Growth Hormone, Glucose, and Free Fatty Acid Levels in Mother and Infant in Normal, Diabetic, and Toxaemic Pregnancies

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Only a few investigations concerning growth hormone (HGH) levels in maternal and cord blood in humans have been made. These were limited to normal pregnancies (Greenwood, Hunter, and Kloppe, 1964; Yen, Pearson, and Stratman, 1965). Though the absolute values of HGH cannot be compared in these two investigations since different methods of measuring the HGH were used, both studies found a higher concentration of HGH in the umbilical arterial plasma than in the umbilical venous and maternal plasma, suggesting an active secretion of HGH by the foetal anterior pituitary. This was further confirmed by the observations made by Cornblath, Parker, Reisner, Forbes, and Daughaday (1965), and Laron, Mannheimer, Pertzelan, and Nitzan (1966), who found, in newborn babies, conspicuously raised plasma growth hormone concentrations, equal to those found in acromegalic subjects.

The present investigation was designed to study the mother-infant relationship of HGH in diabetic and toxaemic pregnancies, about which there is no available information.

Material and Methods

Three groups of subjects were studied: women with a normal pregnancy (Table I), pregnant diabetic women (Table II), and women who developed toxaemia of pregnancy (Table III). During labour all women were routinely given an intravenous drip containing oxytocin 5 units in 500 ml. of a 5% glucose solution. Up to delivery the women usually received about 200-300 ml. Blood was drawn into heparinized tubes from the mother and cord at delivery and from the infant 2 to 4 hours later. The greater time lapse usually took place when the delivery had taken place at night. The blood was stored at -4°C . until centrifugation. Free fatty acids (FFA) and true glucose (GOT) were determined the same day.

Plasma was stored at -20°C . for assay of growth hormone (HGH). The blood or plasma of the mother, cord, and infant were always analysed together, in duplicate. Free fatty acids were determined according to Dole (1956). Blood glucose was measured by the glucose oxidase method using Worthington reagents. Growth hormone was determined by radio-immunoassay, as described elsewhere (Laron and Mannheimer, 1966).

Results

The comparative concentrations of HGH, glucose, and FFA in each mother, the cord blood, and infant, in normal pregnancies, in mothers with diabetes, and with toxaemic pregnancies, are illustrated in Fig. 1-3. The results obtained are summarized in Table IV.

Growth hormone. It is evident that the concentration of plasma growth hormone is much higher in the infant than in the mother. With few exceptions the level of plasma HGH in the cord lay between that in the mother and that in the infant, though in a few instances it was higher than in the infant. In the mothers with diabetes there is a greater individual variation in the plasma HGH than that seen in normal women, but there is no statistical difference between the two means. In the women with toxaemia, however, the mean HGH concentration is significantly higher ($p < 0.02$). In this group the HGH concentration was much higher in the cord blood ($p < 0.01$) than that in the other two groups, and higher values were also found in the infant a few hours after birth. It should be stressed that the values in the cord blood represent the mixture between maternal and infant blood at delivery, whereas the blood from the infant was taken several hours after birth, thus showing concentrations at a somewhat different time. In the infants of diabetic mothers the plasma HGH concentration was significantly lower than in the infants of normal mothers ($p < 0.01$).

TABLE I
Pertinent Data of Mother and Infant in Normal Pregnancies

Case No.	Mother				Infant			
	Name	Age (yr.)	Parity	Delivery	Sex	Weight (g.)	Length (cm.)	Length of Gestation (wk.)
1	K.E.	26	II	Spontaneous	M	3730	52	40
2	D.R.	27	II	Spontaneous	F	3580	50	40
3	D.S.	31	II	Spontaneous	M	2880	54	38
4	H.H.	20	II	Caesarean section	M	3150	48	39
5	A.D.	35	I	Caesarean section	M	3500	53	40
6	Sh.R.	18	I	Caesarean section	F	3100	49	40
7	G.E.	34	III	Vacuum	F	3900	51	40
8	W.G.	28	II	Caesarean section	M	3180	51	38
9	R.S.	23	I	Spontaneous	M	5200	54	40

TABLE II
Pertinent Data of Mother and Infant in Women With Diabetes Mellitus

Case No.	Mother				Infant			
	Name	Age (yr.)	Parity	Delivery	Sex	Weight (g.)	Length (cm.)	Length of Gestation (wk.)
1	S.A.	20	I	Caesarean section	M	4160	53	37
2	K.E.	32	II	Caesarean section	F	3050	50	38
3	M.A.	26	II	Spontaneous	M	3690	54	38
4	Z.S.	28	III	Caesarean section	M	3000	48	37
5	F.G.	40	IX	Caesarean section	M	4300	53	37
6	B.P.	31	II	Caesarean section	F	4200	51	36
7	L.R.	27	III	Caesarean section	M	4400	53	37
8	E.E.	22	II	Spontaneous	M	4000	51	40
9	B.N.	21	I	Spontaneous	F	2600	43	29

TABLE III
Pertinent Data of Mother and Infant in Women With Toxaemia

Case No.	Mother				Infant			
	Name	Age (yr.)	Parity	Delivery	Sex	Weight (g.)	Length (cm.)	Length of Gestation (wk.)
1	G.E.	21	I	Caesarean section	M	1800	42	30
2	E.Z.	38	III	Caesarean section	F	2400	46	38
3	P.L.	24	I	Spontaneous	F	3200	50	39
4	M.D.	30	III	Spontaneous	F	2350	46	38
5	H.S.	33	IV	Spontaneous	M	4320	53	40
6	A.D.	28	I	Spontaneous	M	2950	49	38
7	K.Z.	25	II	Spontaneous	M	3000	49	?
8	N.M.	21	IV	Spontaneous	F	3400	50	39

Blood glucose. All women received about 200 to 300 ml. of a 5% glucose infusion, which most probably had no significant influence on the blood glucose concentration. As compared to normal women, the concentration of blood glucose was higher in the diabetic mothers and lower in the women with toxaemia. There were no significant differences in the cord blood values. After birth the blood sugar in the infants decreased 50% or more within a few hours.

Free fatty acids. Free fatty acids in the plasma were about three times higher in the mother than in the cord blood in normal and diabetic mothers. In toxaemia the proportion was significantly lower ($p < 0.05$). There was no difference between the groups in the levels of FFA in the cord plasma. In the only infant of a diabetic mother tested for FFA, the concentration was lower than in the infants of normal mothers. As shown by Fairweather (1965), oxytocin-induced labour does not affect the serum FFA concentration.

FIG. 1.—Plasma growth hormone (GHG), glucose, and free fatty acids in normal pregnant women at delivery, in the cord, and in the newborn infants.

FIG. 2.—Plasma growth hormone (GHG), glucose, and free fatty acids in pregnant diabetic women at delivery, in the cord, and in the newborn infants.

TABLE
Mean Concentrations of Growth Hormone, Glucose, and Free Fatty Acids in the

Group	GHG (μmg./ml.)						Glucose		
	Mother		Cord		Infant		Mother		No.
	No.	Mean ± S.E.	No.	Mean ± S.E.	No.	Mean ± S.E.	No.	Mean ± S.E.	
Normal	9	15 ± 1.8	9	34 ± 9.7	9	69 ± 14	9	90 ± 8.6	9
Diabetic	9	21 ± 5.2	6	26 ± 8.7	7	40 ± 7.7*	9	114 ± 24	6
Toxaemic	7	24 ± 3.0*	6	93 ± 15*	7	99 ± 42	8	69 ± 3*	6

No. = number of determinations. * Statistically significant difference compared to the values in the normal group. Student's t test.

FIG. 3.—Plasma growth hormone (GHG), glucose, and free fatty acids in women with toxemia of pregnancy at delivery, in the cord, and in the newborn infants.

Discussion

The fact that the plasma of the newborn infant contains a higher concentration of GHG (Cornblath *et al.*, 1965) than does the plasma of the mother (Greenwood *et al.*, 1964), indicates an active secretion of this hormone by the foetus. This hypothesis has recently been substantiated by showing that GHG is not transferred from the mother through the placenta (Gitlin, Kumate, and Morales, 1965; Laron, Mannheim, Pertzalan, Goldman, and Guttman, 1966). The role that growth hormone plays in the normal foetus and newborn infant is not clear, but the raised level could indicate an increased metabolic rate. The usual regulatory mechanism of growth hormone secretion found in adults, such as stimulation by hypoglycaemia and exercise and suppression by glucose administration (Glick, Roth,

Yellow, and Berson, 1965), does not seem to function adequately in the newborn (Cornblath *et al.*, 1965). It was, therefore, of great interest to investigate the materno-foetal relation of growth hormone in diabetes and toxemia, two states of hormonal and metabolic imbalance.

In the normal control group, the concentration of GHG in the cord plasma was twice that in the maternal plasma. This level was also raised as compared to the growth hormone concentration in normal women at rest, but consistent with increases noted during exercise or oestrogen stimulation (Frantz and Rabkin, 1965). In the normal newborn infant the mean GHG level doubled within several hours. This might be partly due to the marked decrease in blood glucose and would infer a normal regulatory mechanism. At the same time

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(mg./100 ml.)			FFA (μEq/l.)					
Cord	Infant		Mother		Cord		Infant	
Mean ± S.E.	No.	Mean ± S.E.	No.	Mean ± S.E.	No.	Mean ± S.E.	No.	Mean ± S.E.
81 ± 12	9	47 ± 4	6	1130 ± 83	8	364 ± 34	8	1195 ± 200
86 ± 7.7	6	37 ± 10	8	1139 ± 41	3	377 ± 99	1	761
94 ± 8.1	3	36 ± 10	3	713 ± 160*	1	400	1	1180

the plasma FFA tripled, which could be a consequence of the rise in HGH (Raben and Hollenberg, 1960).

In the women with diabetes, all of whom received insulin, the plasma HGH was slightly, but not significantly, higher than that in the normal group. Plasma growth hormone in the infants of these diabetic mothers was significantly lower than in normal infants, as was blood glucose. Even the mean HGH concentration in the cord was lower than the normal mean. The lower plasma FFA values found in babies of diabetic mothers by Chen, Adam, Laskowski, McCann, and Schwartz (1965), and in the one case studied by us, may be explained by the low HGH. It is interesting to speculate what causes the low HGH level in these babies, in the presence of low blood glucose. It is possible that foetal HGH secretion is chronically affected by the large amounts of glucose passing through the placenta from the mother and/or by the resulting state of foetal hyperinsulinism (Stimmler, Brazie, and O'Brien, 1964). This finding is certainly the first direct evidence that the large size of babies born to diabetic mothers is not caused by increased amounts of HGH from either the mother or the foetus.

In toxæmia of pregnancy, which is a state characterized by vascular changes and water and salt retention leading to raised blood pressure and oedema, we found significantly raised HGH levels in the women at delivery, in the cord blood, and in the newborn several hours after delivery. The latter values varied considerably so that the mean difference was not statistically significant. On the other hand, blood glucose and FFA were significantly lower in the mothers, with no obvious differences from the normal in the infants. Since the aetiology of toxæmia of pregnancy is still unknown, further investigations will have to be made before an explanation of these findings is reached.

Conclusions

The concentration of plasma growth hormone, glucose, and free fatty acids was studied in three groups of pregnant women, normal, diabetic, and toxæmic, at delivery and in their newborn infants. It was found that HGH levels in the mother were higher at delivery than in the normal fasting state, whereas in the infants they were 2 to 4 times higher

than those of the mother. These findings occurred during concurrent reduction of the infant blood glucose, and are taken as evidence that HGH is actively secreted in the foetus and newborn infant.

Growth hormone concentration was found to be significantly lower in infants of diabetic mothers than in those of normal mothers. However, it was found to be much higher in both mother and infant in cases of toxæmia of pregnancy.

The findings presented are considered further evidence that the large babies of diabetic mothers are not due to increased secretion of growth hormone.

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