Explanations of the obstetric dilemma: evolutionary conflict exacerbates health problems in pregnancy and childbirth

Dakota E. McCoy[1], Jennifer Kotler[1,*], Brianna Weir, J. Arvid Ågren[3,4]

[1]Department of Ecology and Evolution, The University of Chicago, Chicago, IL, USA
[3]Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, OH, USA
[4]Evolutionary Biology, Department of Ecology and Genetics, Uppsala University, Uppsala, Sweden

*Corresponding author: jlkotler@gmail.com

Abstract/Summary:

In their recent *Nature Ecology and Evolution* paper, Webb and colleagues show that chimpanzee pelvises present a tight fit for newborn infants, just like in humans. Their detailed 3D characterization shows that the degree of the squeeze is comparable between humans and chimpanzees, and that both have sexually dimorphic pelvises. The authors challenge the so-called "obstetric dilemma" – the long-standing hypothesis that pregnancy and childbirth are particularly dangerous in humans as a consequence of being both bipedal and large-brained. If cephalopelvic proportions are an insufficient explanation for complications in human pregnancy, new perspectives are required to address this dilemma. Webb and colleagues suggest that humans sit at one end of a spectrum of complicated primate births shaped by a gradual series of obstetric compromises, exemplified by the metric of birth canal contortion. Here, we offer an additional, complementary explanation for difficult human childbirth. Maternal-fetal genetic conflict over resource allocation explains many of the most severe complications of pregnancy and childbirth. Two of the most common complications are hypertension and hemorrhage, both of which result directly from fetal manipulation of maternal vasculature to increase resources flowing to the placenta. We suggest that maternal-fetal conflict is more severe in humans than in other apes as a result of cooperative breeding. Humans have more cooperative child care than other apes, so relatives can help compensate for relatively poorer infant outcomes if the mother is marginally more weakened in pregnancy.

Main Text

Above all else, natural selection prioritizes passing on one's genetic material to a new generation. Why, then, is human pregnancy and childbirth such a risky, uncertain affair? The World Health Organization reports that about 800 women die every day due to complications stemming from pregnancy and childbirth[2]. By traditional medical explanations, human pregnancy optimizes fetal health, maternal health, and easy transmission of nutrients from mother to embryo[3,4]. Early evolutionary explanations for health complications during pregnancy were presented as a result of a narrow maternal pelvis, for bipedalism, and a wide infant head, for our large brains[5]. However, as Webb et al.[1] show, our pelvis-neonate squeeze is comparable

to that of chimps, who tend to have quicker and less complicated births. Their results upturn such straightforward explanations and introduce a model of gradual compromises. Furthermore, the leading causes of maternal deaths are hemorrhage (27.1% of deaths) and hypertension (14.0%), the latter of which is unrelated to obstructed delivery[2].

Birth canal contortion is not the only evolutionary trade-off; maternal-fetal genetic conflict helps explain some of the health outcomes we see in human pregnancy. In mammals broadly, pregnancy is an exception to the general idea that features of bodily function optimize the unitary selective goal of a body passing on its genes. Gestation is a unique phase of mammalian life, where a single body houses two genetically different individuals[6]. Because they do not share 100% of their genes, conflicts develop between mother and embryo[7]. Such conflicts typically play out through marginal shifts in resource allocation. A mother can either invest more in a single child or direct that investment toward producing and supporting other children (e.g., by maintaining adequate body condition). From the evolutionary perspective of a given embryo, however, natural selection has favored behaviors that increase resource extraction from the mother, even if that comes at some expense to their mother's fitness.

Pregnancy is thus an intimate evolutionary arms race. Fetuses are under selection to extract resources; mothers have evolved countermeasures to resist fetal manipulation[8]. As in a tug-of-war, both sides strive mightily to gain millimeters, but a powerful heave or a slip of the fingers sends all participants tumbling. Closely matched contestants maintain the larger posture while gaining small wins in resource availability. But if the rope slips, through small flaws or mutations in the intricate genetic mechanism, both parties may fall to paradoxically harmful effects. A well-studied example of fetal armaments and maternal countermeasures in humans can be seen in maternal blood pressure control. Hypertension is a leading cause of maternal death and gestational health complications across developed and developing regions globally[2]. However, the embryo benefits from relatively higher maternal blood pressure, as it is associated with higher rates of nutrient delivery and increased birth weights[9]. Fetuses are therefore under selection to remodel maternal tissue to wrest control of blood pressure and nutrient delivery from the mother [10,11]. Fetal cells have been shown to progressively invade maternal blood vessels called spiral arteries, remodeling them into wide channels that cannot constrict [12]. Mothers, in turn, have been selected to "tug back," gradually restraining this invasion[13]: in response to the presence of fetal cells, the mother's spiral arteries grow longer and more serpentine, restricting her blood flow[10].

Once maternal arteries are fully remodeled, the volume of maternal blood reaching the embryo is no longer under the control of local maternal tissue[11]. To balance increasing fetal demands on resources, the mother reduces her systemic blood pressure. This resistance to fetal manipulation may explain why pregnant women have high rates of vasodilation in their extremities, lowering systemic blood pressure[10]. Fetal attempts to "pull back" by increasing systemic maternal blood pressure[14], for example by releasing factors that damage maternal vessel endothelium causing

arterioles to constrict[10], can risk maternal health. Importantly, these maternal-fetal adaptations are seen in all pregnancies, not just those that result in life-threatening hypertensive outcomes. However, when blood pressure rises high enough, medical hypertension develops and may become life-threatening. This is an extreme outcome, where all players in the tug-of-war may collapse, even though smaller increases benefit the fetus.

Circulatory damage caused by maternal-fetal conflict also contributes to severe bleeding after childbirth. Postpartum hemorrhage is the most severe and common complication of pregnancy, causing 27.1% of maternal deaths worldwide[2]. Approximately 6% of all births result in postpartum hemorrhage (500mL blood loss or more), and 1.86% of all births lead to severe postpartum hemorrhage (1000mL blood loss or more)[15]. The most important acute cause of postpartum hemorrhage is uterine atony (accounting for ~90% of cases), in which the uterus fails to contract after delivery to clamp blood vessels and stop bleeding[15].

Genetic conflict also helps explain the high prevalence of postpartum hemorrhage in humans. Placentation during human pregnancies is unusually deep and invasive compared to other mammals[16]. Consequently, the placenta does not always separate properly from the uterine wall at birth, causing extreme bleeding. Further, human embryos (more so than other apes) modify maternal uterine blood vessels to increase blood flow to the placenta by both widening the radius and preventing constriction ([10]; see above). Maternal bodies must therefore use myometrial smooth muscle (not arterial smooth muscle) to contract[6], meaning the uterus cannot always contract properly to staunch blood flow after birth. Once again, the subtle impacts of the heightened genetic conflict present in humans can be seen in the high-risk outcomes of human birth relative to that of other apes.

Finally, serious complications resulting from maternal-fetal conflict extend beyond these two instances. For example, gestational diabetes arises from fetally-produced human placental lactogen via a tug-of-war over maternal blood glucose levels[10].

Returning to the original question: Why does maternal-fetal conflict seem more severe in humans than in chimpanzees? Haig presents an explanation in terms of inclusive fitness[6]. Throughout our evolutionary history, birthing women have relied on help from relatives, which other apes rarely do[17–19]. Hrdy[17] writes: “Almost everywhere new human mothers tolerate the proximity of familiar (and one assumes, trusted) conspecifics and voluntarily allow them to hold their newborns, something no other ape will do.” This cooperative breeding likely contributed to our earlier weaning and shorter interbirth intervals among apes[20]. In most other mammals, infant survival depends fully on their mother’s health after birth. Therefore, most mammalian fetuses can only demand so much from their mother at the risk of harming her health at a time when they require her ongoing care. The presence of genetically related helpers who share in the burden of childcare has reduced this selective pressure in humans, allowing for increased fetal demands[6].

To most chimpanzee infants, mother is irreplaceable; in humans, the brakes have been somewhat loosened on the constant tug-of-war, allowing for greater "tugging" by the fetus.

As Webb et al.[1] note, we sit at the unfortunate end of a spectrum of complicated primate births. The lens of evolutionary conflict helps explain why this is. Human pregnancy and childbirth are particularly fraught because gestation is an arena within which agents with different fitness interests struggle for control. "Healthy" pregnancy is not a matter of optimization, but of compromise.

Authorship Contributions

All four authors contributed equally to the development of the manuscript.

Conflicts of Interest

The authors declare no competing interests.

Bibliography

1. Webb, N. M. *et al.* Gradual exacerbation of obstetric constraints during hominoid evolution implied by re-evaluation of cephalopelvic fit in chimpanzees. *Nat. Ecol. Evol.* 1–11 (2024) doi:10.1038/s41559-024-02558-7.
2. Say, L. *et al.* Global causes of maternal death: A WHO systematic analysis. *Lancet Glob. Health* (2014) doi:10.1016/S2214-109X(14)70227-X.
3. Jim, B. & Karumanchi, S. A. Preeclampsia: Pathogenesis, Prevention, and Long-Term Complications. *Semin. Nephrol.* **37**, 386–397 (2017).
4. Pijnenborg, R., Vercruysse, L. & Hanssens, M. The Uterine Spiral Arteries In Human Pregnancy: Facts and Controversies. *Placenta* **27**, 939–958 (2006).
5. Wittman, A. B. & Wall, L. L. The evolutionary origins of obstructed labor: bipedalism, encephalization, and the human obstetric dilemma. *Obstet. Gynecol. Surv.* **62**, 739–748 (2007).
6. Haig, D. Cooperation and conflict in human pregnancy. *Curr. Biol.* **29**, R455–R458 (2019).
7. Trivers, R. L. Parent-Offspring Conflict. *Am. Zool.* **14**, 249–264 (1974).
8. Roberts, R. M. Interferon-τ and Pregnancy. *J. Interferon Cytokine Res.* **16**, 271–273 (1996).

9. Salafia, C. M., Xenophon, J., Vintzileos, A. M., Lerer, T. & Silberman, L. Fetal growth and placental pathology in maternal hypertensive diseases. *Clin. Exp. Hypertens. B.* **9**, 27–41 (1990).
10. Haig, D. Genetic Conflicts in Human Pregnancy. *Q. Rev. Biol.* **68**, 495–532 (1993).
11. Haig, D. Genetic conflicts of pregnancy and childhood. *Evol. Health Dis.* 77–90 (1999).
12. Pijnenborg, R., Robertson, W. B., Brosens, I. & Dixon, G. Review article: Trophoblast invasion and the establishment of haemochorial placentation in man and laboratory animals. *Placenta* (1981) doi:10.1016/S0143-4004(81)80042-2.
13. Haig, D. Putting up resistance: Maternal–fetal conflict over the control of uteroplacental blood flow. in *Endothelial Biomedicine* (2007). doi:10.1017/CBO9780511546198.018.
14. Page, E. W. The relation between hydatid moles, relative ischemia of the gravid uterus, and the placental origin of eclampsia. *Am J Obstet Gynecol* **37**, 291–293 (1939).
15. Carroli, G., Cuesta, C., Abalos, E. & Gulmezoglu, A. M. Epidemiology of postpartum haemorrhage: a systematic review. *Best Pract. Res. Clin. Obstet. Gynaecol.* (2008) doi:10.1016/j.bpobgyn.2008.08.004.
16. Abrams, E. T. & Rutherford, J. N. Framing postpartum hemorrhage as a consequence of human placental biology: An evolutionary and comparative perspective. *Am. Anthropol.* (2011) doi:10.1111/j.1548-1433.2011.01351.x.
17. Hrdy, S. B. Variable postpartum responsiveness among humans and other primates with “cooperative breeding”: A comparative and evolutionary perspective. *Horm. Behav.* **77**, 272–283 (2016).
18. Kenkel, W. M., Perkeybile, A. M. & Carter, C. S. The Neurobiological Causes and Effects of Alloparenting. *Dev. Neurobiol.* **77**, 214–232 (2017).
19. Sear, R. & Mace, R. Who keeps children alive? A review of the effects of kin on child survival. *Evol. Hum. Behav.* **29**, 1–18 (2008).
20. Kotler, J. & Haig, D. The tempo of human childhood: a maternal foot on the accelerator, a

paternal foot on the brake. *Evol. Anthropol. Issues News Rev.* **27**, 80–91 (2018).