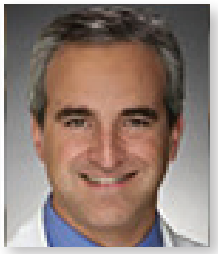
Menstrual Cycle Characteristics and Reproductive Technology



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Knowledge of the physiology of the protein and steroid hormones involved in human reproduction has provided us with the ability to manipulate ovarian function in ways that benefit infertile couples. Pharmacological preparations containing either recombinant or urinary FSH are used to induce superovulation for IVF or intrauterine insemination. Similarly, knowledge of GnRH physiology has allowed us to control ovarian stimulation better and improve outcomes in IVF-embryo transfer.

The primary hormones of menstrual and ovulatory function are either proteins or steroids. Protein hormones include GnRH, FSH, LH, hCG, and the inhibins/activins. GnRH arises from the arcuate nucleus of the hypothalamus, and is secreted into the pituitary portal circulation, where it induces pituitary gonadotrophs to secrete FSH and LH. Effective GnRH secretion requires that it come in periodic pulses, as continuous infusion of GnRH leads to pituitary desensitization and down-regulation.

The major protein hormones in reproductive tissues act through cell membrane receptors coupled to G-proteins. G-proteins are linked to the enzyme, adenylate cyclase, which synthesizes cAMP by removing phosphate groups from ATP. These phosphates bind to either protein kinase A or C, which in turn establish various second messengers that then signal the nucleus to start or stop DNA transcription and mRNA synthesis. The primary mRNA transcripts resulting from FSH receptor activation are mRNAs for the LH receptor and the enzyme aromatase. Aromatase converts ovarian androgens to estrogens. LH receptor activation leads to synthesis of mRNA transcripts for the side-chain cleavage enzyme, which initiates progesterone synthesis.

hCG is a protein hormone derived only from placental secretion. It acts through the LH receptor and has similar effects as LH on luteal function. hCG may be used to induce ovulation on assisted reproductive technology (ART) cycles because it mimics LH action in the ovarian follicle.

Steroid hormones induce DNA synthesis and transcription through cytosolic and nuclear receptors. Unlike protein hormones, steroid hormone-receptor complexes act directly on DNA through response elements adherent to the DNA molecule. These response elements can lead to either suppression or activation of DNA synthesis/transcription.

The primary steroid hormones are androgens, estrogens, and progesterone. Androgen production in the ovary is under control of low-level LH secretion. The primary ovarian androgen is androstenedione, which can be converted to either testosterone by the 17ß-HSOR enzyme or to estrone by aromatase. Testosterone is usually converted directly to estradiol by aromatase.

Estradiol is the primary ovarian estrogen, and is a result of FSH-mediated folliculogenesis. It is derived primarily from conversion of estrone by the 17ß-HSOR enzyme or directly from testosterone by aromatase (as previously mentioned). Estrogens cause endometrial proliferation in the follicular phase of the menstrual cycle and, at high enough levels, cause LH release (and an LH surge in normal cycles).

Progesterone is derived from cholesterol by way of pregnenolone, through the action of the side-chain cleavage and the 3ß-HSD enzymes. Progesterone causes differentiation within the endometrium, so that it becomes capable of implanting an embryo.