

A SELECTION OF OBSTETRIC MEDICINE ARTICLES AND COMMENTARY THAT APPEARED IN THE BRITISH MEDICAL JOURNAL FROM 1999 TO 2000 BY DR. PETER R. GARNER, MD., F.R.C.P., F.A.C.P., Department of Obstetrics/Gynecology and Medicine, University of Ottawa, Ottawa, Canada.

ARTICLE 1

The influence of maternal age at delivery and birth order on risk of Type I Diabetes in childhood: prospective population based family study.

Bingley PJ, Douek IF, Rogers CA, et al. BMJ 2000;31:420-424.

Objective of this trial was to examine the influence of parental age at delivery and birth order on the subsequent risk of childhood Type I Diabetes.

Design. This was a prospective population based family study coming from the Oxford Regional Health Authority in the UK.

Participants. 1375 families were studied in which one child or more had Type I Diabetes.

Main outcome measures. These were disease free survival and hazard ratios for the development of Type I Diabetes in all offspring assessed by Cox proportional hazard regression.

Results. Maternal age at delivery was strongly related to risk of Type I Diabetes in the offspring. The risk increased by 25% for each five year band of maternal age, so that maternal age at delivery of 45 years or more was associated with a relative risk of 3.1, compared with a maternal age of less than 20 years. Paternal age was also associated with a 9% increased for each five year increased in paternal age. The relative risk of diabetes, adjusted for parental age at delivery and sex of offspring decreased with increasing birth order. The overall effect was a 15% risk reduction per child born.

Conclusions. A strong association was found between increasing maternal age at delivery and the risk of Type I Diabetes in the child. The risk was highest in the firstborn child and decreased progressively with higher birth order. The fetal environment seems to have a strong influence on the risk of Type I Diabetes in the child. The increase in maternal age at delivery in the United Kingdom over the past two decades could partly account for the increased incidence of childhood Type I Diabetes over this period.

Commentary. Prior epidemiological studies have shown that if a mother has Type I Diabetes, then the likelihood of her child developing subsequently Type I Diabetes is 2%, whereas if the father has Type I Diabetes the likelihood is 6%. If both parents have Type I Diabetes the risk rises to 20%. The genetics of Type I Diabetes is the geneticist's graveyard, but obviously from this study the genetic risk of developing Type I Diabetes is modified by some intrauterine environmental factor. What this environmental factor is remains speculative. One possibility

supported by epidemiological observations in atopic conditions, including asthma, is that the maturation of the immune system may be influenced by maternal age. Thus, the authors speculate that factors associated with high maternal age influence maturation of the immune system in the offspring, increasing the predisposition towards Type I Diabetes in later life.

An acquired genetic abnormality seems unlikely because, although parental age is associated with several genetic disorders, no chromosomal abnormalities are present in Type I Diabetes. the authors speculate that intrauterine viral infection can influence subsequent risk of diabetes in the child and might account for the higher risk in firstborn children. Whatever the mechanism, the increase in maternal age at delivery in both North American and the United Kingdom could partly account for the increase in incidence of childhood Type I Diabetes.