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EDITORIAL

DIABETIC EMBRYOPATHY

The diabetic mother frequently gives rise to a foetus with several pecularities. A high proportion of her infants are overweight—they often exceed 10 lb.— and this increase in weight is made up of several components. The babies are both over-long and over-fat; they are oedematous and characteristically lose a pound or so of fluid weight during the first few days of life. Their internal organs are large, in particular the heart and liver. They may have an expanded erythron, with widespread haematopoiesis and a high haemoglobin content in their blood. Their general appearance of fat, flabby, rubicund weakness may closely resemble the picture of Cushing's syndrome.

These babies, and also those which escape being overlarge, behave as if they were feeble, undersized, premature infants; they have difficulty in breathing and sucking, and easily regurgitate fluids into their lungs. They are susceptible to birth trauma, infection and hyaline membrane disease so that they may die within the first few days of life unless specially protected. Although their blood-sugar levels may be very low soon after birth, this is probably of no significance, since a normal baby may likewise have extreme hypoglycaemia without any symptoms from it.

Foetuses of diabetic mothers show a greatly increased incidence of major congenital anomalies which, like anencephaly and ectopia cordis, may be incompatible with life. Apart from such anomalies, of course, a number of foetuses are not born alive. They die around the 36th week or earlier and are delivered in a macerated state, or they die nearer term and are obtained in a better state of preservation. Although these stillbirths are near term or even at full term, they are distinguished by active hepatic haematopoiesis, similar to that seen in premature and erythroblastotic infants. Luteal cysts may be found in the ovaries. Warren and Le Compte,[1] and Cardell,[2] in particular, have described the pathological features of these infants in more detail. Probably the most interesting abnormalities are those of the pancreas. Almost invariably the islets of Langerhans in these pancreases are large, and occupy an excessive part of the whole organ. There is both cellular hyperplasia and hypertrophy. Further than this, there is an increased proportion of beta cells in the islets. In the normal newborn infant the alpha cells comprise 60-70% of islet tissue; the ratio of alpha to beta cells is reversed in the infant of the diabetic mother. The histological sections may, moreover, appear to show an unusual degree of granularity in the beta cells, which may indicate an excess of insulin content. In fact, if we take all these items together it looks as if the pancreas of the diabetic's infant may contain up to 30 times the normal amount of insulin.

This abnormal condition of the embryo, or 'embryopathy', as it has rather unfortunately been called, owes its existence to some abnormality in the diabetic mother, since it is not seen in the infants of diabetic fathers. Certainly it has been found that the birth weights of the infants of diabetic fathers are larger on the whole than those of non-diabetics,[3] yet this increase in birth weight is not nearly as striking as is found in the infants of diabetic mothers, and there is no increase whatever in the stillbirth rate in the progeny of diabetic fathers.

Now what types of diabetic are liable to such an embryopathy as has been described? Here we come across some inexplicable discrepancies. In most centres of the world the same type of baby has been found to be produced by the severe, insulin-requiring, growth-onset diabetic, by the mild, diet-controlled diabetic, and even by the prediabetic several years before she shows any obvious metabolic carbohydrate disorder. In Boston and Brussels, apparently, the tendency for foetal loss to occur in the mild diabetic and in the prediabetic is very much less, and the data from these cities seem to be unimpeachable. In Cape Town evidence was found that the tendency to produce stillbirths and large babies extended back indefinitely into the past obstetric history of the diabetic woman, while in her prediabetic phase.[3]

In fact all the above-described features of the diabetic's infant apply with equal force to the infant of the prediabetic. It was van Beek[4] who first pointed out that the enlarged islets of Langerhans were to be found in the stillbirths of women who only later became diabetic. Woolf and Jackson have confirmed this.[5] The mean percentage of islet tissue in stillborn pancreases of control infants was found to be 1·3% by their method, while it was around 7% in erythroblastotics, in children of diabetic mothers and in children of prediabetic mothers. It is extraordinary that once again this similarity is seen between erythroblastosis and diabetes. No other cause for such enlarged islets in the stillborn infant is known. In fact, the finding of enlarged islets in a stillborn which is not erythroblastotic and whose mother is not an overt diabetic is the best possible indication of prediabetes in the mother. Woolf and Jackson's results illustrate this: Pancreases from 109 autopsies on stillbirths were specially examined and their islet contents estimated; 18 were found in which the proportion of islet tissue was over 5·5%, apart from those cases which were known to suffer from Rh incompatibility or whose mothers were diabetic at the time of pregnancy. Of the 18 relevant mothers 12 were traced for follow-up; 5 were found to have become diabetic and 5 gave slightly abnormal glucose curves; in the other 2 there was strong collateral genetic and obstetrical evidence of prediabetes. Thus all 12 mothers were probably prediabetic when they gave rise to the stillborn infants with large islets of Langerhans.

Looked at from another angle, these findings may provide a pointer in hitherto unexplained stillbirths, since the finding of large islets will indicate that maternal diabetes or prediabetes has played a part in the foetal death.

These excursions into the realms of prediabetes may help us in our search for the cause of this strange embryopathy.

It is certainly most unlikely that maternal hyperglycaemia can play any part, since many prediabetics show normal blood-sugar levels during pregnancy, and yet produce abnormal infants. A sensitivity to or excessive production of growth hormone or of glucocorticoids in the diabetic pregnancy has been suggested, and, although Professor Hoet[6] has made some interesting experiments the results of which favour the latter, the evidence is as yet not very good in favour of either. Although the plasma-cortisol level rises during all pregnancies, the levels observed are no higher in the diabetics. There is no tendency for women who are in the early stages of acromegaly or Cushing's syndrome to produce large babies or stillbirths,[7] and this is surely strong evidence against the view that either growth hormone or corticoids are the sole cause of the embryopathy. The large pancreatic islets suggest an excessive stimulation of this tissue. Is the infant's own insulin, acting as a 'growth hormone' itself, in fact the stimulus to the excessive size? And what is the connexion with the large islets in erythroblastosis?

Turning finally to the prevention and management of the embryopathy, in some centres insulin is being given to the prediabetic during pregnancy, even when her blood sugar is normal, in the hope that it may be effective in preventing some of the features of the embryopathy. And yet in the established diabetic, the very best possible control of the mother's diabetes will reduce the incidence of abnormal babies only partially. To obtain a live child it appears to be even more important to induce labour early if the foetus is judged to be large enough, and to manage the baby exactly as though it were truly a premature infant. Before this can be done, of course, it is necessary to make a diagnosis of maternal diabetes or prediabetes, and it is likely that a number of babies may be saved if the latter diagnosis is suspected and the suspicion is acted upon.

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5. Woolf, N. and Jackson, W. P. U. (1957): J. Path. Bact., **74**, 223.
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VAN DIE REDAKSIE

DIE SWAAI VAN DIE PENDULUM IN DIE VERLOSKUNDE

Ons lees gedurig van die swaaiende pendulum in die geskiedenis, maar in geen ander vertakking van die medisyne is dit so opmerklik soos in die verloskunde nie. In die twintiger- en dertiger-jare was die verloskunde daarop toegespits om die moederlike sterftesyfer te verminder terwyl die kind van ondergeskikte belang was. Vandag egter, waar die moederlike sterftesyfer gedaal het tot 'n minimum, is alles weer daarop toegespits om die foetale sterftesyfer af te bring tot 'n minimum. Twintig jaar gelede was dit byna krimineel om 'n keisersnee to maak, en alles is gedoen om 'n vaginale verlossing te bewerkstellig. Vandag word 'n keisersnee baie makliker aangedurf.

Die vraag wat ons dus in die gesig staar is of dit nie tyd is vir die pendulum om terug te swaai nie? Of het dit alreeds te ver geswaai? Word daar nie misbruik gemaak van keisersneë nie? Met die moderne antibiotiese middels, die verbeterde hospitaalgeriewe en die gemak waarmee 'n keisersnee uitgevoer kan word, word daar vandag dikwels nie twee maal gedink voordat 'n keisersnee uitgevoer word nie. Is die tyd van die bekende geduld van die verloskundige dan verby? Gaan die moderne verloskundige dan die kuns van die verloskunde verloor? Die ou gesegde dat ‚die bekwaamheid van 'n verloskundige beoordeel word volgens die manier waarop hy 'n stuit verlos' bestaan amper nie meer nie want hoe dikwels word 'n keisersnee nie gedoen met net 'n stuitligging as indikasie nie?

In hierdie eeu van meganisasie en outomatisasie moet ons egter nie vergeet dat die natuur altyd die beste is nie. Indien 'n vaginale verlossing moontlik is, is dit nog, ten spyte van al die bykomstige tegniese hulpmiddels, vir sowel die moeder as die baba die beste. Die moederlike en foetale mortaliteit by keisersnee is onder die beste omstandighede nog steeds baie hoër as by vaginale verlossings. Ons noem net 3 voorbeelde waaraan die keisersnee die moeder en die baba meer blootstel, naamlik: ruptuur van die uterus met daaropvolgende swangerskappe, pulmonêre embolisme en hyalien-membraan.

Wanneer 'n keisersnee gedoen word vir die jong vrou wat nog 'n lang vrugbare tyd voor haar het, vergeet ons dikwels hoe algemeen ruptuur van die uterus in die daaropvolgende swangerskappe is. Syfers in die literatuur variëer vanaf 0·25%[1] tot 3·3%[2] vir die laer segment, en 2·2%[3] tot 4·2%[4] vir die klassieke keisersnee. As ons dan verder daarop let dat die moederlike mortaliteit by ruptuur van die uterus vanaf 4% tot 50%[4] varieër en die foetale mortaliteit vanaf 40% tot 90%,[4] dan laat dit ons bepaald met angs terugkyk na ons maklike besluite in die verlede. Is ons dan geregverdig om so maklik oor te gaan tot 'n keisersnee as ons die moeder en die baba in daaropvolgende swangerskappe aan so 'n groot gevaar blootstel? Dit is wel waar dat hierdie syfers onder moderne hospitaalbehandeling verminder kan word, maar hoeveel van die verloskunde in ons land word nie nog in huise en onder baie primitiewe toestande gedoen nie?

Die voorkoms van pulmonêre embolisme na normale geboortes variëer vanaf 1 in 3,000[5] tot 1 in 10,000,[6] terwyl dit na buikoperasies — keisersnee ingesluit — variëer vanaf 1 in 400[5] tot 1 in 550. Hier weer, dus, is die kanse van die pasiënt wat 'n keisersnee moet ondergaan 6-20 keer groter as by spontane geboorte om hierdie gevreesde komplikasie te kry.

Wat van die foetus? Dit is keer op keer bewys dat selfs vir die te vroeggebore baba 'n vaginale verlossing beter as 'n keisersnee is. Dit is bevind dat 30%[7] van neonatale sterfgevalle die gevolg van hyalien-membraan is. Hierdie toestand kom grotendeels voor by babas wat met keisersnee gebore is en sommige skrywers beweer selfs dat dit *net* by sulke gevalle voorkom. Moet ons dan nie vra of ons dit nie aan onsself te wyte het dat die bogenoemde toestand vandag so algemeen geword het omdat ons so baie keisersneë doen nie?

Ons wil nie aanbeveel dat ons na die tydperk van 30

jaar gelede, toe alle soorte gevreesde vaginale manipulasies uitgevoer is om vaginale verlossings te bewerkstellig, moet teruggaan nie. Ons moet egter 'n meer gematigde houding in hierdie opsig inneem. In ons land met sy wyduitgestrekte vlaktes waar die verloskunde nog so dikwels onder baie primitiewe toestande moet geskied, moet ons bepaald nie die behendige hande van die knap verloskundige deur onbruik verlore laat gaan nie.

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