References

1. Thomas BJ, Jarrett RJ, Keen H, Ruskin HJ (1982) Relation of habitual diet to fasting plasma insulin concentration and the insulin response to oral glucose. *Human Nutr Clin Nutr* 36c: 49–56
2. Arntzenius AC, Kromhout D, Barth J, Reiber JHC, Bruschke AVG, Buis B, van Gent CM, Kempen-Voogd N, Strikwerda S, van der Velde EA (1985) Diet, lipoproteins, and the progression of coronary atherosclerosis. *N Engl J Med* 312: 805–811

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Glycosylated haemoglobins in normal pregnancy

Dear Sir,

We read with interest the report by Worth et al. on glycosylated haemoglobin in normal pregnancy [1]. However, when comparing our results [2] with their own, the authors missed a crucial point: in our longitudinal study, we did not report the levels of total glycosylated haemoglobin (Hb A₁), but those of the subfraction haemoglobin A_{1c} (Hb A_{1c}), which is, at least theoretically, a more reliable indicator of long-term glycaemia than Hb A₁ [3]. The cation exchange chromatographic macrocolumn method used in our study [2] also permitted measurement of the minor fast haemoglobin components. The values of Hb A₁ can be calculated as the sum of these fractions (Hb A_{1c} plus the minor fast haemoglobins). Because fetal haemoglobin (Hb F) co-elutes with Hb A_{1c} in this method, as it does with Hb A₁ in the cation exchange method employed by Worth et al. [1] (Bio-Rad Hemoglobin A₁ by column test, Bio-Rad Laboratories, Richmond, California, USA), we also reported the levels of Hb F [2] measured by the method of Betke et al. [4]. The changes of corrected levels of Hb A₁ (the apparent Hb A₁ levels minus Hb F) are shown in Figure 1, and were similar

Fig. 1. Haemoglobin A₁ (mean $\pm$ SEM) expressed as a percentage of total haemoglobin and corrected for haemoglobin F in 29 healthy women during pregnancy and 3 months after delivery. Figures in parentheses indicate the number of patients sampled. ☆ $p < 0.01$, ☆☆ $p < 0.001$; significant differences versus post-partum. Δ $p < 0.01$, ΔΔ $p < 0.001$; significant differences versus 38 weeks (Student's paired t-test). Haemoglobin A₁ values from 21 healthy non-pregnant women are also shown

to those reported by Worth et al. [1]. On the other hand, no significant changes of Hb A_{1c} during normal pregnancy and no difference between Hb A_{1c} in pregnant and non-pregnant healthy women were observed in our study [2]. In puerperium (3 months after delivery) Hb A_{1c} was significantly higher than during pregnancy ($p < 0.001$) and in non-pregnant controls ($p < 0.05$), respectively [2].

We agree with the conclusion of Worth et al., that the use of any measurement of glycosylated haemoglobins in pregnancy should take account of pregnancy-specific normal ranges, each laboratory having its own reference values. Moreover, the measurement of Hb A_{1c} in assessing long-term glycaemic control seems to be preferable to that of Hb A₁ especially during pregnancy [2, 5], and comparison between these two parameters should be made with caution. Recently, we have employed an improved method for measuring Hb A_{1c} by rapid fully automated high-performance liquid chromatography, which also determines Hb F, Hb A_{1a}, Hb A_{1b} and Hb A₂ [6]. Thus the method both detects a recent fetomaternal blood transfer, and eliminates the problem of erroneously high glycosylated haemoglobin values due to this phenomenon.

Yours sincerely,

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References

1. Worth R, Potter JM, Drury J, Fraser RB, Cullen DR (1985) Glycosylated haemoglobin in normal pregnancy: a longitudinal study with two independent methods. *Diabetologia* 28: 76–79
2. Ylinen K, Hekali R, Teramo K (1981) Haemoglobin A_{1c} during pregnancy of insulin-dependent diabetics and healthy controls. *J Obstet Gynaecol* 1: 223–228
3. Mayer TK, Freedman ZR (1983) Protein glycosylation in diabetes mellitus – a review of laboratory measurements and of their clinical utility. *Clin Chim Acta* 127: 147–184
4. Betke K, Marti HR, Schlisht I (1959) Estimation of small percentages of foetal haemoglobin. *Nature* 184: 1877–1878
5. Kjaergaard J-J, Ditzel J (1979) Hemoglobin A_{1c} as an index of long-term blood glucose regulation in diabetic pregnancy. *Diabetes* 28: 694–696
6. Stenman U-H, Pesonen K, Ylinen K, Huhtala M-L, Teramo K (1984) Rapid chromatographic quantitation of glycosylated haemoglobins. *J Chromatography* 297: 327–332

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Intact glucose oxidation in human fetal pancreas

Dear Sir,

Harrison et al. have demonstrated for the first time on isolated human islets the sigmoidal nature of glucose-stimulated insulin release and its correlation with enhanced glucose oxidation [1]. Their work should be applauded because many studies of rodent islets may be applicable to man but this should never be assumed. Our own data has shown previously the marked discrepancies between the capacity of fetal mouse pancreas and human fetal pancreas to secrete insulin in response to a glucose stimulus [2, 3].

Subsequent to our finding that human fetal pancreas was unresponsive to glucose, and that a single defect in early glycolysis or deficiency of cyclic AMP was unlikely [3], a defect in glucose oxidation