INSULAR FUNCTION OF MOTHER AND FETUS

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 55, No. 8, pp. 21-24, August, 1963
Original article submitted October 22, 1963

The function of the insular apparatus of the fetus at the end of pregnancy has not yet been determined quantitatively, particularly in man. Facts have been obtained indicating that insulin production by the fetus takes place on a considerable scale. Insulin has been detected in the islet tissue of the fetus of the 5th month of pregnancy [8], newly born infants characteristically have hypoglycemia [11], and the insulin activity of maternal blood of rabbits at term is equal to that of the newly born rabbits [3]. This evidence, however, is indirect; moreover, rabbits are born in a far more mature state than children.

In two studies, the insulin activity of umbilical blood from newly born infants was determined at the same time as the activity of maternal venous blood. In one of these studies [9] the insulin activity of the maternal blood was high, while that of the umbilical blood was negligible, and in the other [6], the insulin activity of the umbilical blood from four women was significantly lower than that of the maternal blood. However, the specificity of the method used by these authors for testing for insulin activity is not beyond reproach. The object of the present investigation was to make parallel determinations of the insulin activity of umbilical blood and maternal venous blood.

EXPERIMENTAL METHOD

Testing for insulin activity was carried out by the method of absorption of glucose by the epididymal fat of the rat [1], with the difference that 3-4 weighed samples of fat were taken from one rat, and of these one was incubated in buffer solution and the others in extracts of serum from maternal venous blood, retroplacental blood, and umbilical blood (obtained by free flow from the umbilical vein immediately after cutting the cord). Blood was taken during parturition. In nearly every case, the parturition was the first or second, with no complication, in a woman aged between 19 and 41 years. The infants weighed 3000-3950 g.

In 10 cases the activity of the venous and retroplacental blood was identical, so that the figures for the umbilical blood and maternal venous blood only will be given. The epididymal fat technique was chosen for the tests not only because of its high sensitivity and adequate simplicity and reliability, but also because it can be used to determine not only the free insulin, but also insulin bound by blood plasma [4].

An essential defect of all methods used to determine insulin activity is that testing is carried out in blood plasma, containing other active substances besides insulin. Insulin was extracted from the blood plasma by a previously developed method [2] using highly porous sulfa-cation exchange resins in the hydrogen form. In this investigation the mark SDV-3 resin, mesh 60-80, swelling coefficient 3.0, were used.

The results were expressed in units of insulin activity and as microunits per milliliter of plasma (μU/ml). In the course of the investigation repeated tests were made with pure insulin, the results of which were used to plot a calibration curve, from which the values of the glucose absorption by the epididymal fat could be converted into values of the insulin activity of the plasma extract. It should be borne in mind that when this method is used to determine insulin activity, only those differences of activity of 100% or more can be regarded as significant.

EXPERIMENTAL RESULTS

Usually 5-10 ml of blood serum was taken for investigation. Tests were conducted on 4-9 rats.

The table reveals the considerable individual differences between indices determined during parallel tests, although the mean values for the maternal and naonatal blood were identical. In order to detect any possible differences

Insulin Activity of Serum from Maternal Venous Blood and Blood from Umbilical Vein

Expt. No.	Insulin activity (in μU/ml)	
	maternal venous blood	blood from umbilical vein
206	250	250
207	76	113
208	282	230
209	170	146
210	180	182
214	560	570
235	274	318
304	139	117
310	83	78
317	230	232
320	242	242
323	126	142
326	153	202
332	172	189
344	93	84
350	265	212
353	380	368
360	204	202
381	350	402
383	230	242
$M \pm m$	226±26,3	223±25,7

in the insulin activity of the maternal and neonatal blood, the results were analyzed statistically using the method of paired comparisons [5], and this also confirmed the absence of differences ($t = 0.152$). No correlation could be found between the insulin activity of the maternal venous blood and its sugar level, or between the insulin activity and the sugar level of the blood from the umbilical vein.

The low values of the insulin activity of the umbilical blood obtained by several workers [6, 9] may be due to two factors. Firstly, they used tests on the rat's diaphragm, a method which detects only the free and not the bound insulin [1]; in its total form the total content of insulin circulating in the fetus is unknown. The fat tissue which we used to test for insulin enables the total (free + bound) insulin of the blood to be determined. Secondly, the blood of mother and fetus differ considerably in their content of many substances, including hormones and insulin antagonists, and this must inevitably affect the result of the determination of insulin activity by a biological method. Indirect evidence of the important role played by antagonists in the production of this difference in insulin activity between the maternal and fetal blood is given by the fact that if maternal blood plasma is diluted, its insulin activity falls, whereas dilution of umbilical blood plasma does not alter its insulin activity [6]. It is clear that this fact can only be explained by the considerable difference in the concentration of insulin antagonists, their concentration being higher in the fetal blood.

The method which we used to isolate the insulin from the blood plasma avoided contamination by a considerable proportion of the antagonists, thereby making the determination much more specific. We are justified in concluding from these facts that the equality of the insulin activity of the maternal and fetal blood which we determined is soundly established. Bearing in mind the high level of insulin activity in women at the end of pregnancy [10], and also the practically complete impermeability of the placenta to insulin [7], it may be asserted that at birth the islet apparatus of the human fetus is in a highly active functional state.

However, our findings are not sufficient to enable the insulin activity of the fetal blood to be judged in the various vascular regions, having regard to the important insulinase role of the liver. Nevertheless, blood enters the umbilical artery from the periphery, and it cannot become richer in insulin as it passes along the umbilical cord; consequently, our results indicate at least that the insulin activity of the peripheral blood of the fetus is very high. The absence of correlation between the insulin activity of the fetal blood and the fetal blood sugar, and also the difference which is known to exist between the fetal and maternal blood sugar levels despite their identical insulin activity, may be interpreted as evidence that insulin takes part in the physiological hypoglycemia of the newborn, and that the hypoglycemia is itself the result of the weakness of the insulin-antagonizing mechanisms.

SUMMARY

Insulin was extracted from blood plasma on strong sulfacationic ion-exchange resin, trade mark SDV – 3, 60-80 mesh, swelling coefficient 3.0 in hydrogen form. Bio-assay for insulin activity was performed by rat epididymal fat pad technique. Insulin activity as assayed in maternal venous and umbilical venous blood at birth and mean error values of insulin activity were 226 ± 26.3 and 223 ± 25.7 μU/ml respectively. There was no difference between insulin activity of maternal venous, retroplacental and umbilical venous blood either in mean values or individually. Since placenta is impermeable to insulin it is presumed that at birth insular function of fetus is relatively high and roughly equal to that of adult women at the end of pregnancy.

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