

The analogy with an orchestra is intended to focus on the need for a conductor to provide the brains in the central to peripheral organization of the heart, and this analogy also applies to the model of Barclay et al.²

In contrast, our model is like a soccer crowd, which demonstrates emergent properties of a semistable system (<http://www.ajog.org/cms/attachment/2035140982/2050479843/mmcl.mp4>). Here coordinated events arise without an obvious initiating factor, and the mechanism clearly requires more than near-neighbor signaling. Although more detailed analogies are possible, we propose that the key to understanding human labor is to acknowledge the importance of action potential propagation at the cell and tissue level but also to consider the need for a second mechanism of tissue recruitment at the organ level. ■

Roger Smith, MD, PhD
 Mohammad Imtiaz, BSc (EE), PhD
 David Banney, MB, BS, BMus (Hons)
 Jonathan W. Paul, BSc (Biotech) (Hons), PhD
 Roger C. Young, MD, PhD
 Hunter Medical Research Institute Mothers and Babies Research Centre
 Lookout Road
 Newcastle, NSW 2310
 Australia
roger.smith@newcastle.edu.au

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Cervical pessary placement for prevention of preterm birth in unselected twin pregnancies: a randomized controlled trial

TO THE EDITORS: We have read with interest the article by Nicolaides et al.¹ It is noteworthy that the authors reported a high rate of removal of the cervical pessary. Specifically, this occurred in 22.3% of cases before 34 weeks of gestation. However, it would be interesting to know the gestational age at delivery (mean, interquartile range, and range) of these patients.

Similarly, it would be relevant to know the percentage of patients with a short cervix; if this figure was high and the pessary was removed shortly thereafter, this could explain the differences in the results of this trial and the subgroup analysis reported by others.²

In a previous study of pessary for prevent preterm birth in singletons, we did not remove the pessary in patients with preterm prelabor rupture of membranes, and this was not associated with differences in the frequency of clinical chorioamnionitis or neonatal sepsis between the pessary and control groups.³

A strength of the study reported in the Journal was that there was systematic training in the measurement of cervical length, which is the method to identify the patient at risk. In

contrast, for the key therapeutic intervention of the trial, many physicians responsible for inserting the pessary did not receive supervised training; this raises the question of whether inadequate placement of the pessary may explain the negative results in the subgroup analysis of patients with twin gestations and a short cervix.

We also noted a case in which cervical edema developed after insertion of the pessary, and this required removal under general anesthesia. It would be helpful to know if that patient had subclinical uterine contractions that may not have been identified prior to insertion of the pessary.

Our experience with insertion of a cervical pessary has led us to routinely ask patients whether they had developed pain and to monitor those with serial cervical length determinations. Patients whose cervix shortens may be developing preterm labor and benefit from tocolysis and corticosteroid administration.^{4,5} We would like to ask whether patients allocated to a cervical pessary and the control group underwent serial cervical length monitoring.

It is noteworthy that the authors reported the use of vaginal progesterone in 2 patients in the control group; in both cases,

the gestational age at delivery was greater than 34 weeks. Given that some recent studies have shown that vaginal progesterone may reduce the rate of preterm birth by 30% and morbidity, could the administration of vaginal progesterone be a confounding factor in the results of the trial?^{5,7}

Finally, the authors used a random-sequence generation without stratification by center; is it possible that such a method could introduce biases in the composition of the study groups? ■

Maria Goya, MD

Luis Cabero, MD, PhD, FACOG, FRCOG

Department of Obstetrics Hospital Universitari

Hospital Vall d'Hebron of Barcelona

Universitat Autònoma de Barcelona

Barcelona 08036, Spain

lcaberor@sego.es

The authors report no conflict of interest.

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REPLY

We thank Drs Goya and Cabero for their comments. Our trial involved 1180 unselected twin pregnancies randomized at 20⁺⁰ to 24⁺⁶ weeks' gestation to cervical pessary vs expectant management; there was no significant difference between the groups in spontaneous birth < 34 weeks (13.6% vs 12.9%),

which was the primary outcome of the study. In both groups there was an inverse correlation between the cervical length at randomization and the rate of spontaneous birth at < 34 weeks, which was not significantly different between the 2 groups.

The pessary was removed at < 34 weeks in 22.3% (131 of 588) of pregnancies, including 100 before elective delivery for medical indications, such as severe preeclampsia, preterm labor or preterm prelabor rupture of membranes, and 31 for patient request.

Subsequently, there was birth at < 34 weeks in 91% of the first group and 23% of the patient request group; in the latter group, the rate of preterm birth was not significantly higher than that in the total group treated with pessary placement. Consequently, in most cases the pessary was removed because the patients were about to deliver and such delivery could not have been prevented had the pessary been left in situ.

In the paper we acknowledge that a potential limitation of our study is that many research team doctors were involved in the insertion of the pessary and they did not receive supervised training in doing so. It is therefore not possible to be certain that there was appropriate insertion in all cases. However, the same was also true for the study of Liem et al,¹ and therefore, this cannot be the explanation for the differences in the results of the 2 trials.

Serial measurements of cervical length and use of tocolytics and steroids would not have influenced the results of the trial because women in the control group received the same obstetrical care as those in the pessary group. Progesterone was administered to 2 patients in the control group; had this not been done and both patients delivered preterm, this would not have affected the conclusions of the study.

Randomization resulted in 2 groups with similar maternal and pregnancy characteristics. ■

Professor Kypros H. Nicolaides

Harris Birthright Research Centre for Fetal Medicine

King's College London

London SE5 9RS, United Kingdom

kypros@fetalmedicine.com

kypros@technocom.com

The author reports no conflict of interest.

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