

Insulin Levels in the Umbilical Vein and in the Umbilical Artery of Newborns of Normal and Gestational Diabetic Mothers*

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Summary. Insulin levels (by double antibody radio-immunological assay) were studied in the venous blood of mothers at vaginal delivery and in the umbilical vein and artery of their newborns. — In 14 normal mothers the insulin levels after 10 hours fasting were 18.5 ± 3.6 μ U/ml (mean \pm S.E.M.). In their newborns (mean: 3.420 kg, all < 4.000 kg, 38–41 weeks gestation) the insulin levels were low and similar in the umbilical vein (5.6 ± 0.7 μ U/ml) and in the umbilical artery (6.6 ± 0.7 μ U/ml). The plasma glucose levels in the mothers were 99.7 ± 3.9 mg/100 ml and in the umbilical vein 77.3 ± 3.7 mg/100 ml and the umbilical artery 65.5 ± 3.2 mg/100 ml. They were significantly different from each other. — Eleven normal mothers receiving a glucose infusion (ca. 15 g/3 hours) during delivery had 42.0 ± 9.9 μ U/ml insulin in their venous blood. In their newborns with a normal birthweight (mean: 3.585 kg, all < 4.000 kg) the insulin levels were not increased either in the umbilical vein (7.0 ± 1.0 μ U/ml) or in the artery (7.9 ± 1.0 μ U/ml). The plasma glucose levels in the mothers were 128.0 ± 7.7 mg/100 ml, and in the umbilical vein 105.0 ± 7.5 mg/100 ml and in the umbilical artery 88.8 ± 8.6 mg/100 ml. The plasma glucose levels were significantly different from each other. — In six infants with "large birthweight" (> 4.100 kg) born to untreated mothers with gestational diabetes the insulin levels were superior to the values found in normal newborns. In three of these infants, born to mothers who did not receive a glucose infusion, the insulin levels in the umbilical vein were 38, 42 and 13 μ U/ml, and in the artery they were 17, 34.5 and 18.5 μ U/ml. The other three mothers received a glucose infusion, their newborns had in the umbilical vein an insulin level of 15.5, 65 and 19 μ U/ml and in the artery 20, 72.5 and 14 μ U/ml. — In conclusion, the normal infant at birth has a low insulin level, which is equal in the umbilical vein and artery. In 6 heavy infants born to untreated latent diabetic mothers, the insulin levels were significantly higher than in normals, and the levels in the umbilical vein and the artery were different from one another. This latter data on hyperinsulinism is discussed in relation with hyperplasia of the islets of Langerhans observed in stillborn infants of mothers with insulin-dependant diabetes or gestational diabetes.

L'insulinémie dans l'artère et la veine ombilicales chez les nouveau-nés de mères normales et de mères atteintes de diabète de grossesse non traité.

Résumé. L'insuline dosée par la méthode radioimmunologique aux doubles anticorps est déterminée dans le sang veineux de la mère au moment de l'accouchement et dans la veine et l'artère ombilicales des nouveau-nés. — L'insulinémie de 14 mères normales après 10 heures de

jeûne est de 18.5 ± 3.6 μ U/ml (moyenne, écart-type de la moyenne). Les taux d'insuline dans le sang de leurs nouveau-nés (moyenne: 3.420 kg; tous < 4.000 kg; 38 à 41 semaines de grossesse) sont bas dans la veine (5.6 ± 0.7 μ U/ml) comme dans l'artère ombilicale (6.6 ± 0.7 μ U/ml). Les glycémies plasmatiques chez les mères sont 99.7 ± 3.9 mg/100 ml et dans la veine ombilicale (77.3 ± 3.7 mg/100 ml) et dans l'artère ombilicale (65.5 ± 3.2 mg/100 ml). Les glycémies des trois compartiments sont significativement différentes entre elles. — Onze mères normales qui ont reçu une perfusion glucosée (± 15 g/3 heures) pendant le travail, présentent au moment de l'accouchement une insulinémie qui s'élève à 42.0 ± 9.9 μ U/ml. Leurs nouveau-nés, de poids normal à la naissance (moyenne: 3.585 kg; tous < 4.000 kg) n'ont pas d'augmentation de l'insulinémie ni dans la veine ombilicale (7.0 ± 1.0 μ U/ml) ni dans l'artère ombilicale (7.9 ± 1.0 μ U/ml). Les glycémies plasmatiques chez les mères sont 128.0 ± 7.7 mg/100 ml et dans la veine ombilicale 105.0 ± 7.5 mg/100 ml et dans l'artère ombilicale 88.8 ± 8.6 mg/100 ml. Les glycémies des trois compartiments sont significativement différentes entre elles. — Chez 6 enfants de poids excessif (> 4.000 kg) nés de mères atteintes de diabète de la grossesse non traité, l'insulinémie est supérieure aux valeurs de nouveau-né normal. Trois de ces enfants, dont la mère n'a pas été perfusée, ont des taux d'insuline dans la veine ombilicale de 38, 42 et 13 μ U/ml et dans l'artère de 17, 34.5 et 18.5 μ U/ml. Les trois autres parturientes reçoivent une perfusion de glucose. L'insulinémie dans la veine ombilicale chez leurs nouveau-nés est respectivement de 15.5, 65 et 19 μ U/ml et de 20, 72.5 et 14 μ U/ml dans l'artère. — En conclusion, les enfants normaux à la naissance ont des taux d'insuline bas et identiques dans l'artère et la veine ombilicales. Chez les gros enfants de mères atteintes de diabète de grossesse non traité, l'insulinémie est significativement plus élevée que chez les enfants normaux. Les valeurs trouvées dans la veine ombilicale sont différentes de celles de l'artère ombilicale. Cet hyperinsulinisme confirme les observations concernant l'hyperplasie des îlots de Langerhans observée chez les enfants mort-nés de mère diabétique ou atteinte de diabète de la grossesse. Le parallélisme entre l'hyperinsulinémie foetale et le poids excessif à la naissance est souligné.

Blutinsulinspiegel in der Arteria und Vena Umbilicalis bei Neugeborenen gesunder Mütter und von Müttern mit unbehandeltem Schwangerschaftsdiabetes.

Zusammenfassung. Mit der radioimmunologischen Doppelantikörpermethode wurde der Insulinspiegel im Venenblut der Mutter im Augenblick der Geburt und in der Nabelschnurarterie und -vene des Neugeborenen bestimmt. — Der Insulinspiegel von 14 stoffwechselgesunden Müttern nach zehnstündigem Fasten betrug 18.5 ± 3.6 μ E/ml (Mittelwert mit Standardabweichung). Der Blutinsulinspiegel ihrer Neugeborenen (Körpergewicht im Mittel 3.420 kg, alle < 4.000 kg bei 38 bis 41 Schwangerschaftswochen) war sowohl in der vena umbilicalis (5.6 ± 0.7 μ E/ml) als auch in der arteria umbilicalis (6.6 ± 0.7 μ E/ml) niedrig. Der Plasmaglucosespiegel bei den Müttern

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betrug 99.7 ± 3.9 mg/100 ml, in der vena umbilicalis 77.3 ± 3.7 mg/100 ml und in arteria umbilicalis 65.6 ± 3.2 mg/100 ml, wobei sich die Werte signifikant voneinander unterscheiden. — Elf stoffwechselgesunde Mütter, die während der Geburtsperiode eine Glucoseinfusion (± 15 g/3 Stunden) erhielten, zeigten im Augenblick der Entbindung einen Insulinspiegel von 42.0 ± 9.9 μ E/ml. Ihre normalgewichtigen Neugeborenen (Durchschnittsgewicht: 3.585 kg; alle < 4.000 kg) wiesen weder in der vena (7.0 ± 1.0 μ E/ml) noch in der arteria umbilicalis (7.9 ± 1.0 μ E/ml) eine Erhöhung des Blutinsulinspiegels auf. Die Glucosekonzentration im Plasma der Mütter beträgt 128.0 ± 7.7 mg/100 ml, in der vena umbilicalis 105.0 ± 7.5 mg/100 ml und in arteria umbilicalis 88.8 ± 8.6 mg/100ml. Diese Werte unterscheiden sich signifikant voneinander. — Bei sechs „Riesenkindern“ (> 4.000 kg), die von nicht behandelten während der Schwangerschaft zuckerkranken Müttern geboren werden, war der Blutinsulinspiegel höher als beim normalen Neugeborenen. Drei dieser Kinder, deren Mütter keine Infusion erhalten hatten, zeigten in der vena umbilicalis einen Insulinspiegel von 38, 42 und 13 μ E/ml, in der arteria umbili-

calis von 17, 34.5 und 18 μ E/ml. Die drei übrigen Mütter erhielten eine Glucoseinfusion. Ihre Neugeborenen hatten Insulinspiegel von 15.5, 65 und 19 μ E/ml in der vena umbilicalis und 20, 72.5 und 14 μ E/ml in der arteria umbilicalis. — Somit können wir schlußfolgern, daß normale Kinder bei der Geburt einen niedrigen Insulinspiegel haben, der in der arteria und vena umbilicalis gleich ist. Bei „Riesenkindern“ von Müttern mit nicht behandeltem Schwangerschaftsdiabetes ist der Blutinsulinspiegel signifikant höher als bei normalen Kindern. Die Werte gemessen in der vena und arteria umbilicalis sind unterschiedlich. Dieser Hyperinsulinismus bestätigt die Beobachtung der Hyperplasie der Langerhans'schen Inseln bei totgeborenen Kindern diabetischer oder praediabetischer Mütter. Auf den Parallelismus zwischen fetalem Hyperinsulinismus und Geburtsübergewicht wird hingewiesen.

Key-words: Insulin levels, Blood sugar, Gestational diabetes, Birthweight, Placental weight, Umbilical blood insulin, Umbilical bloodsugar, Normal parturients, Latent diabetic parturients.

A glucose concentration in blood which declines rapidly to values below those observed in normal newborns is a major characteristic of the heavy infant of a diabetic mother. This condition is related to the hyperplasia of the islets of Langerhans (DRISCOLL et al., 1960; NAYE et al., 1966) and a state of functional hyperinsulinism (BAIRD and FARQUHAR, 1962; CORNBATH and SCHWARTZ, 1966). The same histological features of the islets of Langerhans have been shown to occur in heavy newborns of untreated mothers with latent or potential diabetes (DUBREUIL and ANDERODIAS, 1920; MILLER, 1946; WOOLF and JACKSON, 1957; NAYE et al., 1966).

The object of this study was to measure separately the insulin content in the umbilical vein and in the artery, to ascertain if any difference could be demonstrated between the release of insulin by the pancreas in normal infants and in newborns with a heavy birthweight.

Material and Methods

Parturients: In a first group, 14 parturients were defined as normal by the following criteria: the mothers had no personal, obstetrical or family history suggestive of diabetes mellitus; they were between 16 and 37 years old; their weight was normal and their pregnancy was uncomplicated. Vaginal delivery occurred spontaneously between the 38th and 41st week. The newborns weighed under 4.000 kg and had no respiratory distress syndrome, with an Apgar between eight and ten. The mothers were fasting for at least ten hours before delivery.

The second control group of 11 parturients met the same criteria as the first but received during delivery a glucose infusion of 15 g in three hundred milliliters water during three hours. The glucose infusion was also used as a vehicle for oxytocin.

The third group consisted of six mothers with gestational diabetes whose clinical symptoms are reported in Table 2.

Blood samples: All blood samples were collected in dry test-tubes containing powdered heparin in a concentration of 25 to 35 U. of heparin per ml of blood. Blood was taken simultaneously from the mother and the newborn. Blood collection from the mother was done from the forearm vein. If glucose was infused, care was taken to collect the sample from the opposite arm. To collect blood from the newborn a needle was introduced into one of the two umbilical arteries still pulsating and into the umbilical vein. All three samples were collected simultaneously within 3 minutes after birth. All blood samples were immediately centrifuged and the plasma separated, freeze-dried and stored at -10°C . until assayed for blood sugar and insulin.

Blood glucose was estimated by means of the Autoanalyser, using a ferricyanide method (Hoffman, 1937).

Insulin assay: The insulin levels were assayed by the double antibody radioimmunoassay technique of MORGAN and LAZAROW (1963). Human Insulin¹, Insulin-¹²⁵I and an insulin-binding reagent kit, which was supplied by the Radiochemical Centre, Amersham, England, were used. All assay operations were carried out at 4°C . Except for the step of separating the precipitate from the supernatant, which was done in a cooled centrifuge at 3000 r.p.m. for 45 minutes, the instructions prescribed were closely followed throughout. The precipitate was washed once, and centrifuged again for 15 minutes. The radioactivity of the precipitate was counted in a Single Channel-Gamma Spectrometer (Philips). Duplicate assays were carried out on each sample and the mean value was expressed in μ U of insulin per ml of plasma. The insulin levels observed

¹ Obtained by courtesy of Dr. J. SCHLICHTKRULL, Novo Research Institute, Copenhagen-Denmark.

in 12 normal adults (ranging in age from 25–35 years) in the morning hours, after twelve hours fasting, were $8.45 \pm 0.4 \mu\text{U/ml}$ (mean and S.E.M.).

Results

In fourteen normal mothers who did not receive an infusion of glucose the plasma glucose levels after ten hours fasting were $99.7 \pm 3.9 \text{ mg}/100 \text{ ml}$ (mean and S.E.M.). In their newborns with a mean weight of 3.420 kg (all less than 4.000 kg) the glucose levels were $77.3 \pm 3.7 \text{ mg}/100 \text{ ml}$ in the umbilical vein and $65.5 \pm 3.2 \text{ mg}/100 \text{ ml}$ in the umbilical artery (Table 1; controls).

The difference between the glucose levels in the mothers and in the umbilical vein was $22.4 \text{ mg}/100 \text{ ml}$; between the glucose levels in the mother and in the umbilical artery it was 34.2 mg , and between the umbilical vein and artery was $11.8 \text{ mg}/100 \text{ ml}$. These differences are, according to the method of variances, statistically significant ($F = 9.07$; $d.f. = 1; 13$; $p < 0.01$). The correlations of the plasma glucose between the mother and the umbilical vein, between the mother and the umbilical artery and between the umbilical vein and artery are significant at the respective levels of $p < 0.02$; $p < 0.05$ and $p < 0.001$.

In their newborns with a mean birthweight of 3.585 kg (all less than 4.000 kg) the glucose concentration in the umbilical vein was $105.0 \pm 7.5 \text{ mg}/100 \text{ ml}$ and in the umbilical artery $88.8 \pm 8.6 \text{ mg}/100 \text{ ml}$. The difference between the maternal glucose level and the umbilical vein level was $23 \text{ mg}/100 \text{ ml}$, between the maternal glucose level and the umbilical artery $39.2 \text{ mg}/100 \text{ ml}$ and between the umbilical vein and artery $16.2 \text{ mg}/100 \text{ ml}$. These differences are, according to the method of variances, statistically significant (< 0.01). The correlations of the glucose levels, between the mother and the umbilical vein, between the mother and the umbilical artery and between the umbilical vein and artery are statistically significant at the respective levels of $p < 0.05$; $p < 0.05$ and $p < 0.001$.

In this group of parturients who were given the infusion of glucose the insulin levels were $42.0 \pm 9.9 \mu\text{U/ml}$ in the mother, and $7.0 \pm 1.0 \mu\text{U/ml}$ in the umbilical vein and $7.9 \pm 1.0 \mu\text{U/ml}$ in the artery of their newborns. The difference between the insulin levels of the mother and the umbilical vein was $35 \mu\text{U/ml}$, and between the insulin levels of the mother and the umbilical artery was $34.1 \mu\text{U/ml}$. These differences are significant ($p < 0.01$). There is a significant correlation between the insulin level of the mother and the insulin level of

Table 1. Plasma glucose and insulin levels of normal mothers and their newborn infants with normal birthweight

	Plasma glucose (mg/100 ml)			Plasma insulin (I.M.I. : $\mu\text{U/ml}$)		
	Controls ($n = 14$) mean \pm S.E.M.	Infused ($n = 11$) mean \pm S.E.M.	Differences (between means)	Controls ($n = 14$) mean \pm S.E.M.	Infused ($n = 11$) mean \pm S.E.M.	Differences (between means)
Mother: antecubital vein	99.7 ± 3.9	128.0 ± 7.7	28.3^2	18.5 ± 3.6	42.0 ± 9.9	23.5^1
Newborn: umbilical vein	77.3 ± 3.7	105.0 ± 7.5	27.5^2	5.6 ± 0.7	7.0 ± 1.0	1.4^3
umbilical artery	65.5 ± 3.2	88.8 ± 8.6	23.3^1	6.6 ± 0.7	7.9 ± 1.0	1.3^3

t-test: ¹ : $p < 0.02$; ² : $p < 0.002$; ³ : N.S.

In the same group (Table 1; controls), the insulin levels of the mothers were $18.5 \pm 3.6 \mu\text{U/ml}$ (mean; S.E.M.) and of the newborns $5.6 \pm 0.7 \mu\text{U/ml}$ in the umbilical vein and $6.6 \pm 0.7 \mu\text{U/ml}$ in the artery. The difference between the insulin levels of the mother and of the umbilical vein was $12.9 \mu\text{U/ml}$ and between the insulin levels of the mother and the umbilical artery was $11.9 \mu\text{U/ml}$. These differences are statistically significant ($p < 0.01$). There is no significant difference between the insulin levels of the umbilical vein and of the artery ($1 \mu\text{U/ml}$). The correlation between the insulin levels of the umbilical vein and artery is statistically significant ($p < 0.01$). There is no correlation between the glucose and the insulin levels of the mother, or the insulin level of the mother and the insulin level in the umbilical vessels.

A second group of eleven normal mothers (Table 1; infused) received a glucose infusion (ca. 15 g/3 hours) containing small amounts of oxytocin during delivery. Their venous glucose levels were $128.0 \pm 7.7 \text{ mg}/100 \text{ ml}$.

the umbilical vein ($p < 0.05$) and the insulin level of the artery ($p < 0.05$). There is also a correlation between the glucose of the mother and the insulin level of the umbilical vein ($p < 0.05$). There is no correlation in the insulin levels of the umbilical vein and artery.

The data in these two groups of normal parturients were then compared with each other: the differences were analyzed according to the student t-test and are reported in Table 1. The glucose infusion significantly increased the glucose levels in the maternal vein, in the umbilical vein and the artery. Glucose infusion significantly increased the insulin level of the blood of the mother but not in the cord blood.

In a third group, glucose and insulin levels were recorded in mothers with untreated gestational diabetes and in their newborns with large birthweight ($> 4.100 \text{ kg}$). The clinical data of the mothers and their newborns are reported in Table 2, their glucose levels in Table 3, and their insulin levels in Table 4. The infant of patient no. 509 was born without arterio-venous dif-

ference for glucose presumably due to his distress syndrome (CRAWFORD, 1965). Three (no. 330, 408, 509) of the six mothers received glucose infusions of the same order as the subjects of the second group. The individual insulin levels in the umbilical vein and artery were higher than in normals and the levels in the umbilical vein and the artery were different from one another.

that in the umbilical vein, and in the latter it was higher than in the artery.

When the mother was infused with glucose² the maternal plasma glucose rose significantly as did the umbilical venous and arterial plasma glucose. The increase of the plasma glucose in the mother was of the same order of magnitude as the elevation in the glucose content of the umbilical vein and in the artery. The

Table 2. Clinical data of mothers with untreated gestational diabetes (vaginal delivery)

Case	Mother				Newborn				Placenta
	Age (year)	Weight (kg)	Par./Grav.	GTT ¹	Weeks	Weight (kg)	Agpar	Aspect	Weight (g)
No. 247	30	144	5/6		37	4.940	9	cushingoid ²	860
No. 337	44	99	8/9	abnormal	37	4.320	9	cushingoid	700
No. 340	35	99	1/2	abnormal	38	4.030	10	normal	950
No. 330	21	83.5	1/2	abnormal	41	4.600	8	normal	810
No. 408	41	90	4/5	abnormal	38	4.650	9	cushingoid	1000
No. 509	37	140	3/5	abnormal	38	5.140	5	cushingoid	1050

¹ GTT of the latent diabetic type presents at least two blood-sugar values higher than the upper limit of normal, provided that fasting levels remain below 130 mg/100 ml.

Normal GTT: values not exceeding 100, 180, 140, 110 and 110 mg/100 ml at times: 0, 45, 90, 135 and 180 minutes after 100 g glucose loading respectively.

² Cushingoid refers to the typical aspect of the infant of the diabetic or latent diabetic mother described by FARQUHAR (1959) and HOET et al. (1960).

Table 3. Plasma glucose levels of untreated gestational diabetic mothers and their newborn infants with large birthweight (> 4,000 kg)

Case	Plasma glucose (mg/100 ml)		
	Mother	Newborn	
	Antecubital vein (M.V.)	Umbilical vein (U.V.)	Umbilical artery (U.A.)
No. 247	66	62	47
No. 337	120	86	51
No. 340	88	65	50
No. 330 + Glucose inf.	110	70	46
No. 408 + Glucose inf.	135	100	78
No. 509 + Glucose inf.	156	112	115

In Fig. 1 are shown the insulin levels in the umbilical vein and in the artery in relation with the birthweight. It is noticeable that the highest insulin levels occur in infants with a birthweight greater than 4,000 kg.

Discussion

The blood supply between mother and foetus gives an opportunity to analyse the carbohydrates and the insulin that are brought to the foetus by the umbilical vein and that are returned to the placenta through the two umbilical arteries. In the group that did not receive the infusion, the glucose content of the blood in the antecubital vein of the mothers was higher than

Table 4. Plasma insulin levels of untreated gestational diabetic mothers and their newborn infants with large birthweight (> 4,000 kg)

Case	Plasma insulin (I.M.I.: μ U/ml)		
	Mother	Newborn	
	Antecubital vein (M.V.)	Umbilical vein (U.V.)	Umbilical artery (U.A.)
No. 247	56	38	17
No. 337	27	42	34.5
No. 340	17.5	13	18.5
No. 330 + Glucose inf.	85	15.5	20
No. 408 + Glucose inf.	23	65	72.5
No. 509 + Glucose inf.	21	19	14

gradient was similar to the one observed in the non-infused mother.

The correlation between the plasma glucose in the maternal vein, the umbilical vein and in the artery is present in the infused as in the non-infused group. CRAWFORD (1965) analyzing the slopes of the glucose concentration from the maternal artery to the umbilical

² The same amount of oxytocin (3 units Voegtlin) used in the glucose solution was diluted and did not modify the glucose, nor the insulin levels in non-pregnant women. In parturients, saline perfusion with oxytocin (3 units Voegtlin) did not modify these two parameters. Therefore the glucose-oxytocin perfusion will be referred to as glucose perfusion.

vein and from the umbilical vein to the artery, suggested that "the balance of the maternal-foetal glucose concentration was maintained in a minute to minute fashion, even in the face of a rapidly changing concentration of maternal blood sugar".

The mean insulin concentration at birth found in the umbilical vein of a normal foetus from a non-in-

umbilical vein and in the artery. The glucose-insulin homeostatis in the foeto-placental unit seems to be a stable one, which is not easily changed by the supply of glucose readily offered by placental passage from the mother to the foetus.

The foetal pancreas appears to be less sensitive to the glucose stimulation than the mother's pancreas, as an increase of 27 mg/100 ml in glucose concentration in the mother elevated the insulin level in the mother, whereas the glucose addition in the foetus did not modify the foetal insulin level. Previous authors have already suggested that the pancreas of the normal newborn did not react briskly to glucose. BAIRD and FARQUHAR (1962) demonstrated this by administering glucose through the umbilical vein, and MILNER and HALES (1965) observed a slow maximal insulin increase in umbilical vein blood when glucose was injected in the mother during parturition. These latter authors included in their normal infants newborns whose birthweight went up to 4.500 kg, who may be responsible for the statistical increase of the insulin levels.

It appears that the glucose-insulin homeostasis of the normal foeto-placental unit relies completely on the flexible and rapidly changing glucose-insulin equilibrium in the mother.

The normal ratio of insulin levels between mother and foetus was no longer observed when the mother presented untreated gestational diabetes. The insulin levels observed in the umbilical vein and artery of heavy weight newborns were higher than the levels observed in normal infants. Both BAIRD and FARQUHAR (1962) using a biological assay and JORGENSEN et al. (1966) using a radioimmunological method have observed in overweight newborns from treated diabetic mothers a brisk, immediate insulin response to glucose administration. Their pancreas seems to have been sensitized to glucose during their foetal life. A similar functional hyperinsulinism to account for the rapid fall of blood sugar concentration immediately after birth has been postulated in children born from mothers with gestational diabetes (CORNBATH and SCHWARTZ, 1966).

A correlation between high insulin levels in total cord blood and the excessive birthweight is recorded by DITSCHUNEIT et al. (1966) and SHIMA et al. (1966), but these authors did not investigate separately the umbilical vein and artery. HELWIG (1940) and CARDELL (1953) previously reported a direct correlation between the mean surface area of the islets of Langerhans and the birthweight of infants from treated diabetic women. In addition, our results show a difference between the insulin content of the umbilical vein and

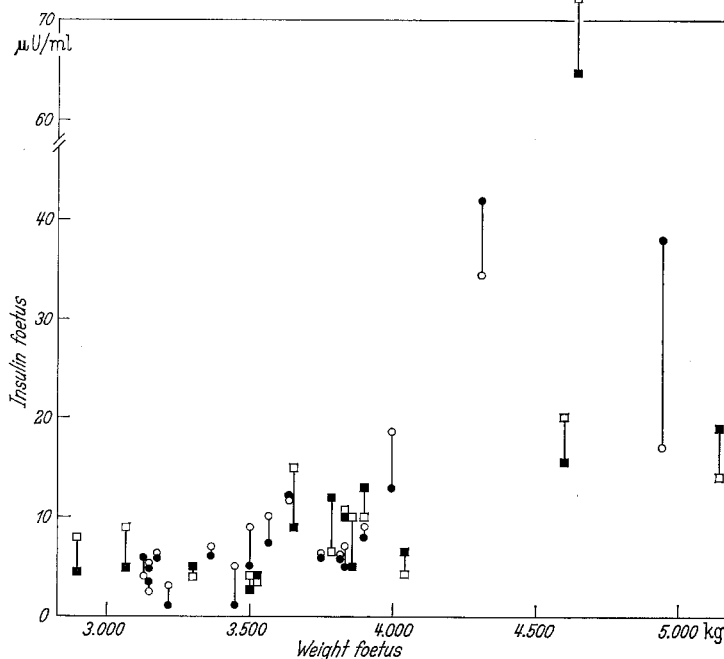


Fig. 1. Relation between birthweight of the foetus and the insulin levels in the umbilical vessel
 ● Umbilical vein, ○ umbilical artery = Newborns of mothers without glucose infusion;
 ■ Umbilical vein, □ umbilical artery = Newborns of mothers with glucose infusion.

fused, normal mother was $5.6 \pm 0.7 \mu\text{U/ml}$, which compares well with $9.0 \pm 1.0 \mu\text{U/ml}$ observed by MILNER and HALES (1965) under the same conditions, and with $5.93 \pm 0.64 \mu\text{U/ml}$ reported by DITSCHUNEIT et al. (1966); but it is different from that reported by SPILLACY et al. (1964), who found $42 \mu\text{U/ml}$. Our levels in the umbilical vein are significantly lower than the fasting level of normal adults ($8.45 \pm 0.4 \mu\text{U/ml}$). The changes of the insulin levels that occur during infusion did not parallel the modifications of the glucose levels. The difference in the insulin level between the venous blood of non-infused mothers and the umbilical vein blood was $12.9 \mu\text{U/ml}$, and it was the same for the umbilical artery. For the infused parturients this difference between the mother and the umbilical vein was $35 \mu\text{U/ml}$ and remained the same for the umbilical artery.

In the non-infused mother, the ratio of the maternal insulin level to the insulin level in the umbilical cord was three to one, and during glucose infusion this ratio was six to one. The difference in the ratio is due to the increase in the insulin level of the mother and to the constancy of the foetal insulin level in both groups. Newborns with normal birthweight and normal placental weight maintained similar insulin levels in the

the artery, but this difference, which did not exist in normal infants, was not always in the same direction; the levels in the vein were sometimes higher than in the artery and vice versa. These results suggest that factors which maintain the constancy of the insulin levels in the foeto-placental unit are modified in these cases.

It is apparent from our data that the stable glucose-insulin homeostasis observed in the normal infant has changed in these heavy birthweight infants born from untreated mothers with gestational diabetes to an unpredictable glucose-insulin relationship.

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