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DOI:
10.1016/j.ajog.2019.02.008

Document Version
Peer reviewed version

Citation for published version (Harvard):
MacKie, F, Morris, RK & Kilby, M 2019, 'Reply to: Twin-twin transfusion syndrome: need for mechanistic studies: Twin-twin transfusion syndrome: need for mechanistic studies', *American journal of obstetrics and gynecology*, vol. 220, no. 5, pp. 508. https://doi.org/10.1016/j.ajog.2019.02.008

Accepted Manuscript

Reply to: Twin-twin transfusion syndrome: Need for mechanistic studies

Fiona L. Mackie, MBChB, R. Katie Morris, PhD, Professor Mark D. Kilby, DSc

PII: S0002-9378(19)30349-7

DOI: https://doi.org/10.1016/j.ajog.2019.02.008

Reference: YMOB 12550

To appear in: *American Journal of Obstetrics and Gynecology*

Received Date: 15 January 2019

Accepted Date: 3 February 2019

Please cite this article as: Mackie FL, Morris RK, Kilby MD, Reply to: Twin-twin transfusion syndrome: Need for mechanistic studies, *American Journal of Obstetrics and Gynecology* (2019), doi: https://doi.org/10.1016/j.ajog.2019.02.008.

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Fiona L MACKIE MBChB, Centre for Women's & Children Health, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, UK.

R. Katie MORRIS PhD, Centre for Women's & Children Health, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, UK. West Midlands Fetal Medicine Centre, Birmingham Women's and Children's NHS Foundation Trust, Mindelsohn Way, Edgbaston, B15 2TG, UK.

Professor Mark D. KILBY DSc, Centre for Women's & Children Health, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, UK. West Midlands Fetal Medicine Centre, Birmingham Women's and Children's NHS Foundation Trust, Mindelsohn Way, Edgbaston, B15 2TG, UK.

Conflict of interest: the authors report no conflicts of interest

Funding: FLM is funded by the Richard and Jack Wiseman Trust but they had no involvement in the reply.

Corresponding author: Fiona L MACKIE MBChB, Centre for Women's & Children Health, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, UK. +441216264535 (work) fionamackie@doctors.org.uk

Word count: 293

We thank Professor Ross et al. for their interest in our publication 'Early prognostic factors of outcomes in monochorionic twin pregnancy: systematic review and meta-analysis' (Mackie 2018), and for kindly highlighting important areas of future research.

We agree that unbalanced placental vascular anastomoses are pivotal to the pathophysiology of twin-twin transfusion syndrome (TTTS). Computational and mathematical studies, including those performed by Professor Ross, have demonstrated that fluid mechanics are involved in TTTS and have improved knowledge surrounding TTTS. However, to our knowledge there have been no studies able to translate the models' findings into real-life measurable parameters as it is very difficult to visualise placental anastomoses, irrespective of type, using colour flow or power Doppler, especially in the first trimester. Professor Christoph Lees is examining the use of advanced dynamic flow (ADF) and superb micro-vascular imaging (SMI) Doppler, although this is an early-stage research tool (personal communication).

The study by Nakata et al. (Nakata 2004) that Professor Ross et al. reference that evaluates invasive intra-amniotic Doppler placental anastomoses blood flow measurement received criticism regarding the lack of validation of the technique and the findings (Taylor 2004), and as far as the authors are aware, these findings have not been validated in real-life, nor have the findings of the computational modelling studies. Thus the search continues for novel first trimester predictive markers for

TTTS, which is hampered by the lack of animal models. We are exploring other aspects of TTTS pathogenesis, by investigating the use of maternal serum analytes and microRNA as predictive tests, which would be evaluated in conjunction with ultrasound assessment (Mackie 2017). Currently, as there is no prevention for TTTS, even with the identification of a 'high-risk' group, sequential ultrasound monitoring of the amniotic fluid deepest vertical pools would be required.

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