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Islet autoantibodies in cord blood could be a risk factor for future diabetes

Dear Sir,

Bonfanti et al. present an interesting investigation in their letter and make comparisons with our recent study [1]. Their material differs from ours on several important points. Our study included 81 children with an age at diagnosis of Type I (insulin-dependent) diabetes mellitus from 0.9 years to 14.9 years (median 8.4 years). We had a different methodology because frozen sera were used allowing analysis of GAD65Ab, ICA512Ab and IAA as well as ICA. Apart from those differences it is important to emphasise that no child who developed Type I diabetes before 5 years of age, had cord blood GAD65Ab, ICA512Ab or IAA in our study. This is in complete agreement with the findings by Bonfanti et al. In another study of islet autoantibodies, one out of six children developing Type I diabetes at an age of 11–29 months had ICA in the cord blood [2].

The cord blood autoantibody-positive children in our study did not have an earlier clinical onset of Type I diabetes compared with the antibody-negative ones. Intrauterine factors could still have an important role. This is suggested by the findings that congenital rubella is associated with a greatly increased risk of Type I diabetes 10–30 years after the intrauterine infection.

Transport of maternal IgG over the placenta barrier is an active Fc- γ receptor-mediated process. It starts in the 17th week of gestation and gives the newborn full-term baby an IgG concentration which is 150% of that of the mother [3]. In our study, sera were also available from the mother at the time of delivery in 13 out of 14 children with islet autoantibodies. Positivity of the concomitant autoantibody in the mother could only be detected in 2 out of 13 subjects. This is in contrast to our earlier study of non-diabetic children born to non-diabetic mothers that develop Type I diabetes 1–18 years after pregnancy. All children ($n = 14$) with islet antibodies in cord blood, had mothers seropositive for the same autoantibodies [4].

The possibility of fetally produced autoantibodies is not completely excluded. The ability of the fetus to react with antenatal active immunisation and IgG production has been shown earlier. Vaccination against tetanus of the mother between 5–8 months of gestation, resulted in neonatally detected anti-tetanus IgG and IgM produced by the fetus [5]. An earlier

study implicated that antibodies are produced by the fetus when one of the infants with antibody-positivity at birth continued to be IAA positive at follow-up at 2 years of age [6]. Concordant with this is our observation that the ICA antigen is present in the fetal pancreas which shows the possibility of autoimmune reactions against beta cells in utero [7]. We have earlier shown the presence of non-islet pancreatic autoantibodies in two children with permanent neonatal Type I diabetes mellitus [8].

The main finding in our study was: although offsprings to mothers with Type I diabetes were excluded, the children later developing Type I diabetes had statistically significantly higher prevalence of cord blood islet autoantibodies compared with control subjects. This implicates cord blood islet autoantibodies as a risk factor for future Type I diabetes independently of the origin of these autoantibodies.

Yours sincerely,

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