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LETTER

Mitogenic effect of insulin and developmental programming

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To the Editor: We read with great interest the 'For debate' article by Draznin in the February issue of *Diabetologia* on the mitogenic effect of insulin as a possible causal factor for cancer [1]. This association is of great scientific interest and could have a major impact on the clinical management of the many thousands of patients treated with insulin worldwide. Furthermore, this finding can be extended to the occurrence of cancer within the framework of developmental programming. Developmental programming is the process of an insult in utero and/or in early postnatal life inducing a permanent response in the fetus and the newborn, leading to enhanced susceptibility to later diseases.

In diabetic pregnancies, the insulin-producing beta cells of the fetus are hyperactive, leading to hyperinsulinism and macrosomia [2, 3]. Women who were macrosomic at birth have an increased incidence of breast cancer in later life [4], and it has been postulated that hyperinsulinism during fetal life has a mitogenic effect on the developing breast [5]. Moreover, studies have shown that fetal macrosomia is related to different tumours of the central and peripheral nervous system in later life [6, 7].

We would like to underline the fact that the mitogenic effect of insulin suggested by Draznin is indeed a problem during fetal life, because high levels of insulin place the developing organs under stress during critical periods of differentiation. The treatment of the diabetic pregnant woman should focus on preventing hyperinsulinism in the fetus. The fetuses of mothers who are obese during pregnancy are often observed to have hyperinsulinism and macrosomia [8]. Since obesity is an important health problem, of even epidemic proportions, it is clear that efforts should be made to reduce obesity among women of reproductive age. This, as well as universal screening for, and adequate treatment of, diabetes during pregnancy may help to reduce the risk of cancer in the offspring by preventing fetal hyperinsulinism.

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