3. The authors have used prophylactic hydrocortisone in all ewe fetuses to avoid fluctuations in blood pressure and to prevent hypotension, which is very common in this age group. But it should be used more cautiously in human fetuses, given the fact that there is proven long-term neurologic adverse effects on the developing brain with exposure to corticosteroids; further studies are warranted on this matter.
4. The procedure of transition from intrauterine period to extra uterine environment (artificial womb) required nearly 15 minutes. The readers would be interested to know how stabilization was done in the transition period and what extra support was needed. Because a 15-minute period may be long enough for the initiation of first breath, thereby resulting in infliction of lung injury.
5. Differences in the maturation process of fetal lung and brain in ewes and humans may have resulted in a favorable outcome for fetal ewes; the same result might not be replicated in human fetuses.
6. Because the fetus will be grown in artificial environment, it will be exposed to all types of noxious stimulus, to the risk of infection, and to the risk of brain injury, compared to natural pregnancy of the same gestation.
7. Last, there are some long-standing unsolved ethical issues that need to be answered before this technology gets adapted to humans.
   - What should be the ideal gestation age for use of this technology? Although the authors have mentioned it to be of 20−24 weeks gestation, with passage of time and increase in awareness, this technology will be used/misused in a wider gestation.
   - Similarly, it might push the limit of viability and force the age of abortion lower.
   - It might replace the role of a woman in natural pregnancy, which might be considered risky and stigmatized. People will adapt to partial ectogenesis, even without any valid underlying reason. This might result in questioning facilities like "maternity leave" in employment for women.
   - Who should use? Use of artificial womb technology may give a false sense of security and promote its use in lower middle income countries where there is a lack of adequate infrastructure and supportive care. It might promote unjustified use of limited resources especially in lower middle income countries.
   - Legal rights? Because the hypothetical human fetus (so called *gestateling*) would be growing in the artificial womb, who will bear the legal responsibility? Is it the neonatologist? The obstetricians? Or the fetal surgeons. Would it have all legal rights like that of a born neonate?

Finally, we would conclude that this is definitely cutting edge technology. Until the challenges that are related to technical limitation, the provision of adequate nutrition, the prevention of infection, and the ethical issues are addressed systematically, there is a long way to go before it replace the natural womb. ■

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REPLY

We thank Drs Sahoo and Gulla for their commentary on our recent publication[1] that described the preclinical development of an artificial placenta for extremely preterm infants. As discussed in our submission, an abbreviated study period was selected because of a lack of performance data for extremely preterm fetuses that are supported via an artificial placenta-based platform; moreover, there are good data to show that a significant percentage of morbidity and death occurs acutely after extreme preterm birth,[2] hence the duration of the studies undertaken. Drs Sahoo and Gulla are also quite correct to suggest, as we have done previously, that there are, of course, significant differences between ovine-based model systems and human beings.

The correspondents raise several interesting points in relation to the use of therapeutic steroids and antimicrobial agents during this experiment, highlighting the potential risk of their application. Although we do not disagree with the need to proceed cautiously, it is important to assess the use of these agents against the current expected outcomes for extremely preterm infants using existing technology, which are more often than not extremely poor.[3]

From an ethical standpoint, we agree that a robust conversation should take place well in advance of artificial placenta technology being adopted for use in the clinic. However, we do not share the same concerns as the correspondents regarding the potential for misuse of this platform. Given the profound improvements in preterm outcomes once 26−28 weeks gestation is achieved, it seems quite unlikely that an artificial placenta would be used across a wide range of

gestational ages. Moreover, because the use of an artificial placenta requires catheterization of umbilical vasculature and a system with sufficiently low resistance so as not to compromise the fetal heart, it seems unlikely that fetuses much below 20 weeks gestation could be adapted to or maintained on an artificial placenta.

Because, from a functional perspective, current artificial placenta-based systems essentially are limited to gas exchange and the delivery of nutrition and medication, it is not possible to use this technology to supplant the role of women in natural pregnancy. As is the case with current intensive neonatal care programs, the high-cost of using this technology similarly will do much to prevent its misuse. The question of legal status is indeed an interesting one; however, it does seem counterintuitive to introduce differential legal status and protections (relative to those currently conveyed to extremely preterm infants) simply on the basis of the application of an alternative means of providing gas exchange, nutrition, and medication.

Last, we are in complete agreement that, based on current publicly available data, there are many more years of work necessary before clinical application of this technology should be considered. We are very much of the view that moves to introduce this technology to the clinic in the near future should be viewed as extremely premature. ■

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Breastfeeding outcomes after assisted conception

Check for updates

TO THE EDITORS: We appreciate Barrera et al[1] for their analysis of breastfeeding outcomes among women who conceived spontaneously compared with women who underwent assisted conception. The authors reported shorter breastfeeding durations in women who conceived via assisted reproductive technologies (ART) compared with spontaneous conception, possibly explained by the greater likelihood of multiples birth and preterm infants that are observed in women who have conceived via ART. However, we find it important to draw attention to several limitations of this study.

First, we contend that the data that were collected from the cross-sectional surveillance system were inadequate in addressing the objective of the study: assessing breastfeeding outcomes. Given the ambiguity behind this phrase, we believe that a prospective cohort design with multiple questionnaires that are administered at different time points spanning the intrapartum and postpartum periods would be more appropriate in elucidating breastfeeding outcomes.

Second, although we acknowledge the predesigned format of the questionnaire, additional information is warranted to analyze clinically relevant factors in breastfeeding cessation. Further clarification is required if breastfeeding cessation originated from the infant or the mother. We propose that additional questions may include (1) exclusivity of breastfeeding, (2) the introduction of formula for nutritional supplementation because it is associated with shorter duration of breastfeeding,[2] (3) maternal intrapartum conditions, and (4) maternal attitudes toward breastfeeding. Open-ended questions that are not restricted to set options could generate a more meaningful classification regarding reasons behind breastfeeding cessation.

Third, despite the authors' intention to disentangle any causal relationships between ART and early breastfeeding cessation by adjusting for possible confounders, we identified several notable factors that were not included in the study design nor the authors' discussion. Early breastfeeding cessation is associated with risk factors that include lower breastfeeding self-efficacy, introduction of a pacifier, and work-related factors such as early return to paid work.[3,4] Furthermore, it is important to acknowledge the lack of