

Progesterone and Implantation

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Progesterone is a critical mediator of endometrial receptivity. The pathway between ovulation and progesterone production from the corpus luteum involves complex paracrine mechanisms involving the Indian Hedgehog signaling pathway allowing communication between epithelial and stromal compartments. In normal, fertile women progesterone initiates a large number of mediators that ultimately down-regulate estrogen receptors, a key step in implantation success. In certain inflammatory conditions, such as endometriosis and hydrosalpinx, these pathways are disrupted, leading to progesterone resistance. The link between these reversible inflammatory conditions and implantation failure have remained poorly understood. Increasingly, women with unexplained infertility or pregnancy loss are recognized to have defects in their endometrial response to progesterone, maintaining an excessive endogenous estrogen response that favors proliferation and is anti-apoptotic. Progesterone resistance and estrogen dominance are central to the association between inflammation and infertility. This presentation will focus on the normal progesterone signaling pathways for successful pregnancy but also examine the mechanisms of how disruption in progesterone signaling occurs, leading to endometrial receptivity defects, infertility and IVF failure.