Alastair H. MacLennan, Suzanna C. Thompson, Jozef Gecz
Cerebral palsy: causes, pathways, and the role of genetic variants
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even potentially lifesaving to underline the fact that a woman with an unscarred uterus can be 100% sure of avoiding uterine rupture if they avoid medical induction and augmentation. ■

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REPLY

We appreciate Ms Cohain's interest in our manuscript and concerns regarding the association between oxytocin use and uterine rupture.[1] Unfortunately, oxytocin use was only one obstetric covariate and not our main focus. In addition, the facts presented in Ms Cohain's letter are incorrect; 4 women with primary uterine rupture were neither induced nor received oxytocin augmentation. The claim that "the unscarred uterus that is not artificially forced to contract, will not contract so hard as to explode itself" should not, as the majority of situations in medicine and in obstetrics, be considered absolute. We speculate that underlying undiagnosed connective tissue aberrations or genetic factors may have influenced the development of uterine rupture in these 4 women. Unfortunately, our study design precludes an investigation of causation.

The incidence of oxytocin use was greater in unscarred cases (80% vs 37%, odds ratio 6.7, $P < .001$). This statistic shows an association between oxytocin use in unscarred uterine ruptures compared with scarred uterine ruptures but does not prove causation. Our comment that the increased rate of oxytocin use in primary uterine rupture cases "likely reflect differences in provider management among women with a scarred uterus" is our acknowledgement that association and causation are separate and that all statistics must be interpreted within clinical practice. Furthermore, this statement reflects provider differences in the management of women with and without a uterine scar, because many obstetric providers minimize the use of labor induction and oxytocin augmentation in the setting of a previous uterine scar. The use of oxytocin may increase the risk for primary uterine rupture, because it is a known risk factor for rupture of the scarred uterus.[2]

Ms Cohain references Tversky and Kahneman's "Belief in the Law of Small Numbers" to question our results and interpretation.[3] We acknowledge the (thankfully) few primary uterine rupture cases as a study limitation. Tversky and Kahneman caution the observer from making assumptions from small numbers (although they never define what constitutes a "small number"—in their paper, 20 subjects is seen as a reasonable sample size). As physician scientists, however, we must make do with clinical realities.

In conclusion, we urge all clinicians providing obstetric care to women to recognize that risk factors and associations are powerful tools but they are not absolutes. Although extremely rare, devastating obstetric outcomes such as primary uterine rupture (even in the labor absence of induction or augmentation) may occur in any gravida, with potentially catastrophic morbidity and mortality. ■

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Cerebral palsy: Causes, pathways, and the role of genetic variants

TO THE EDITORS: I read with great interest the article by MacLennan et al[1] on cerebral palsy (CP), in which the authors provided a comprehensive outline of the varied pathogenesis as well as associated clinical risk factors relevant to the practicing clinician.

I was, however, surprised to read that a strong emphasis was not placed on the use of magnesium sulphate in reducing the risk of CP. Although this was mentioned under the "Interventions to prevent CP" subheading, it was limited to a small paragraph, leaving potential readers saddened or

discouraged by the lack of therapeutic options available to prevent such a disabling disorder. Again, under the "Future clinical applications" subheading, the authors declared that the long-term goal is the prevention of CP—with no mention or any arguments made as to the future role of such therapy.

Since 2010, both the United States and Australasia have been on the forefront in establishing national guidelines on the use of magnesium sulphate for neuroprotection of very preterm infants.[2] As referenced by the authors, this was based on good-quality randomized controlled trials and meta-analyses that demonstrated its effectiveness. Although other countries such as Canada have followed through, the United Kingdom remained guarded and cited the large number needed to treat for benefit (as compared with antenatal administration of corticosteroids to prevent respiratory distress syndrome) as 1 of the possible reservations.[3] I appreciate that the available data are limited for late-preterm and term infants, and hope that the MAGENTA study[4]—an ongoing randomised controlled trial assessing antenatal magnesium sulphate administration between 30 and 34 weeks gestation—will provide further evidence to support to such a policy.

The magnitude might be small, but antenatal administration of magnesium sulphate may be the greatest primary preventive intervention that we obstetricians should practice on a daily basis to prevent CP. ■

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REPLY

We thank Dr Lim for his interest in our review of the causes, pathways, and, in particular, the role of genetic variants that may contribute to cerebral palsy.[1] It was a big topic, and with limited space we focused on causation and the increasing evidence for genetic causation in many of the cerebral palsies. We are very aware and supportive of the admirable work in our department of Professor Caroline Crowther's team and many others on the use of magnesium sulphate in very-preterm labor to help reduce slightly the risk of cerebral palsy in this subgroup. We applaud this clinical intervention. However, for major progress to be made in reducing all types of cerebral palsy, we need to conduct much more neurodevelopmental research extending back to conception. ■

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