## REPLY

Check for updates

We appreciate the thoughtful comments of Dr Worley and his dedication to the care of this special group of children that we set out to help by exploring the possibility of fetal surgery for myelomeningocele more than 20 years ago. To address his concerns specifically:

1. We agree that 30 months of age is too young to make definitive assessments in children who grow and mature at varying rates. Thirty months was selected as the earliest time for which there existed validated tools to make an initial attempt at understanding the impact of fetal surgery on motor function. On both the Bayley and Peabody motor scales, the prenatal surgery group had better motor function than the postnatal group, even though those in the prenatal surgery group had more severe anatomic levels of lesions. We very much look forward to the upcoming publication of MOMS 2 results, which evaluates the children at ages 6−10 years.
2. Male sex was acknowledged to be an identified finding, and we await longer-term follow-up data from MOMS 2.
3. The issue of the role of spinal cord tethering and other postnatal surgeries and their role in long-term motor function impairment is important. The relationship of these interventions to long-term outcomes as well as their impact on cost and quality of life need to be further evaluated.
4. We agree that the issue of walking independently, while statistically true as narrowly defined in this rigorous trial, minimizes the complexity of this disorder and does not reflect the full impact of the initial location of the lesion and the role played on the future motor outcome of the child.

In addition to the improvement in hindbrain herniation and the decreased need for cerebrospinal fluid diversion, one of the important outcomes of the MOMs trial was the demonstration that there is hope for real amelioration of this disease. Previously the medical community believed that myelomeningocele was a fixed defect by 6 weeks of gestation. The MOMS trial has shown that there is ongoing damage in the prenatal period that could be prevented and/or repaired in utero. There are at least 10 laboratories today that are studying ways to improve the motor function with a variety of in utero treatment strategies including stem cells and other tissue engineering techniques as well as exploring ways to reduce the impact on pregnant women and their future reproductive potential. ■

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# Purinergic, P2X3 positive cells in amniotic membranes

Check for updates

We congratulate Dr Feng et al on their innovative studies demonstrating infection-induced thrombin production in preterm premature rupture of the membranes (PPROM).[1] Are similar results demonstrable in vivo using noncultured tissues, and which comes first: the infection or thrombin production? Or does prior denervation of the lower genital tract promote opportunist infection and a diverse cascade of pathologic changes in preterm labor/PPROM?[2]

Our observations in PPROM in simple, rolled membrane preparations demonstrate significant infiltration of both sets of membranes with sheets of inflammatory cells (Figure, A). However, in uncomplicated term pregnancies, we note a layer of cells that express purinergic, P2X3 "stretch" receptors that de-layers in labor (Figure, B and C). We are interested in their relationship to aquaporin (water) channels because aquaporins 1, 3, 8, and 9 are known to be present in membranes;[3] however, it is too early to draw firm conclusions about any associations yet. ■

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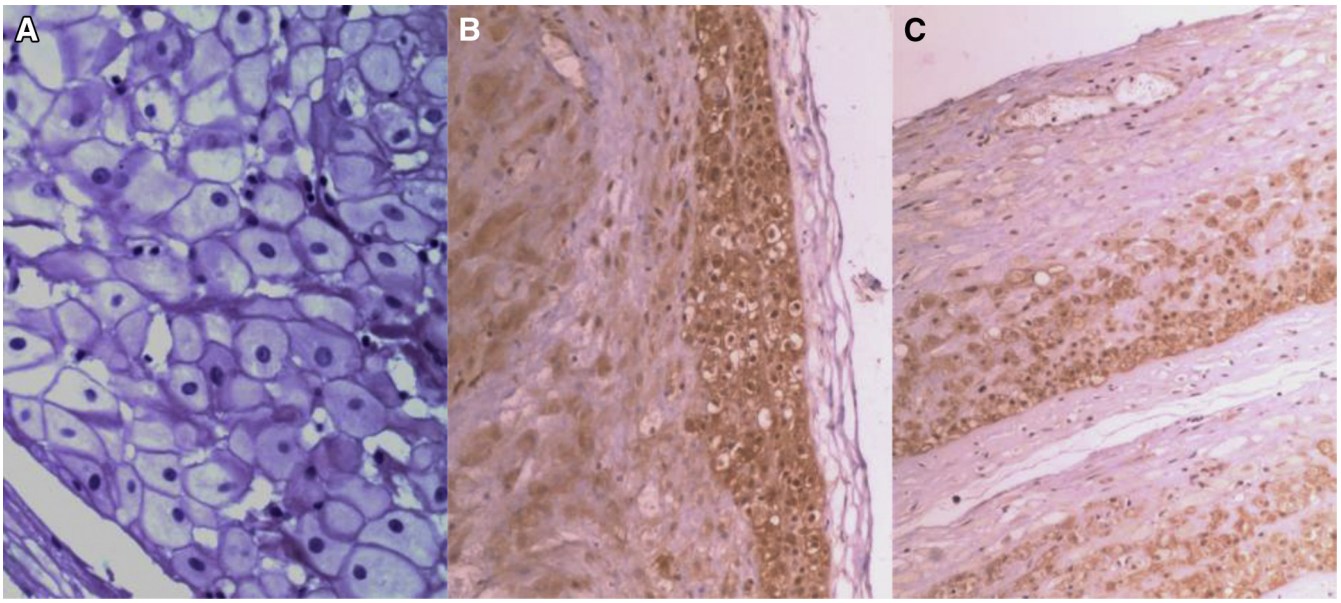
**FIGURE**
**Inflammatory cells, P2X3-positive cells, and de-layering of P2X3-positive layer of cells**




**A,** Sheets of inflammatory cells obliterate the membranes adjacent to the site of membrane rupture in a rolled membrane preparation (hematoxylin and eosin, magnification, ×200). **B,** A discrete layer of P2X3-positive cells in maternal chorion after cesarean delivery at term **(B)** (anti-P2X3, magnification, ×100). **C,** De-layering of the P2X3-positive layer of cells following spontaneous labor at term (anti-P2X3, magnification, ×100).

*P2X3*, P2X purinoceptor 3.

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## REPLY



We appreciate the thoughtful comments of Dr Quinn and colleagues regarding our recent article.[1] In response to their first question, we demonstrated only the results in vitro cell or tissue explants. The cause-effect is an important question; however, our model is not designed to answer a cause-effect relationship but primarily to show how infection can exaggerate a response with thrombin, a known agent that weakens membranes. Depending on the specific type of underlying pathology, thrombin may come first or in other cases infection may arise first.

It is also difficult to predict that denervation of vaginal epithelium is predisposing ascending infection. Vaginal epithelial cell exfoliation has been reported as a mechanism of ascending infection with Group B streptococcus but unsure that can be the reason for genital mycoplasma ascension.

Finally, congratulations on your new discoveries. ■

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