Male Reproductive System

Mimi Jakoi, PhD
Jennifer Carbrey, PhD

The underlined headings correspond to the 2 Male Reproductive System videos.

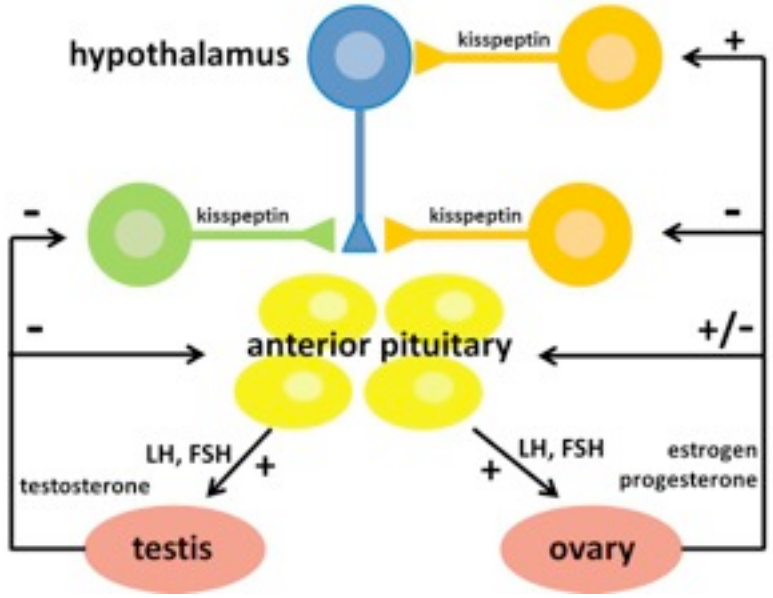
1. Hypothalamus-Pituitary-Gonad Axis

Sexual Differentiation

The chromosomal determinants of genetic sex are the XX or XY chromosome combination. Expression of the SRY gene on the Y chromosome results in testes being formed instead of ovaries. Whether or not an individual has testes or ovaries determines their gonadal sex. The gonads (either testes or ovaries) are the source of gametes (sperm or ova) as well as sex hormones which determine the external and internal genitalia (phenotypic sex). The SRY gene is necessary for maleness but not sufficient. For example, the testosterone receptor gene on the X chromosome is also required.

The Common Axis

There are many similarities between the hypothalamus-pituitary-gonad axis in males and females. The process of producing sperm or ova is coordinated by the hypothalamus which secretes GnRH (gonadotropin-releasing hormone) in a pulsatile manner. In turn, GnRH stimulates the pituitary to secrete FSH (follicle-stimulating hormone) and LH (luteinizing hormone) (Fig. 1). In both males and females, androgens (like testosterone) produced in the gonad is needed for development of the ovum or sperm. Production of inhibin B by cells in the testis or ovary decreases FSH secretion while sex hormones like testosterone and estrogen regulate GnRH, LH, and FSH secretion (Fig. 1).



Maturation of the H-P-Gonad Axis

In humans, the hypothalamus-pituitary-gonad axis differentiates in a sex-specific manner. In the adult male, GnRH secretion has a continuous (24-hr) pulsatile pattern and in the adult female, a cyclic (28 day) pulsatile pattern.

How does this maturation occur? The hypothalamus functions like a thermostat which responds negatively or positively to the levels of circulating gonadal steroids (testosterone or estrogen). During development, it is initially

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very sensitive to the negative feedback of these steroids and becomes progressively less so as puberty approaches. By puberty, its sensitivity to circulating gonadal steroids has changed from a super-sensitive state to a lower state of sensitivity. This continues until the feedback actions characteristic of the adult are established. This maturation is now understood to involve another set of hypothalamic neurons, ones that release the neurotransmitter kisspeptin (Fig. 1). In the absence of either kisspeptin activity or its receptor (GPR54) activity, the individual (male or female) fails to enter puberty and is infertile. It is the kisspeptin neurons which have receptors for the gonadal steroids and are responsible for the negative feedback to the GnRH producing neurons (Fig. 1).

During fetal life, testosterone is secreted by the testes independent of GnRH control. This early rise in testosterone imprints the hypothalamus as male. Later, at birth, a second surge in testosterone results in permanent virilization of the hypothalamus which imprints the GnRH secretion pattern as 24-hour and pulsatile. Throughout childhood until puberty, testosterone remains low. At puberty the plasma level increases to adult levels, remains elevated until middle age, and then declines somewhat later in life.

2. Sperm and Hormone Production

Sperm Production

In the adult male, in response to GnRH, the pituitary secretes FSH and LH. These hormones act on the testes to regulate sperm production (spermatogenesis) and sex hormone synthesis. Spermatogenesis occurs in the testes. Unlike the female, the stem cell population, spermatogonia, of the male can undergo continuous division renewing the developing sperm population throughout the life of the male. FSH acts on the sertoli cells of the seminiferous tubules of the testis. Sertoli cells surround the stem cells and developing sperm, isolating them from the rest of the body (blood-testes barrier). FSH initiates spermatogenesis by promoting the germs cells to undergo division. Cohorts of functional sperm take 90 days to fully mature. A fertile sperm count is 200-400 million sperm/5 mL of semen.

In addition, FSH induces the expression of androgen binding protein (ABP) on the cell surfaces of the sertoli cells. ABP binds testosterone (androgen). The testosterone-ABP complex provides a local supply of testosterone in high concentration near the developing sperm which is critical for the maturation of the sperm.

FSH also increases the secretion of inhibin B by the sertoli cells which acts to negatively regulate FSH release by the pituitary.

The target cell for LH is the leydig cell of the testes. Leydig cells secrete testosterone for use as a paracrine within the testes and as a hormone by the peripheral target tissues. Leydig cells also produce dihydrotestosterone (DHT).

Role of Testosterone in Sperm Production

Testosterone is a steroid hormone. As with all steroid hormones, it binds to nuclear receptors to initiate transcription. Locally, within the testes, testosterone binds to androgen receptors in sertoli cells leading to increased transcription, synthesis, and secretion of androgen binding protein (ABP) and maturation of sperm in spermatogenesis.

Testosterone alone cannot initiate spermatogenesis. FSH is required. But once initiated, FSH is no longer required and testosterone alone can maintain sperm maturation.

Testosterone also circulates in the plasma bound to a carrier protein. In the peripheral target tissues, it acts as an anabolic hormone responsible for the growth and function of accessory sex structures (penis, seminal vesicle, prostate) and to increase lean muscle mass.

Testosterone Conversion

In many target tissues, testosterone acts as a prohormone. It is converted to a more potent androgen called dihydrotestosterone (DHT) by the enzyme, 5-alpha reductase. DHT is responsible for development and maintenance of the male secondary sex characteristics including beard growth, deep voice, and growth of the prostate.

In the ovary and breast (of males and females), testosterone is converted to estrogen by the enzyme aromatase.

Sex Steroids and the Male Skeleton

Both testosterone and estrogen are required for optimal bone deposition and skeletal growth in men and women. Gender differences in bone mineral density are established during puberty, resulting in a higher peak bone mass in men compared to women. In addition, men lose less bone mass during aging. It is now established that bone expresses aromatase activity and that estrogen and testosterone have separate roles in bone homeostasis. In males and females, estrogen and estrogen receptor activity stimulate longitudinal growth and induce epiphyseal growth plate closure at the end of puberty. In contrast, androgen and androgen receptor activation play little role in epiphyseal growth plate closure, but are involved in elongation of the skeleton and maintenance of bone mass.

Two different types of mutations reported in human males reveal the role of estrogen in bone homeostasis. Receptor resistance in which the estrogen receptor is inactivated results in continual longitudinal growth of the skeleton. Insufficiency of estrogen in which the aromatase gene is inactivated results in undetectable plasma estrogen levels, but normal plasma testosterone levels, low bone density, and continual longitudinal growth of the skeleton. Administration of estrogen to these individuals induces epiphyseal closure limiting the elongation of the skeleton.