Beyond the obstetric dilemma: evolutionary maternal-fetal conflict causes health problems in pregnancy and childbirth

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Abstract *(150 words)*

In excellent recent work, Webb and colleagues challenged the so-called "obstetric dilemma"—the long-standing hypothesis that human childbearing is particularly dangerous because we have a narrow pelvis but large infant heads (we are bipedal and smart). They showed that humans and chimpanzees have a comparable fetal-pelvic squeeze. What, then, causes risky childbirth in humans? Webb and colleagues describe a gradual series of physical obstetric compromises: e.g., our contorted birth canal allows bipedal movement but requires the fetus to rotate during birth. We propose an additional obstetric compromise between the evolutionary interests of mother and fetus, who experience genetic conflict over resource allocation. The fetus manipulates maternal vasculature to boost resources flowing to the placenta, benefiting itself but increasing the risk of maternal hypertension and hemorrhage. Following Haig, we suggest that maternal-fetal conflict harms human mothers more than other mammals because our cooperative infant care permits more damage to maternal health (when it grants some resource benefit to the fetus).

Lay Summary *(50 words)*

Pregnancy and childbirth seem more dangerous for humans than our closest primate relatives. Historically, this was thought to result from a large infant head and a small maternal pelvis. However, new evidence shows that chimpanzees experience a comparable "squeeze." Here, we show that evolutionary conflict between maternal and fetal genes over resources contributes to severe complications of childbirth in humans.

Main Text

1. Childbearing is risky for humans due to obstetric compromises: bipedalism vs. large-headed infants; maternal vs. fetal interests

Above all else, natural selection prioritizes passing on one's genetic material to offspring. 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[1]. By traditional medical explanations, human pregnancy optimizes fetal health, maternal health, and easy transmission of nutrients from mother to embryo[2,3]. Evolutionary biologists have long explained health complications during pregnancy as a result of a narrow maternal pelvis, for bipedalism, and a wide infant head, for our large brains[4]. This is termed the obstetric dilemma. However, Webb et al.[5] recently showed that our pelvis-neonate squeeze is comparable to that of chimps, who tend to have quicker and less complicated births, thereby upturning the straightforward head-is-too-big-for-pelvis explanations. Webb and colleagues[5] convincingly argue that humans sit at the unfortunate end of a spectrum of complicated primate births shaped by a gradual series of obstetric compromises. As human ancestors became large-bodied and, eventually, bipedal, we evolved shorter hip bones and a stiffer pubic symphysis, contorting our birth canal and requiring the infant to rotate during birth[5]. This compromise—mandatory rotation during birth to allow bone structure for large-bodied bipedalism—likely prolongs and complicates labor.

However, obstructed labor only causes 2.8% of maternal deaths worldwide, trailing the most common causes: severe blood loss (hemorrhage, 27.1% of deaths) and hypertension (14.0%)[1]. Obstructed labor can exacerbate hemorrhage [see, e.g.,[6]] and other problems, but hemorrhage usually arises from uterine atony (80%) and placental features (such as placenta previa and anomalous vasculature) [7,8] rather than delivery complications due to bone structure. In short, we suspect that another culprit—another obstetric compromise, to use Webb's apt terminology—further complicates childbearing, causing postpartum hemorrhage and hypertension.

Here, we argue that maternal-fetal genetic conflict is another obstetric compromise that causes some of the worst health outcomes of human pregnancy and childbirth. Just as a contorted birth canal compromises between bipedalism and birthing a large-headed infant[5], selection also navigates a compromise between maternal and fetal interests. Mammalian pregnancy is an exception to the idea that a body optimizes its phenotype for the unitary goal of passing on its genes. During pregnancy, a single body houses two genetically different individuals[9]. Because they do not share 100% of their genes, mother and embryo do not share 100% of their interests; they experience conflicts[10]. Embryos are selected to extract more resources than mothers are selected to provide. Mother and embryo clash[1] over marginal shifts in resource allocation. A mother can either invest more in a single child or use that investment to produce and support other children (e.g., by maintaining adequate body condition). From the evolutionary perspective of a given embryo, selection favors traits that extract more resources from the mother, even at some expense to her health and fitness. In **Section 2**, we demonstrate concrete evidence that maternal high blood pressure and hemorrhage result from fetal adaptations to control and extract resources.

[1] We adopt teleological language for clarity; see [11]

Pregnancy is thus an intimate evolutionary arms race. Fetuses are under selection to extract resources; mothers have evolved countermeasures to resist fetal manipulation[12]. As in a tug-of-war, both sides strain to gain millimeters, and even a small slip of the fingers sends all participants tumbling. Tug-of-wars seem, deceptively, like a stable equilibrium because the rope hardly moves for closely matched contestants. In normal pregnancies, mother and embryo are healthy. But tugs-of-war are unstable: if the rope slips, both parties go flying. Similarly, with small mutations in the intricate genetic mechanisms of pregnancy or tweaks to the environment, both mother and embryo experience surprisingly severe health complications. The genetic conflicts of pregnancy largely play out through the mechanism of imprinted genes. "Imprinted genes" are expressed differently when inherited from mothers or fathers; many such genes control resource demands during pregnancy, and mutations in these genes cause different– and extreme– health consequences depending on which copy is altered. For example, if a cluster of imprinted genes on Chromosome 15 is deleted, this deletion causes Prader-Willi Syndrome when paternally inherited and Angelman syndrome when maternally inherited–with opposite effects on maternal resource demands [13–17]. Pregnancy seems paradoxically risky, but the paradox is explained when we consider the conflict intrinsic to gestation.

Other mammals also face obstetric compromises over pelvic structure and maternal-fetal resource allocation, but humans seem to be *most* affected. Why? As for pelvic structure, our bipedal lifestyle puts us at the contorted end of the spectrum among apes. Then why do we have the most intense maternal-fetal clashes over how to allocate resources? In **Section 3,** we outline Haig's hypothesis that our evolutionary history of cooperative infant care relaxes selection on maternal health after birth; grandmothers and aunts help care for babies, freeing selection to favor more demanding embryos that extract more from mother at a larger cost to her health. Thus, two of humanity's strangest attributes—our bipedal lifestyle and our extreme cooperativity—make childbearing riskier.

2. Maternal high blood pressure, postpartum hemorrhage, and other complications result from fetal attempts to increase nutrient flow

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[1]. The embryo benefits from relatively higher maternal blood pressure, as it is associated with higher rates of nutrient delivery and increased birth weights[18]. Fetuses are therefore under selection to remodel maternal tissue to wrest control of blood pressure and nutrient delivery from the mother[19,20]. Fetal cells have been shown to progressively invade maternal blood vessels called spiral arteries, remodeling them into wide channels that cannot constrict[21]. Mothers, in turn, have been selected to gradually restrain this invasion[22]: in response to the presence of fetal cells, the mother's spiral arteries grow longer and more serpentine, restricting her blood flow[19].

Once maternal arteries are fully remodeled, local maternal tissue can no longer control the volume of maternal blood reaching the embryo[20]. To counteract increasing fetal demands on resources, the mother restricts blood flow by reducing her systemic blood pressure. This resistance to fetal manipulation may explain why pregnant women have high rates of vasodilation in their extremities, because this lowers systemic blood pressure[19]. The fetus responds by increasing systemic maternal blood pressure[23], e.g., releasing factors that damage maternal vessel endothelium causing arterioles to constrict[19]. These fetal strategies can harm 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 severe hypertension harms mother and likely also the fetus, even though smaller blood pressure increases benefit the fetus.

Severe bleeding after childbirth results directly from maternal-fetal conflict over resources. Postpartum hemorrhage is the most severe and common complication of pregnancy, causing 27.1% of maternal deaths worldwide[1]. 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)[24]. 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[24]. 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 ([19]; see above). Maternal bodies must therefore use myometrial smooth muscle (not arterial smooth muscle) to contract[9], meaning the uterus cannot always contract properly to staunch blood flow after birth.

Genetic conflict over placenta development also helps explain the high prevalence of postpartum hemorrhage in humans. Placentation during human pregnancies is unusually deep and invasive compared to other mammals[25]. This allows the fetus to have direct access to maternal arterial blood, limiting maternal control over nutrient provision and giving the fetus a path to release hormones and other substances directly into maternal circulation[19]. Consequently, the placenta does not always separate properly from the uterine wall at birth, causing extreme bleeding. Indeed, the deeper the placenta's invasion into the uterine muscle wall, the greater the risk of postpartum hemorrhage in humans (n=435 patients with placenta previa; [26]). 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 those of other mammals.

The examples presented above represent only two examples of serious pregnancy and birth complications resulting from maternal-fetal conflict. Several other examples have been described in the literature, including gestational diabetes, which arises from fetally produced human placental lactogen via a tug-of-war over maternal blood glucose levels[19], and hyperemesis gravidarum, which results from placentally produced GDF15[27].

3. Human child-bearing is riskier than in many other mammals because we evolved substantial alloparenting

Here, we argue that maternal-fetal conflict drives risky pregnancies. However, *all* eutherian pregnancies have, in principle, some degree of maternal-fetal conflict (a tug-of-war at their core). What makes humans special? Why does maternal-fetal conflict seem more severe in humans than in chimpanzees and, indeed, than in most other mammals? Haig presents an explanation in terms of inclusive fitness[9]. Throughout our evolutionary history, birthing women have relied on help from relatives, which other apes rarely do[28–30]. Hrdy[28] 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 substantially impacted certain areas of human evolution, e.g., driving our earlier weaning and shorter interbirth intervals compared to other apes[31]. Here, we suggest that cooperative breeding also complicates birth outcomes.

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 and, thus, themselves. But humans were somewhat freed from this selective constraint by the presence of helpers who relieved the unique demands on the mother. Haig[9] writes, "As a consequence, the indirect costs to babies of increased demands on mothers during pregnancy were relaxed in the human lineage, and fetuses responded evolutionarily by increasing their demands." 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—and *only* 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[9]. To most chimpanzee infants, mother is irreplaceable; not so in humans.

Conclusion

Approaching the seemingly paradoxical risks of pregnancy and birth with maternal-offspring conflict in mind helps clarify an evolutionary history that leaves humans in a uniquely complex and dangerous position. As Webb et al.[5] 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. Say L, Chou D, Gemmill A *et al.* Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health* 2014;**2**:e323–33.

2. Jim B, Karumanchi SA. Preeclampsia: Pathogenesis, Prevention, and Long-Term Complications. *Semin Nephrol* 2017;**37**:386–97.

3. Pijnenborg R, Vercruysse L, Hanssens M. The Uterine Spiral Arteries In Human Pregnancy: Facts and Controversies. *Placenta* 2006;**27**:939–58.

4. Wittman AB, Wall LL. The evolutionary origins of obstructed labor: bipedalism, encephalization, and the human obstetric dilemma. *Obstet Gynecol Surv* 2007;**62**:739–48.

5. Webb NM, Fornai C, Krenn VA *et al.* Gradual exacerbation of obstetric constraints during hominoid evolution implied by re-evaluation of cephalopelvic fit in chimpanzees. *Nat Ecol Evol* 2024;**8**:2228–38.

6. Hofmeyr G j. Obstructed labor: using better technologies to reduce mortality. *Int J Gynecol Obstet* 2004;**85**:S62–72.

7. Wetta LA, Szychowski JM, Seals MsS *et al.* Risk Factors for Uterine Atony/Postpartum Hemorrhage Requiring Treatment after Vaginal Delivery. *Am J Obstet Gynecol* 2013;**209**:51.e1-51.e6.

8. Stafford IA, Belfort MA, Dildy GA. Etiology and Management of Hemorrhage. In: Phelan JP, Pacheco LD, Foley MR, et al. (eds.). *Critical Care Obstetrics*. 1st ed. Wiley, 2018, 569–98.

9. Haig D. Cooperation and conflict in human pregnancy. *Curr Biol CB* 2019;**29**:R455–8.

10. Trivers R. Parent-Offspring Conflict. *Am Zool* 1974;**14**:249–64.

11. Ågren JA, Patten MM. Genetic conflicts and the case for licensed anthropomorphizing. *Behav Ecol Sociobiol* 2022;**76**:166.

12. Roberts RM. Interferon-tau and pregnancy. *J Interferon Cytokine Res Off J Int Soc Interferon Cytokine Res* 1996;**16**:271–3.

13. Kotler J, Mehr SA, Egner A *et al.* Response to music in Angelman syndrome contrasts with Prader-Willi syndrome. *Evol Hum Behav* 2019;**40**:420–6.

14. Kotler J, Balko K, Berall G *et al.* Nutritional Phases in Prader-Willi Syndrome: Evolutionary and Clinical Interpretations. *J Evol Med* 2016;**4**:1–7.

15. Mehr SA, Kotler J, Howard RM *et al.* Genomic Imprinting Is Implicated in the Psychology of Music. *Psychol Sci* 2017;**28**:1455–67.

16. Úbeda F. Evolution of genomic imprinting with biparental care: implications for Prader-Willi and Angelman syndromes. *PLoS Biol* 2008;**6**:1678–92.

17. Haig D, Wharton R. Prader-Willi syndrome and the evolution of human childhood. *Am J Hum Biol Off J Hum Biol Counc* 2003;**15**:320–9.

18. Salafia CM, Xenophon ,J., Vintzileos ,A. M. *et al.* Fetal Growth and Placental Pathology in Maternal Hypertensive Diseases. *Clin Exp Hypertens B* 1990;**9**:27–41.

19. Haig D. Genetic Conflicts in Human Pregnancy. *Q Rev Biol* 1993;**68**:495–532.

20. Haig D. Genetic conflicts of pregnancy and childhood. *Evol Health Dis* 1999;**77**:77–90.

21. Pijnenborg R, Robertson WB, Brosens I *et al.* Review article: trophoblast invasion and the establishment of haemochorial placentation in man and laboratory animals. *Placenta* 1981;**2**:71–91.

22. Haig D. Putting Up Resistance: Maternal–Fetal Conflict over the Control of Uteroplacental Blood Flow. In: Aird WC (ed.). *Endothelial Biomedicine*. Cambridge: Cambridge University Press, 2007, 135–41.

23. Page EW. The relation between hydatid moles, relative ischemia of the gravid uterus, and the placental origin of eclampsia. *Am J Obstet Gynecol* 1939;**37**:291–3.

24. Carroli G, Cuesta C, Abalos E *et al.* Epidemiology of postpartum haemorrhage: a systematic review. *Best Pract Res Clin Obstet Gynaecol* 2008;**22**:999–1012.

25. Abrams ET, Rutherford JN. Framing postpartum hemorrhage as a consequence of human placental biology: an evolutionary and comparative perspective. *Am Anthropol* 2011;**113**:417–30.

26. Chen C, Liu X, Chen D *et al.* A risk model to predict severe postpartum hemorrhage in patients with placenta previa: a single-center retrospective study. *Ann Palliat Med* 2019;**8**:61121–621.

27. Crespi BJ. Nausea, vomiting and conflict in pregnancy. *Evol Med Public Health* 2024;**12**:75–81.

28. Hrdy SB. Variable postpartum responsiveness among humans and other primates with “cooperative breeding”: A comparative and evolutionary perspective. *Horm Behav* 2016;**77**:272–83.

29. Kenkel WM, Perkeybile AM, Carter CS. The Neurobiological Causes and Effects of Alloparenting. *Dev Neurobiol* 2017;**77**:214–32.

30. Sear R, Mace R. Who keeps children alive? A review of the effects of kin on child survival. *Evol Hum Behav* 2008;**29**:1–18.

31. 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* 2018;**27**:80–91.