"MATERNAL, FOETAL, AND NEONATAL CALCIUM, PHOSPHORUS AND GLUCOSE VALUES WITH SPECIAL EMPHASIS ON THE ROLE OF THE PLACENTA IN THEIR REGULATION".

by

ABD EL-KHALIK KHATTAB
M.B., Ch.B. (Cairo), M.D. (Cairo), M.R.C.P. (Ed.),
M.R.C.P. (Glasg.), D.C.H., D.M.

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Although the metabolism of calcium and phosphorus in the neonatal period has been the subject of considerable investigation, yet there is still much that is unknown about the factors which affect the blood concentrations of both substances in the newborn. In this respect, the role which the placenta plays both in health and in disease is ill understood.

Much work has been done on the changes that occur during pregnancy in serum-calcium, and phosphorus levels. Similarly, many workers have studied the changes that take place in these two substances in the blood of the newborn infant. Less attention has been paid to the changes - both maternal and foetal - that take place during labour and delivery.

To combine the three aspects of the problem, antenatal, natal and postnatal in one study with an attempt to relate and/or to correlate them to each other seemed to be a worth while investigation.

It was also thought that if this combined study was done first in normal pregnancy and then in abnormal conditions, especially toxaemic pregnancies, a comparison between the normal and these abnormal conditions could be made.

Alongside these extensive studies on neonatal calcium and phosphorus, but separately glucose values in the newborn babies have received great attention during the past few years. This has resulted in more cases of neonatal hypoglycaemia being discovered and adequately managed. It is surprising, however, that no attempts have/

have been made to combine both studies together in the same patient or to correlate glucose values with those of calcium and/or phorphorus. This is in spite of the apparently close relation that the three substances bear to each other in the neonatal period.

So it was felt that - apart from the combined antenatal, natal and postnatal study of the changes that occur in the blood-calcium, phosphorus and glucose, a more intensive study of the changes in the neonatal period would be valuable.

Starting with the full-term baby, we could draw a base line of the changes that occur in the calcium, phosphorus and glucose blood-values in the first four days of life.

To this base line, some abnormal babies could be compared. In our series, these included prematurity, postmaturity, twin-pregnancies and babies of diabetic mothers.

There was more than one reason for including glucose in the same study with calcium and phosphorus. The co-existence of hypocalcaemia and hypoglycaemia in the newborn is not uncommon (Cornblath, Wybregt and Klein, 1964). Also symptoms and signs are similar in both conditions (Cornblath et al, 1964). Another reason is that babies of diabetic mothers commonly have both hypocalcaemia (Zetterstrom and Arnold, 1958), and (Craig and Buchanan, 1958) and hypoglycaemia (Baird and Farquhar, 1962).

I. COMBINED ANTENATAL, NATAL AND POSTNATAL STUDY IN NORMAL CASES

ANTENATAL PERIOD

1. Serum-calcium and phosphorus during pregnancy.

Ever since the development of modern methods of chemical blood-analysis,/

analysis, the significance of the variations of the calcium and inorganic phosphorus of the serum, specially during pregnancy, has been the subject of interest and study. Morley (1913) reported a lowering of serum-calcium during pregnancy, labour and puerperium. Widdows (1923) introduced the innovation of following individual cases over an extended period. By this method, she reached the conclusion that there was a tendency first to a reduction in the calcium content of blood in late pregnancy, which was not manifest in all cases and later to an increase directly after confinement even during lactation.

Handelman, Rose and Sherwin (1926) found that calcium conc. was normal during gestation, slightly decreased immediately after parturition, but with a rise to a high normal value before dismissal from hospital. Stieglitz (1927) found a mild hypo-calcaemia during the last months of pregnancy, a rise after delivery and a transient fall at the onset of lactation. Bokelmann and Bock (1928) reported a slight reduction in the total serum-calcium during pregnancy, but relatively high, an actual increase at the onset of delivery, although it fell again to the low level of the latter half of pregnancy by the end of the delivery. Mull and Bill (1934) carried out 4896 calcium and phosphorus determinations upon 900 patients in their prenatal dispensaries. They concluded that during pregnancy, there is a distinct seasonal difference in the serum-calcium, since blood-specimens drawn during the months January - May inclusive, average less at every stage of the pregnancy than those drawn during the remaining 7 months. Following delivery, the difference tends to disappear.

There is also a significant decline in calcium, approximately 5% due to the pregnancy itself up to 6 - 7 weeks before delivery, then a slight rise until delivery, followed by a sharp increase. They also observed that close successive pregnancies tended further to diminish the serum calcium levels of the individual patient during subsequent periods of gestation.

Concerning phosphorus, Mull et al found no seasonal variation, but due to the pregnancy itself, there was a significant fall in the average values, about 6% until the 11th - 13th week before delivery, followed by an equal rise until term. There was no evidence of a lowered phosphorus level as a result of previous pregnancies.

2. Blood-glucose during pregnancy.

Morriss (1917) found normal blood-sugar values in the maternal blood during pregnancy and puerperium, with a range of 90 - 110 mg./100 ml. He found that the same finding was reported in the previous literature and he quoted the following table:

N.B. - This table is quoted from Morriss (1917)

Investigator	Range	Mean
1. Schirokauer	85 - 112	-
2. Kampf	-	79
3. Benthin	54 - 96	-
4. Bergsma	70 - 136	91
5. Frank	80 - 120	95
6. Neubauer & Novak	50 - 90	-
7. Jacobson	94 - 105	98
8. Morriss	98 - 116	103

LABOUR TIME

1. Serum calcium values during normal labour and delivery.

This includes both maternal as well as foetal blood. As previously mentioned, Bokelmann and Bock reported a high, an actual increase of maternal serum calcium at the onset of delivery, although it fell again to the low level of the latter half of pregnancy by the end of delivery.

Concerning foetal blood.

Mull et al. (1932) have shown that the serum of the foetus from the umbilical cord is higher in calcium (11.7 mg.%) than the maternal blood (9.8 mg.%) at the time of delivery. The cord blood inorganic phosphorus averaged 5.8 mg.% compared to maternal blood at delivery (5.3 mg.%). Mull (1936) found that the levels of cord blood, although without an exception were higher than the maternal blood, yet were dependent on those of the maternal circulation. Denzer, Reiner and Weiner (1939) found that cord blood calcium was 1 - 3 mgs. higher than those of the mother. Moreover, Serdyn Kov and Morosova, (1928), Bokelmann et al. (1928) and Hellmuth (1925) all found that the foetal calcium was definitely higher than the maternal blood calcium, the first named to the extent of about 20%.

So in regard to the calcium concentration in the umbilical cord blood, there is entire agreement. But, all those investigators did not give separate consideration to umbilical artery as distinguished from umbilical vein.

Hallman and Salmi (1953) were the first to discuss values for umbilical/

umbilical artery and vein separately. They found that calcium concentration in the umbilical vein blood was about 0.3 - 2.3mgs./100 ml. higher than in blood taken from the umbilical artery. They also found that the calcium content of the blood entering the placenta through the umbilical artery and of the infant's blood after birth to be approximately of the same level and both were higher than maternal levels, just before or immediately after delivery. From this, it became evident that at or immediately after delivery, one has to deal with three different values:- (a) maternal blood.
(b) umbilical vein blood: which reflects foetal blood.
(c) umbilical artery blood; which is the same as the baby's blood.
According to the literature, maternal plasma calcium is 1.77 mgms./100 ml. lower than that of umbilical vein calcium, and on an average by 0.80 mg./100 ml. lower than that of the umbilical artery (Hallman et al. 1953). The latter workers found that the average maternal plasma calcium was 10.01 mg./100 ml. of blood, and the extremes being 8.7 mg./100 ml. and 12.3 mg./100 ml. of blood. They also found that the umbilical vein calcium varied from 9.8 - 16.1 mg./100 ml. blood, with an average of 11.78 mg./100 ml. At the same time and by the same workers calcium in the umbilical artery blood was found to be 10.86 mg./100 ml. In each case, umbilical vein calcium was higher than umbilical artery calcium, the difference averaged 0.92 mg./100 ml., with a range of 0.2 - 2.9 mg./100 ml.

Bakwin and Bakwin (1932) and Mull and Bill (1932) noticed a slight correlation between the calcium values of maternal and placental/

placental blood. A higher calcium concentration in the cord blood was usually accompanied by a higher than normal maternal calcium value.

2. Blood phosphorus during normal labour and delivery.

Concerning phosphorus, it is usually the inorganic phosphate which is referred to when unspecified figures of blood phosphorus are quoted, (Smith, 1959). Stearns (1939) found that the inorganic phosphate of the infant's blood at birth is - like the calcium - higher than the maternal blood calcium. According to Needham (1931), the maternal blood is richer in proteins, total and lipid phosphorus, in phosphatides, total fatty acids, total cholesterol and glucose, while the foetal blood is richer in non - protein nitrogen, free amino-acid nitrogen, nucleoprotein and specially in inorganic phosphorus, lactic acid, total ash, sodium, potassium and calcium. This applies to Man as well as to most of the mammals. These findings about inorganic phosphate in labour go with what Riesenfeld and Handelman (1925) found in a study of 1439 cases at labour. They found that in only 5.4% of cases was the mother's blood more in inorganic phosphate than the infant's blood at birth. The same findings were found by Widdowson and McCance (1959).

Denzer et al. (1939) also found higher phosphorus values in the cord blood than in the maternal blood. They concluded that generally speaking inorganic phosphorus is higher in the blood of the newborn than in cord blood or maternal blood. So, while the average

concentration/

concentration of phosphorus in cord blood was 6.06 mgs./100 ml., in the babies' blood immediately after birth it was 7.11 mg./100 ml. a figure which was higher than in the babies' blood a few days later. Todd, Chuinard and Wood (1939) comparing calcium and phosphorus content of fontanelle blood with that of cord blood, found that an actual difference exists between both. Calcium was lower and phosphorus was higher in fontanelle blood than in cord blood, meaning that babies' blood calcium at birth is lower and phosphorus is higher than in cord blood.

In this respect, Fuchs and Fuchs (1956) could show that in the guinea pig, the foetal plasma contained twice as much inorganic phosphate as the maternal plasma, and so the transfer of phosphate from the mother to the foetus takes place against a concentration gradient.

3. Glucose concentrations during normal labour and delivery.

As was followed in calcium and phosphorus, this includes:-

(a) Maternal blood glucose during labour.

(b) Foetal blood glucose as reflected in blood from the placental end of the umbilical vein.

(c) Neonatal blood at birth.

Concerning maternal blood glucose during labour, Morriss (1917) found that it was normal during early labour, but in 28 cases in which blood was taken at the end of the second stage of labour, he found that the blood sugar was slightly higher than normal adult levels (132 mg./100 ml.). Morriss explained this rise by being partly due to the mother's voluntary effort to expel the foetus, which is accentuated/

accentuated by the use of an anaesthetic. Ketteringham and Austin(1938) also found that the mean value for maternal blood glucose at the time of delivery (taken by a finger prick) was 124.6 mg./100 ml. In 60% of their cases (the total number was 50) the range was 110 - 140 mg./100 ml., nearly 40 - 50 mg./100 ml. higher than the normal adult range. They also found that in 28 of their cases the blood sugar values at the time of delivery were 28 mg./100 ml. higher than during the first stage of labour. They also mentioned that both the anaesthesia and the muscular effort of labour contribute to the increase in blood sugar values.

4. Transplacental passage of glucose.

Nearly all mammals with very few exceptions exhibit a gradient of blood glucose concentration from the maternal to the foetal blood, the foetal blood sugar following maternal levels, at least during the latter part of pregnancy and during labour (Pedersen 1952). Glucose passes freely through the placenta according to the gradient of concentration.

The ratio maternal/foetal blood sugar has been studied by simultaneous determinations on the mother and infant at the moment of birth. Human experiments were first reported by Merletti (1905) and later by Ballerini (1908). Since then a considerable amount of literature has accumulated on the subject, partly because rapid micro methods for the determination of blood sugar values came into use. The period 1925 - 1950 witnessed a particularly large number of/

of publications. Studies of this nature must evidently comprise both the spontaneous blood sugar values and also the augmented blood sugar values following artificial enhancement of maternal blood sugar by giving glucose to the mother.

Comparing human foetal blood sugar concentration to that of the mother at the time of birth, Morriss (1917) found averages of 115 mg. and 132 mg./100 ml. for foetal and maternal values respectively. In his study, he included 28 mothers and babies of 24 of them and he considered blood taken from the placental end of the cord to represent foetal blood.

Ketteringham and Austin (1938) studying glucose values at birth in 50 women and in the babies of 47 of those mothers, found that the mean values were - 124.6 mg. and 103.6 mg./100 ml. for maternal and baby's blood respectively. The maternal blood was taken by a finger prick, and the baby's blood was taken by a heel stab. They concluded that 94% of infants in their series had blood glucose values at the moment of birth that were lower than those of their mothers.

Windle (1940) wrote that dextrose could pass from the mother to the foetus across the placental barrier in all mammals, and that the foetal blood sugar concentration is always lower than that of the maternal blood. He added that a similar condition prevails in most mammals, except sheep and goats. In the latter, Passmore and Schlossmann/

Schlossmann (1938) found that - unlike most animals - the foetal blood had a higher glucose value than the maternal and that intravenous glucose infusions into the mother showed that glucose diffused in both directions.

Smith (1959) also discussed glucose transmission through the human placenta. His opinion is that although glucose passes from the mother to the foetus across the placenta, this does not appear to occur by free diffusion.

Hartmann (1955) discussed the situation at birth in the following way:-

When whole blood samples are obtained as nearly simultaneously as possible from -

1. The mother's capillary or vein.
2. The infant's umbilical vein.
3. The umbilical cord (mixed blood).
4. The infant's heel capillaries.
5. The umbilical artery.

the mother's sugar is always the highest, and the glucose concentration diminishes gradually in the previously mentioned order.

The difference in blood sugar concentration between the umbilical vein and umbilical artery at birth was also found by Bell, Cunningham, Jowett, Millet and Brooks (1928). They found that the blood sugar of the umbilical vein was 84 mg. and of the umbilical artery to be 75 mg./100 ml. of blood.

So there is nearly general agreement that at the time of delivery maternal/

maternal blood glucose is always higher than the baby's blood glucose.

However, an exception to this statement was found in Holman and Mathieu's results (1934). These workers compared blood taken from the maternal end of the severed cord as soon as possible after birth with blood simultaneously taken from the median basilic vein of the mother. In 100 cases they found that the mean values for blood glucose in the maternal and cord blood were 100.5 mg. and 95.4 mg./ 100 ml. respectively. They concluded that in normal cases the blood sugars of the mother and her baby are practically the same and that this ratio is probably maintained in abnormal cases as well.

5. Correlation of the mother's and infant's blood sugar at birth.

A positive correlation between the blood sugar of the mother and her baby is often noted at the moment of birth. Ketteringham and Austin (1938) found a correlation coefficient of + 0.6. Yet, Smith (1945) stated that the amounts of sugar in the two circulations seem to be neither wholly independent of each other nor on the other hand, closely related.

Naeslund (1928) and Dahl (1928) have often been quoted on this subject. Both interpreted their results to the effect that free diffusion does not take place.

Pedersen (1952) has plotted the corresponding values for the blood sugar at the moment of birth for the mother and peripheral blood of the baby, using for this Naeslund's results. He also plotted values for maternal blood and umbilical vein on scatter diagrams/

diagrams. For the latter he used Dahl's results. The diagram formed on the basis of Naeslund's series shows a rather marked positive correlation between the blood sugar of the mother and the baby following oral glucose administration to the mother. Dahl's series also shows a marked positive correlation with regard to the spontaneous blood sugar values. But in 9 experiments done with glucose given to the mother, only two were close to, and seven were far from the regression **line** of the spontaneous values.

Pedersen (1952) also found a distinctly positive correlation between the maternal blood sugar and the sugar content of the blood obtained from the umbilical artery at the moment of birth.

These calculations stress that the experiments have shown the same positive correlation between the blood sugar values of the mother and the infant.

6. Induced changes in the maternal blood glucose during labour.

Induced changes in the maternal blood glucose during labour will be reflected on the placental and foetal blood glucose. In rats suffering from diabetes induced by alloxan or by pancreatectomy, the blood sugar of the newborn follows the greatly enhanced values in the mother (Friedgood 1945), and there is a highly positive correlation between the maternal and foetal blood sugar values. The hyperglycaemia seen at birth in the offspring of diabetic rats subsides during the first day of life (Friedgood and Miller 1945). Morriss (1917) also found that deliveries by obstetrical/

obstetrical procedures are associated with higher values of maternal blood glucose than spontaneous deliveries, due to the effect of the anaesthetic. More important still, is that the relatively hyperglycaemic maternal levels are always associated with high blood sugar in the foetus. He also made the very interesting observation that there is prompt disposal of this excess glucose on the part of the infant, but trying to explain this phenomenon he could not reach a definite conclusion.

Holman et al. (1934) reported a pregnant woman who developed toxaemia in the last month of pregnancy. Because of this, she was given 300 ml. of 25% glucose solution intravenously 15 minutes before delivery. As a result her blood glucose went up to 427 mg./100 ml. and consequently the baby's blood glucose was 439 mg./100 ml., so glucose diffused very quickly from the maternal to the foetal circulation. They found that, on the other hand, if the maternal blood glucose was low during pregnancy and labour, this would result in low levels of blood glucose in the infant at birth.

In 1939 Ketteringham and Austin performed what they called "the indirect intravenous glucose tolerance test" on the newborn babies by giving intravenous glucose to the parturient mother. Each patient was given 500 ml. of a 10% glucose solution intravenously half to one hour before delivery and the blood sugar was determined at birth in both the mother and baby, and again during the subsequent/

subsequent four hours on the infant only.

Their study included 7 mothers and their 8 babies (one of the patients had twins). Their findings were:-

Maternal blood glucose at delivery	= 400	- 550	mg./100 ml.
Baby's blood glucose at birth	= 192.3	- 267.8	mg./100 ml.
Baby's blood glucose after one hour	= 110	- 140	mg./100 ml.
Baby's blood glucose after two hours	= 45	- 65	mg./100 ml.
Baby's blood glucose in the subsequent two hours	= 45	- 80	mg./100 ml.

These workers were very impressed by the rate at which glucose was eliminated from the infant's blood. In their opinion, this was interpreted as a sign of lively "pancreatic activity" in the newborn baby.

In 1952 Pedersen reviewed the literature on the subject. He concluded that tests following oral or intravenous glucose administration to the mother shortly before delivery have shown that the blood sugar of the infant is dependent on and follows that of the mother.

In experimental conditions, however, the maternal and foetal blood glucose concentrations are seldom or never the same. He suggested that it would be interesting to perform tests following artificial depression of the maternal blood sugar. This was later carried out and confirmed by Hartmann (1955), who found that maternal hypoglycaemia was reflected by a simultaneous reduction of glucose/

glucose concentration in the umbilical veins to levels less than those of the mother's blood.

In this respect the relation between the maternal and foetal blood sugars in diabetes mellitus must be of great interest. There is usually a foetal hyperglycaemia compared to normal babies, but the levels are always lower than those of the mother. Browne & Browne (1960) quoted the example of a diabetic case with the following results:-

Mother's blood sugar immediately after delivery	= 450 mg./100 ml.
Cord blood sugar	= 200 mg./100 ml.
Baby immediately after birth	= 156 mg./100 ml.
Liquor amnii sugar	= 90 mg./100 ml.

NORMAL NEWBORN BABIES

1. Serum calcium in the full-term newborn baby.

Bruck and Weintraub (1955) studied the serum calcium concentration in the blood in 21 full-term babies. They found that in every case the first calcium value after birth as estimated by a heel stab was lower than the cord blood, with a difference of 0.8 - 4.6 mgms./100 ml. in the first twenty-four hours after birth. They also found no relation between cord values and subsequent calcium levels in the infant. They also found that in all these full-term babies, the serum calcium was higher than 8 mg.% except in/

except in only two cases when it was lower than 8 mg./100 ml. They also mentioned that the general trend of serum calcium concentration in the newborn was a moderate decline, its degree probably related to the length of time before the infant is fed and to the degree of prematurity. The lack of correlation between serum calcium of the cord blood and serum calcium of peripheral blood of infants in the neonatal period was previously stressed by Denzer, Reiner and Weiner (1939). These workers also found in an early study of serum calcium in the newborn that the striking feature in calcium values during the first ten days of life was the deep depression that occurs in the first four days. Thereafter, it gradually rises till by the seventh day it attains a point a little higher than in later infancy.

Gittleman, Pincus, Schmerzler and Saito (1956) made a special study of calcium values on the first day of life and they concluded that in the full term baby a serum calcium below 8 mgms./100 ml. on the first day of life is abnormal. They found that the incidence of hypocalcaemia (below 8 mg./100 ml.) on the first day in mature infants born to mothers per vagina who had uncomplicated pregnancies and labours to be 1.2%. Mitchell and Stevenson (1932) in a study of serum calcium in 55 healthy full-term babies, found only one case with a serum calcium below 8 mg./100 ml. Dodd and Rapoport (1949) studied 48 cases, in all of which the serum calcium was higher than 8 mg./100 ml. Both Bakwin (1937) and Kendig (1942) reported that a serum calcium below 8 mg./100 ml. in the newborn confirmed the presence of tetany in a suspected case. Craig and Buchanan/

Buchanan (1958) diagnosed neonatal tetany when the baby showed evidence of exaggerated neuromuscular irritability and confirmed the diagnosis by a serum calcium below 8 mgm./100 ml.

2. Plasma phosphorus in the full-term newborn baby.

McCance and Widdowson (1959) studied the values of blood phosphorus in the mother, cord and babies at 48 hours of age, as well as on the 7th. day and they also studied the phosphorus excretion on the first day, second and seventh days of life. They found that cord blood contains more inorganic phosphate than maternal blood and that it increases more in the first 48 hours of life, but later values will depend on whether the baby is breast fed or artificially fed. The latter have a higher blood phosphorus than the breast fed babies. The differences between human and cow's milks have been emphasised by Gardner and Butler (1950) in explaining the hyperphosphataemia and hypocalcaemia in the neonatal period. Gittleman & Pincus (1951) showed that infants receiving vitamin D supplements had a more marked tendency to hyperphosphataemia and hypocalcaemia than infants receiving a similar diet without vitamin D. Bakwin (1937) mentioned that during the first few days of life the serum calcium diminishes, when the maximum drop occurs about 3 - 5 days after birth. This is associated with a steady rise of the inorganic phosphate concentration in the blood.

3. Blood glucose in the full-term newborn baby.

Despite the vast amount of work that has been done on this subject and the large number of publications written about it, still the/

the blood glucose level in the normal full-term baby is not well defined and is given a very wide range of 20 - 80 mg./100 ml. of blood.

Few references only are quoted here as examples - Cobliner (1911) was the first to record blood sugar determinations for infants, but his estimations were only made on infants from 9 - 21 days old. In this age group he found an average value of 85 mg./100 ml.

Mogwitz (1914) was the first to determine the fasting blood sugar in newborn infants ranging from 7 hours to 3 weeks old. He reported values that varied from 70 - 103 mg./100 ml.

Greenwald and Pennell (1930) carried out 191 determinations on 94 normal newborn infants to determine the average concentration of the fasting blood sugar. The Folin micro method was used. They found the range to be 60 - 100 mg./100 ml., with an average of 76 mg./100 ml. They failed to find any relation between either birth-weight or variations in weight and the blood glucose concentration.

Ketteringham and Austin (1938) in a series of 47 newborn infants found that the blood sugar was:-

At birth	124.6	mg./100 ml.
10 minutes after birth	103.6	mg./100 ml.
3 - 6 hours	66.8	mg./100 ml.
Between 6 - 24 hours	68.3	mg./100 ml.
First 2 days of life	55 - 75	mg./100 ml.

They found that within 3 - 6 hours after birth the blood sugar drops to the normal infant's range.

Norval, Kennedy and Berkson (1949) in a series of 51 normal newborn infants and using the modified Somogyi's method, studied the blood glucose values in the first 6 days of life. A total of 612 determinations were done and the mean value of blood sugar during the six days was 61.0 $\pm$ 0.63 mg./100 ml. with a standard deviation of 15.6 mg./100 ml. Analysing the blood sugar values in relation to age, they found an average increase of 2.8 mg./100 ml. per day during the first six days of life. They also found no evidence of stabilisation of the blood sugar during this period.

Farquhar (1954) in a study of neonatal glucose values in the full-term baby in a trial to correlate the changes that take place in the glucose values with the eosinophil count found -

The average glucose value at birth fell by 11.2 mg./100 ml. in the first two hours, by 1.1 mg./100 ml. in the following two hours and by 0.1 mg./100 ml. in the next two hours. He also found that the mean blood sugar varied from -

65.5 mg./100 ml. on the 2nd day of life

87.7 mg./100 ml. on the 9th day, and

81.3 mg./100 ml. on the 10th day.

Hartmann (1955) found that blood glucose tends to fall for 3 - 4 hours after birth and then increase spontaneously thereafter. After the 1st day, in a full-term baby of a normal mother, the hypoglycaemic levels continue for about 5 days. The average is increased/

increased gradually to a plateau which is reached on the 10th - 14th day after birth.

Stur (1964) in a study of blood glucose concentration in 10 healthy mature newborn babies found that capillary blood glucose was:-

39 mg./100 ml. at 3 hours after birth.

45 mg./100 ml. at 6 hours.

42 mg./100 ml. at 24 hours.

40 mg./100 ml. at 49 hours.

Pedersen (1952) found a negative correlation between the maternal blood sugar during the latter half of pregnancy and the infant's blood glucose during the first 24 hours. He also found a positive correlation between the maternal blood sugar during labour and immediately before or after delivery, and the infant's blood sugar in the first 24 hours of life.

Remarkably low blood glucose values were discovered without any symptoms or signs of hypoglycaemia and were commented upon by Hartmann and Jandon (1937), Norval, Kennedy and Berkson (1949) and also by Farquhar (1954).

Symptomatic neonatal hypoglycaemia is a rare condition. Brown and Wallis (1963) found only 10 cases of symptomatic neonatal hypoglycaemia amongst all the newborn babies they have seen in the period August 1960 - June 1963. Also Neligan, Robson and Watson (1963) found 12 cases only of symptomatic neonatal hypoglycaemia amongst approximately 6000 babies born in the period September 1959 - October 1962.

II. TWIN STUDY

Since there are so many factors that affect the calcium, phosphorus and glucose values in the newborn, some of them being maternal, others are placental and some are foetal, it was thought that twin study would be ideal to eliminate all the maternal factors and so the foetal factors could be compared with special reference to the birth weight.

The biochemistry of twins has not been extensively studied in the previous literature.

As to calcium concentrations in twins, Craig and Buchanan (1958) studied serum calcium in four sets of twins and all were found to have hypocalcaemia. A feature of each of the four sets was that the total serum calcium level was lower in the second twin that what it was in the first live born infant. They did not give an explanation for this phenomenon. Gittleman (1957) also found that the total serum calcium levels in twins of the same pregnancy were usually different.

Concerning glucose values in twins, this has not been mentioned previously in the literature, although Wybregt, Reisner, Patel, Nellhans and Cornblath (1964) mentioned that this is to be published. Since dysmaturity is agreed upon by most workers as the common predisposing factor for neonatal hypoglycaemia (Cornblath, Wybregt, Brens and Klein 1964; Wybregt et al., 1964; Haworth et al., 1963; Brown et al., 1963, and Neligan et al., 1963) it was thought that twins would provide the best chance of investigating the effect of this factor, specially if they show marked discrepancy of birth/

birth weights. Studying twins, would naturally eliminate other factors that might affect the blood glucose value as much as possible.

III. THE PLACENTAL DYSFUNCTION SYNDROME

The third part of this work dealt with conditions which are known to be occasionally associated with placental dysfunction.

The aim of this part was to study placental function in the transmission of calcium, phosphorus and glucose from the maternal to the foetal blood and to see whether this transmission was impaired.

Another aspect was to see the effect of these conditions on the values in the newborn.

The conditions taken for this study included premature deliveries, prolonged pregnancies, toxaemias of pregnancy and elderly primiparae.

1. Premature infants.

First day hypocalcaemia in premature babies was described by Gittleman et al., (1956), Craig et al., (1958), and Bruck et al., (1955). Gittleman and Pincus (1951) noticed a positive correlation between the birth weight of the premature and the concentration of calcium in its plasma. Zetterstrom and Arnold (1958) mentioned that hypocalcaemia and hyperphosphataemia are the reflection of functional immaturity of the newborn baby.

The increased incidence of hypoglycaemia in prematures was reported by van Creveld (1929), Cornblath et al., (1955), Wybregt et al., (1964) and Haworth et al., (1963).

2. Postmature Infants.

Concerning calcium, phosphorus and glucose values in postmatures, perhaps placental function comes to act. Pendleton (1959)/

(1959) mentioned that postmature babies are more susceptible to neonatal hypoglycaemia than full term babies, the underlying factor being placental insufficiency. Increased calcification of the placenta has been observed in postmaturity and since deposition of calcium in the term placenta is a feature of placental ageing, (McKay, Hertig, Adams and Richardson (1958), one would expect placental insufficiency to be a feature of postmaturity.

3. Toxaemias of pregnancy

Toxaemic mothers may have hypoglycaemia during pregnancy (Holman et al, 1934). Also toxaemias are known to be commonly associated with placental insufficiency (Nelson 1964) and (Browne 1963). As to the effect on the baby, Cornblath et al. (1955) have shown that pre-eclampsia in the mother if complicated by difficult labour or delivery and low birth weight of the baby will lead to neonatal hypoglycaemia on the second day of life. As to calcium, Gittleman et al. (1956) reported that babies whose mothers had complicated or abnormal pregnancies and/or labours would commonly develop hypocalcaemia on the first day of life.

IV. BABIES OF DIABETIC MOTHERS

These may show hypoglycaemia, hypocalcaemia and hyperphosphataemia. Offergeld (1906) was the first to determine the blood sugar in an infant born of a diabetic mother. He found the following blood sugar values -

In the comatose mother	800 mg./100 ml.
In the umbilical vein	235 mg./100 ml.
In the umbilical artery	218 mg./100 ml.
In the baby	2200 mg./100 ml.

Certainly the baby's value was not correct.

Pedersen (1952) from his own results and from a review of the previous literature, found that the correlation that exists between the baby's blood sugar at birth and the maternal blood sugar is the same in diabetics as in non-diabetics, i.e. positive with maternal levels at delivery, but negative with maternal levels during pregnancy.

But in contrast to normal babies who show a positive correlation between blood sugar and birth weight, babies of diabetic mothers show a negative correlation, i.e. the higher the birth weight, the lower the blood glucose value.

He concluded that if infants of diabetic mothers were to have a high blood sugar value during the first 24 hours of life, the maternal blood sugar must be kept normal during pregnancy and high at delivery.

According to Pedersen (1952), Komrower (1954) and Farquhar (1956), there is general agreement that the blood sugar level will show/

show a more consistent and rapid fall in babies of diabetic mothers than in normal babies. This hypoglycaemia is at its maximum height at 2 - 3 hours of age (Farquhar 1956) and is spontaneously corrected in 4 - 6 hours to recur on the second day and it is not before a few days that the glucose level becomes stabilized.

As to calcium values, hypocalcaemic tetany was reported in six out of nine babies born of diabetic mothers (Craig et al. 1958). The same workers reported hypocalcaemic tetany in a baby of a pre-diabetic patient who was obese and had a pre-diabetic glucose tolerance test. Zetterström and Arnold (1958) also found hypocalcaemia in 19 babies born of diabetic mothers, some of the babies presented with tetany as well.

Concerning the inorganic phosphate in babies of diabetic mothers, hyperphosphataemia was found by Reardon, Feild and Baumann (1955) and later by Zetterström et al. (1958).

MATERIAL

GROUP I. COMBINED ANTE-NATAL, NATAL AND POST-NATAL STUDY IN THE NORMAL.

For this study 28 mother-baby pairs were taken, and on these 193 triple estimations* of calcium, phosphorus and glucose were carried out (579 total). All these cases were of normal pregnancy, normal labour and delivery. The criteria considered in this series for normal pregnancy, labour and delivery were -

(a) No excessive gain in weight or marked oedema during pregnancy.

(b) Blood pressure not exceeding $140/_{90}$.

(c) Period of gestation = 38 - 42 weeks.

(d) No history of any medical or obstetric complication during pregnancy.

(e) Labour was uneventful and delivery was spontaneous.

(f) Babies were of normal birth weight (above 5 pounds 8 ounces) (2500 gms.) and of normal progress during the period they were in hospital.

Because of the last requirement five cases had to be ultimately excluded from this normal group because four of the babies turned out to be of low birth weight (below 5 pounds 8 ounces (2500 gms.), and the fifth baby had neonatal convulsions. Although the levels of calcium, phosphorus and glucose during pregnancy/

* The term "Triple Estimation" refers to calcium, phosphorus and glucose estimations done on the same specimen of blood.

pregnancy were normal in those five cases, it was felt that they must be excluded. Thus the study ended with 23 cases of normal pregnancy, labour and delivery and babies of normal birth weight.

GROUP II. PATIENTS ON INTRAVENOUS GLUCOSE INFUSIONS DURING LABOUR.

For this study seven patients were taken when it had been decided by the obstetrician that they should receive glucose by the intravenous drip method either because of the presence of acetone bodies in the urine or because of the use of oxytocin in the glucose drip as a method of induction of labour. On these patients, therefore, calcium, phosphorus and glucose estimations were carried out for the first time only during labour.

A total of 35 triple estimations (105 total number) were done. The seven patients were divided into two sub-groups -

(a) Normal.

There were 6 patients who were considered normal according to the criteria of normality previously mentioned.

(b) Pre-eclamptic.

This was only one patient who had severe pre-eclampsia (blood pressure of $160/_{118}$, albuminuria with massive oedema of legs and feet and a trace of oedema of the face). For comparison this case had to be studied and results interpreted separately.

GROUP III. FULL TERM NORMAL NEWBORN INFANTS.

In addition to the 23 infants in Group I a further group of 32 infants whose mothers have not been examined were also studied, bringing the total number in this group (Group III) to 55 babies. These infants were born after normal labour and delivery. The pregnancy was also uneventful. All the infants were full term (38 - 42 weeks of gestation) and were of average normal birth weight (none of them had a birth weight below 5 pounds 8 ounces - 2500 gms.). None of these infants at any time showed any abnormal clinical symptoms or signs.

The number of estimations carried out on the 55 babies was 164 triple estimations (492 total).

GROUP IV. TWIN STUDY

For this study 16 sets of twins were taken. A total of 96 triple estimations (total 288) were carried out on these twins. All the 32 infants were tested on the first day and again on the fourth day, but it was only possible to examine the foetal* blood in nine sets and the neonatal* in seven sets of this group.

Pregnancies were normal and deliveries varied between spontaneous, breech and forceps delivery. Clinically they were all normal except for the third set in the series, i.e. Anderson Twins - clinically they were male and female, but the female twin showed some clinical data suggestive of Turner's syndrome. This was found on chromosome study to be XY/XX mosaicism. The male twin while in the nursery developed torsion of the left testicle for which he had to have orchidectomy done. Cytologically he also showed XY/XX mosaicism. Examination of the placenta and blood showed that they were uniovular.

* The meaning of the terms foetal and neonatal blood in this series will come later under "methods."

GROUP V. THE PLACENTAL DYSFUNCTION SYNDROME.

This group included the following -

1. Pre-eclamptic toxaemia.

There were 16 cases, 12 of them were mild pre-eclampsia, i.e. blood pressure not exceeding $150/_{90}$, trace of albumin was present in the urine and oedema being absent or only slight. The remaining 4 cases were severe toxaemia - with blood pressure more than $150/_{90}$, albuminuria and marked oedema. All the babies in this severe group were of low birth weight (below 5 lbs. 8 ozs. - 2500 gms.)

A total of 327 estimations (109 triple estimations) were carried out on this group.

2. Elderly primigravidae

In this group, which consisted of four patients, the only deviation from the normal was the old age of the mother when she first conceived. They were 37 years, 39 years, 43 years and 40 years old.

A total of 60 estimations (20 triple estimations) were done on this group.

3. Dysmaturity.

This series consisted of five babies.* In this group the babies/

* Four of the five babies were those who were excluded from the normal Group I on account of low birth weight.

babies were all of low birth weight with normal or prolonged gestational age, three of the former and two of the latter. (42 weeks and 43 weeks).

A total of 105 (35 triple estimations) were done on this group.

4. Immature deliveries.

There were four cases, who were studied for the first time at delivery, and in which the period of gestation was less than 37 weeks, and in three of the four babies the birth weight was below 5 pounds 8 ounces (2500 gms.). The periods of gestation were 37 weeks, 36 weeks, 37 weeks and 35 weeks and the corresponding birth weights were 8 lbs. 1 oz. (3580 gms.), 4 lbs. 9½ ozs. (2042 gms.), 5 lbs. 4 ozs. (2332 gms.) and 4 lbs. 6½ ozs.(1958 gms.) respectively.

A total of 51 (17 triple estimations) were done.

5. Prolonged pregnancy.

Three cases.

In this sub-group, which was studied for the first time at delivery, the gestation continued beyond 42 weeks, but differed from the group of dysmaturity in that the birth weight of the babies was not low. It was 8 lbs. 14 ozs. (3944 gms.), 7 lbs. 1 oz. (3136 gms.), and 8 lbs. 5½ ozs. (3706 gms.).

A total of 36 (12 triple estimations) were carried out on this sub-group.

6. Placenta praevia.

Only one case was studied, in which a total of 15 (5 triple) estimations/

estimations were done.

GROUP VI. BABIES OF DIABETIC AND PRE-DIABETIC MOTHERS.

In this sub-group it was possible to examine two cases only because these were the only two diabetic patients that came to the maternity department during the period of study.

The first case - Baby Reid. She was born at 36 weeks of gestation by a lower segment Caesarean section, which was done because of the diabetic state. This was proved by the past obstetric history, the blood glucose and glucose tolerance test done on the mother. At birth the baby weighed 8 lbs. 12 ozs. (3888 gms.) and showed manifestations of respiratory distress.

A total of 36 (12 triple) estimations were carried out on this case.

The second case - Baby White. He was born at 37 weeks of gestation by a classical Caesarean section, which was done because of the pre-diabetic state and the pre-eclamptic toxaemia of the mother. (Blood pressure during pregnancy was $160/_{95}$, there was oedema of the legs, hands and trunk, and there was albumin ¼% in the urine). The pre-diabetic state was proved by the past obstetric history and the glucose tolerance test. At birth the baby weighed 7 pounds (3108 gms.).

A total of 27 (9 triple) estimations were carried out on this case.

METHODS.

This section includes -

1. Blood sampling.
2. Biochemical methods.

BLOOD SAMPLING

GROUP I. COMBINED STUDY OF NORMAL CASES.

Of the 23 cases in this group -

22 were tested at 36 weeks.

21 were tested at 38 weeks.

All were tested at delivery.

All babies were tested on the 1st day and again on the 4th day.

Tests at delivery

These included -

(a) Maternal blood.

This was taken from the mother by venupuncture towards the end of labour, i.e. at the end of the 2nd stage or beginning of the 3rd stage of labour.

(b) Foetal blood.

This was taken by puncturing the placental end of the umbilical vein using a syringe and needle immediately after the placenta was delivered.

(c) Neonatal blood.

This was taken by a heel stab done on the baby as soon as he was transferred to the nursery. In most cases this was within half an hour of birth.

1st day specimen: was taken by a heel stab done on the baby at 12 hours of life and before the first feed was given.

4th day specimen: was taken by a heel stab done on the baby on the 4th day in the fasting state.

GROUP II. PATIENTS ON INTRAVENOUS GLUCOSE DURING LABOUR.

In these cases calcium, phosphorus and glucose estimations were only carried out for the first time at delivery. No pregnancy levels were recorded. Maternal, foetal and neonatal blood specimens were taken as in Group I concerning the procedure and time. Also first and fourth day specimens were obtained from the babies.

GROUP III. FULL TERM NORMAL NEWBORN BABIES.

The 23 babies of Group I who were included also in this group were tested on the first and fourth days of life.

Of the remaining 32 babies, 27 were tested daily for the first four days of life, while in the other 5 it was possible to examine them on the first and fourth days only.

In all these babies blood was collected by a heel stab.

GROUP IV. TWIN STUDY.

Of the 16 sets of twins all 32 babies were tested on the first day and again on the fourth day, but it was possible to test foetal blood in 9 sets and neonatal blood in 7 sets only.

GROUP V. THE PLACENTAL DYSFUNCTION SYNDROME.

1. Pre-eclamptic toxaemia: of the 16 cases (mild and severe) -

15 were tested at 36 weeks.

14 were tested at 38 weeks.

all were tested during labour.

all babies were tested on 1st day and on 4th day.

2. For the rest of all this group (elderly primigravidae, dysmatures, immature deliveries, prolonged pregnancy and placenta praevia) all were tested as usual for maternal, foetal, neonatal and baby's blood on the 1st and 4th days. An exception to this was the second case of the immature deliveries and the third case of prolonged gestation, in which it was not possible to test labour samples (maternal, foetal and neonatal).

GROUP VI. BABIES OF DIABETIC MOTHERS.

1st case - Baby Reid.

Maternal, foetal and neonatal specimens were taken as usual at the time of birth. Then specimens of blood were obtained from the baby on the 1st, 2nd, 3rd, 4th, 5th, 6th, 7th, 12th and the 14th day after birth. All the specimens were taken while the baby was fasting (about 3 hours after the last feed).

2nd case - Baby White.

Maternal, foetal and neonatal specimens were taken as usual at the time of birth. Then specimens of blood were obtained from the baby on the 1st, 2nd, 3rd, 5th, 7th and 9th day after birth. They were all taken in the fasting state.

METHOD OF COLLECTION OF BLOOD

1. Maternal and foetal samples.

After the venupuncture (maternal and umbilical vein respectively) at the time of delivery blood was collected in long plastic disposable tubes. About 2.5 - 3 ml. of blood were received in a plain tube (used later for calcium estimation) and a similar amount received in a fluoride oxalate tube (used later for glucose and phosphorus estimations).

2. Blood from the baby.

Obtained by a heel stab, blood was received in small plastic disposable tubes of 2 ml. capacity each. About 1 ml. of blood was received in a plain tube (used for calcium estimation) and a similar amount was received in a fluoride oxalate tube (used for phorphorus and glucose estimations).

BIOCHEMICAL METHODS

These included -

1. Estimation of calcium in serum.
2. Estimation of phosphorus in plasma.
3. Estimation of glucose in blood.

ESTIMATION OF CALCIUM IN SERUM

The method used was "The E.D.T.A. method of Wilkinson". (Wilkinson 1957).

Principle of the method.

Murexide in alkaline solution is a specific indicator for calcium in serum. When calcium is added to an alkaline solution of murexide, a calcium murexide complex is formed. When E.D.T.A. (ethylene-diamine-tetra-acetic acid) is added to this complex it absorbs calcium, thus changing the calcium murexide complex once more to the free dye. The colour change of the calcium murexide complex to the free dye is gradual and the visual end point of titration with E.D.T.A. is not sharp.

Comparison of the murexide method with the oxalate precipitation method.

Wilkinson (1957) in a study of the normal serum calcium in 710 cases found that the average was 9.63 mg. per 100 ml. using the murexide method. At the same time, using the oxalate method, he found/

found the average serum calcium was 10.48 mg. per 100 ml. in 710 normal cases. He concluded that the murexide method gave figures which were 0.70 - 0.85 mg. per 100 ml. lower than those obtained by the oxalate precipitation method.

Comparison of both methods was also done by Lehmann (1953) and Eldjarn et al. (1955).

Advantages of the murexide method.

1. It required only 0.1 ml. of serum from capillary blood, which was easily obtained by a heel stab while the oxalate method required 2.0 ml. of serum from blood obtained by venipuncture.
2. Recoveries obtained by the murexide method suggested that they were complete and that the method is specific for calcium.

Apparatus.

1. Photoelectric absorptiometer with spectrum filter 606 (Peak 5750 - 5800 A). Connections to the bulb should be soldered for stability. A simple light shutter is necessary.
2. A 1 cm. cuvette of approximately 6 ml. capacity is reserved for the estimation.
3. Micrometer syringe burette delivering to $\pm$ 0.00005 ml. accuracy equipped with a bent glass delivery tip. The capacity of the burette is = 0.5 ml.

Reagents.

1. Glass distilled water was used throughout the procedure.

2. Murexide indicator

This was freshly prepared each time for use by dissolving approximately 6 mg. of murexide (ammonium purpurate acid) in 100 ml. of water in a polythene bottle. The strength of the solution was adjusted so that the scale reading was always in the range 58 - 62. The polythene container was always washed out after use as traces of the old indicator are known to depress the colour change with calcium.

3. E.D.T.A. solution (4.8 gm. per litre)

The di-sodium salt of ethylene-diamine-tetra-acetic acid (Hopkin and Williams 98% purity) was dried at 110° C. for 4 hours and then placed in the dessicator overnight. 4.8 gm. of the salt was dissolved in water and made up to 1 litre, and then was stored in a polythene bottle.

4. Potassium hydroxide (1 normal solution) stored in a polythene bottle.

5. Calcium standard (Neutral 10 mg. per 100 ml.)

0.250 gm. of pure dry calcium carbonate was dissolved in 6 ml. of normal hydrochloric acid. This was then heated in a beaker on boiling water bath to drive off any excess hydrochloric acid. Then this was cooled. The contents of the beaker were then transferred quantitatively to a 1 litre flask with water and then made up to the mark.

Procedure

1. All the pipettes, the cuvette and the polythene bottle for the indicator solution were always rinsed with distilled water, but not dried, before and after use.
2. The burette was then washed several times with E.D.T.A. solution and filled. No lubricant was used on the plunger.
3. 2.5 ml. of murexide indicator solution were placed in the cuvette.
4. 0.2 ml. of potassium hydroxide solution was added to the indicator.
5. The cuvette was then placed in the titrator and the burette was adjusted so that the tip was just below the level of the liquid.
6. The stirrer and galvanometer were then switched on. The sensitivity was adjusted so that the meter read 50.
7. 0.1 ml. of calcium standard solution was added from a wash-out pipette. The meter reading was noted.
8. 20 divisions (0.004 ml.) of E.D.T.A. solution were then added and the reading noted.
9. The addition and meter readings were repeated till the latter reached a peak and then stayed constant or fell slightly after two additions of E.D.T.A.
10. The scale reading was plotted against the volume of E.D.T.A. added and the point of intersection of the two straight lines denoted the end point.

0.02 ml. of E.D.T.A. = 10 μg of calcium.

11. The cuvette and pipette were rinsed with distilled water and the procedure was repeated using 0.1 ml. of serum delivered from a dried 0.1 ml. washout pipette.

Calculation

$$\frac{\text{Titration of serum}}{\text{Titration of standard}} \times 10 \text{ mg. calcium per 100 ml.}$$

Detection of blanks in the reagents.

0.1 ml. of standard solution and 0.2 ml. of potassium hydroxide solution were added to 2.5 ml. of murexide solution. The titration was carried out as usual. After two decreasing scale readings a second 0.1 ml. of standard was added, then it was mixed, read and titrated to the end point.

End point reading 2 - end point reading 1 = true standard reading.

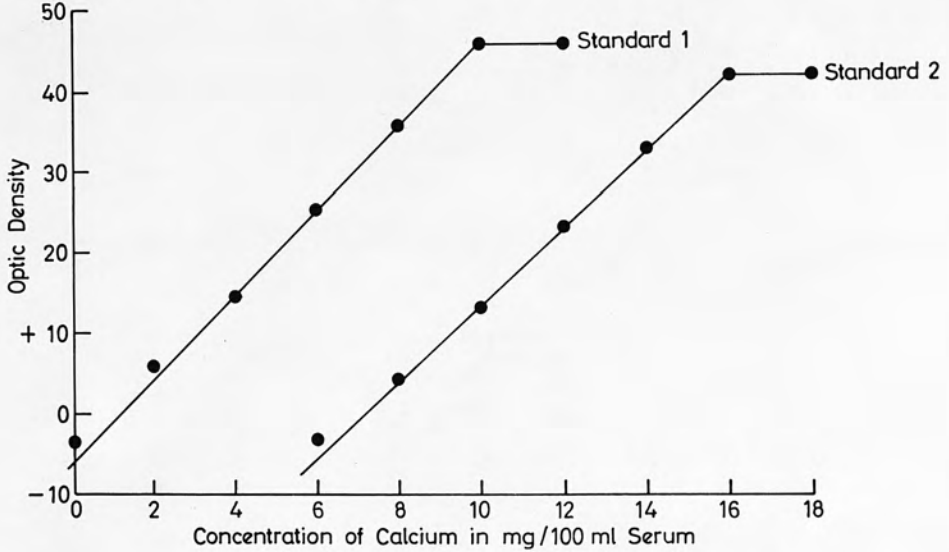
True standard reading 1 - true standard reading = blank.

THE CALCIUM METHOD

Readings for the standards :-

(1). <0-6·0-14·5-25·5-36·0-46·0-46·0 = 10·0 mg %

(2). <0-4·5-13·5-23·5-33·0-42·0-42·0 = 10·0 mg %



ESTIMATION OF PHOSPHORUS (AS INORGANIC PHOSPHATE) IN PLASMA

For this the phosphomolybdate method of McDonald (1957) was used.

Principle of the method.

The method depends on the formation of phosphomolybdate when plasma is added to ammonium molybdate and the subsequent extraction of the phosphomolybdate into an organic solvent. An intense blue colour is formed when the extracted phosphomolybdate is reduced by stannous chloride.

The most important source of error comes with long delays in removing the plasma from the red cells when phosphorus may be split from esters in the cells giving an incorrectly high result. The supernatant after protein separation will keep for at least 48 hours.

Plasma phosphorus should always be estimated in the fasting state.

Reagents.

1. 60% perchloric acid HC/O_4.
2. 4% perchloric acid prepared by diluting the 60% 1:15.
3. Extraction solution: 15 parts petroleum ether (B.P. = 100 - 120 ^{o}) + 85 parts iso-butyl alcohol.
4. 5% ammonium molybdate = $(NH4)_2$ MoO4 in 4 N H_2 50_4 (sulphuric acid).
5. 43% stannous chloride $SnCl_2$ 2 H_2O in concentrated hydrochloric acid HCl. This should be freshly diluted each day/

day in a dilution of 1 : 400 with 18 N sulphuric acid. (10 µl in 4.0 ml.)

6. Standard solutions

(a) Stock containing 1 mg. of phosphorus per ml. This is prepared by dissolving 4.394 gm. of potassium monobasic phosphate (KH_2 Po_4) and diluting it to 1 litre with water. A few drips of chloroform CHCl are added as a preservative.

(b) Intermediate containing 100 micrograms per ml. This is prepared by adding 10 ml. of stock standard solution to 3.3 ml. of 60% perchloric acid then diluting it to 100 ml. with water.

(c) Working containing 1 microgram per ml. This is prepared by diluting 1.0 ml. of the intermediate standard solution to 100 ml. with 2% perchloric acid.

Procedure

1. Into a glass-stoppered test tube 2.4 ml. of water was pipetted, 0.1 ml. of plasma was washed, and 2.5 ml. of 4% perchloric acid were added. Then the contents of the tube were well mixed and allowed to stand for at least 15 minutes, then centrifuged (the supernatant fluid could keep overnight satisfactorily in the refrigerator.)

2. Into a clean glass-stoppered tube 2 ml. of the supernatant fluid were pipetted. For the blank, 2 ml. of 2% perhloric acid were used instead. For the standard, 2 ml. of the working standard were used.

   To these 2 ml. 0.5 ml. of ammonium molybdate solution and 2.5 ml. of the extracting solution were added. The contents of the tube were mixed by shaking the tube vigorously for 90 seconds, then it was briefly centrifuged.

3. Into a clean glass-stoppered tube 2 ml. of the supernatant fluid were pipetted, then 0.3 ml. of absolute ethanol and 0.2 ml. of the stannous chloride-sulphuric acid reagent were added. All were mixed well.

4. The result was read after 15 minutes in the spectrophotometer at 680 using a dry cuvette.

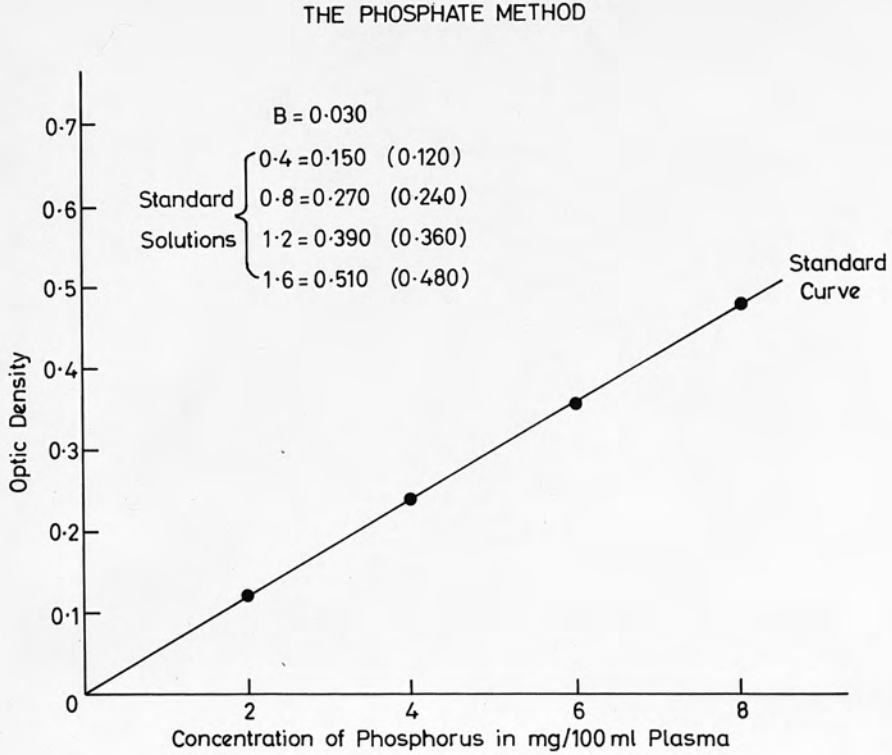
Calcultation of the result

$$\frac{\text{(optic density of the sample - o.D. of the blank}}{\text{(o.D of the standard - o.D. of the blank)}} \times \frac{2}{0.04} \times \frac{100}{1000}$$

$$= \frac{\text{(o.D. of the tst - o.D. of blank}}{\text{(o.D. of the standard - o.D. of blank)}} \times 5 = \text{mg. of phosphorus}$$

per 100 ml.of plasma.

The standard curve is linear up to the equivalent of 10 mg. per 100 ml.


THE PHOSPHATE METHOD
B = 0·030
Standard Solutions
0·4 = 0·150 (0·120)
0·8 = 0·270 (0·240)
1·2 = 0·390 (0·360)
1·6 = 0·510 (0·480)
Standard Curve
Optic Density
0·7
0·6
0·5
0·4
0·3
0·2
0·1
0
2
4
6
8
Concentration of Phosphorus in mg/100 ml Plasma

ESTIMATION OF GLUCOSE IN WHOLE BLOOD

This was done using the enzymatic test for "true glucose". (Huggett and Nixon 1957) (Keilin and Hartree 1945) 1948

Solutions required.

1. Glugose reagent: Buffer/enzyme mixture.

$Na\ H_2\ Po_4\ \ 2\ H_2O$	Sodium orthophosphate dihydrogen.
$Na_2\ Po_4\ \ 2\ H_2O$	Sodium orthophosphate monohydrogen.
GoD	Glucose oxidase
PoD	Peroxidase
	Chromogen
	o - dianisidine hydrochloride.

2. Glucose standard solution : D - glucose. DAB 6

3. Perchloric acid : 0.33 M for deproteinisation.

Principle of the method.

1. D - glucose is oxidised by glucose oxidase enzyme to gluconolactone which with water will form gluconic acid.

$$\text{Glucose} + H_2O + O_2 \xrightarrow{\text{GoD}} \text{gluconic acid} + H_2O_2$$

2. Hydrogen peroxide formed will oxidise the hydrogen donor DH_2 (o - Dianisidine) which will be converted into a reddish brown dye D

$$H_2O_2 + DH_2 \xrightarrow{\text{PoD}} 2\ H_2O + D$$

So the total reaction is -

$$\text{Glucose} + O_2 + DH_2 \xrightarrow[\text{PoD}]{\text{GoD}} \text{gluconic acid} + H_2O + D$$

3. The amount of dyestuff is determined colorimetrically at 436 mμ (or a similar wave length). The amount of brown dyestuff/

dyestuff formed is thus a measure of the amount of glucose participating since the reactions proceed quantitatively.

Advantages of this procedure.

1. In view of the high specificity of GoD for D- glucose, this procedure may be considered the only method for determining "true glucose". So this test is specific for D- glucose. Results are not affected by other sugars eg. fructose, lactose, galactose and pentoses. Mannose yields a positive but a much weaker reaction than glucose. No pathological conditions cause mannose to appear in the blood.
2. Other reducing agents eg. glucuronic acid, creatine and uric acid do not interfere with the reaction.
3. Elevated glutathione concentrations and extremely large doses of vitamin C may cause the impression that the values are too low.
4. The average error margin for this routine method is below $\pm$ 5%.

Preparation of solutions

1. Buffer/enzyme mixture. The material in the plastic foil bag was dissolved and brought up with redistilled water to 600 ml. in a beaker, then 1.8 ml. of 0.3% of chloroform were added to diminish bacterial contamination.
   This mixture was stable for at least three weeks in the refrigerator.

2. Chromogen. This was prepared by dissolving the substance in the bottle labelled "chromogen" in 8.0 ml. of redistilled water, and then the solution was kept in the brown bottle provided. Stability of this solution was unlimited.

3. Glucose reagent. This was prepared freshly every day by mixing the buffer enzyme mixture with the chromogen solution. It was prepared freshly to avoid too rapid oxidation of O - Dianisidine hydrochloride in solution. It was prepared by adding 1 volume of chromogen solution to 100 volumes of buffer/enzyme mixture and vigorous stirring. The resultant glucose reagent was then poured into a brown glass-stoppered bottle. It was stable only until the next morning.

4. Glucose standard. Containing 91 mg. per 100 ml.

5. Perchloric acid. 2.85 ml. of 70% perchloric acid were diluted with redistilled water to 100 ml.

A new blank and a new glucose standard were always used for each test series.

Procedure.

1. Into a centrifuge tube 1.00 ml. of perchloric acid and 0.1 ml. of whole blood were successively pipetted. The pipette was rinsed by repeatedly drawing up and blowing out the mixture. Proper mixing was then completed with a plastic spatula.

2. The mixture was then centrifuged for 5 - 10 minutes at 3000 revolutions per minute or more.

3. The supernatant fluid was then pasteur-pipetted into a dry test tube and 0.2 ml. of it were used for the test. Sometimes the blood sample could not be processed immediately. In such cases it was at least pipetted into perchloric acid. After deproteinization and centrifuging the supernatant fluid was decanted and could then be kept in the refrigerator until the next day.

4. A reagent blank and a glucose standard were used for each test series. For series determinations, as was usually the case, as a first step 0.2 ml. of the respective decantate were pipetted into the prepared test tube. Then the glucose reagent was added at 30 second intervals which was also observed during measurement. This would ensure a uniform incubation period of 35 minutes for all samples and the glucose standard.

   Into one test tube were pipetted successively -

   (a) Reagent blank — 0.2 ml. of redistilled water + 5.0 ml. of glucose reagent.

   (b) Glucose standard — 0.2 ml. of glucose standard sol. + 5.0 ml. of glucose reagent.

   (c) Sample (blood) — 0.2 ml. of deproteinized supernatant sol. + 5.0 ml. of glucose reagent.

All the specimens were done in duplicates.

The two solutions in each test tube were mixed well by repeated swirling and then the mixture was allowed to stand for 35 minutes at room temperature. The glucose standard and the samples were always kept under identical conditions of light. Direct sunlight was always avoided, but indirect sunlight or dispersed daylight were known not to affect the reagents.

5. After the 35 minute period the difference in colour between the sample (or the glucose standard) and the reagent blank was measured in a 10 mm. cell at 436

N.B. The glucose reagent might darken due to oxidation (the error was eliminated by using the reagent blank) and after prolonged standing might form absorbances which were somewhat lower (the error was compensated by the glucose standard).

6. Calcultation.

The calibration curve in this method was linear up to values of more than 350 mg. per 100 ml. of blood glucose. In order to obtain the glucose content per ml. of blood the measurement was related to the absorbance of the glucose standard solution. The glucose standard contained 18.2 of glucose per test run which is equal to 1 mg. per ml. of blood.

So $\frac{\text{sample}}{\text{standard}}$ = mg. per ml. blood or = mg.% glucose

RESULTS.

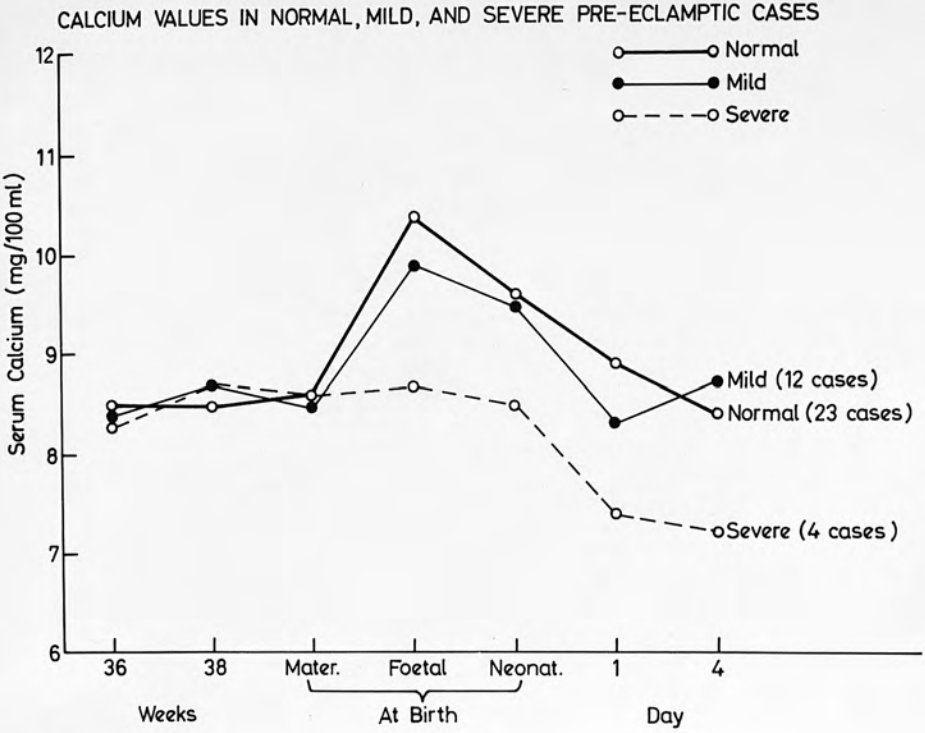
GROUP I: COMBINED ANTENATAL, NATAL AND POSTNATAL STUDY

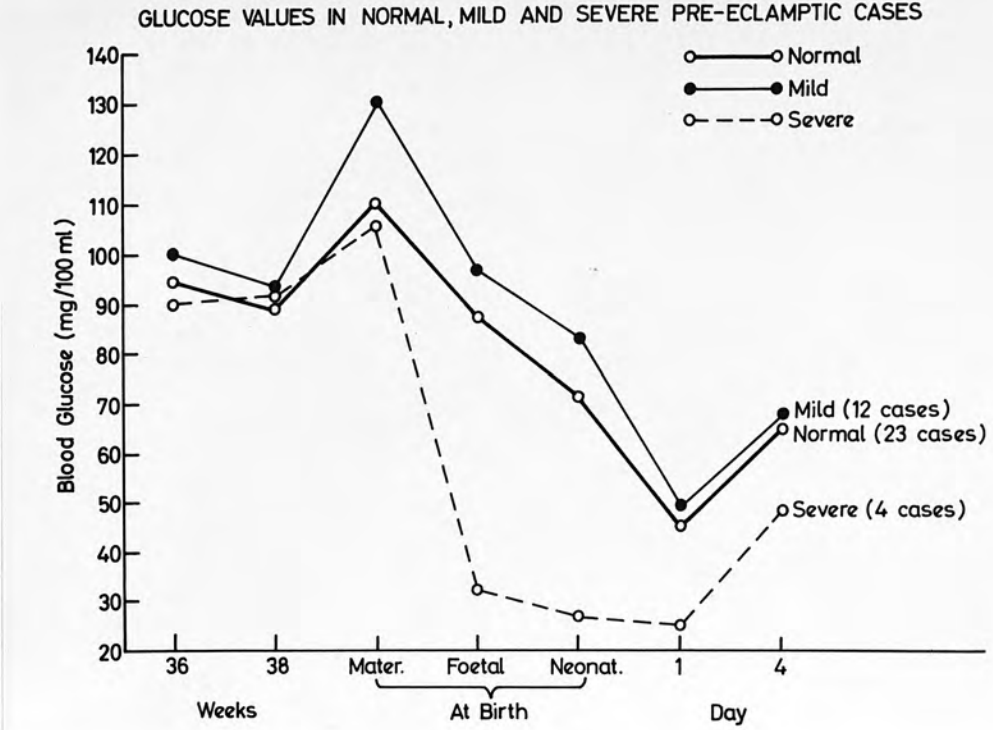
TABLE I.

Mean values and standard deviations
in normal mothers and babies

Substance	value	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.50	8.50	8.60	10.40	9.60	8.90	8.40
	S.D.	0.28	0.24	0.40	1.00	0.82	0.73	0.48
	No.	22	21	23	23	23	23	23
Phosphorus	M.V.	2.70	2.80	2.50	4.10	4.40	4.90	6.20
	S.D.	0.65	0.81	0.65	0.87	1.16	1.09	1.23
	No.	22	21	23	23	23	23	23
Glucose	M.V.	94.00	89.00	110.00	87.00	71.00	45.00	65.00
	S.D.	13.30	9.43	19.57	22.93	19.42	17.61	12.04
	No.	22	21	23	23	23	23	23

M.V. = Mean value
S.D. = Standard deviation
No. = Number of cases studied


CALCIUM VALUES IN NORMAL, MILD, AND SEVERE PRE-ECLAMPTIC CASES
Normal
Mild
Severe
Serum Calcium (mg/100 ml)
12
11
10
9
8
7
6
Mild (12 cases)
Normal (23 cases)
Severe (4 cases)
36
38
Mater.
Foetal
Neonat.
1
4
Weeks
At Birth
Day


GLUCOSE VALUES IN NORMAL, MILD AND SEVERE PRE-ECLAMPTIC CASES
Normal
Mild
Severe
Blood Glucose (mg/100 ml)
140
130
120
110
100
90
80
70
60
50
40
30
20
Mild (12 cases)
Normal (23 cases)
Severe (4 cases)
36
38
Mater.
Foetal
Neonat.
1
4
Weeks
At Birth
Day

GROUP II. PATIENTS ON INTRAVENOUS GLUCOSE INFUSIONS DURING LABOUR

TABLE 2

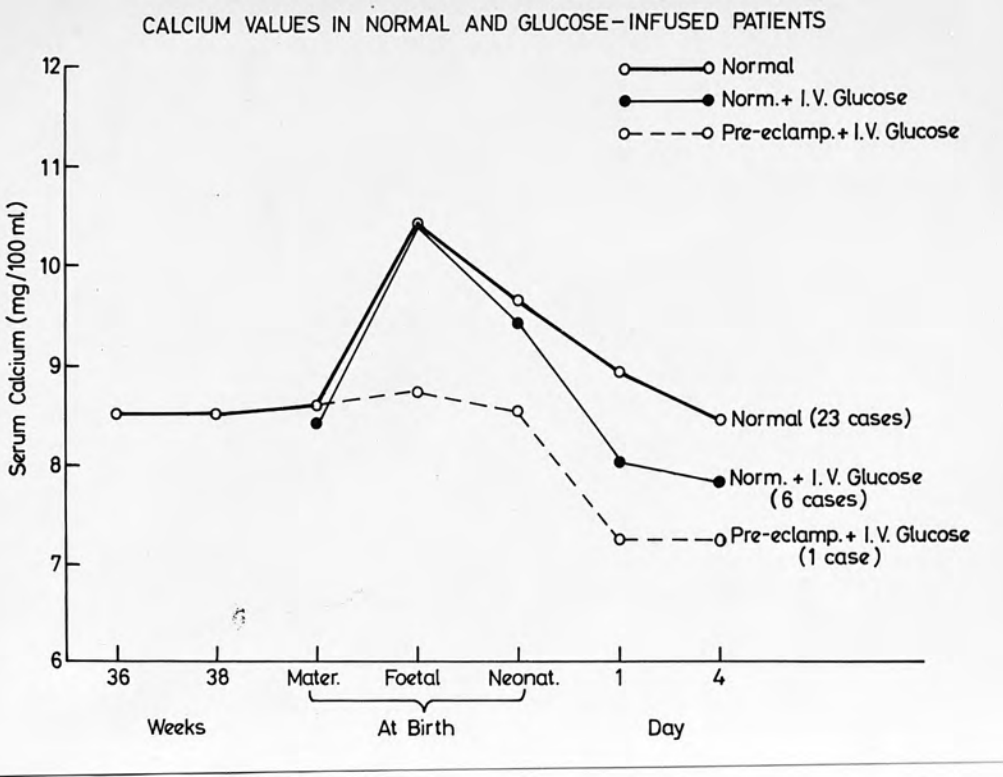
Normal cases on glucose infusions

Substance	Value	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.40	10.40	9.40	8.00	7.80
	S.D.	0.41	0.30	0.55	0.70	0.48
	No.	6	6	6	6	6
Phosphorus	M.V.	2.70	4.30	4.50	4.90	6.10
	S.D.	0.79	0.75	0.67	1.29	1.40
	No.	6	6	6	6	6
Glucose	M.V.	154.00	124.00	108.00	54.00	75.00
	S.D.	28.16	40.74	38.08	16.49	12.65
	No.	6	6	6	6	6

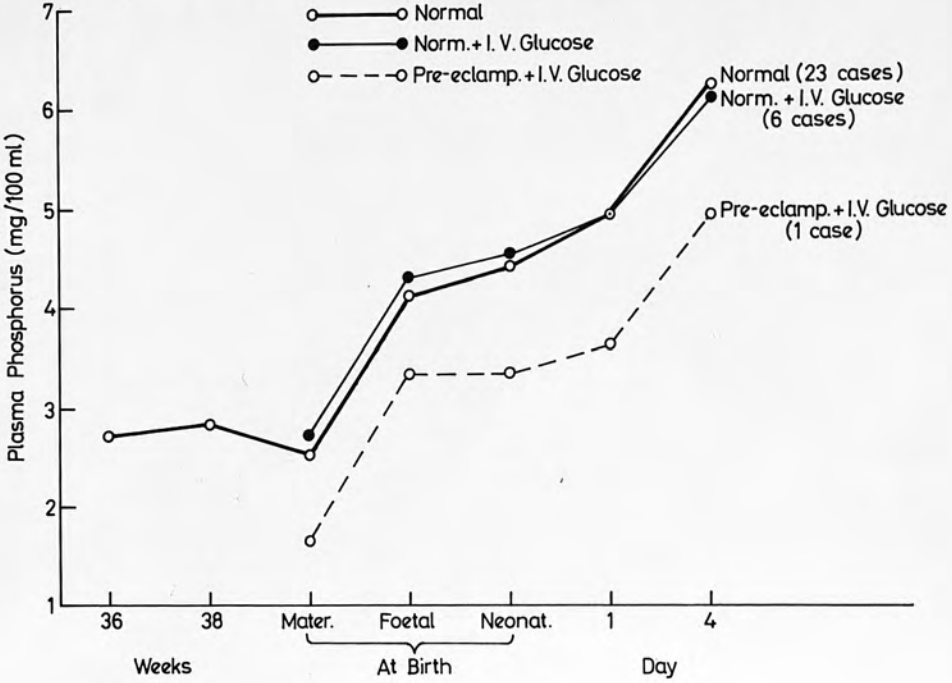
TABLE 3

Pre-eclamptic patient on I.V. glucose

Substance	Value	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.6	8.7	8.5	7.2	7.2
Phosphorus	M.V.	1.6	3.3	3.3	3.6	4.9
Glucose	M.V.	388.0	94.0	81.0	28.0	34.0


CALCIUM VALUES IN NORMAL AND GLUCOSE-INFUSED PATIENTS
Normal
Norm.+ I.V. Glucose
Pre-eclamp.+ I.V. Glucose
Serum Calcium (mg/100 ml)
12
11
10
9
8
7
6
Normal (23 cases)
Norm. + I.V. Glucose
(6 cases)
Pre-eclamp.+ I.V. Glucose
(1 case)
36
38
Mater.
Foetal
Neonat.
1
4
Weeks
At Birth
Day

PHOSPHORUS VALUES IN NORMAL AND GLUCOSE-INFUSED PATIENTS



GROUP III: FULL-TERM NORMAL NEWBORN INFANTS

TABLE 4

Mean values and standard deviations
in full-term newborn infants

Substance	Value	Neonatal	1st. day	2nd. day	3rd. day	4th. day
Calcium	M.V.	9.60	8.90	8.50	8.30	8.30
	S.D.	0.82	0.62	0.50	0.47	0.57
	No.	23	55	27	27	55
Phosphorus	M.V.	4.40	4.70	4.70	5.10	6.10
	S.D.	1.16	1.19	1.16	1.74	1.30
	No.	23	55	27	27	55
Glucose	M.V.	71.00	50.00	55.00	65.00	71.00
	S.D.	19.42	18.79	17.32	20.22	15.33
	No.	23	55	27	27	55

GROUP III: TWIN STUDY

TABLE 5

Results according to birth order

(1) first in order
(2) second in order

Substance	Value	Foetal 1	Foetal 2	Neonatal 1	Neonatal 2	1st. day 1	1st. day 2	4th. day 1	4th. day 2
Calcium	M.V.	10.40	10.10	9.40	8.80	7.80	7.50	8.00	7.80
	S.D.	1.04	0.70	0.33	0.56	0.66	0.64	0.79	0.71
	No.	9	9	7	7	16	16	16	16
Phosphorus	M.V.	4.20	4.90	4.80	4.30	4.40	4.50	5.00	5.30
	S.D.	0.93	1.25	1.05	0.89	0.96	1.21	1.27	1.36
	No.	9	9	7	7	16	16	16	16
Glucose	M.V.	72.00	70.00	55.00	69.00	42.00	44.00	63.00	61.00
	S.D.	31.24	34.04	15.13	16.15	18.33	17.80	20.25	16.61
	No.	9	9	7	7	16	16	16	16

GROUP III: TWIN STUDY

TABLE 6

Results according to birth weight (1) the larger
(2) the smaller

Substance	Value	Foetal 1	Foetal 2	Neonatal 1	Neonatal 2	1st. day 1	1st. day 2	4th. day 1	4th. day 2
Calcium	M.V.	10.20	10.30	9.00	9.20	7.70	7.70	7.80	8.00
	S.D.	9.82	0.97	0.30	0.69	0.66	0.66	0.81	0.70
	No.	9	9	7	7	16	16	16	16
Phosphorus	M.V.	4.50	4.50	4.40	4.70	4.00	4.90	5.00	5.50
	S.D.	1.39	0.87	0.89	1.11	0.82	1.18	1.00	0.49
	No.	9	9	7	7	16	16	16	16
	M.V.	79.00	63.00	66.00	47.00	46.00	40.00	68.00	59.00
	S.D.	27.05	35.63	13.96	21.52	15.72	19.60	15.72	16.73
	No.	9	9	7	7	16	16	16	16

GROUP V. THE PLACENTAL DYSFUNCTION SYNDROME

TABLE 7

Mild and moderate pre-eclampsia

Substance	Value	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.40	8.70	8.50	9.90	9.50	8.30	8.70
	S.D.	0.39	0.39	0.39	0.81	0.82	0.64	0.48
	No.	11	10	12	12	12	12	12
Phosphorus	M.V.	2.70	2.60	3.00	4.50	4.70	5.50	6.20
	S.D.	0.83	0.42	0.75	1.08	1.19	1.11	2.03
	No.	11	10	12	12	12	12	12
Glucose	M.V.	100.00	93.00	130.00	96.00	83.00	49.00	67.00
	S.D.	3.87	4.36	22.74	23.41	19.65	20.93	19.39
	No.	11	10	12	12	12	12	12

GROUP V. THE PLACENTAL DYSFUNCTION SYNDROME

TABLE 8

Severe pre-eclampsia

Substance	Value	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.30	8.70	8.60	8.70	8.50	7.40	7.20
	S.D.	0.54	0.41	0.10	0.14	0.17	0.39	0.10
	No.	4	4	4	4	4	4	4
Phosphorus	M.V.	2.60	3.00	2.70	4.20	4.90	5.50	6.50
	S.D.	0.44	0.36	1.04	1.01	1.17	1.44	1.51
	No.	4	4	4	4	4	4	4
Glucose	M.V.	90.00	92.00	106.00	32.00	27.00	25.00	48.00
	S.D.	3.74	4.47	29.15	5.00	1.58	2.12	27.62
	No.	4	4	4	4	4	4	4

TABLE 9

Elderly primigravida

Substance	Value	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.80	8.80	8.50	10.40	10.20	8.00	8.80
	S.D.	0.14	0.56	0.43	0.82	0.73	0.81	0.70
	No.	4	4	4	4	4	4	4
Phosphorus	M.V.	2.30	2.60	2.30	3.50	3.50	4.10	5.90
	S.D.	0.41	0.50	0.35	0.10	0.05	0.46	0.85
	No.	4	4	4	4	4	4	4
Glucose	M.V.	88.00	90.00	122.00	98.00	87.00	34.00	67.00
	S.D.	12.37	8.66	29.44	19.82	16.79	14.78	16.76
	No.	4	4	4	4	4	4	4

TABLE 10

Dysmatures with normal gestation

Substance	Value	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.50	8.40	8.50	9.90	9.00	7.60	9.40
	S.D.	0.26	0.24	0.26	0.76	0.17	0.14	0.14
	No.	3	3	3	3	3	3	3
Phosphorus	M.V.	2.30	2.40	2.50	3.80	4.40	5.70	7.90
	S.D.	0.41	0.22	0.10	0.17	0.84	0.54	1.22
	No.	3	3	3	3	3	3	3
Glucose	M.V.	94.00	90.00	76.00	53.00	44.00	32.00	65.00
	S.D.	23.04	20.30	17.80	19.31	16.46	5.00	5.92
	No.	3	3	3	3	3	3	3

TABLE 11

Dysmatures with prolonged gestation

Substance	Value	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.60	8.70	7.40	7.40	7.20	7.30	7.90
	S.D.	-	-	-	0.78	0.50	0.14	0.22
	No.	1	1	2	2	2	2	2
Phosphorus	M.V.	2.30	2.00	1.90	5.60	6.60	6.00	6.20
	S.D.	-	-	0.36	1.27	0.36	1.49	1.84
	No.	1	1	2	2	2	2	2
Glucose	M.V.	81.00	34.00	103.00	32.00	28.00	25.00	69.00
	S.D.	-	-	3.61	1.00	1.41	3.61	16.28
	No.	1	1	2	2	2	2	2

TABLE 12

Immature delivery

Substance	Value	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.80	10.50	9.80	8.70	8.20
	S.D.	0.36	0.41	0.40	0.86	0.76
	No.	3	3	3	4	4
Phosphorus	M.V.	2.30	3.60	4.30	5.80	6.50
	S.D.	0.33	0.17	0.22	1.63	1.75
	No.	3	3	3	4	4
Glucose	M.V.	103.00	68.00	48.00	30.00	56.00
	S.D.	7.07	3.46	00.00	8.77	16.88
	No.	3	3	3	4	4

TABLE 13

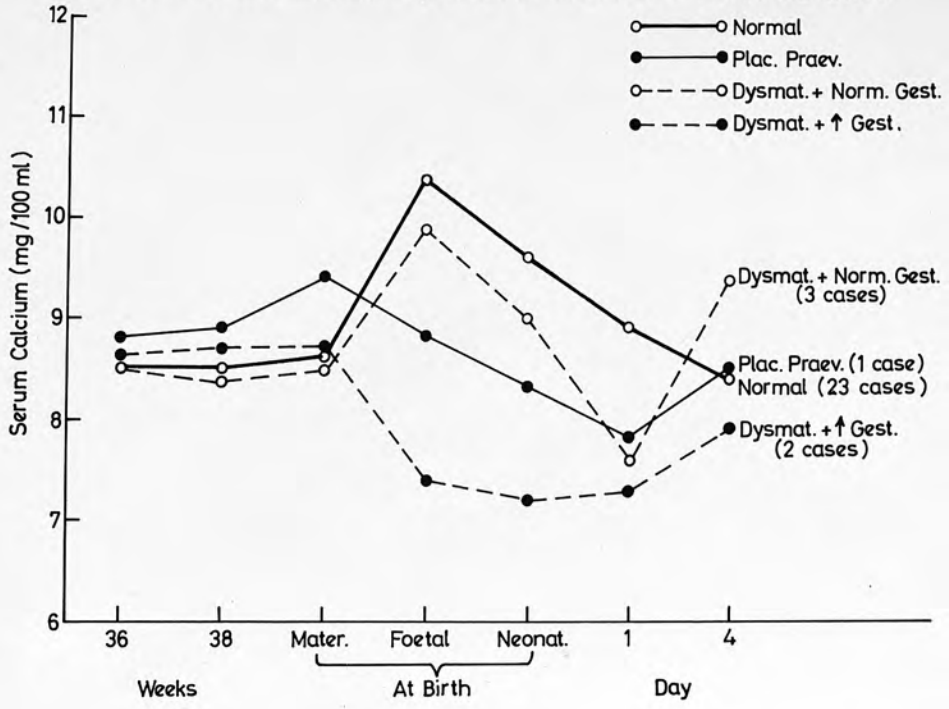
Prolonged gestation

Substance	Value	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	M.V.	8.70	9.60	8.90	8.20	7.80
	S.D.	0.28	1.56	1.20	0.26	0.62
	No.	2	2	2	3	3
Phosphorus	M.V.	2.30	4.90	5.70	4.20	5.20
	S.D.	0.28	1.06	0.57	1.18	0.48
	No.	2	2	2	3	3
Glucose	M.V.	115.00	79.00	61.00	72.00	73.00
	S.D.	1.00	1.00	5.00	14.25	5.92
	No.	2	2	2	3	3

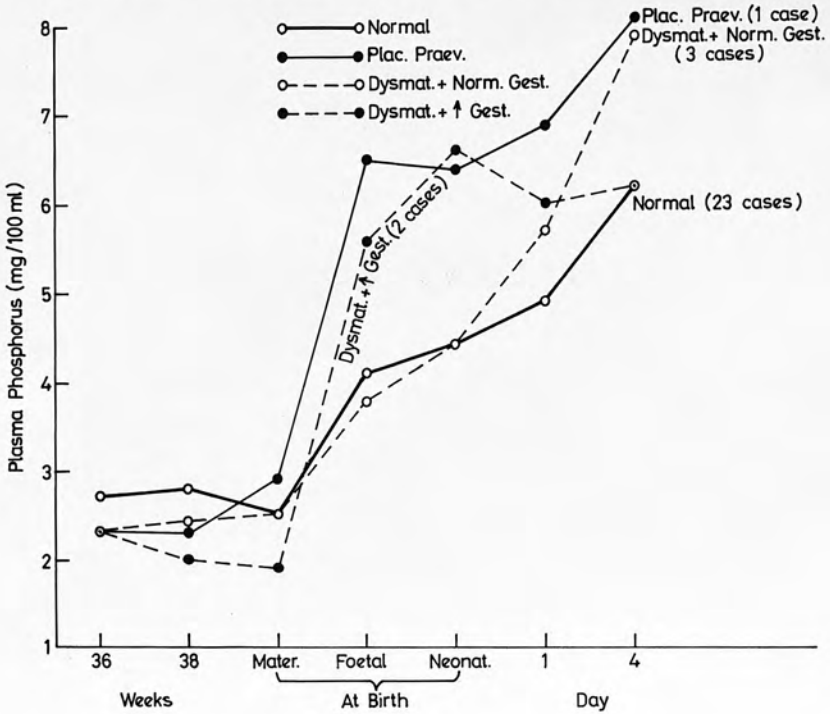
TABLE 14

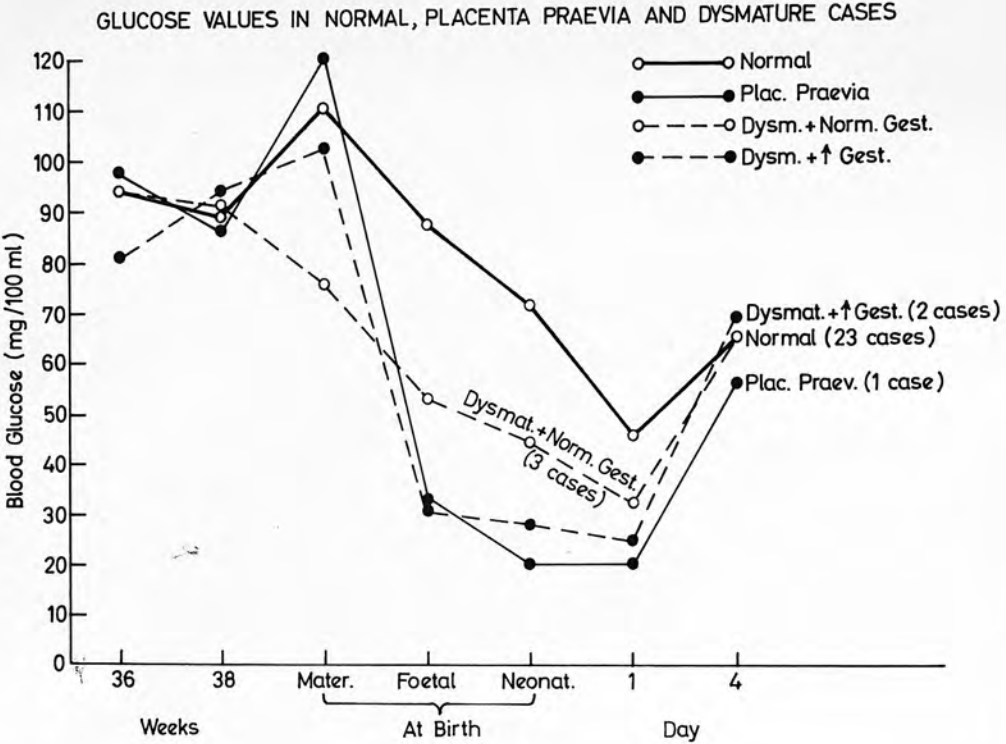
Placenta praevia (one case)

Substance	36 weeks	38 weeks	Maternal	Foetal	Neonatal	1st. day	4th. day
Calcium	8.80	8.90	9.40	8.30	8.30	7.80	8.50
Phosphorus	2.30	2.30	2.90	6.50	6.40	6.90	8.40
Glucose	98.00	86.00	120.00	33.00	20.00	20.00	56.00


CALCIUM VALUES IN NORMAL, PLACENTA PRAEVIA AND DYSMATURE CASES
Normal
Plac. Praev.
Dysmat. + Norm. Gest.
Dysmat. + ↑ Gest.
Serum Calcium (mg/100 ml)
12
11
10
9
8
7
6
Dysmat. + Norm. Gest. (3 cases)
Plac. Praev. (1 case)
Normal (23 cases)
Dysmat. + ↑ Gest. (2 cases)
36
38
Mater.
Foetal
Neonat.
1
4
Weeks
At Birth
Day

PHOSPHORUS VALUES IN NORMAL, PLACENTA PRAEVIA AND DYSMATURE CASES




GLUCOSE VALUES IN NORMAL, PLACENTA PRAEVIA AND DYSMATURE CASES
Normal
Plac. Praevia
Dysm. + Norm. Gest.
Dysm. + ↑ Gest.
Blood Glucose (mg/100 ml)
120
110
100
90
80
70
60
50
40
30
20
10
0
Dysmat. + ↑ Gest. (2 cases)
Normal (23 cases)
Plac. Praev. (1 case)
Dysmat. + Norm. Gest. (3 cases)
36
38
Mater.
Foetal
Neonat.
1
4
Weeks
At Birth
Day

GROUP VI. BABIES OF DIABETIC MOTHERS

TABLE 15

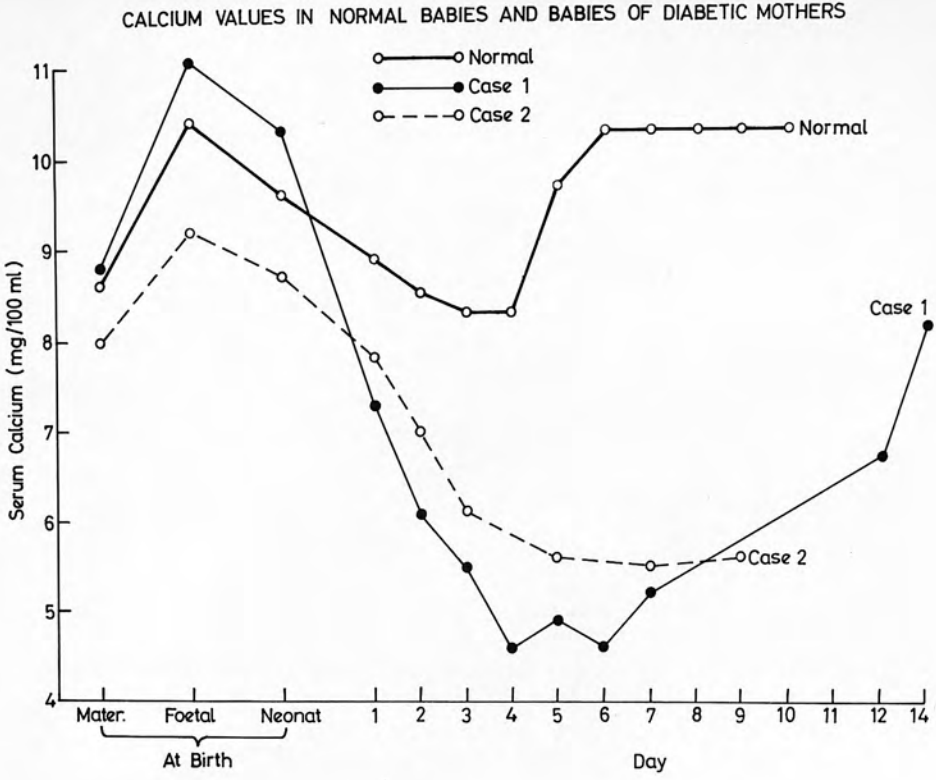
1st. Case: Baby Reid

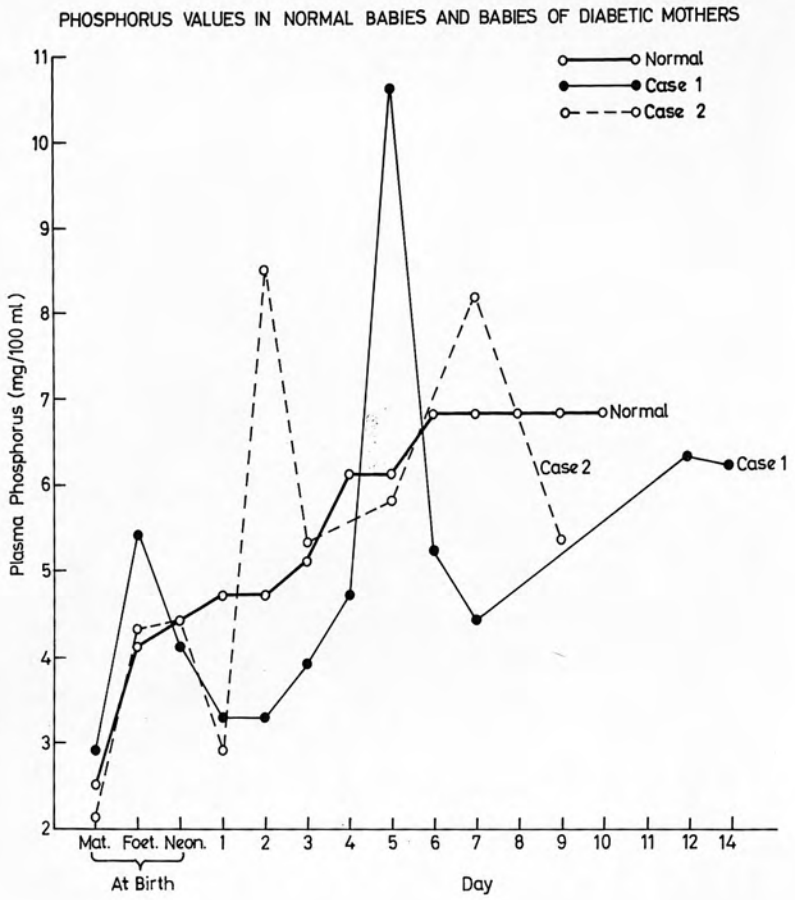
Substance	Maternal	Foetal	Neonatal	Day 1	Day 2	Day 3	Day 4	Day 4	Day 5	Day 6	Day 7	Day 12	Day 14
Calcium	8.8	11.1	10.3	7.3	6.1	5.5	4.6	4.6	4.9	4.6	5.2	6.7	8.1
Phosphorus	2.9	5.4	4.1	3.3	3.3	3.9	4.5	4.9	10.7	5.2	4.4	6.3	6.1
Glucose	137.0	100.00	77.0	23.0	14.0	25.0	19.0	14.0	36.0	37.0	42.0	70.0	85.0

TABLE 16

2nd. Case: Baby White

Substance	Maternal	Foetal	Neonatal	Day 1	Day 2	Day 3	Day 3	Day 7	Day 9
Calcium	8.0	9.2	8.7	7.8	7.0	6.1	5.6	5.5	5.6
Phosphorus	2.1	4.3	4.4	2.9	8.5	5.3	5.8	8.2	5.3
Glucose	88.0	28.0	25.0	53.0	27.0	57.0	69.0	39.0	72.0


CALCIUM VALUES IN NORMAL BABIES AND BABIES OF DIABETIC MOTHERS
Normal
Case 1
Case 2
Normal
Case 1
Case 2
Serum Calcium (mg/100 ml)
11
10
9
8
7
6
5
4
Mater.
Foetal
Neonat
At Birth
1
2
3
4
5
6
7
8
9
10
11
12
14
Day


PHOSPHORUS VALUES IN NORMAL BABIES AND BABIES OF DIABETIC MOTHERS
Normal
Case 1
Case 2
Plasma Phosphorus (mg/100 ml.)
11
10
9
8
7
6
5
4
3
2
Normal
Case 2
Case 1
Mat.
Foet.
Neon.
1
2
3
4
5
6
7
8
9
10
11
12
14
At Birth
Day

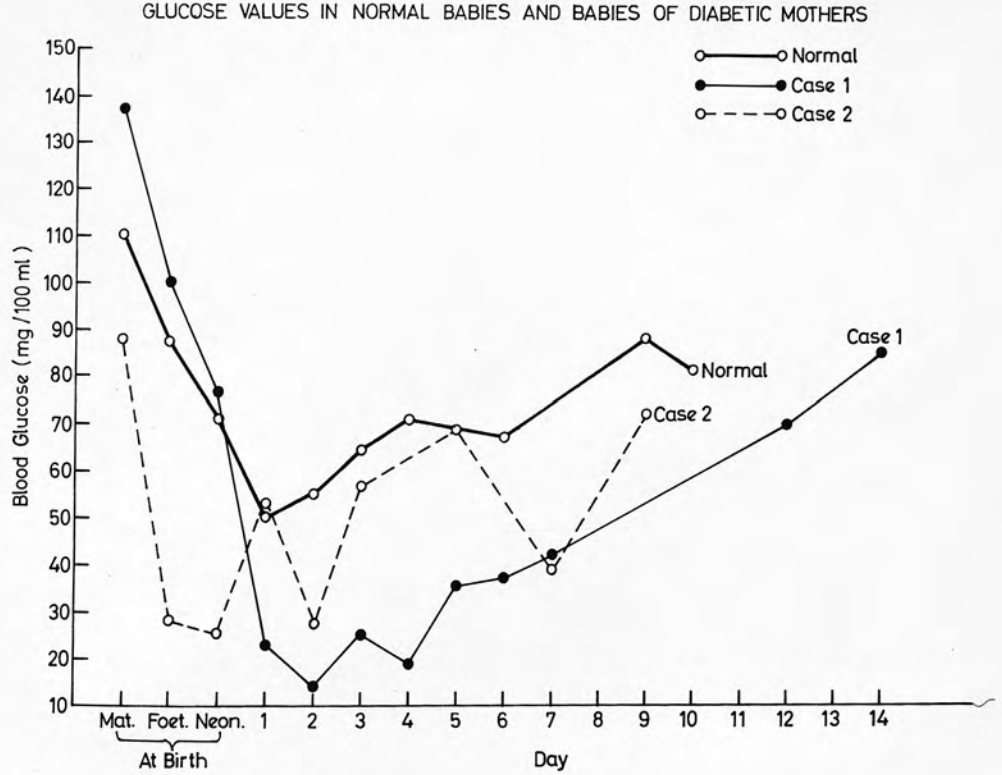

GLUCOSE VALUES IN NORMAL BABIES AND BABIES OF DIABETIC MOTHERS
Normal
Case 1
Case 2
Blood Glucose (mg/100 ml)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Case 1
Normal
Case 2
Mat.
Foet.
Neon.
At Birth
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Day

TABLE 17

CORRELATIONS OF MATERNAL, FOETAL AND NEONATAL SERUM CALCIUM, PHOSPHORUS AND GLUCOSE LEVELS

(23 paired samples in each)

Substance	Correlated Values	r	S.E.	p
Calcium	Maternal and foetal	+ 0.36	0.21	0.08
	Maternal and neonatal	+ 0.57	0.21	<0.01
	Foetal and neonatal	+ 0.87	0.21	<0.0001
Phosphorus	Maternal and foetal	+ 0.45	0.21	0.03
	Maternal and neonatal	+ 0.38	0.21	0.07
	Foetal and neonatal	+ 0.71	0.21	0.001
Glucose	Maternal and foetal	+ 0.82	0.21	0.0001
	Maternal and neonatal	+ 0.70	0.21	0.001
	Foetal and neonatal	+ 0.72	0.21	0.001

TABLE 18

CORRELATIONS OF NEONATAL, 1st DAY AND 4th DAY SERUM CALCIUM, PHOSPHORUS AND GLUCOSE LEVELS

(23 paired samples in each)

Substance	Correlated Values	r	S.E.	p
Calcium	Neonatal and 1st day	+ 0.36	0.21	0.08
	Neonatal and 4th day	+ 0.28	0.21	0.18
	1st day and 4th day	+ 0.31	0.21	0.14
Phosphorus	Neonatal and 1st day	+ 0.16	0.21	0.44
	Neonatal and 4th day	- 0.24	0.21	0.25
	1st day and 4th day	+ 0.25	0.21	0.23
Glucose	Neonatal and 1st day	+ 0.05	0.21	0.81
	Neonatal and 4th day	- 0.42	0.21	0.04
	1st day and 4th day	+ 0.61	0.21	< 0.01

TABLE 19

CORRELATIONS BETWEEN SERUM CALCIUM, PHOSPHORUS AND GLUCOSE LEVELS IN THE NEWBORN INFANT

(55 cases)

Time	Correlated Values	r	S.E.	p
1st day	Calcium and phosphorus	- 0.007	0.13	0.96
	Calcium and glucose	- 0.095	0.13	0.46
	Phosphorus and glucose	- 0.310	0.13	0.02
4th day	Calcium and phosphorus	- 0.180	0.13	0.17
	Calcium and glucose	+ 0.100	0.13	0.44
	Phosphorus and glucose	- 0.083	0.13	0.53

TABLE 19

CORRELATIONS BETWEEN SERUM CALCIUM, PHOSPHORUS AND GLUCOSE LEVELS IN THE NEWBORN INFANT

(55 cases)

Time	Correlated Values	r	S.E.	p
	Calcium and phosphorus	- 0.007	0.13	0.96
1st day	Calcium and glucose	- 0.095	0.13	0.46
	Phosphorus and glucose	- 0.310	0.13	0.02
	Calcium and phosphorus	- 0.180	0.13	0.17
4th day	Calcium and glucose	+ 0.100	0.13	0.44
	Phosphorus and glucose	- 0.083	0.13	0.53

TABLE 20

Correlations between changes which occur in the levels of serum calcium, phosphorus and glucose:- (23 paired samples in each).

Substance	Correlated values	r	S.E.	P
Calcium and phosphorus	Rise of Ca and p from maternal to foetal values	- 0.17	0.21	0.41
	Fall of Ca and rise of p from foetal to 12 hours	+ 0.14	0.21	0.50
Calcium and glucose	Rise of Ca and fall of Gl from matern. to foetal	+ 0.01	0.21	0.96
	Fall of Ca and Gl from foetal to 12 hours	+ 0.34	0.21	0.11
Phosphorus and glucose	Rise of p and fall of Gl from mater. to foetal	-.0.09	0.21	0.67
	Rise of p and fall of Gl from foetal to 12 hours	+ 0.06	0.21	0.77

TABLE 21

Correlation of foetal blood calcium, phosphorus and glucose values with the baby's birth weight
(23 normal cases)

Substance	r	S.E.	P
Calcium	- 0.10	0.21	0.63
Phosphorus	- 0.05	0.21	0.81
Glucose	+ 0.08	0.21	0.70

TABLE 22

Correlation of the baby's blood calcium, phosphorus and glucose values at birth with the birth weight
(23 normal cases)

Substance	r	S.E.	P
Calcium	- 0.06	0.21	0.77
Phosphorus	- 0.15	0.21	0.47
Glucose	- 0.09	0.21	0.67

DISCUSSION.

I. COMBINED ANTENATAL, NATAL AND POSTNATAL STUDY IN NORMAL CASES

ANTENATAL PERIOD

1. Maternal values during pregnancy.

During the latter part of pregnancy, i.e. from the 36th week onwards, it is clear from this study that the serum calcium decreases, that the phosphorus decreases, while the blood glucose remains within the normal adult range.

From the previous literature it appears that there is general agreement about the hypocalcaemia during pregnancy. Morley (1913), Widdows (1923), Stieglitz (1927), Bokelman and Bock (1928) and Mull and Bill (1934) all found hypocalcaemia during pregnancy in their cases, but Handelman et al (1926) found that the serum calcium was normal during pregnancy and it only dropped immediately after parturition, but their series consisted of only 10 cases.

In spite of this general agreement about the hypocalcaemia, little is mentioned in the previous literature about its cause. However, there are two possible explanations -

(a) The work of Gittleman et al (1956) gives the impression that it is due to excessive adrenocorticosteroid hormone secretion during pregnancy and it has been shown by Hopkins et al. (1953) that both adrenocorticotriphic hormone and cortisone diminish the calcium concentration of human serum. In favour of this view, is the fact/

fact that the lowest serum calcium during pregnancy is encountered at about six weeks before parturition, at a time when these hormones reach their maximum concentration both in blood as well as in urine.

(b) Mull and Bill (1934) also found that the lowest calcium concentration was at about 4 - 7 weeks preceding parturition, although they explained it in a different way. They assumed that the greatest demand for calcium made on the maternal system by the growing foetus comes during the period of 4 - 7 weeks preceding delivery. As an evidence for their explanation they found that there was a slight lowering of serum calcium during pregnancy through close successive pregnancies (they explained the word "close" as within 18 months or less).

The present study also showed hypophosphataemia during pregnancy. This was also found by Mull et al. A mechanism similar to that responsible for the hypocalcaemia is suggested, i.e. increased demand on the maternal phosphorus by the growing foetus.

2. Blood glucose during pregnancy.

As to the blood glucose during pregnancy, the present work shows that it is within normal adult limits (89 - 94 mg. per 100 ml.) This goes/

goes with what Morriss (1917) has already found and also with previous workers results which were quoted by Morriss.

LABOUR TIME

Serum Calcium, Phosphorus and Glucose During Normal Labour and Delivery.

Before discussing the results, the method of obtaining blood at delivery will be discussed first, as it was felt that this might have a bearing on the interpretation of our results.

Most of the early workers on calcium and phosphorus of the newborn considered cord values to represent the baby's blood at birth, so Mull and Bill (1934) and Denzer et al. (1939) considered cord values for calcium to represent neonatal values, and Riesenfeld, Handelman and Rose (1925) considered phosphorus of blood taken from the cut end of the cord to represent neonatal phosphorus values, while Bakwin (1937) considered both cord calcium and cord phosphorus to represent baby's values at the moment of birth.

In our work we were not in full agreement with this. Theoretically the umbilical cord has two arteries and a vein. The umbilical vein blood is actually foetal blood and not neonatal blood. It is the umbilical artery blood which is equivalent to that of the baby at the moment of birth and this was shown by Hallman et Salmi (1954).

Differences between umbilical artery and umbilical vein concentration of calcium were found by Hallman et al. who were the first to give separate consideration to both values regarding calcium.

Also differences in glucose content between umbilical artery (75 mg./100 ml.) and umbilical vein (84 mg./100 ml.) were found by Bell and Cunningham (1928) and later confirmed by Hartmann (1955).

From this it is clear that umbilical artery and vein are different in their calcium and glucose contents, and the artery represents the baby at birth while the vein represents the foetus before birth.

It is true that at birth the cut end of the cord is mostly umbilical vein because the umbilical arteries tend to close up of themselves and in any case do so before the veins, but still cord blood (taken from the cut end at birth) cannot be taken as equivalent to umbilical vein blood for two reasons -

1. Todd, Chuinard and Wood (1939) mentioned that it is impossible for all specimens obtained from the cut end of the cord to be well mixed and free from variations in concentration and viscosity. They simulated the process of "milking" of the umbilical cord to obtain blood from its cut end, a procedure commonly practiced, to milking of the finger or ear before or after pricking it for haematological examination. The latter technique is now criticised by many haematologists. On these bases those workers stressed that determinations of calcium and phosphorus on the cord blood do not provide a true indication of the calcium/

calcium and phosphorus content of the circulating blood of the foetus or the newborn.

2. The fact that the glucose content of the umbilical vein is not equal to that of the cut end of the cord was clearly shown in Hartmann's findings (1955). He has shown that the situation at birth was as follows -

When whole blood samples are obtained as nearly simultaneously as possible and tested for glucose content they showed the following decreasing order -

(a) Mother's capillaries or veins (highest)

(b) Umbilical vein.

(c) Umbilical cord (mixed blood).

(d) Infant's heel capillaries.

(e) Umbilical artery (lowest).

From the previous discussion,it is clear that ideally, at the moment of birth, pure umbilical vein blood (taken by a syringe and needle from the vein itself) and pure umbilical artery blood (similarly taken from the artery itself) represent foetal and neonatal bloods respectively, but because of the nature of the umbilical artery and its prompt contraction after birth it is very difficult to get blood from it (Morriss 1917). That is why in the present/

present work the baby's heel was resorted to.

In the present work foetal blood was the blood aspirated directly from the umbilical vein and neonatal blood was that obtained from the baby's heel at birth.

The present work shows the following results -

1. At the time of birth calcium in the foetal blood is higher than neonatal calcium. The latter is higher than the maternal serum calcium at delivery.
2. Neonatal plasma phosphorus is higher than the foetal phosphorus and the latter is higher than maternal plasma phosphorus.
3. Glucose is highest in the maternal blood, lower in foetal blood and lowest in the neonatal.
4. Both calcium and phosphorus in the maternal blood at delivery are lower than those of normal adults.
5. At the time of birth there is a highly significant positive correlation between calcium, phosphorus and glucose values of foetal blood and those of the neonatal blood ($P = 0.0001$ in case of calcium, $P = 0.001$ for both phosphorus and glucose.) Also there is a significantly positive correlation between maternal values and both foetal and neonatal values.

(Correlations of maternal and foetal values show that P = 0.08 for calcium, = 0.03 for phosphorus and = 0.0001 for glucose. Correlations of maternal and neonatal values show that P = 0.01 for calcium, 0.07 for phosphorus and = 0.001 for glucose.)

6. At the time of birth there is no significant correlation between the birth weight and foetal and neonatal calcium, phosphorus and glucose values.

7. There is no significant correlation between the changes which occur in blood calcium, phosphorus and glucose values from maternal to foetal values, nor from foetal to first day values.

The findings concerning serum calcium at delivery as reported by previous workers can be summarised in the following table -

Reference	Foetal	Neonatal	Maternal	Foetal - Neonatal	Neonatal - Maternal	Other Observations
Hallman et Salmi (1954 - 1955)	9.8 - 16.1 Mean = 11.8	8.9 - 13.2 Mean = 10.9	8.7 - 12.3 Mean = 10	0.2 - 2.9 Mean = 0.92	0.80	umbilical artery calcium = neonatal calcium
Mull and Bill (1934)			Mean = 9.8		1 - 3	cord calcium = 11.7
Bakwin and Bakwin (1932)					1 - 3	
Denzer et al. (1939)						cord blood is 1 - 3 mg. maternal

N.B. All the above values are given in mgms. per 100 ml. of serum.

So it is obvious that our results, in agreement with other workers results, show that foetal serum calcium and neonatal serum calcium are higher than the maternal calcium at or immediately after birth.

Several explanations and theories have been put forward to explain this difference -

(a) Diffusion theory.

According to this view diffusion is the main process by which calcium passes from the mother to the foetus across the placenta, but this could not explain the higher foetal and neonatal levels. If diffusion was the responsible process it would be expected to find a reversed calcium gradient, i.e. maternal serum calcium higher than foetal and neonatal, which is not the case.

(b) Storage theory.

Bokelmann and Bock (1928) assumed that the placenta acts as a calcium store supplying it to the foetus in increasing amounts, particularly during the last intra uterine months when the foetal growth is at its maximum.

(c) The closed circuit theory.

Schick (1939) explained the difference by considering the foetal circulation to be a closed circuit. The foetus excretes calcium in very small amounts only in the meconium and deposits some of its/

its calcium in bone. Another part may return through the placenta to the maternal circulation. The end result will be that the larger part of foetal calcium circulates in the closed circuit of the foetal circulation. By such a mechanism the high level of foetal serum calcium might be explained.

(d) The pumping theory.

Lamers (1912) explained the high foetal and neonatal serum calcium immediately after birth by increased uterine contractions during labour pumping more calcium from the maternal blood into the placenta and consequently into the baby more than at any other time, but if this was the true explanation one would expect to find all blood constituents other than calcium to be higher in the foetal and neonatal bloods than in the maternal. This is not the case. The present work showed that although calcium and phosphorus were so yet glucose was different. Thus glucose values were found to be higher in the maternal than in foetal or neonatal bloods.

In this respect Bogert and Plass (1923) disputed the concept of increased uterine contractions as an explanation. Their findings of higher calcium/

calcium and phosphorus, but lower proteins in placental blood than in the maternal, point clearly to a specific active placental function.

(e) The anoxic theory.

Hallman and Salmi (1954 - 1955) stressed the important role of anoxia causing the high calcium value observed in the placental blood compared to maternal serum calcium. They found that this value seemed even to be higher in the cyanotic newborn baby with poor respiration than in the normal newborn. According to their theory it is well known that the foetus lives in anoxia during the intra-uterine period and that the degree of this anoxia increases in the last intra-uterine weeks. At birth the oxygen content of the blood of the baby is lower than normal, particularly so in asphyxiated infants. They assumed that anoxia in such cases primarily increases placental function causing the movement of more calcium into the placenta and a rise in its calcium content. However, it is felt that this is not a satisfactory explanation. If increased placental function secondary to anoxia is the cause of the high foetal serum calcium one would naturally expect all other blood blood constituents other than calcium and phosphorus

to/

to be higher in foetal blood more than in the maternal, which is not the case.

Moreover it is difficult to assess the role of anoxia in the observed changes in calcium and phosphorus, as no simultaneous determinations of the oxygen content of the blood were made in Hallmann's series and the duration of anoxia, a probably significant factor, was unknown.

(f) The acidosis theory.

It is well known that the infant is born in a state of acidosis. Possibly this acidosis is of significance with regard to the high calcium level of foetal blood as compared to maternal blood and to the diversity of changes in calcium levels of the newborns in good and poor condition.

Against this argument is the fact that Marples and Lippard (1932) found that acidosis in the newborn is mostly compensated for so that changes in the PH (hydrogen iron concentration) of the blood of the newborn do not occur as a rule, although the indications of acidosis - low carbon dioxide values and increased chloride levels - are noticeable in the blood, so if acidosis is compensated for one would expect its influence to be minimal.

In conclusion it may be said that at the moment of birth serum calcium is higher in foetal than in neonatal blood and that it is higher in the latter than in maternal blood, so the foetus retains part of the calcium received. Such retention is naturally necessary for satisfation of the calcium requirement for growth. In numerous cases, however, specially in the infants born in poor condition, this difference in calcium levels is so great that it cannot be explained on the basis of satisfaction of the foetal calcium requirement alone. It is hard to account for the difference in calcium or for its large variation. One might assume that it is connected in some way with increased placental function or with the circulatory changes that take place immediately after birth.

Plasma phosphorus at birth.

The present work shows that immediately after birth the phosphorus concentration in the maternal blood is lower than that of the foetal blood. It also shows that the neonatal plasma phosphorus is higher than the foetal level and accordingly than the maternal as well.

The findings of previous workers concerning plasma phosphorus at birth are summarized in the following table -

Reference	Maternal Value	Cord Value	Neonatal (heel stab)	No. of Cases
1. Riesenfeld et al. (1925)	1.50 - 5.2 Mean = 3.10	1.9 - 7.2 Mean = 4.12		1439
2. Bruck & Weintraub (1955)		Mean = 6.62	7.49	21
3. Denzer et al. (1939)		6.06	7.11	

The figures overleaf show that cord blood and neonatal blood at birth are different in their phosphorus contents. This criticises the conclusions reached by Riesenfeld et al. (1925) in considering the blood from the cut end of the cord to represent the baby's blood at birth, although their series was a very big one of 1439 cases studied at labour.

It is our assumption that the higher phosphorus content of foetal and neonatal bloods can be explained by retention by the foetus, augmented perhaps by increased placental function at the moment of birth and by circulatory changes taking place in the placenta at that time.

Blood glucose at birth.

The present work shows that maternal blood glucose at delivery is usually within the normal adult range. This does not entirely agree with what Morriss et al. (1917) and Ketteringham et al. (1938) found. They found that although the blood glucose of the mother was normal during the first stage of labour, yet it tended to rise at the end of the second stage. However, both groups mentioned that the difference was slight and both attributed at least part of this rise to the effect of the anaesthetic. Since our cases were mostly spontaneous deliveries they did not require any anaesthetic or, if any was used, it was too light to be enough by itself to raise the blood sugar.

This work also shows that immediately after delivery glucose concentration/

concentration is higher in the maternal blood than in foetal blood and that the latter has more glucose levels than the neonatal blood glucose.

This transplacental gradient of blood glucose with the highest levels in the maternal circulation, followed by the foetal and lowest in neonatal blood is agreed upon by Merletti (1905), Ballerini (1908), Morriss (1917), Ketteringham and Austin (1938), Windle (1940), Smith (1945), and Hartmann (1955). However, Morriss tested the maternal and foetal bloods only, taking the latter from the cut end of the cord and he did not test the baby's blood at birth. On the other hand Ketteringham tested both the maternal and neonatal capillary blood and he did not test the foetal blood.

Perhaps the most relevant work to the present work is that of Hartmann (1955) in which he showed that if blood samples were obtained as nearly simultaneously as possible, the maternal blood was the highest in glucose, followed by the umbilical vein, then the cut end of the cord, followed by the infant's heel capillary blood and the lowest values were found in blood obtained from the umbilical artery.

<u>As to the correlations of these different values at birth</u>.

The results of the present work show that at the moment of birth a highly significant positive correlation exists between the maternal and foetal blood glucose (coefficient of correlation $R = + 0.82$, standard error S.E. = 0.21 and $P = 0.0001$) also between/

between maternal and neonatal blood glucose (R = + 0.70, S.E. = 0.21 and P = 0.001), and also between foetal and neonatal blood glucose (R = + 0.72, S.E. = 0.21 and P = 0.001).

A positive correlation between the blood glucose of the mother and her baby at the moment of birth was previously reported by Ketteringham and Austin (1938). They found a coefficient of correlation of + 0.6 but they did not give any figures for the standard error or probability. Also a positive correlation between the maternal blood glucose and umbilical artery glucose was obtained by Pedersen (1952) but he did not give any figures.

Importance of the positive correlation between the maternal, foetal and neonatal blood glucose values.

There are two points of interest that emerge from this inter-relationship -

(a) The positive correlation and the decrease of blood sugar concentration normally occurring from the mother to the baby indicates a diffusion process through the placenta as far as glucose transmission is concerned.

(b) The existence of a positive correlation between the blood sugar of the baby and the mother at birth and the fact that there is no limit (threshold value) to the level of the infant's blood sugar, explain why the blood sugar of the infant/

> infant may be at different levels at birth, depending on the maternal blood sugar. In normal subjects the latter may vary within wide limits, probably from 60 - 200 mg. per 100 ml. of blood without any glucose administration, and so the infant's blood sugar will vary a great deal as well. It follows that at birth it is impossible to establish "a normal value" for the infant's blood sugar in the ordinary sense and its blood glucose can only be assessed in relation to the maternal value at birth. This is the simplest explanation of the wide variations in the infant's blood sugar at birth, which most authors have found shrouded in mystery.

The present work also shows that there is no significant correlation between the birth weight and both foetal and neonatal blood calcium, phosphorus and glucose values. The absence of correlation between the birth weight and the serum calcium in the newborn was reported by Bakwin and Bakwin (1932). They also found no striking difference in the variability of calcium levels at different birth weight levels.

On the other hand, Gittleman et al. (1956) obtained a significant positive correlation between the weight of the infant and/

and the mean content of calcium in the plasma.

Concerning the blood glucose, Kendig (1942) in 191 determinations done on 94 normal newborn infants found no relation between the birth weight and the blood sugar concentration at birth. He also found no relation between the variations in weight and the blood sugar concentration. This was later confirmed by Farquhar (1954) who found from scatter diagrams no correlation between the birth weight and blood sugar level.

On the other hand, Pedersen (1952) in a study of the various factors that affect the blood glucose level in the newborn found that in infants of non diabetic women there was a positive correlation between the birth weight and blood glucose level. Conversely, in infants of diabetic patients, the blood sugar level was negatively correlated to the birth weight.

INTRAVENOUS GLUCOSE ADMINISTRATION TO THE MOTHER

The results of the present work show that in the six normal cases in which intravenous glucose was given during labour the maternal blood glucose increased, also the foetal and neonatal levels, indicating the ability of the normal placenta to transmit this extra load of glucose.

This finding is in agreement with what Holman et al.(1934), Ketteringham et al. (1938), Friedgood (1945), and Pedersen (1952) have all reported.

More interesting still is the finding in our series of the rapid drop in blood glucose that occurred in these babies of transfused patients in the first few hours of life, so the mean value of blood glucose dropped from 108 mg. per 100 ml. to 54 mg. per 100 ml. For this finding there is support from previous literature. Friedgood and Miller (1945) found that the hyperglycaemia in the offsprings of diabetic rats (made diabetic by alloxan injection) subsides during the first day of life. Also Morriss (1917) found that in hyperglycaemic mothers (result of obstetric procedures) the baby is also hyperglycaemic compared to normal newborn babies, but there is prompt disposal of glucose on the part of the baby. He tried to explain this phenomenon in one of two ways -

(a) Rapid oxidation. This was discredited by the results of relative rapidity of glycolysis in the/

the maternal and foetal circulations. Maternal and foetal blood samples were placed in a thermostat at 38°c. and determinations of glucose were made from time to time. It was found that sugar decreased in both at the same rate.

(b) Storage. The rapid subsidence of this neonatal hyperglycaemia could be due to unusual facilities for storage of carbohydrates on the part of the foetus.

The same results were obtained by Ketteringham and Austin (1939) in what they called "The indirect intravenous glucose tolerance test" performed on the newborn babies by intravenous injection of glucose in their mothers during labour. Their results (which were mentioned in the introduction) show clearly how within two hours the newborn gets rid of excess glucose. In their opinion this interesting phenomenon is a reflection of what they called "A lively pancreatic activity" in the newborn baby.

From all what was discussed, as a result of our own findings and supported by other workers' findings, there is an entire agreement/

agreement about the ability of the normal placenta to transmit glucose from the mother to the baby both with normoglycaemic as well as with hyperglycaemic maternal levels.

The argument is about how the placenta does this function. In this respect Pedersen (1952) reported that the passage of different substances through the placenta is an intricate and interesting problem which has not yet been solved with respect to all substances concerned. Some light was thrown on the subject when the significance of the nature of the substances, the shape of the placenta and duration of pregnancy was recognised (Huggett 1950). As far as glucose is concerned, it passes freely through the placenta according to the gradient of concentration.

There are three theories for this transplacental passage of glucose -

(a) Diffusion

(b) Diffusion - utilization.

(c) Active secretion.

(a) Diffusion theory.

According to this theory the passage of glucose through the placenta is a passive process Needham (1931) looked upon the placenta as an inert semipermeable membrane and that substances passed from the mother to the foetus or in the reverse/

reverse direction, by diffusion and filtration, and that physical processes alone govern the transmission and that the molecular size of the substance plays an important part in determining which shall and which shall not cross the barrier. This is well established for gases, dextrose and a number of chemical compounds of relatively low molecular weight. The positive correlation that we have found between the maternal, foetal and neonatal blood glucose levels at birth and the decrease of blood sugar concentration normally occurring from the mother to the baby is the main argument used by the adherents of the diffusion theory.

(b) Diffusion - utilization theory.

The main objection to the diffusion theory is that complete equilibrium of concentration between maternal and foetal blood sugars should be reached in every case. This equilibrium is prevented by the tendency of the maternal blood glucose to be nearly always appreciably higher or rarely lower than the foetal, so passage of glucose could be explained as a relatively slow/

slow diffusion through the placenta combined with foetal consumption of glucose. Absence of equilibrium between maternal and umbilical vein blood glucoses may be due to foetal consumption of glucose.

It is certain that the balance between maternal and foetal glucose levels takes some time. This is evident from Pedersen's trial (1952) to plot the concentration of foetal blood glucose against the maternal, after the latter has been augmented by intravenous glucose, scatter diagram for which he used Dahl's (1928) results. He found that two only out of nine of the foetal values would correlate with maternal values at the moment of birth, but taking neonatal values half an hour later seven out of the nine correlated, meaning that it took time for such a balance to occur.

From this emerged the second theory, i.e. the diffusion - utilization theory, held mainly by Pedersen. The infant's blood sugar is primarily determined by the maternal blood sugar, modified by the time factor and the infant's consumption of glucose. That is why the infant's sugar is always lower

than/

than the maternal at birth.

(c) The secretory theory.

The facts that complete equilibrium is hardly ever attained between blood sugar values of the mother and infant, the latter always showing lower values and the higher the maternal blood sugar at birth the more marked the difference between the values of the mother and her baby, are all against diffusion. This has been interpreted as "something" in the placenta must prevent free diffusion. This is probably what made Smith (1945) state that "the amounts in the two circulations seem to be neither wholly independent of each other nor on the other hand closely related".

Both Naeslund (1928) and Dahl (1928) interpreted their results to the effect that free diffusion does not take place, so it must be an active secretory process involving some enzymatic activity in the placental tissue that is responsible for the transmission of glucose. In this respect Hofbauer (quoted from Morriss 1917) demonstrated the presence of glycolytic ferments in glycerine extracts of the placenta, so their function is to prepare glycogen stored in the placenta for passage to the foetus, but whether this is so or not still is not very clear.

II. CALCIUM, PHOSPHORUS AND GLUCOSE VALUES IN THE FIRST FOUR DAYS OF LIFE

Neonatal serum calcium values.

The present work shows the following -

1. In the full term newborn baby serum calcium on the first day of life is more than 8 mg./100 ml. (8.9 mg./100 ml.)
2. Serum calcium value at birth is higher than at 12 hours after (9.6 and 8.9 mg./100 ml. respectively).
3. The trend of the serum calcium pattern in the first four days of life is a gradual decline from -

   8.9 mg./100 ml. on the first day.

   8.5 mg./100 ml. on the second day.

   8.3 mg./100 ml. on the third day.

   8.3 mg./100 ml. on the fourth day.
4. Calcium values at birth, on the first day and on the fourth day show a positive correlation, but it is not significant.
5. There is no significant correlation between calcium and either phosphorus or glucose values on the first day of life or on the fourth day.
6. Although there is a positive correlation between the rate of fall of serum calcium from foetal to first day values and rate of the corresponding fall in glucose/

glucose values, yet this correlation is not statistically significant.

The finding of serum calcium in the full term newborn baby on the first day to be above 8 mg./100 ml. has been found before by Mitchell et al. (1932), Bakwin (1937), Kendig (1942), Dodd et al. (1949), Bruck and Weintraub (1955), Gittleman et al. (1956), and by Craig and Buchanan (1958). In mature infants born vaginally after uncomplicated pregnancies and labours, Gittleman et al. found hypocalcaemia (below 8 mg./100 ml.) in only 1.2% of newborn babies. Mitchell reported a figure of 1.8%.

While factors such as pregnancy and labour, birth weight, and maturity affect the serum calcium level on the first day of life, it seems unlikely that diet affects it, specially that most of the full term newborn babies are not fed during the first 12 hours after birth.

Concerning the trend of serum calcium in the neonatal period, Bakwin (1937) found a gradual decrease in calcium. This was also reported by Denzer et al. (1939) and Todd et al. (1939). Our results confirmed these findings. Denzer et al. stressed the deep depression that occurs in the serum calcium level during the first four days of life, after which it gradually rises. Those workers trying to explain this post natal drop in serum calcium did not find that the weight at birth, the degree of loss in weight, the type/

type of feed, race, serum proteins, or inorganic phosphorus content of the blood play any role in this fall. Assuming that the parathyroids were the cause, they compared the calcium values with those of phosphorus. They found that when serum calcium decreased below 10 mg./100 ml. the inorganic phosphorus did not rise, so hypoparathyroidism by itself could not explain this drop, but those workers found that the height of serum calcium of the umbilical cord blood at birth controlled this fall. If the cord calcium was low the post natal drop was slight to prevent the occurrence of tetany.

In conclusion, although there is a post natal drop of serum calcium in the first four days of life, yet there are protective mechanisms preventing this drop from reaching tetanic levels. These mechanisms are the high calcium level of the cord at birth, the tendency of the newborn infant to have acidosis, and the anti-tetanogenic properties of breast milk.

The absence of a significant correlation between calcium values at birth and on subsequent days which was found in the present work, was previously mentioned by Bruck et al. (1955) and earlier by Denzer et al. (1939).

Neonatal plasma phosphorus values

The present work shows the following results -

1. Plasma phosphorus on the first day of life is higher/

higher than foetal levels (4.7 and 4.4 mg./100 ml. respectively.)

2. The trend of plasma phosphorus is a rise from the first day values of 4.7 mg./100 ml. to fourth day values of 6.1 mg./100 ml.

3. There is a significantly negative correlation between phosphorus and glucose on the first day of life. However, this correlation is gradually lost on subsequent days.

4. There is no significant correlation between plasma phosphorus at birth, on the first day and on the fourth day of life.

5. There is no correlation between calcium and phosphorus on the first day or on the fourth day.

The gradual rise of plasma phosphorus was also mentioned by Bakwin (1937), Gardner et al. (1950), Gittleman et al. (1951) and McCance and Widdowson (1959).

To explain this rise in phosphorus from the first to the fourth days McCance et al found that during the first 48 hours of life the urine of the newborn baby hardly contains any phosphorus, except if labour is prolonged or difficult. They also found that the early starvation period every newborn baby undergoes will cause tissue breakdown with the release of inorganic phosphate in the plasma and its/

its subsequent rise, so both early starvation and the poor renal clearance of phosphorus are the main causes of the rising phosphorus in the first 48 hours of life. (McCance & Widdowson 1954).

The renal clearance of phosphorus was earlier investigated by Heubner (1910) in his own baby, and later by McCrory et al. (1950).

After the first 48 hours diet is the main factor that controls plasma phosphorus. Generally speaking artificially fed babies have a higher blood phosphorus than breast fed babies. The dietetic factor has been investigated in great detail by Lenstrup (1926). He has shown that the total phosphate content of human milk is about one seventh that of cow's milk. In addition the calcium and phosphorus ratio of human milk is 2:1 and of cow's milk is 1:1. As a result artificially fed infants receive less calcium relative to phosphorus than breast fed babies. Gardner and Butler (1950) attribute both the hyperphophataemia and the hypocalcaemia to this dietetic factor, but Graham et al. (1953) found it very difficult to agree with the concept that high phosphate intake, besides causing the hyperphosphataemia, does in any consistent way cause hypocalcaemia in the newborn.

It is of interest to mention that infants receiving vitamin D supplements had a more marked tendency to hyperphosphataemia and hypocalcaemia than infants receiving a similar diet but without vitamin D (Gittleman et al. 1951, Albright et al. 1946, and Pincus et al. 1954).

Since most of the babies in our study were artificially fed, at least/

least after the second day, the hyperphosphataemia found was not unexpected.

It is difficult to explain the significantly negative correlation that was found between blood glucose and phosphorus on the first day of life. However, there is some evidence to support the theory that phosphate, amino acids and glucose are reabsorbed through a similar if not a common transport pathway. It may be explained by competition for a transport mechanism common to all three substances, or by toxic inhibition by the hexoses or their metabolites of the mechanisms responsible for the reabsorption of phosphate and amino acids.

In this respect it is interesting to mention that Fox, Thier, Rosenberg and Segal (1964) found that the intravenous infusion of glucose in man will lead to impaired renal tubular function, hence to increased phosphate excretion and consequently to hypophosphataemia.

Neontal blood glucose values

The present work shows the following -

1. In the full term newborn baby the average blood glucose value at birth was 71 mg./100 ml.
2. During the first 12 hours after birth there was a drop of blood glucose to an average of 50 mg./100 ml., but at what time exactly this drop/

drop occurred could not be shown clearly in this work.

In this respect previous workers, Ketteringham and Austin (1939), Farquhar (1954) and Hartmann (1955) found that the maximum drop in blood glucose value occurs during the first two hours after birth.

3. There is a gradual rise of blood glucose level during the first four days of life from -
50 mg./100 ml. on the first day
55 mg./100 ml. on the second day
60 mg./100 ml. on the third day, and
71 mg./100 ml. on the fourth day.
Therefore the rise was about 5 - 10 mg./100 ml. each day. Norval et al. (1949) found that the average rise in blood glucose during the first six days of life was 2.8 mg./100 ml. per day.

4. There was a significantly positive correlation between blood glucose on the first day and that on the fourth day.

5. The significantly negative correlation between phosphorus values and glucose values on the first day of life has already been mentioned.

6. There is a positive correlation between the rate of fall of calcium from foetal to first day values and the corresponding fall in glucose values./

values. However, this correlation is not statistically significant.

From the present work and previous work by others (Hartmann and Jamdon 1937, Van Creveld 1929, Desmond et al. 1950, Farquhar 1954, Hartmann 1955, Cornblath et al. 1956 and Stur 1964), it is certain that the blood sugar drops markedly after birth, the maximum drop being in the first two hours after birth, after which it tends to rise gradually, but still the level is lower than normal adult levels.

Concerning the aetiology of this physiological hypoglycaemia of the newborn, there are different views on the subject -

1. Immaturity of the liver, with a consequent lack of glycogen. This was suggested by Van Creveld (1929). It is true that the lowest post-natal levels correspond roughly to the days of loss of weight and minimal calorie intake, but the newborn is born with an adequate glycogen store in his liver which is built up during the last trimster of pregnancy (Windle 1940). This means that the low blood sugar levels of the newborn are not initially due to lack of glycogen as was suggested by Van Creveld. Recently Cornblath et al. (1964) found that there was no hyperglycaemic response to glucagon and epinephrine in the newborn baby, but this response became normal after parenteral glucose administration and steroid or adrenocorticotrophin injection. Because/

Because of this they favoured the depleted liver glycogen theory.

2. Lack of hepatic glycogenolysis.

Against this theory is the finding of Desmond, Hild and Gost (1950). Those workers have shown that the blood sugar level of the newborn does rise when adrenaline is injected at any time from birth, although they mentioned that it was true that flatter curves occur in the first few days of life than later.

3. Absolute hyperinsulinism.

Nakamura (1924) described an excess of islet cells in the foetuses and newborn infants, but according to Baird and Farquhar (1962) Beta-cell hyperplasia does not always mean hyperinsulinism. Fisher and Scott (1934) found pancreatic insulin levels in the newborn calf to be more than adult levels. White (1949) discarded the idea of hyperinsulinism as the mechanism of hypoglycaemia in babies of diabetic mothers because in her opinion such a process should inevitably be continuous and should eventually produce a zero level of blood glucose. Such an argument would also apply to the normal baby.

4. Relative hyperinsulinism.

Hartmann and Jaldon (1937) believed in relative hyperinsulinism/

hyperinsulinism without necessarily hyperplastic beta cells, there being incomplete development of opposing mechanisms.

5. Insulin hypersensitivity.

Wachter (1949) spoke of an absolute hypersensitivity to insulin in the first few days of life. In favour of this they, both Hartmann et al. (1937) and Wachter (1949) separately found that adrenaline injection in a newborn baby produces a normal rise of the blood sugar, but if insulin was previously injected, adrenaline will not produce such a rise. Also an abnormally sensitive insulin release mechanism was shown by Cornblath et al. (1964) by the prolonged hypoglycaemia that occurs in the newborn baby after leucine and tolbutamide injection

6. Neonatal polycythaemia.

Hypoglycaemia has been frequently reported with neonatal polycythaemia (Cornblath et al. 1964). They explained the hypoglycaemia by the reduced blood flow, and by the high rate of glycolysis present in the erythrocytes of the newborn baby. The hypoglycaemia found in all Cornblath's polycythaemic babies responded to glucose.

7. Local capillary hypoglycaemia.

Stur (1964) mentioned that there is a slight

decrease/

decrease in the blood glucose value during the first few hours of life, probably due to fasting, but this alone does not account for the markedly low blood glucose levels found in capillary blood. The marked hypoglycaemia in capillary blood is due to diminished circulation in the peripheral skin capillaries, which means a longer period of utilization of glucose in the capillaries, so the very low glucose levels in capillary blood are not typical for the situation in the whole body. Stur found a marked difference in blood glucose of capillary blood (obtained by a heel stab) and venous blood (obtained from the inferior vena cava by catheter during exchange transfusion) done simultaneously on the same case in 12 Rh. babies who required an exchange transfusion. Glucose of venous blood was higher than that of capillary blood. He reported that the hypoglycaemia found in capillaries is a local condition of the skin and does not indicate hypoglycaemia in the vital organs of the body. On the contrary, it is part of a mechanism to provide encough glucose for those organs by restricting the supply of glucose to the skin. That is why many cases of the so called "physiological hypoglycaemia/

hypoglycaemia of the newborn" are asymptomatic, since the vital organs are in actual fact receiving an adequate supply of glucose.

In this respect Stur found that the low capillary blood glucose levels during the first two days of life were still compatible with the ability to maintain energy producing processes necessary for preservation of sodium and potassium levels in the erythrocytes.

8. The hepatic threshold theory.

From the previous discussion it appears that a condition of hypersensitivity to insulin may exist in the newborn baby, but why does it exist ? Pedersen (1952) put forward the theory that the maternal blood glucose level during pregnancy will determine the rate of production of insulin by the foetus, which latter will set the liver threshold at a certain level. During the first week and due to the withdrawal of maternal glucose, the liver threshold is increased.

Later on Farquhar (1954) modified the hypothesis as follows - There is an excess of maternal adreno-corticotrophin levels during pregnancy. These will cross the placenta and stimulate the infant's adrenal glands. This produces the foetal reticular zone,/

zone, which with the help of glucose diffusing through the placenta will set the liver threshold at a high level. This in turn will stimulate the pancreas and will cause this state of hyperinsulinism.

At delivery, with clamping of the cord, the supply of glucose from the maternal blood is cut off, but the state of hyperinsulinism is still going on, producing glycogenesis which will result in hypoglycaemia in the first four hours after birth.

The arrest of the temporary hypoglycaemia after four hours made White (1949) discard the concept of hyperinsulinism, but Farquhar explains this arrest by the spill-over of maternal adrenocortico-trophic hormones to the foetus which increases during labour. This is also augmented by the increase of foetal adrenocorticotrophin production, due to the physiological stress of adaptation of the newborn to extra-uterine life as the start of respiration, thermal regulation and so on.

So both maternal and foetal adrenocorticotrophins will arrest any further fall in the neonatal blood sugar.

It is of interest to mention that Miller (1941) mentioned/

mentioned that even sometimes this pituitary adrenal axis of the foetus is stimulated before birth in stress conditions as asphyxia neonatorum. In this way the hyperglycaemia of asphyxiated infants can be explained.

III. TWIN STUDY

The present work shows the following -

1. Serum calcium in twins on the first day of life is below 8 mg./100 ml. i.e. twins commonly show the so-called "first day hypocalcaemia".
2. Serum calcium is lower in the second twin than in the first twin throughout the various times of estimation, i.e. foetal blood, at birth, on the first day and on the 4th day as well.
3. Birth weight does not affect the serum calcium level in twins.
4. Blood glucose is lower in the lighter of the two twins, but birth order seems to have no effect on the blood glucose.

Hypocalcaemia on the first day of life in twins has been previously reported by Craig and Buchanan (1958). Those workers also found in four sets of twins whom they studied that serum calcium in all the sets was lower in the second twin than the first. They also mentioned that a personal communication from Gittleman (1957) indicated that serum calcium is different in the two twins but made no further specifications. The present work shows the same findings. In addition, it shows that birth weight does not affect the serum calcium level. This agrees with what Bakwin and Bakwin (1932) found. They/

They observed no statistical correlation between birth weight and serum calcium in the newborn baby, nor does there seem to be any striking difference in the variability of serum calcium at different birth weight levels. This also agrees with our findings in the full-term newborn baby study in that there is no significant correlation between birth weight and foetal or neonatal serum calcium levels. However, Gittleman et al. (1956) obtained a significantly positive correlation between the weight of the infant and the mean content of calcium in the plasma.

No explanation was given for the hypocalcaemia of the second twin relative to the first in the previous literature. To find an explanation for this difference from our data the individual sets of twins were considered separately, with special regard to the time interval that elapsed between the delivery of both. It was found that of the 16 sets -

(a) 9 sets showed a higher serum calcium in the first twin than the second. In 7 out of the 9 sets the interval between the two deliveries was more than 30 minutes, it was between 30 - 45 minutes.

(b) 5 sets showed no marked difference in serum calcium between the two twins of each set. In all the 5, the time interval was less than 30 minutes, varying between 5 - 26 minutes.

(c) The remaining two sets showed a higher serum calcium/

calcium in the second than in the first twin. In one set the interval was 2 minutes and the first twin was born after a forceps delivery, while in the second set the difference in time was 15 minutes and both were born after forceps delivery.

The impression is that the difference in serum calcium between two twins may be determined by the time interval between the two deliveries. The longer this interval is, the more marked the difference in serum calcium will be. The assumption is that the stress to which the baby is exposed during delivery is associated with excessive secretion of corticosteroids, and corticosteroids lower the serum calcium. In twins, the second is more exposed to stress than the first, specially if the time interval between the two is marked, and consequently more under steroid effect than the first and so tends to be more hypocalcaemic than the first twin. Perhaps the finding of Gittleman et al (1956) of hypocalcaemia in babies born after prolonged labour lends support to our hypothesis.

Concerning phosphorus in twins, it was found that in seven of the 16 sets of twins studied, phosphorus was higher in the smaller of the two twins. In the remaining 9 sets there was no marked difference. Whether this relative hyperphosphataemia in the small twin speaks of functional immaturity as Zetterstrom and Arnold (1958) mentioned, or whether it indicates renal inability in the small twin to excrete phosphorus, as McCance and Widdowson mentioned, is not very clear.

As to the blood glucose values in twins, this work shows that it is the birth weight and not the birth order that affects the glucose level. It was found that the mean value for the smaller twins was lower than that for the bigger twins.

Studying the results in the individual sets, glucose value was lower in the smaller twin in 12 of the 16 sets. In the remaining four sets no marked difference was noticed in glucose values of the two twins, but in those four sets the difference in birth weight was - 2 ounces (56 gms.), 9 ounces (252 gms.), half an ounce (14 gms.) and 1 pound 2 ounces (500 gms.) respectively.

So the relative hypoglycaemia is associated with relative dysmaturity (low birth weight relative to period of gestation). Previous workers (Haworth et al. 1963, Brown et al. 1963, Neligan et al. 1963 and Cornblath et al. 1964) stressed the importance of dysmaturity in the causation of neonatal hypoglycaemia, but all those workers were dealing with single babies and not twins. This work on twins balancing many of the other factors shows clearly the effect of dysmaturity. The accepted concept now is that dysmaturity is associated with depleted liver glycogen and this has been found by Shelley (1960).

IV. THE PLACENTAL DYSFUNCTION SYNDROME.

This group consisted of cases of different clinical patterns, grouped together under the previous heading because of the known fact that some of those abnormal states may be associated with abnormal placentae -(**Flexner 1948, Clifford 1954 & 1957, Walker 1954, Browne 1963**)

1. Toxaemias of pregnancy.

The 12 mild cases did not show any deviations from the normal.

On the other hand, the 4 cases of severe toxaemia, showed abnormally low values for calcium and glucose in the foetal blood, baby's blood at birth, on the first day and on the fourth day. Phosphorus values were either normal or higher than normal. It is concluded that it is only the severe and not the mild toxaemia that affects the placenta. The effect is one of degeneration. This was evident macroscopically in two of the four placentae where multiple infarctions, some calcification with a gritty sensation were found. The biochemical evidence for degeneration was failure of the placenta to transmit calcium and glucose from the maternal to the foetal circulation, while phosphorus was normal or high, being a product of degeneration.

In favour of this assumption are the findings of Sjostedt, Engleson and Rooth (1958). Those workers found that in dysmature babies with prolonged gestation, there was low birth weight, hypoxia/

hypoxia, a rise of haemoglobin percentage and a rise of the non-protein nitrogen. They considered these findings indicative of a reduction in the diffusion capacity of the placenta caused by ischaemia or destruction of the placental tissue. This destruction was confirmed more by a rise in pentoses and protein bound hexoses in the blood in these cases.

In this respect, McCance and Widdowson (1954) found that the level of blood urea in cord blood at birth was 39.9 mg. per 100 ml. in 6 dysmature babies, while it was only 30.9 mg. per 100 ml. in 4 normal babies. Phosphorus can be considered as a production of tissue destruction, the same as urea.

The hypocalcaemia and hypoglycaemia noticed in the babies in these four cases could thus be interpreted as secondary to failure of placental transmission.

2. Dysmaturity.

This term is used here to indicate low birth weight irrespective of the period of gestation. It follows that this dysmaturity could be associated with -

(a) Premature deliveries.

(b) Normal gestation.

(c) Prolonged gestation.

(a) In dysmatures with premature deliveries, the foetal values/

values were normal, and the only noticeable change was the hypoglycaemia that was found on the first day and also on the fourth day.

It is assumed that premature deliveries will not affect the placenta, and the hypoglycaemia of the baby is probably due to depleted liver glycogen. The hypocalcaemia noticed by Gittleman et al. (1956) in premature babies was not found in this work, but perhaps the number of our cases was small, and that more would be needed to put forward firm conclusions.

(b) In dysmatures with normal gestation, foetal values were normal, again indicating normal placental function. Macroscopically the placentae were normal. The low blood glucose levels are thus due to the dysmaturity and not to any placental derangement.

(c) In dysmaturity associated with prolonged pregnancy there were low blood glucose and calcium in the foetal blood, neonatal blood and in the baby on the first and fourth days of life.

The assumption is that the prolonged gestation (beyond 42 weeks) caused the placenta to degenerate and hence to fail to transmit. calcium and glucose to/

to the foetus. Accordingly the hypoglycaemia and hypocalcaemia in the neonatal period could be explained.

In favour of this assumption of placental derangement is the fact that the placenta was gritty, calcified and showed multiple infarctions in one case.

In the group of prolonged pregnancy, but with normal birth weight, it was interesting to find the values to be normal. Macroscopically the placentae were also normal.

From this it can be concluded that with prolonged pregnancy the placenta may - in some and not all cases - start to degenerate. If it does so this will be shown by -

(a) Low birth weight of the baby.

(b) A macroscopically abnormal placenta with infarctions and calcifications.

(c) Failure of transmission of calcium and glucose from the mother to the foetus, leading to hypocalcaemia and hypoglycaemia of the foetal as well as the neonatal blood.

In the cases with prolonged pregnancy, but in which the placenta remains normal, normal findings are to be expected -

(a) Normal birth weight of the baby.

(b) A normally looking placenta.

(c) Normal biochemistry in the foetal as well as in the neonatal blood.

A degenerated placenta may also be encountered in severe toxaemias of pregnancy and in placenta praevia as well. On the other hand, elderly primigravidae, premature deliveries, dysmature babies with normal gestational age, as well as mild toxaemias are all associated with normal placentae.

The previous literature gives support to our hypothesis. So Jeacock (1963) found that the human placenta at term is often gritty, while the premature placenta is soft. Also x-rays have indicated that the term but not the premature placenta may be calcified. Also it is thought that excessive amounts of calcium may be present in postmature placentae.

Fujikura (1963) found that moderate and marked degrees of calcium deposits in the term placentae (by gross and microscopic examinations) seemed to diminish with advancing maternal age, specially after 25 years of age. This may be interpreted with our findings that elderly primigravidae do not suffer from placental dysfunction.

Hartley (1954) found that placental calcification could be detected by x-rays from 32 weeks onwards and that calcification might be seen in prolonged pregnany and is a herald of foetal death.

Before leaving this section of discussion on the placental dysfunction group it must be admitted that the number of cases in this/

this group was small and those conclusions could be regarded as preliminary. This study could be regarded as a pilot one, paving the way to further studies on the same line.

V. BABIES OF DIABETIC MOTHERS.

The two cases studied in this group show the following -

1. At birth the placenta in the first case could transmit efficiently calcium, glucose and phosphorus, as indicated by the absence of any hypocalcaemia or hypoglycaemia in foetal or neonatal blood at birth.

On the other hand, the placenta in the second case could partially transmit calcium, but failed to transmit glucose. The latter is indicated by the marked hypoglycaemia in both foetal and neonatal bloods at birth. The second case in addition to being a pre-diabetic case suffered also from severe pre-eclampsia (with a blood pressure of $160/_{95}$, oedema of the hands and feet, and albuminuria).

So it can be concluded that in uncomplicated diabetic cases the placenta is still efficient in transmission of glucose. This has been found previously by Browne (1963) and earlier by Offergeld (1906) who was the first to determine the blood sugar in an infant born of a diabetic mother.

2. The two babies showed marked hypocalcaemia - all the calcium values were below 8 mg. per 100 ml. except in the first baby when it went up to 8.1 mg./100 ml. on the fourteenth day. The lowest figures in both cases were about the fourth day. The two striking features in both were -

(a) In spite of the very low calcium levels (4 mg./100 ml. on one occasion), no symptoms or signs of tetany developed.

(b) The hypocalcaemia did not respond to calcium therapy.

Hypocalcaemia was found by Craig (1958) in six our of nine babies born of diabetic mothers and also in one baby of a pre-diabetic mother. Also hypocalcaemia in similar babies was reported by Zetterstrom and Arnold (1958).

Concerning the cause of this hypocalcaemia, it is likely to be a summation of several factors. So in addition to the temporary decline in the serum calcium which occurs normally after birth there are three other predisposing factors -

(a) Most of those babies are born prematurely and as suggested by Bruck and Weintraub, there is a higher frequency of hypocalcaemia in prematures, although this has not been confirmed in the present work.

(b) Babies exposed to difficult or prolonged labour or any operative interference on the mother commonly have hypocalcaemia, due to excess corticosteroids. Both babies in this study were born after a Caesarean section.
In this respect it is interesting to mention that Zetterstrom and Arnold (1958) found that babies of diabetic mothers who were born after Caesarean section showed more profound hypocalcaemia than those born after spontaneous delivery.

(c) Craig suggested that disturbance of the normal hormonal adjustments of pregnancy and specially of adrenocortical function in diabetic mothers might be a determining factor in the occurrence of hypocalcaemia in their babies. Inthis regard it is of interest to note the similarity between those bloated, full-faced, plethoric infants of diabetic mothers and patients suffering from fluid and electrolyte disturbances following cortisone therapy.

3. Both babies at some stage of the follow-up showed hyper-phosphataemia. The first baby showed a plasma phosphorus of 10.8 mg. per 100 ml. on the 5th day, while the second had a plasma phosphorus of 8.5 mg. per 100 ml. on the 2nd day. Although these high levels were recorded only once in each baby, yet they are interesting. The literature is scanty concerning this point, but Zetterstrom et al. (1958) and Reardon and her co-workers (1955) found hyperphosphataemia. Zetterstrom attributed it to functional immaturity of those babies and he did not go any further. In this respect two explanations are offered -

(a) Those babies are exposed to stress of prolonged or difficult labour. McCance suggested that stress causes increased tissue destruction with liberation of urea and phosphate. The finding of high blood urea in some of those babies is in favour of this theory.

(b) Babies of diabetic mothers are usually starved for longer than usual (48 hours or more). As previously mentioned by McCance, starvation leads to excess tissue destruction and so raises blood phosphorus. This is why Zetterstrom is of the opinion that those babies should not be starved too long.

It is of interest that the hyperøphosphataemia found in our two cases did not coincide in time with the minimum level of serum calcium encountered. The same finding was commented upon by Zetterstrom et al.

4. The present work shows that these babies had <u>hypoglycaemia</u>. The first case started from the 1st day and it was not before the 5th or 6th day that it started to be stabilized. The second baby started the hypoglycaemia on the 2nd day and although it was not prolonged yet the blood glucose was very unstable.

The two striking features were -

(a) No symptoms or signs were directly attributed to this hypoglycaemia.

(b) No dramatic response of the blood glucose to glucose both intravenously and orally occurred in the first case.

Pedersen (1952), Komrower (1954) and Farquhar (1956) reported

on/

on hypoglycaemia in babies of diabetic mothers. The lowest values for blood glucose are reached at 2 - 3 hours of age and is spontaneously corrected in 4 - 6 hours to recur on the 2nd day. Farquhar (1956) has shown that these babies could tolerate very low blood glucose levels without any symptoms. The most accepted explanation for this hypoglycaemia is that maternal hyperglycaemia will produce foetal hyperinsulinism which lowers the blood sugar of the baby.

The arrest of this hypoglycaemia is brought about by two factors -

(a) The withdrawal of the stimulus to excess insulin when the cord is clamped and cut.

(b) The opposing factors to insulin as the diabetogenic hormones of the pituitary gland, the pancreas and the chromaffin tissue. So it is expected that this hypoglycaemia corrects itself within four hours.

Why it persisted over four days in both of our cases is not very clear. The suggestion is that although maternal hyperglycaemia was cut off, yet hyperinsulinism continued, augmented perhaps by some delay in the development of the opposing mechanisms.

It should be concluded that these two cases provide a base line for further research on the same basis.

Clinical significance of hypoglycaemia in babies of diabetic mothers.

(1) Farquhar (1956) found no correlation between the development/

development of a morbid neonatal course and the blood sugar level at the time or the extent and rapidity of the fall.

(2) No relationship exists between the degree of hypoglycaemia or the gradient of the change in levels and abnormal incidents later in the first two weeks of life.

(3) Probably there is no relationship between the blood sugar changes and subnormal intelligence in later childhood. In this respect Farquhar found that 71 out of 80 of those babies were normal in physical and mental development.

(4) Since the mechanism of hypoglycaemia in these babies is foetal hyperinsulinism due to maternal hyperglycaemia, it follows that lower maternal blood glucose levels during pregnancy would result in higher levels in the newborn and so the fall after birth would not be excessive. So if the mother's blood sugar level during pregnancy is kept within normal levels by adequate control hypoglycaemia in the newborn could be prevented.

(5) In spite of the hypoglycaemia glucose should not be given for asymptomatic cases because -

(a) If given orally glucose may result in vomiting with the danger of inhalation.

(b) Parenteral isotonic solutions given to these/

these babies will result in an increase in the abnormal volume of water in their bodies.

(c) The intravenous administration of hypertonic solutions to those babies will increase the intravascular fluid volume and so embarrass the heart.

(d) Glucose administration in those babies as was shown in the first one in this work, fails to raise the blood glucose.

(e) It may hinder to establish the correct diagnosis.

SUMMARY AND CONCLUSIONS.

SUMMARY AND CONCLUSIONS.

1. In 23 normal pregnancies and labours the following results were obtained -

(a) At 36 weeks of pregnancy: serum calcium was below normal adult levels (8.5 mg. per 100 ml.), phosphorus below normal (2.7 mg. per 100 ml.), but blood glucose within normal limits (94 mg. per 100 ml.)

(b) At 38 weeks of pregnancy: serum calcium, phosphorus and blood glucose were 8.5, 2.8, 89.0 mg. per 100 ml. respectively, again with mild hypocalcaemia and hypo/phosphataemia, but with normal blood glucose values for an adult.

(c) At delivery: serum calcium was highest in the foetal blood (10.4 mg. per 100 ml.), followed by neonatal values (9.4 mg. per 100 ml.) and lowest in the maternal blood (8.6 mg. per 100 ml.) Possible explanations concerning the role of the placenta were given.

Plasma phosphorus was highest in neonatal blood (4.4 mg. per 100 ml.), lowest in maternal blood (2.5 mg. per 100 ml.) and foetal values were inbetween (4.1 mg. per 100 ml.)

Blood glucose was highest in maternal blood (110 mg. per 100 ml.) followed by foetal blood (87.0 mg. per 100 ml.) and lowest in neonatal blood (71.0 mg. per 100 ml.)

Passage of glucose from the mother to the foetus across a transplacental gradient, by diffusion, diffusion-utilization/

utilisation or by active secretion has been discussed

(d) First day values: within 12 hours after birth, the babies' serum calcium falls, phosphorus rises and glucose values drop (8.9, 4.9, 45.0 mg. per 100 ml. respectively).

(e) Fourth day values: There is a further drop in serum calcium (8.4 mg. per 100 ml.), a further rise in phosphorus (6.2 mg. per 100 ml.) and also a rise in blood glucose (65.0 mg. per 100 ml.)

(f) Correlations: At the time of delivery there is a highly significant positive correlation between maternal, foetal and neonatal calcium, phosphorus and glucose values, with P varying from less than 0.0001 up to 0.08. The clinical implication of this finding has been discussed. There is no significant correlation between the birth weight of the baby, and foetal and neonatal values for calcium, phosphorus and glucose.

2. In six normal cases, a glucose-infusion during labour raised the maternal blood glucose, with the placenta having been capable of transmitting this extra load of glucose to the foetus. In a patient with severe pre-eclampsia, the placenta could not transmit a similar extra load of glucose. This was taken as an indirect proof of placental insufficiency in the latter case.

3. In 55 normal full-term newborn babies the following results were obtained -

(a) Serum calcium: drops very gradually from 9.6 mg. per 100 ml./

100 ml. at birth to 8.9, 8.5, 8.3 and 8.3 mg. per 100 ml. on the first, second, third and fourth days of life respectively. Early starvation, temporary functional hypoparathyroidism and hyperphosphataemia may be aetiologic factors in this drop.

(b) Plasma phosphorus: rises gradually from 4.4 mg. per 100 ml. at birth to 4.7, 4.7, 5.1 and 6.1 mg. per 100 ml. on the first, second, third and fourth days of life respectively. Early starvation with tissue destruction, renal immaturity with phosphate retention and excessive phosphate intake in cow's milk were put forward to explain this hyperphosphataemia.

(c) Blood glucose: drops from 71.0 mg. at birth to 50 mg. per 100 ml. on the 1st day, probably due to hyperinsulinism. Then it rises to 55, 65, 71 mg. per 100 ml. on the 2nd, 3rd and 4th days respectively, possibly due to development of insulin antagonists of the anterior pituitary and adrenals.

(d) Correlations: A significantly positive correlation between glucose on 1st day and glucose on 4th day has been found (P = less than 0.01). A significantly negative correlation between glucose and phosphorus on 1st day has been found (P = 0.02).

4. In 16 sets of twins first day hypocalcaemia was demonstrated, also the average serum calcium was higher in the first than in the second, while the blood glucose was higher in the larger of the twins. The effect of birth order on serum calcium was explained through the hypocalcaemic/

hypocalcaemic action of corticosteroids, while the effect of birth weight on blood glucose was explained through the hepatic glycogen stores.

5. Placental insufficiency as indicated by inability of the placenta to transmit calcium and glucose from the mother to the foetus has been demonstrated in 4 cases of severe pre-eclampsia, in 2 cases of prolonged gestation with dysmaturity and in one case of placenta praevia.

On the other hand, the placental transmission of calcium and glucose was normal in 2 prolonged gestations but with normal birth weight babies, in 3 immature deliveries, in 4 elderly primigravidae, and in 12 mild cases of pre-eclampsia.

6. In two babies of diabetic mothers, hypocalcaemia, hyperphosphataemia and hypoglycaemia has been demonstrated in the neonatal period.

Placental transmission was intact in the first case, but impaired in the second, probably because of a super-imposed toxaemia.

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APPENDIX.

INDIVIDUAL RESULTS.

I - Antenatal, natal and postnatal Study in the normal group:-

Case No.	(1) At 36 Weeks			(2) At 38 Weeks		
	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.2	2.9	92.0	8.5	2.7	94.0
2	8.7	2.2	106.0	8.2	2.0	79.0
3	8.6	2.2	80.0	8.8	3.2	87.0
4	8.5	4.6	86.0	8.6	5.1	84.0
5	8.4	2.7	89.0	8.5	3.3	91.0
6	9.1	3.4	74.0	8.8	2.9	85.0
7	8.0	3.2	85.0	8.8	2.3	73.0
8	9.0	2.8	75.0	8.6	2.4	101.0
9	8.4	1.7	102.0	8.3	1.6	97.0
10	8.2	2.9	89.0	8.4	2.8	92.0
11	8.2	2.6	91.0	8.6	2.7	78.0
12	8.5	2.5	100.0	8.7	3.0	94.0
13				8.1	3.1	88.0
14	8.7	3.7	108.0	8.3	4.7	73.0
15	8.4	2.7	92.0	8.1	2.7	90.0
16	8.3	2.7	93.0	8.8	2.3	102.0
17	8.5	2.6	96.0			
18	8.9	3.0	91.0	8.5	3.0	96.0
19	8.7	1.9	132.0	8.7	2.5	93.0
20	8.6	2.3	117.0			
21	8.8	1.8	104.0	8.8	1.9	110.0
22	8.6	2.5	95.0	8.8	3.0	84.0
23	8.4	2.4	90.0	8.6	2.6	84.0
Total	187.7	59.3	2087.0	179.5	59.8	187.5
M.V.	8.5	2.7	94.0	8.5	2.8	89.0
S.D.	0.28	0.66	13.30	0.24	0.81	9.43

Case	(3) Maternal at delivery			(4) Foetal blood			(5) Baby at birth		
No.	Calcium	phosphorus	glucose	Calcium	phosphorus	glucose	Calcium	phosphorus	glucose
1	8.3	2.5	110.0	10.0	3.0	82.0	9.1	3.5	64.0
2	9.0	3.3	81.0	12.4	4.5	63.0	11.3	5.0	51.0
3	8.8	2.7	91.0	11.0	4.0	55.0	10.0	3.4	52.0
4	9.0	3.0	128.0	11.3	4.5	97.0	10.8	6.4	91.0
5	9.3	2.7	129.0	11.5	4.5	124.0	10.5	4.8	120.0
6	8.5	1.4	120.0	9.8	3.6	95.0	9.5	4.0	85.0
7	8.8	2.1	120.0	12.0	3.8	89.0	9.8	3.8	89.0
8	8.7	1.9	124.0	10.6	2.4	93.0	9.8	2.7	85.0
9	8.6	1.9	119.0	12.0	3.3	89.0	10.7	3.1	87.0
10	7.9	1.7	80.0	9.4	4.1	73.0	8.5	4.0	73.0
11	8.2	3.9	99.0	9.2	3.9	79.0	8.6	4.6	65.0
12	8.5	2.5	125.0	10.7	5.5	92.0	9.8	7.0	82.0
13	8.5	2.9	99.0	10.7	3.8	70.0	9.7	3.9	61.0
14	8.4	2.5	92.0	8.2	3.6	45.0	8.0	3.4	36.0
15	8.1	2.7	112.0	10.0	3.8	108.0	8.4	4.5	81.0
16	8.8	1.6	97.0	10.4	3.4	92.0	10.0	3.6	50.0
17	9.3	3.2	128.0	8.8	6.6	105.0	8.6	6.2	78.0
18	8.2	3.2	100.0	10.0	3.9	71.0	9.2	4.0	61.0
19	8.6	1.9	135.0	10.5	3.9	127.0	9.7	2.6	61.0
20	8.5	2.8	150.0	10.4	4.5	138.0	9.7	4.5	97.0
21	8.1	1.9	121.0	10.1	4.5	83.0	9.3	4.6	60.0
22	9.4	3.3	75.0	10.2	4.8	73.0	10.1	4.8	49.0
23	8.8	2.0	100.0	10.5	3.5	63.0	9.6	6.0	59.0
Total	198.3	57.6	2535.0	239.7	93.4	2006.0	220.7	100.4	1637.0
M.V.	8.6	2.5	110.0	10.4	4.1	87.0	9.6	4.4	71.0
S.D.	0.40	0.65	19.57	1.00	0.87	22.93	0.82	1.16	19.42

Case	(6) Baby on 1st day			(7) Baby on 4th day		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.3	3.6	56.0	8.5	5.7	74.0
2	9.9	5.4	31.0	8.9	6.6	70.0
3	9.7	5.5	20.0	9.4	5.9	66.0
4	9.2	6.3	40.0	8.2	6.7	54.0
5	8.5	5.5	45.0	8.0	5.8	65.0
6	8.8	5.7	37.0	8.3	5.8	54.0
7	9.2	5.5	32.0	8.1	7.5	62.0
8	8.6	4.1	31.0	8.8	9.0	64.0
9	9.9	4.1	27.0	9.1	5.0	45.0
10	9.6	4.4	40.0	9.0	7.3	65.0
11	9.6	4.9	28.0	7.7	5.7	63.0
12	8.6	4.5	54.0	8.1	5.9	60.0
13	8.5	4.0	77.0	9.1	6.0	92.0
14	7.5	5.1	28.0	8.7	8.0	53.0
15	8.2	3.8	50.0	7.9	4.5	57.0
16	7.9	6.5	63.0	8.2	6.9	78.0
17	8.6	4.3	46.0	7.6	7.3	62.0
18	8.5	4.0	43.0	8.1	3.7	64.0
19	8.7	3.5	85.0	8.0	7.0	88.0
20	8.5	6.0	67.0	8.2	6.5	53.0
21	10.5	7.8	34.0	8.6	6.5	55.0
22	9.6	5.5	38.0	8.6	6.2	82.0
23	8.8	3.8	73.0	8.2	4.0	80.0
Total	205.2	113.8	1045.0	193.3	143.5	1506.0
M.V.	8.9	4.9	45.0	8.4	6.2	65.0
S.D.	0.73	1.09	17.61	0.48	1.23	12.04

II - Glucose infused patients:-

(1) Maternal blood

Case No.	Calcium	Phosphorus	Glucose
1	7.9	2.4	141.0
2	8.0	2.8	106.0
3	8.4	2.9	186.0
4	9.0	2.0	143.0
5	8.2	4.1	242.0
6	8.6	2.0	103.0
Total	50.1	16.2	921.00
M.V.	8.4	2.7	154.00
S.D.	0.41	0.78	28.16

(2) Foetal blood

Case No.	Calcium	Phosphorus	Glucose
1	10.9	3.8	111.0
2	10.3	4.0	83.0
3	10.6	3.5	167.0
4	10.4	4.1	119.0
5	10.4	5.4	180.0
6	10.0	5.1	86.0
Total	62.6	25.9	746.0
M.V.	10.4	4.3	124.0
S.D.	0.30	0.75	40.74

(3) Baby at birth

Case No.	Calcium	Phosphorus	Glucose
1	8.8	3.7	98.0
2	9.2	4.2	79.0
3	9.6	4.3	140.0
4	10.4	4.3	99.0
5	9.2	5.3	165.0
6	9.2	5.4	64.0
Total	56.4	27.2	645.0
M.V.	9.4	4.5	108.0
S.D.	0.55	0.67	38.08

(4) Baby on the 1st day

Case No.	Calcium	Phosphorus	Glucose
1	6.9	3.3	67.0
2	8.3	5.7	40.0
3	8.6	5.1	80.0
4	8.4	3.4	43.0
5	7.3	6.5	56.0
6	8.4	5.4	40.0
Total	47.9	29.4	326.0
M.V.	8.0	4.9	54.0
S.D.	0.70	1.29	16.49

(5) Baby on the 4th day

Case No.	Calcium	Phosphorus	Glucose
1	8.0	5.0	78.0
2	7.7	6.8	72.0
3	7.6	4.3	87.0
4	8.4	5.6	51.0
5	7.0	8.0	81.0
6	8.0	7.1	80.0
Total	46.7	36.8	449.0
M.V.	7.8	6.1	75.0
S.D.	0.48	1.40	12.65

III - Full-term normal newborn babies:-

(1) First day of life:-

Case No.	Calcium	Phosphorus	Glucose	Case No.	Calcium	Phosphorus	Glucose	Case No.	Calcium	Phosphorus	Glucose
1	8.8	4.3	88.0	21	8.8	5.8	66.0	41	7.5	5.1	28.0
2	9.0	3.5	41.0	22	8.2	4.6	23.0	42	8.2	3.8	50.0
3	8.7	4.2	93.0	23	8.3	3.8	33.0	43	7.9	6.5	63.0
4	9.1	5.2	48.0	24	8.9	4.6	51.0	44	8.6	4.3	46.0
5	9.1	9.1	32.0	25	9.2	4.9	48.0	45	8.5	4.0	43.0
6	9.3	3.5	65.0	26	8.3	4.8	60.0	46	8.7	3.5	85.0
7	8.8	4.0	37.0	27	10.0	3.3	66.0	47	8.5	6.0	67.0
8	9.4	3.2	54.0	28	8.3	3.6	56.0	48	10.5	7.8	34.0
9	9.0	4.0	33.0	29	9.9	5.4	31.0	49	9.6	5.5	38.0
10	9.2	4.0	40.0	30	9.7	5.5	20.0	50	8.8	3.8	73.0
11	9.3	3.8	39.0	31	9.2	6.3	40.0	51	8.3	5.7	40.0
12	8.3	4.4	30.0	32	8.5	5.5	45.0	52	8.6	5.1	80.0
13	9.6	4.4	50.0	33	8.8	5.7	37.0	53	8.4	3.4	43.0
14	8.6	3.6	59.0	34	9.2	5.5	32.0	54	7.3	6.5	56.0
15	9.6	3.5	81.0	35	8.6	4.1	31.0	55	8.4	5.4	40.0
16	9.1	5.3	39.0	36	9.9	4.1	27.0				
17	9.5	4.3	85.0	37	9.6	4.4	40.0				
18	9.0	4.3	31.0	38	9.6	4.9	28.0				
19	9.0	3.2	87.0	39	8.6	4.5	54.0				
20	9.1	2.6	62.0	40	8.5	4.0	77.0				
Total	489.4	256.1	2740.0								
M.V.	8.9	4.7	50.0								
S.D.	0.62	1.19	18.79								

(2) Second day of life:-

Case No.	Calcium	Phosphorus	Glucose
1	8.6	4.5	60.0
2	8.5	4.0	43.0
3	8.4	4.3	70.0
4	8.7	5.3	45.0
5	8.7	8.9	34.0
6	8.3	5.2	62.0
7	8.3	4.4	74.0
8	9.1	3.3	69.0
9	8.7	4.8	43.0
10	8.7	4.7	47.0
11	8.9	4.2	50.0
12	8.3	5.0	57.0
13	9.5	4.5	79.0
14	8.2	3.0	50.0
15	8.9	4.4	84.0
16	7.0	4.1	45.0
17	8.1	4.5	28.0
18	8.6	4.9	29.0
19	8.8	4.0	76.0
20	8.5	2.9	82.0
21	8.5	7.3	76.0
22	9.0	5.3	64.0
23	8.2	3.4	24.0
24	7.7	5.3	35.0
25	8.2	5.3	51.0
26	7.6	4.7	54.0
27	8.5	4.5	66.0
Total	228.5	126.7	1497.0
M.V.	8.5	4.7	55.0
S.D.	0.50	1.16	17.32

(3) Third day of life:-

Case No.	Calcium	Phosphorus	Glucose
1	8.2	4.7	65.0
2	8.5	4.7	55.0
3	8.3	5.0	65.0
4	8.7	6.0	50.0
5	8.5	9.0	60.0
6	8.2	5.2	72.0
7	8.8	3.5	84.0
8	8.0	3.5	78.0
9	8.4	5.4	72.0
10	8.3	5.6	69.0
11	8.7	5.6	69.0
12	8.2	6.3	73.0
13	9.4	4.2	80.0
14	7.9	5.9	60.0
15	9.2	3.6	82.0
16	8.1	5.6	71.0
17	8.3	3.0	34.0
18	8.5	5.2	34.0
19	8.8	2.5	100.0
20	7.9	3.6	100.0
21	7.8	8.2	84.0
22	8.3	3.0	42.0
23	7.4	4.4	26.0
24	7.6	8.0	24.0
25	8.0	8.4	84.0
26	9.0	4.8	54.0
27	8.6	3.1	71.0
Total	225.6	138.0	1758.0
M.V.	8.3	5.1	65.0
S.D.	0.47	1.74	20.22

(4) Fourth day of life:-

Case No.	Calcium	Phosphorus	Glucose	Case No.	Calcium	Phosphorus	Glucose	Case No.	Calcium	Phosphorus	Glucose
1	8.0	5.0	87.0	21	8.0	7.9	84.0	41	8.7	8.0	53.0
2	8.8	5.0	91.0	22	9.2	3.9	70.0	42	7.9	4.5	57.0
3	8.3	5.3	74.0	23	7.5	6.2	42.0	43	8.2	6.9	78.0
4	8.9	6.7	51.0	24	7.3	7.9	42.0	44	7.6	7.3	62.0
5	8.0	9.0	97.0	25	8.4	6.0	45.0	45	8.1	3.7	64.0
6	8.0	6.9	84.0	26	9.0	5.4	51.0	46	8.0	7.0	88.0
7	9.0	4.6	87.0	27	8.9	6.2	83.0	47	8.2	6.5	53.0
8	8.5	4.3	91.0	28	8.5	5.7	74.0	48	8.6	6.5	55.0
9	8.0	5.6	74.0	29	8.9	6.6	70.0	49	8.6	6.2	82.0
10	8.4	5.5	100.0	30	9.4	5.9	66.0	50	8.2	4.0	80.0
11	10.2	6.1	83.0	31	8.2	6.7	54.0	51	7.7	6.8	72.0
12	8.0	6.8	71.0	32	8.0	5.8	65.0	52	7.6	4.3	87.0
13	8.9	5.9	73.0	33	8.3	5.8	54.0	53	8.4	5.6	51.0
14	8.9	8.4	92.0	34	8.1	7.5	62.0	54	7.0	8.0	81.0
15	8.4	4.0	85.0	35	8.8	9.0	64.0	55	8.0	7.1	80.0
16	8.4	6.0	79.0	36	9.1	5.0	45.0				
17	8.1	6.0	58.0	37	9.0	7.3	65.0	Total	460.3	335.1	3896.0
18	8.1	6.4	77.0	38	7.7	5.7	63.0	M.V.	8.3	6.1	71.0
19	8.4	5.4	61.0	39	8.1	5.9	60.0	S.D.	0.57	1.30	15.33
20	8.7	3.4	87.0	40	9.1	6.0	92.0				

IV - Twin Study.

(1) Foetal blood:

Case	The heavier			The lighter		
No.	Calc.	Phos.	Gluc.	Ca	P	Gl
1	9.1	4.3	70.0	9.8	3.7	79.0
2	11.8	3.6	144.0	10.5	5.1	134.0
3						
4						
5						
6						
7	10.1	2.9	55.0	10.8	3.9	55.0
8						
9	11.0	7.0	78.0	12.0	4.3	90.0
10	9.9	5.4	77.0	9.1	4.4	35.0
11	9.6	4.6	66.0	9.1	6.4	37.0
12						
13	9.8	6.1	53.0	10.2	4.7	13.0
14						
15	10.7	3.9	80.0	11.4	4.7	71.0
16	10.0	3.1	90.0	10.2	3.5	58.0
Total	92.0	40.9	713.0	93.1	40.7	572.0
M.V.	10.2	4.5	79.0	10.3	4.5	63.0
S.D.	0.82	1.39	27.06	0.97	0.87	35.64

(2) Baby at birth:

The heavier			The lighter		
Ca	P	Gl	Ca	P	Gl
8.7	4.6	68.0	9.6	4.5	67.0
8.9	4.3	80.0	7.8	3.5	69.0
8.7	3.3	67.0	9.1	3.2	34.0
9.3	5.9	48.0	8.9	5.2	37.0
9.5	5.1	47.0	9.6	5.6	9.0
9.1	4.0	73.0	9.9	6.3	60.0
9.1	3.6	78.0	9.3	4.4	50.0
63.3	30.8	461.0	64.2	32.7	326.0
9.0	4.4	66.0	9.2	4.7	47.0
0.30	0.89	13.96	0.69	1.11	21.52

Twins.

(3) Baby on 1st day.

Case	The heavier			The lighter		
No.	Ca	P	Gl	Ca	P	Gl
1	6.4	4.1	28.0	6.8	5.0	21.0
2	8.5	3.7	70.0	7.5	6.7	48.0
3	7.0	3.3	50.0	7.7	5.2	16.0
4	7.4	3.6	43.0	7.3	3.8	25.0
5	7.3	5.1	30.0	6.8	5.9	15.0
6	7.8	6.0	68.0	7.2	7.3	60.0
7	8.7	3.5	39.0	8.8	4.0	49.0
8	7.6	3.8	47.0	8.7	5.1	43.0
9	7.3	3.2	39.0	8.5	3.5	39.0
10	7.7	3.4	79.0	7.1	4.6	58.0
11	8.7	4.4	46.0	7.7	4.4	36.0
12	7.1	3.3	57.0	7.5	3.4	79.0
13	8.2	4.7	25.0	8.4	4.2	70.0
14	8.1	3.6	30.0	8.6	3.8	25.0
15	7.0	4.8	41.0	7.4	6.5	30.0
16	7.7	4.0	49.0	7.7	4.7	22.0
Total	122.5	64.5	741.0	123.7	78.1	636.0
M.V.	7.7	4.0	46.0	7.7	4.9	40.0
S.D.	0.66	0.82	15.72	0.66	1.18	19.60

(4) Baby on 4th day.

The heavier			The lighter		
Ca	P	Gl	Ca	P	Gl
8.9	4.4	67.0	9.2	4.0	58.0
9.0	4.5	88.0	8.6	5.1	61.0
7.2	4.4	77.0	7.9	8.7	54.0
8.1	6.1	53.0	7.9	5.9	53.0
7.5	4.1	60.0	7.0	4.9	53.0
7.9	3.7	95.0	7.0	4.4	82.0
7.1	6.3	52.0	8.6	4.7	40.0
7.2	6.5	87.0	7.8	6.2	91.0
6.3	4.3	47.0	6.8	3.5	56.0
8.2	3.9	82.0	8.1	4.9	70.0
9.1	6.3	69.0	8.0	6.0	72.0
8.2	3.9	83.0	9.1	3.0	83.0
8.0	6.3	54.0	8.0	7.4	42.0
7.7	5.1	46.0	8.3	4.8	36.0
7.1	5.0	62.0	7.5	7.3	37.0
7.8	5.7	70.0	7.6	7.0	56.0
125.3	80.5	1092.0	127.4	87.8	944.0
7.8	5.0	68.0	8.0	5.5	59.0
0.81	1.01	15.72	0.700	0.49	16.73

Twins.

(1) Foetal blood:

Case	First twin			Second twin		
No.	Ca	P	Gl	Ca	P	Gl
1	9.8	3.7	79.0	9.1	4.3	70.0
2	11.8	3.6	144.0	10.5	5.1	134.0
3						
4						
5						
6						
7	10.1	2.9	55.0	10.8	3.9	55.0
8						
9	12.0	4.3	90.0	11.0	7.0	78.0
10	9.1	4.4	35.0	9.9	5.4	77.0
11	9.6	4.6	66.0	9.1	6.4	37.0
12						
13	9.8	6.1	53.0	10.2	4.7	13.0
14						
15	11.4	4.7	71.0	10.7	3.9	80.0
16	10.2	3.5	58.0	10.0	3.1	90.0
Total	93.8	37.8	651.0	91.3	43.8	634.0
M.V.	10.4	4.2	72.0	10.1	4.9	70.0
S.D.	1.04	0.93	31.24	0.70	1.25	34.04

(2) Baby at birth:

First twin			Second twin		
Ca	P	Gl	Ca	P	Gl
9.6	4.5	67.0	8.7	4.6	68.0
8.9	4.3	80.0	7.8	3.5	69.0
9.1	3.2	34.0	8.7	3.3	67.0
9.3	5.9	48.0	8.9	5.2	37.0
9.5	5.1	47.0	9.6	5.6	90.0
9.9	6.3	60.0	9.1	4.0	73.0
9.3	4.4	50.0	9.1	3.6	78.0
65.6	33.7	386.0	61.9	29.8	482.0
9.4	4.8	55.0	8.8	4.3	69.0
0.33	1.05	15.13	0.56	0.89	16.16

Twins.

(3) Baby on 1st day:-

Case No.	First Twin Ca	First Twin P	First Twin Gl	Second Twin Ca	Second Twin P	Second Twin Gl
1	6.8	5.0	21.0	6.4	4.1	28.0
2	8.5	3.7	70.0	7.5	6.7	48.0
3	7.0	3.3	50.0	7.7	5.2	16.0
4	7.3	3.8	25.0	7.4	3.6	43.0
5	7.3	5.1	30.0	6.8	5.9	15.0
6	7.8	6.0	68.0	7.2	7.3	60.0
7	8.7	3.5	39.0	8.8	4.0	49.0
8	8.7	5.1	43.0	7.6	3.8	47.0
9	8.5	3.5	39.0	7.3	3.2	39.0
10	7.1	4.6	58.0	7.7	3.4	79.0
11	8.7	4.4	46.0	7.7	4.4	36.0
12	7.5	3.4	79.0	7.1	3.3	57.0
13	8.2	4.7	25.0	8.4	4.2	70.0
14	8.1	3.6	38.0	8.6	3.8	25.0
15	7.4	6.5	30.0	7.0	4.8	41.0
16	7.7	4.7	22.0	7.7	4.0	49.0
Total	125.3	70.9	675.0	120.9	71.7	70.20
M.V.	7.8	4.4	42.0	7.5	4.5	44.0
S.D.	0.66	0.96	18.33	0.64	1.21	17.80

(4) Baby on 4th day:-

First Twin Ca	First Twin P	First Twin Gl	Second Twin Ca	Second Twin P	Second Twin Gl
9.2	4.0	58.0	8.9	4.4	67.0
9.0	4.5	88.0	8.6	5.1	61.0
7.2	4.4	77.0	7.9	8.7	54.0
7.9	5.9	53.0	8.1	6.1	53.0
7.5	4.1	60.0	7.0	4.9	53.0
7.9	3.7	95.0	7.0	4.4	82.0
7.1	6.3	52.0	8.6	4.7	40.0
7.8	6.2	91.0	7.2	6.5	87.0
6.8	3.5	56.0	6.3	4.3	47.0
8.1	4.9	70.0	8.2	3.9	82.0
9.1	6.3	69.0	8.0	6.0	72.0
9.1	3.0	83.0	8.2	3.9	83.0
8.0	6.3	54.0	8.0	7.4	42.0
7.7	5.1	46.0	8.3	4.8	36.0
7.5	7.3	37.0	7.1	5.0	62.0
7.7	4.7	22.0	7.7	4.0	49.0
127.6	80.2	1011.0	125.1	84.1	970.0
8.0	5.0	63.0	7.8	5.3	61.0
0.79	1.27	20.25	0.71	1.36	16.61

V - Placental dysfunction syndrome:-

(a) Mild pre-eclampsia:-

Case	(1) At 36 Weeks			(2) At 38 Weeks		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.8	1.7	86.0	9.2	2.3	77.0
2	8.3	4.6	105.0	8.3	2.0	81.0
3	7.7	3.3	97.0	8.3	2.9	94.0
4	8.5	2.5	104.0	8.7	2.9	120.0
5	8.2	2.9	92.0			
6	8.9	2.5	103.0	9.1	2.8	98.0
7	8.9	2.7	90.0	9.4	2.9	78.0
8	8.3	2.2	78.0			
9	7.9	1.6	107.0	8.0	1.9	103.0
10				8.6	3.1	83.0
11	8.3	3.1	117.0	8.7	2.9	105.0
12	8.3	3.1	117.0	8.7	2.4	93.0
Total	92.1	30.2	1096.0	87.0	26.1	932.0
M.V.	8.4	2.7	100.0	8.7	2.6	93.0
S.D.	0.39	0.83	3.87	0.39	0.42	4.36

(b) Severe pre-eclampsia:-

1	8.5	2.2	86.0	8.6	3.4	74.0
2	8.7	2.4	100.0	9.0	2.8	94.0
3	7.5	3.2	75.0	8.1	3.2	93.0
4	8.5	2.5	99.0	8.9	2.6	108.0
Total	33.2	10.3	360.0	34.6	12.0	369.0
M.V.	8.3	2.6	90.0	8.7	3.0	92.0
S.D.	0.54	0.44	3.74	0.41	0.36	4.47

(a) Mild pre-eclampsia:-

Case	(3) Maternal at delivery			(4) Foetal blood			(5) Baby at birth		
No.	Calcium	phosphorus	glucose	Calcium	phosphorus	glucose	Calcium	phosphorus	glucose
1	8.6	4.0	145.0	9.8	7.0	110.0	9.1	7.0	92.0
2	8.5	4.0	94.0	7.8	3.3	71.0	7.4	3.0	66.0
3	8.5	3.3	97.0	9.9	4.0	82.0	10.3	4.1	71.0
4	8.8	2.5	172.0	10.4	3.9	139.0	9.5	3.9	95.0
5	8.7	2.3	145.0	9.7	4.7	96.0	9.4	5.5	66.0
6	8.9	2.6	123.0	10.2	4.3	91.0	10.1	4.3	81.0
7	9.1	3.0	137.0	9.7	4.0	111.0	9.8	4.9	111.0
8	8.7	1.6	108.0	10.3	3.8	52.0	10.3	3.8	52.0
9	7.7	2.1	146.0	10.7	3.0	116.0	10.2	3.4	106.0
10	8.2	3.4	143.0	9.0	5.4	110.0	8.9	5.4	109.0
11	8.5	3.3	128.0	10.5	5.2	92.0	9.0	5.0	65.0
12	8.0	3.5	121.0	10.6	4.8	77.0	9.8	6.3	77.0
Total	102.2	35.6	1559.0	118.6	53.4	1147.0	113.8	56.6	991.0
M.V.	8.5	3.0	130.0	9.9	4.5	96.0	9.5	4.7	83.0
S.D.	0.39	0.75	22.74	0.81	1.08	23.41	0.82	1.19	19.65
			(b)	Severe pre-eclampsia:-					
1	8.5	3.4	83.0	8.6	5.5	29.0	8.6	5.5	25.0
2	8.7	3.8	139.0	8.9	4.5	38.0	8.5	6.0	28.0
3	8.5	2.1	97.0	8.7	3.5	30.0	8.2	4.9	27.0
4	8.6	1.6	388.0	8.7	3.3	94.0	8.5	3.3	81.0
Total	34.3	10.9	319.0	34.9	16.8	97.0	33.8	19.7	80.0
M.V.	8.6	2.7	106.0	8.7	4.2	32.0	8.5	4.9	27.0
S.D.	0.10	1.04	29.15	0.14	1.01	5.00	0.17	1.17	1.58

(a) Mild pre-eclampsia:-

Case	(6) Baby on 1st day			(7) Baby on 4th day		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	7.3	8.0	49.0	9.5	5.9	71.0
2	7.4	4.0	31.0	8.9	5.1	69.0
3	8.2	4.8	30.0	7.9	6.4	66.0
4	9.2	4.8	67.0	8.6	5.0	88.0
5	8.8	6.5	36.0	8.9	12.0	79.0
6	7.9	4.7	19.0	8.7	6.2	23.0
7	8.1	5.8	63.0	8.3	7.3	81.0
8	8.7	4.7	22.0	9.0	5.2	55.0
9	8.9	4.6	69.0	9.4	4.3	61.0
10	8.8	5.6	48.0	7.8	6.7	79.0
11	7.6	5.6	83.0	8.9	6.1	87.0
12	8.7	7.2	65.0	8.3	4.5	41.0
Total	99.6	66.3	582.0	104.2	74.7	800.0
M.V.	8.3	5.5	49.0	8.7	6.2	67.0
S.D.	0.64	1.11	20.93	0.48	2.03	19.39

(b) Severe pre-eclampsia:-

1	7.4	6.0	24.0	7.2	6.6	51.0
2	7.0	7.0	27.0	7.0	8.5	19.0
3	7.9	5.2	23.0	7.2	6.0	74.0
4	7.2	3.6	28.0	7.2	4.9	34.0
Total	29.5	21.8	74.0	28.6	26.0	144.0
M.V.	7.4	5.5	25.0	7.2	6.5	48.0
S.D.	0.39	1.44	2.12	0.10	1.51	27.62

(c) Dysmatures with normal gestation:-

Case	(1) At 36 Weeks			(2) At 38 Weeks		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.6	2.5	93.0	8.1	2.2	86.0
2	8.2	2.5	118.0	8.6	2.5	112.0
3	8.7	1.8	72.0	8.4	2.6	72.0
Total	25.5	6.8	283.0	25.1	7.3	270.0
M.V.	8.5	2.3	94.0	8.4	2.4	90.0
S.D.	0.26	0.41	23.04	0.24	0.22	20.3

Case	(3) Maternal at delivery			(4) Foetal blood			(5) Baby at birth		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose	Calcium	Phos.	Glucose
1	8.4	2.6	95.0	10.6	3.8	70.0	9.2	4.0	54.0
2	8.3	2.4	72.0	10.0	3.6	32.0	9.0	3.9	25.0
3	8.8	2.5	60.0	9.1	3.9	57.0	8.9	5.4	53.0
Total	25.5	7.5	227.0	29.7	11.3	159.0	27.1	13.3	132.0
M.V.	8.5	2.5	76.0	9.9	3.8	53.0	9.0	4.4	44.0
S.D.	0.26	0.1	17.8	0.76	0.17	19.31	0.17	0.84	16.46

Case	(6) Baby on 1st day			(7) Baby on 4th day		
No.	Calcium	Phosphorus	Glycose	Calcium	Phosphorus	Glucose
1	7.7	4.0	37.0	9.3	6.5	69.0
2	7.7	7.0	27.0	9.3	8.5	58.0
3	7.5	6.1	32.0	9.5	8.7	67.0
Total	22.9	17.1	96.0	28.1	23.7	194.0
M.V.	7.6	5.7	32.0	9.4	7.9	65.0
S.D.	0.14	1.54	5.0	0.14	1.22	5.92

(d) Dysmatures with prolonged gestation:-

Case	(1) At 36 Weeks			(2) at 38 Weeks		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.6	2.3	81.0	8.7	2.0	94.0
2	-	-	-	-	-	-

	(3) Maternal at delivery			(4) Foetal			(5) Baby at birth		
	Calcium	Phosphorus	Glucose	C	P	G	Calc.	Phos.	Glucose
1	8.7	1.6	100.0	6.8	6.5	32.0	6.8	6.3	29.0
2	8.7	2.1	105.0	7.9	4.7	31.0	7.5	6.8	27.0
Total	17.4	3.7	205.0	14.7	11.2	63.0	14.3	13.1	56.0
M.V.	8.7	1.9	103.0	7.4	5.6	32.0	7.2	6.6	28.0
S.D.	00.0	0.36	3.61	0.78	1.27	1.0	0.5	0.36	1.41

	(6) Baby on 1st day			(7) Baby on 4th day		
	C	P	G	C	P	G
1	7.2	4.9	27.0	7.7	4.9	81.0
2	7.4	7.0	22.0	8.0	7.5	58.0
Total	14.6	11.9	49.0	15.7	12.4	139.0
M.V.	7.3	6.0	25.0	7.9	6.2	69.0
S.D.	0.14	1.49	3.61	0.22	1.84	16.28

(e) Elderly primigravidoe:-

Case	(1) At 36 Weeks			(2) At 38 Weeks		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.8	2.6	91.0	8.6	3.2	82.0
2	8.6	2.2	98.0	8.3	2.5	102.0
3	8.9	2.6	93.0	9.6	2.5	91.0
4	8.9	1.8	70.0	8.7	2.0	86.0
Total	35.2	9.2	352.0	35.2	10.2	361.0
M.V.	8.8	2.3	88.0	8.8	2.6	90.0
S.D.	0.14	0.41	12.37	0.56	0.5	8.66

Case	(3) Maternal at delivery			(4) Foetal blood			(5) Baby at birth		
No.	Calcium	Phosphorus	Glucose	Calc.	Phos.	Glucose	Calcium	Phos.	Glucose
1	8.3	2.8	123.0	11.0	3.5	98.0	10.7	3.6	93.0
2	8.0	2.3	158.0	9.2	3.4	126.0	9.1	3.5	107.0
3	9.0	2.2	119.0	10.7	3.6	83.0	10.4	3.5	76.0
4	8.7	2.0	86.0	10.8	3.6	85.0	10.5	3.5	70.0
Total9	34.0	9.3	486.0	41.7	14.1	392.0	40.7	14.1	346.0
M.V.	8.5	2.3	122.0	10.4	3.5	98.0	10.2	3.5	87.0
S.D.	0.43	0.35	29.44	0.82	0.1	19.82	0.73	0.05	16.79

Case	(6) Baby on 1st day			(7) Baby on 4th day		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.3	4.1	50.0	8.0	4.7	90.0
2	7.1	3.5	31.0	8.7	5.8	67.0
3	7.8	4.6	38.0	9.7	6.5	62.0
4	9.0	4.2	17.0	8.9	6.5	50.0
Total	32.2	16.4	136.0	35.3	23.5	269.0
M.V.	8.0	4.1	34.0	8.8	5.9	67.0
S.D.	0.81	0.46	13.78	0.7	0.85	16.76

(f) Immature deliveries:-

Case	(1) Maternal at delivery			(2) Foetal blood			(3) Baby at birth		
No.	Calcium	Phosphorus	Glucose	Calcium	Phos.	Glucose	Calcium	Phosphorus	Glucose
1	9.2	2.1	96.0	10.9	3.5	70.0	10.0	4.5	48.0
2	-	-	-	-	-	-	-	-	-
3	8.5	2.7	110.0	10.6	3.8	64.0	9.9	4.1	48.0
4	8.8	2.2	104.0	10.1	3.5	70.0	9.4	4.2	48.0
Total	26.5	7.0	310.0	31.6	10.8	204.0	29.3	12.8	144.0
M.V.	8.8	2.3	103.0	10.5	3.6	68.0	9.8	4.3	48.0
S.D.	0.36	0.33	7.07	0.41	0.17	3.46	0.4	0.22	00.0

	(4) Baby on 1st day			(5) Baby on 4th day		
	C	P	G	C	P	G
1	9.7	7.5	19.0	9.1	8.0	46.0
2	7.8	6.5	33.0	8.5	6.8	41.0
3	8.2	3.7	29.0	7.6	4.0	79.0
4	9.1	5.4	40.0	7.5	7.3	57.0
Total	34.8	23.1	121.0	32.7	26.1	223.0
M.V.	8.7	5.8	30.0	8.2	6.5	56.0
S.D.	0.86	1.63	8.77	0.76	1.75	16.88

(g) Prolonged Pregnancy.

Case	(1) Maternal at delivery			(2) Foetal blood			(3) Baby at birth		
No.	Calcium	Phosphorus	Glucose	Calc.	Phos.	Gluc.	Calcium	Phosphorus	Glucose
1	8.5	2.1	114.0	10.7	4.1	79.0	9.8	5.3	57.0
2	8.9	2.5	115.0	8.5	5.6	80.0	8.1	6.1	64.0
3	-	-	-	-	-	-	-	-	-
Total	17.4	4.6	229.0	19.2	9.7	159.0	17.9	11.4	121.0
M.V.	8.7	2.3	115.0	9.6	4.9	79.0	8.9	5.7	61.0
S.D.	0.28	0.28	1.0	1.56	1.06	1.0	1.2	0.57	5.0

Case	(4) Baby on 1st day			(5) Baby on 4th day		
No.	Calcium	Phosphorus	Glucose	Calcium	Phosphorus	Glucose
1	8.0	3.9	88.0	7.6	5.0	71.0
2	8.1	5.5	62.0	7.3	5.7	80.0
3	8.5	3.2	65.0	8.5	4.8	69.0
Total	24.6	12.6	215.0	23.4	15.5	220.0
M.V.	8.2	4.2	72.0	7.8	5.2	73.0
S.D.	0.26	1.18	14.25	0.62	0.48	5.92