

McLean Lab: Relevant Reproduction



Paternal Impacts on Gestational Diabetes and Preeclampsia



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Maternal contributions to pregnancy and life after pregnancy have long been a research focus (Coussons-Read, 2013). However, this focus has expanded into the paternal role on pregnancy success (Khoshkerdar et al., 2021). Not only are paternal contributions able to impact fetal health and development but have shown impactful effects on maternal health. Two of the most common pregnancy complications are preeclampsia and gestational diabetes which has recently been connected to interactions between the maternal environment and paternal semen (Khoshkerdar et al., 2021). These serious conditions can impact fetal and maternal health after birth.

Maternal hormone concentrations fluctuate during pregnancy to induce physiological changes necessary to support the fetus (Soma-Pillay et al., 2016). Before pregnancy, the pancreas will release insulin to compensate for this increasing presence for blood glucose (Soma-Pillay et al., 2016). During pregnancy, the mother may not produce enough insulin or may not be as efficient in utilizing insulin (Soma-Pillay et al., 2016). The consequence of this is a condition known as gestational diabetes mellitus (GDM). One potential association with the development of GDM is age of the father. Khandwala et al. (2018) found that when a pregnancy was created with fathers aged 45 years old and older there was 34% increase of GDM. Maternal GDM can increase the offspring's risk of glucose intolerance and increase the difficulty to lose weight, showing a lasting impact of this gestational disease (Bakos et al., 2010).

Preeclampsia is a condition in which the mother has increased blood pressure and/or protein in the urine (Fox et al., 2019). This condition begins at around 20 weeks of pregnancy and may present with no other symptoms. Risk factors for preeclampsia include high body fat, genetics (Fox et al., 2019). Low placental and fetal weights are symptoms as a result of preeclampsia (Fox et al., 2019). Recent research has implicated the father can increase the risk for this condition as well. Paternal impact on preeclampsia has been connected to the male epigenome, length of relationship, and maternal immune response to paternal antigens. The epigenome consists of the markers and nonstandard molecules of DNA. These molecules interact with the DNA and other proteins that aid in transcription of the DNA. Changes in the epigenome frequently relate to additional methylation on the DNA. Methylation occurs naturally with age and this methylation can impact spermatogenesis. Frequently, methylation occurs on imprinted genes and can negatively impact maternal and/or fetal health. The increase in methylation of *Kxng1ot* has shown to decrease placental weight and fetal weight (Denomme et al., 2020). In addition to increased methylation, short term exposure to seminal secretions has been shown to impact the risk of preeclampsia. In mothers with preeclampsia, there was twice the likelihood that exposure to paternal seminal secretions were for less than six months. There was also correlation to maternal hypertension and babies that were small for their gestational age (Kho et al., 2009). Conversely, Zhang & Patel (2007) found that exposure to paternal antigens for a length of time before the induction of pregnancy may decrease the likelihood of preterm birth, low fetal birthweight, and preeclampsia.

In summation, father's health, diet, and lifestyle can impact gestation, offspring development, and maternal health. Future research should include a more diverse paternal population to better elucidate reproductive success while minimizing long-term maternal and fetal impacts.



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Works Cited

- Bakos, H., R. Henshaw, and M. Mitchell. 2010. Paternal body mass index is associated with decreased blastocyst development and reduced live birth rates following assisted reproductive technology. *Fertility and Sterility*. Available from: [https://www.fertstert.org/article/S0015-0282\(10\)02846-3/fulltext](https://www.fertstert.org/article/S0015-0282(10)02846-3/fulltext)
- Coussons-Read, M. E. 2013. Effects of prenatal stress on pregnancy and human development: Mechanisms and pathways. *Obstetric medicine*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5052760/>
- Denomme, M. M., J. C. Parks, B. R. McCallie, N. I. McCubbin, W. B. Schoolcraft, and M. G. Katz-Jaffe. 2020. Advanced paternal age directly impacts mouse embryonic placental imprinting. *PLOS ONE*. Available from: <https://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0229904>
- Fox, R., J. Kitt, P. Leeson, C. Y. L. Aye, and A. J. Lewandowski. 2019. Preeclampsia: Risk factors, diagnosis, management, and the cardiovascular impact on The offspring. *Journal of clinical medicine*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6832549/>
- Khandwala, Y. S., V. L. Baker, G. M. Shaw, D. K. Stevenson, Y. Lu, and M. L. Eisenberg. 2018. Association of paternal age with perinatal outcomes between 2007 and 2016 in the United States: Population Based cohort study. *The BMJ*. Available from: <https://www.bmj.com/content/363/bmj.k4372>
- Kho, E. M., L. M. E. McCowan, R. A. North, C. T. Roberts, E. Chan, M. A. Black, R. S. Taylor, and G. A. Dekker. 2009. Duration of sexual relationship and its effect on preeclampsia and small for gestational age perinatal outcome. *Journal of Reproductive Immunology*. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S0165037809002599?via%3Dihub>
- Khoshkerdar, A., E. Eryasar, H. L. Morgan, and A. J. Watkins. 2021. Reproductive toxicology: Impacts of paternal environment and lifestyle on maternal health during pregnancy. *rep*. Available from: <https://rep.bioscientifica.com/view/journals/rep/162/5/REP-20-0605.xml>
- Soma-Pillay, P., C. Nelson-Piercy, H. Tolppanen, and A. Mebazaa. 2016. Physiological changes in pregnancy. *Cardiovascular journal of Africa*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#:~:text=There%20is%20a%20significant%20increase,than%20in%20the%20respiratory%20rate.>
- Zhang, J., and G. Patel. 2007. Partner change and perinatal outcomes: A systematic review. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1365-3016.2007.00837.x>