

COMMENTS AND
RESPONSES

**Response to
Comment on:
Chakera et al.
Antenatal Diagnosis
of Fetal Genotype
Determines if
Maternal
Hyperglycemia due
to a Glucokinase
Mutation Requires
Treatment.
Diabetes Care
2012;35:1832-
1834**

We appreciate the comments by Tartaglia et al. (1) in response to our study. We agree with Tartaglia et al. that maternal glucose management in glucokinase (*GCK*) pregnancy should be guided by knowledge of whether the fetus has inherited the mutation from the mother. In our article (2), we propose that fetal genetic testing should be performed if chorionic villus sampling (CVS) or amniocentesis is performed for another reason. Amniocentesis/CVS cannot be recommended as a routine procedure in the management of pregnant women with *GCK* mutations, as the 1% miscarriage rate is unacceptably high and outweighs the potential benefits of knowing fetal *GCK* genotype.

At present, fetal growth on ultrasound is used as a surrogate marker for fetal *GCK* status with increasing growth seen when the fetus has not inherited the mutation. Tartaglia et al. raise a valid point that the optimal cutoff is unclear, especially given uncertainty in measurements. If the fetus does not inherit the *GCK* mutation, maternal hyperglycemia results in an approximately sixfold increase in macrosomia, with mean increase in corrected birth weight of 700 g, ~1 SD difference (3). Using data from Hindmarsh et al. (4), we estimate that if the abdominal circumference exceeds the 75th percentile, the odds ratio that the child is unaffected is increased by 3.5-fold. If the abdominal circumference exceeds the 90th percentile, this odds ratio increases to sevenfold. The variability in measurement will determine the confidence limits around these estimates, but this will be reduced if repeated measures are used. For this reason we suggest having two values over the 75th percentile in scans separated by 2 weeks before starting insulin. One advantage of this cutoff is that it has an evidence base to support it because Buchanan et al. (5) used this cutoff in a randomized controlled trial.

Ultimately, noninvasive prenatal diagnosis (6) will replace the need to make an indirect assessment based on ultrasound and result in individualized care for pregnant women with *GCK* mutations.

ALI J. CHAKERA, MBCHB^{1,2}
VICTORIA L. CARLETON, MBBS^{3,4}
BEVERLEY SHIELDS, PHD¹
GLYNIS P. ROSS, MBBS³
ANDREW T. HATTERSLEY, DM^{1,2}

From the ¹Peninsula College of Medicine and Dentistry, University of Exeter, Exeter, U.K.; the ²Department of Diabetes and Endocrinology,

Royal Devon and Exeter Hospital, Exeter, U.K.; the ³Department of Endocrinology, Royal Prince Alfred Hospital, Sydney, Australia; and ⁴The University of Sydney, Sydney, Australia.

Corresponding author: Glynis P. Ross, glynis.ross@sswahs.nsw.gov.au.

DOI: 10.2337/dc12-1497

A.J.C. and V.L.C. contributed equally to this work.

© 2013 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

References

1. Tartaglia E, Iafusco D, Giuliano P, et al. Comment on: Chakera et al. Antenatal diagnosis of fetal genotype determines if maternal hyperglycemia due to a glucokinase mutation requires treatment. *Diabetes Care* 2012;35:1832–1834 (Letter). *Diabetes Care* 2013;36:e14. DOI: 10.2337/dc12-1364
2. Chakera AJ, Carleton VL, Ellard S, et al. Antenatal diagnosis of fetal genotype determines if maternal hyperglycemia due to a glucokinase mutation requires treatment. *Diabetes Care* 2012;35:1832–1834
3. Spyer G, Macleod KM, Shepherd M, Ellard S, Hattersley AT. Pregnancy outcome in patients with raised blood glucose due to a heterozygous glucokinase gene mutation. *Diabet Med* 2009;26:14–18
4. Hindmarsh PC, Geary MP, Rodeck CH, Kingdom JC, Cole TJ. Intrauterine growth and its relationship to size and shape at birth. *Pediatr Res* 2002;52:263–268
5. Buchanan TA, Kjos SL, Montoro MN, et al. Use of fetal ultrasound to select metabolic therapy for pregnancies complicated by mild gestational diabetes. *Diabetes Care* 1994;17:275–283
6. Lo YM. Fetal nucleic acids in maternal blood: the promises. *Clin Chem Lab Med* 2011;50:995–998