CORRELATION BETWEEN GLUCAGON, INSULIN AND GLYCAEMIA AFTER ORAL LOADING WITH GLUCOSE AT VARIOUS STAGES OF PREGNANCY

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SUMMARY

The Authors studied the progress of glycaemia, insulinaemia and glucagonaemia after oral loading of 100 g of glucose in a group of women at different ages of pregnancy (30th-40th week).

Their results demonstrate with regard to the glycaemic curve, a slowing to the initial glycaemic values. This then tended to return at least partially to normal during the last weeks of pregnancy.

As regards insulin the Authors noted a gradual increase of its secretion as pregnancy progressed. In the case of glucagon there was inhibition of the alpha cells, expressed as hypoglucagonaemia; the hyperglucagonaemia observed 30 min. after oral loading with glucose might be interpreted as direct stimulation of the alpha cells by cholecystokinin.

In determining glucidic homeostasis in pregnancy, there has been much confusion and divergence (as amply documented in the literature) ([1, 3]) with reference to the production and secretion of glucagon as a hyperglycaemic factor, and especially to the action of certain substances that are able to modify its plasma concentration.

In normal people hyperglycaemia gives rise to a block in the secretion of glucagon ([4, 5]), and vice versa hypoglycaemia, prolonged fasting, protein foods or amino acids (arginine), some intestinal hormones such as cholystokinin (pancreozymin), vagal stimuli and free fatty acids are suitable stimuli for its secretion.

In pregnancy, according to some Authors ([7]), glucagon under basic conditions does not deviate as compared to its effect in non-pregnant women: in this connexion, experiments performed on gravid rats ([6, 2]) have demonstrated normal glucagonaemia despite a fast of 5 days.

Greater difficulties arise in the interpretation of glucagon modifications after a "glucidic meal". After an oral load of 100 g of glucose there is an exaggerated reduction of glucagonaemia ([1]); vice versa, this hypoglucagonaemia is less evident after the same load introduced intravenously.

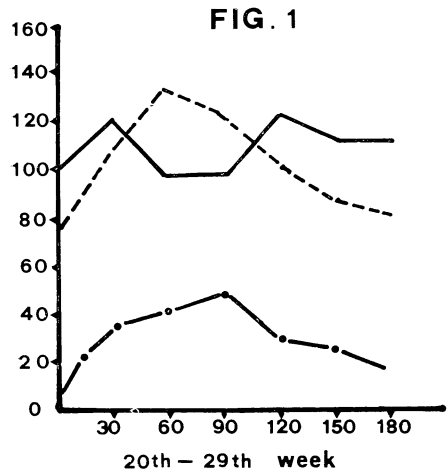
Independently of the route of administration, glucose and thus the glycaemic level always effectively stimulate the alpha cells; this, synergistically with insulin, may be a valid mechanism in normoglycaemia and sudden glycaemic variations in pregnancy, which might be injurious to the product of conception, can thus be avoided.

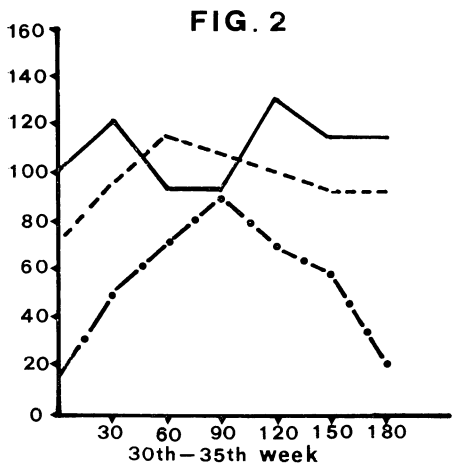
Starting from these presuppositions, we initiated a preliminary investigation on the secretion of both glucagon and insulin at various ages of pregnancy, under basic conditions and on loading wiht glucose.

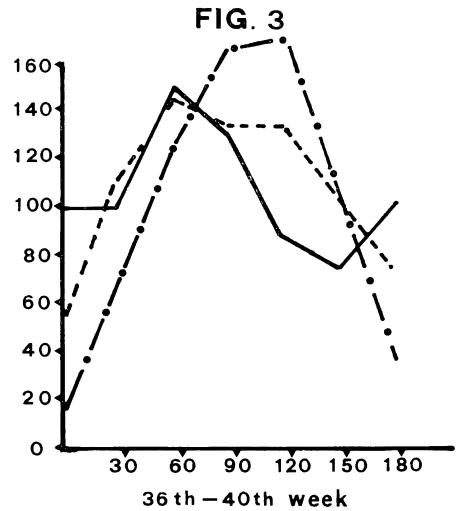
MATERIAL AND METHODS

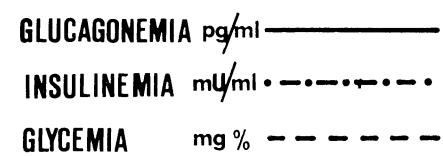
We have examined a group of thirty women between the 20th and 40th week of pregnancy, in the period January-August 1977.

None of these women had shown any signs









of clinical diabetes, nor any positive history of diabetes, nor any signs of EPH gestosis, kidney disease, Rh isoimmunization or obesity.

The usual blood chemistry tests, and the 24-hour glycaemic profile performed seven days before the oral glucose loading tests, gave results within the limits of normal. Samples were obtained in the morning (8 a.m.) for the analysis of glycaemia, glucagon and insulin 100 g of glucose were then given by mouth. Subsequent samples were obtained every 30 minutes up to 180 minutes, and from these samples, graphs were made, dosing glucose, insulin and glucagon.

We subdivided the subjects examined into three groups, based on the number of weeks of pregnancy:

a) group I : 20th-29th week of pregnancy
b) group II : 30th-35th week of pregnancy
c) group III: 36th-40th week of pregnancy.

For each of these groups, the mean of the values obtained at any given moment was worked out (30 min., 60 min., 120 min., 150 min., 180 min.). From the various curves a mean curve was obtained, and for each of its individual value the standard deviation was calculated.

The glycaemia was analysed by the hexokinase enzymatic method, the reactions being performed on the auto-analyzer. Insulin was analyzed by the radio-immunological method, using the Dow Lepetit kit; and glucagon by the 30 K pancreatic glucagon radio-immunological method.

RESULTS

The results we obtained are illustrated in figs. 1, 2 and 3; they are expressed as values of glycaemia, insulinaemia and glucagonaemia at various ages of pregnancy.

The values for glycaemia showed a slight change on oral loading with glucose; this was expressed as a slowing on returning to the initial glycaemic values.

This change was evident in both the first and the second group, or from the 20th to the 35th week of gestation; the course then tended to return partly to normal in the last weeks of pregnancy (36th-40th week).

Insulin was observed to increase gradually as pregnancy progressed; this was more marked between the 36th and 40th week, although not sufficiently to bring the glycaemia back to its initial values after loading with glucose.

The basic values for glucagonaemia, according to our data, did not vary from those found in non-pregnant women.

After glucose loading there was inhibition of the secretion of the alpha cells in all three groups considered, which was expressed as hypoglucagonaemia. The hyperglucagonaemia that we encountered at the 30th minute after loading with glucose, which was particularly evident between the 20th and 29th week and the 36th - 40th week, may be interpreted as the consequence of direct stimulation of the alpha cells by cholecystokinin, secreted following the oral administration of glucose, and vagal stimuli.

DISCUSSION

As indicated above, there was throughout gestation a slight change of tolerance on oral loading with glucose, which was expressed as a slow return to the initial glycaemic values, despite an evident increase in insulin production. This increase, however, was not sufficient to bring the glycaemia back to normal values within the unit of time under consideration (180 min.).

This is evidently to a great extent connected with the presence of hyperglycaemic factors typical of pregnancy, such as HPL of placental origin, and perhaps also the "consumption" factor exercised by placental tissue, with a high level of insulin breakdown.

Up to the 35th week, the beta cells were stimulated as glycaemia increased (after loading), together with progressive hyperinsulinaemia and simultaneous block of the alpha cells and relative diminution of the glucagonaemic level.

This seems to be a normal response of the alpha cells to the hyperglycaemic stimulus.

With regard to the third period of gestation (36th-40th week), paradoxical hyperglucagonaemia was present with respect to the hyperglycaemic stimulus. This may be interpreted, perhaps, as due to activation of the alpha cells on the part of intestinal hormones (cholecystokinin), or vagal stimuli.

Although some aspects of the function exercised by glucagon are not easy to interpret, the fact remains that the combined activity of insulin and glucagon, as well as the action of other typically placental hormones, can maintain glycaemia levels in healthy women such that maternal, and still more foetal, glucidic homoestasis is not altered.

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