

## Evaluation of the effects of steroid hormones on collagen fibers in the endometrial stroma of ovulation-stimulated mice

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### Abstract

Successful blastocyst implantation requires a suitable uterine environment. Ovarian hormones are responsible for endometrial maturation. The aim of this study is to investigate the effects of steroid hormones on collagen fibers and the diameter of endometrial glands in the endometrial stroma of ovulated mice. In this study, mice were divided into five groups after stimulation of ovulation and pregnancy: 1) Control 2) Experimental control 3) Estrogen 4) Progesterone, 5) Estrogen with progesterone 5 days after pregnancy, mice were killed by cervical vertebral dislocation and their uterus was sampled and prepared for light microscope. The results obtained from this study showed that progesterone administration reduces the thickness of collagen fibers in the endometrium, while injection of estrogen with progesterone can cause the growth of collagen fibers in the endometrium and increase the diameter of glands compared to progesterone. Also, histomorphometric results obtained from this study showed that the size of glandular diameter between groups was significant except in the estrogen and estrogen with progesterone groups. The results of this study also showed that progesterone compared to the control group cannot provide a suitable environment for implantation and the addition of estrogen to progesterone can create a better situation for implantation in the luteal phase.

**Key words:** Ovulation, Implantation, Collagen, Estrogen, Progesterone

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## References

- Arian Manesh, M., Saleh Nia, M. & Nik Nafs, B. (2002). The effect of progesterone administration after ovulation stimulation on rat endometrial ultrastructure in pre-implantation time. *Yakhteh* 4 (14), 61–65.
- Basir, G. S., O, W. S., Yu Ng, E. H., & Ho, P. C. (2001). Morphometric analysis of peri-implantation endometrium in patients having excessively high oestradiol concentrations after ovarian stimulation. *Human Reproduction*, 16(3), 435-440.
- Brosens, J. J., & Gellersen, B. (2006). Death or survival–progesterone-dependent cell fate decisions in the human endometrial stroma. *Journal of molecular endocrinology*, 36(3), 389-398.
- Crow, J., Wilkins, M., Howe, S., More, L., & Helliwell, P. (1991). Mast cells in the female genital tract. *International Journal of Gynecological Pathology: Official Journal of the International Society of Gynecological Pathologists*, 10(3), 230-237.
- Cha, J., Sun, X., & Dey, S. K. (2012). Mechanisms of implantation: strategies for successful pregnancy. *Nature medicine*, 18(12), 1754-1767.
- Carbone, K., Pinto, N. M., Abrahamsohn, P. A., & Zorn, T. M. (2006). Arrangement and fine structure of collagen fibrils in the decidualized mouse endometrium. *Microscopy research and technique*, 69(1), 36-45.
- De Paiva, S., Abrahamsohn, P. A., & Zorn, T. M. T. (1994). Histochemical demonstration of phospholipid containing choline in the cytoplasm of murine decidual cells. *Cells Tissues Organs*, 150(2), 119-126.
- Danielsson, K. G., Swahn, M. L., Westlund, P., Johannisson, E., Seppälä, M., & Bygdeman, M. (1997). Effect of low daily doses of mifepristone on ovarian function and endometrial development. *Human reproduction (Oxford, England)*, 12(1), 124-131.
- Engmann, L., DiLuigi, A., Schmidt, D., Benadiva, C., Maier, D., & Nulsen, J. (2008). The effect of luteal phase vaginal estradiol supplementation on the success of in vitro fertilization treatment: a prospective randomized study. *Fertility and sterility*, 89(3), 554-561.
- Fox, C., & Lessey, B. A. (2018). Signaling between embryo and endometrium: Normal implantation. In *Recurrent Implantation Failure* (pp. 1-19). Springer, Cham.
- Fatemi, H. M., & Van Vaerenbergh, I. (2015). Significance of premature progesterone rise in IVF. *Current Opinion in Obstetrics and Gynecology*, 27(3), 242-248.
- Garrido-Gomez, T., Dominguez, F., Quiñonero, A., Diaz-Gimeno, P., Kapidzic, M., Gormley, M., ... & Simón, C. (2017). Defective decidualization during and after severe preeclampsia reveals a possible maternal contribution to the etiology. *Proceedings of the National Academy of Sciences*, 114(40), E8468-E8477.
- Greca, C. D. P. S., Nader, H. B., Dietrich, C. P., Abrahamsohn, P. A., & Zorn, T. M. T. (2000). Ultrastructural cytochemical characterization of collagen-associated proteoglycans in the endometrium of mice. *The Anatomical Record: An Official Publication of the American Association of Anatomists*, 259(4), 413-423.
- Hewitt, S. C., Grimm, S. A., Wu, S. P., DeMayo, F. J., & Korach, K. S. (2020). Estrogen receptor  $\alpha$  (ER $\alpha$ )-binding super-enhancers drive key mediators that control uterine estrogen responses in mice. *Journal of Biological Chemistry*, 295(25), 8387-8400.
- Hubayter, Z.R. and Muasher, S.J., 2008. Luteal supplementation in in vitro fertilization: more questions than answers. *Fertility and sterility*, 89(4), pp.749-758.
- Kolibianakis, E. M., Venetis, C. A., Papanikolaou, E. G., Diedrich, K., Tarlatzis, B. C., & Griesinger, G. (2008). Estrogen addition to progesterone for luteal phase support in cycles stimulated with GnRH analogues and gonadotrophins for IVF: a systematic review and meta-analysis. *Human reproduction*, 23(6), 1346-1354.
- Krüssel, J. S., Bielfeld, P., Polan, M. L., & Simón, C. (2003). Regulation of embryonic implantation. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 110, S2-S9. King, A., 2000. Uterine leukocytes and decidualization. *Human reproduction update*, 6(1), pp.28-36.
- Klemmt, P. A., Liu, F., Carver, J. G., Jones, C., Brosi, D., Adamson, J., ... & McVeigh, E. (2009). Effects of gonadotrophin releasing hormone analogues on human endometrial stromal cells and embryo invasion in vitro. *Human reproduction*, 24(9), 2187-2192.
- Kumar, R., Zakharov, M. N., Khan, S. H., Miki, R., Jang, H., Toraldo, G., ... & Jasuja, R. (2011). The dynamic structure of the estrogen receptor. *Journal of amino acids*, 2011.

- Klonos, E., Katopodis, P., Karteris, E., Papanikolaou, E., Tarlatzis, B., & Pados, G. (2020). Endometrial changes in estrogen and progesterone receptor expression during implantation in an oocyte donation program. *Experimental and therapeutic medicine*, 20(6), 1-1.
- Lindhard, A., Bentin-Ley, U., Ravn, V., Islin, H., Hviid, T., Rex, S., ... & Sørensen, S. (2002). Biochemical evaluation of endometrial function at the time of implantation. *Fertility and Sterility*, 78(2), 221-233.
- Mascarenhas, M., Kamath, M. S., Chandy, A., & Kunjummen, A. T. (2015). Progesterone/estradiol ratio as a predictor in the ART cycles with premature progesterone elevation on the day of hCG trigger. *Journal of reproduction & infertility*, 16(3), 155.
- Okada, H., Tsuzuki, T., & Murata, H. (2018). Decidualization of the human endometrium. *Reproductive medicine and biology*, 17(3), 220-227.
- Oliveira, S. F., Abrahamsohn, P., & Zorn, T. M. T. (1998). Autoradiography reveals regional metabolic differences in the endometrium of pregnant and nonpregnant mice. *Brazilian journal of medical and biological research*, 31(2), 307-312.
- Proctor, A., Hurst, B. S., Marshburn, P. B., & Matthews, M. L. (2006). Effect of progesterone supplementation in early pregnancy on the pregnancy outcome after in vitro fertilization. *Fertility and sterility*, 85(5), 1550-1552.
- Simón, C., Martín, J. C., & Pellicer, A. (2000). Paracrine regulators of implantation. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 14(5), 815-826.
- Spieß, K., Teodoro, W. R., & Zorn, T. M. (2007). Distribution of collagen types I, III, and V in pregnant mouse endometrium. *Connective tissue research*, 48(2), 99-108.
- Simon, C., Domínguez, F., Valbuena, D., & Pellicer, A. (2003). The role of estrogen in uterine receptivity and blastocyst implantation. *Trends in Endocrinology & Metabolism*, 14(5), 197-199.
- Sharma, A., & Kumar, P. (2012). Understanding implantation window, a crucial phenomenon. *Journal of human reproductive sciences*, 5(1), 2.
- Salehnia, M., Arianmanesh, M., & Beygi, M. (2006). The impact of ovarian stimulation on mouse endometrium: a morphometrical study.
- Teh, W. T., McBain, J., & Rogers, P. (2016). What is the contribution of embryo-endometrial asynchrony to implantation failure? *Journal of assisted reproduction and genetics*, 33(11), 1419-1430.
- Wu, D., Kimura, F., Zheng, L., Ishida, M., Niwa, Y., Hirata, K., ... & Murakami, T. (2017). Chronic endometritis modifies decidualization in human endometrial stromal cells. *Reproductive biology and endocrinology*, 15(1), 1-10.
- Young, S. L. (2013). Oestrogen and progesterone action on endometrium: a translational approach to understanding endometrial receptivity. *Reproductive biomedicine online*, 27(5), 497-505.
- Zheng, H. T., Zhang, H. Y., Chen, S. T., Li, M. Y., Fu, T., & Yang, Z. M. (2020). The detrimental effects of stress-induced glucocorticoid exposure on mouse uterine receptivity and decidualization. *The FASEB Journal*, 34(11), 14200-14216.