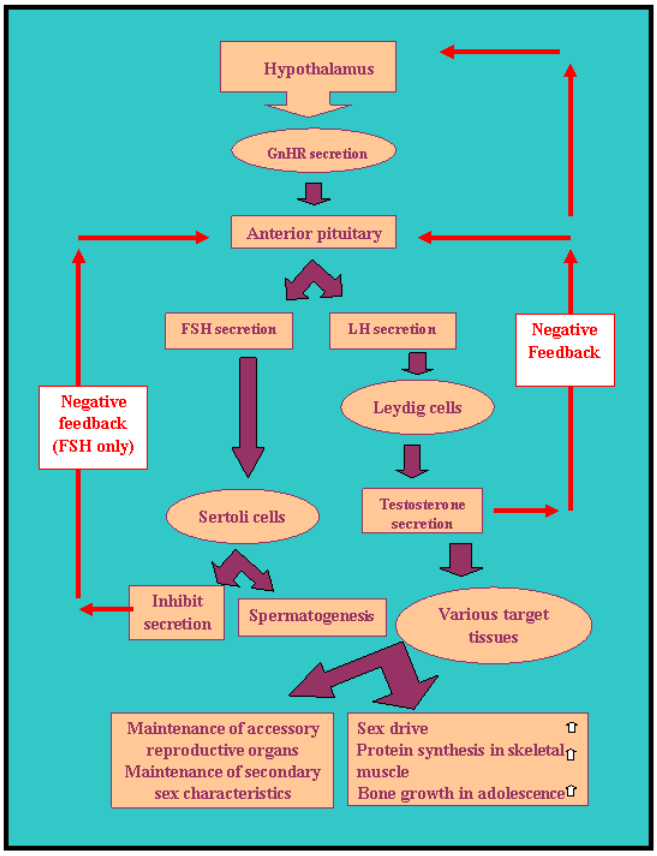
5.7.4

Male Reproductive Endocrine Axis

Before discussing the role of the various hormones involved in regulating the male reproductive system lets review the cells of the testes. Recall that within the testes are numerous, coiled seminiferous tubules (see image below). Surprisingly if all of these tubes were connected end-to-end they would stretch nearly a half a mile. Seminiferous tubules contain two types of cells.

The **Sertoli cells** (also known as **sustentacular** cells) attach to the basal lamina (basement membrane) of the tubules and surround the germ cells. Within the adult testes, the germ cells can be found at various stages of development (this will be explained later). The Sertoli cells protect and nourish the developing germ cells.

Outside of the seminiferous tubules are the testosterone producing **Leydig cells** or **interstitial cells of Leydig**. Several hormones are involved in regulating the male reproductive processes, they include: **Gonadotropin Releasing Hormone** (**GnRH**) secreted by the hypothalamus; **Follicle Stimulating Hormone** (**FSH**) for sperm production in Sertoli cells; and **Luteinizing Hormone** (**LH**) which binds to Leydig (interstitial) cells and for the production of testosterone. Both FSH and LH are secreted by the anterior pituitary (Note that these two hormones are named after their functions in the female); **Testosterone** secreted by the Leydig Cells; and **Inhibin** secreted by the Sertoli cells.



Male Reproductive Hormones Chart.

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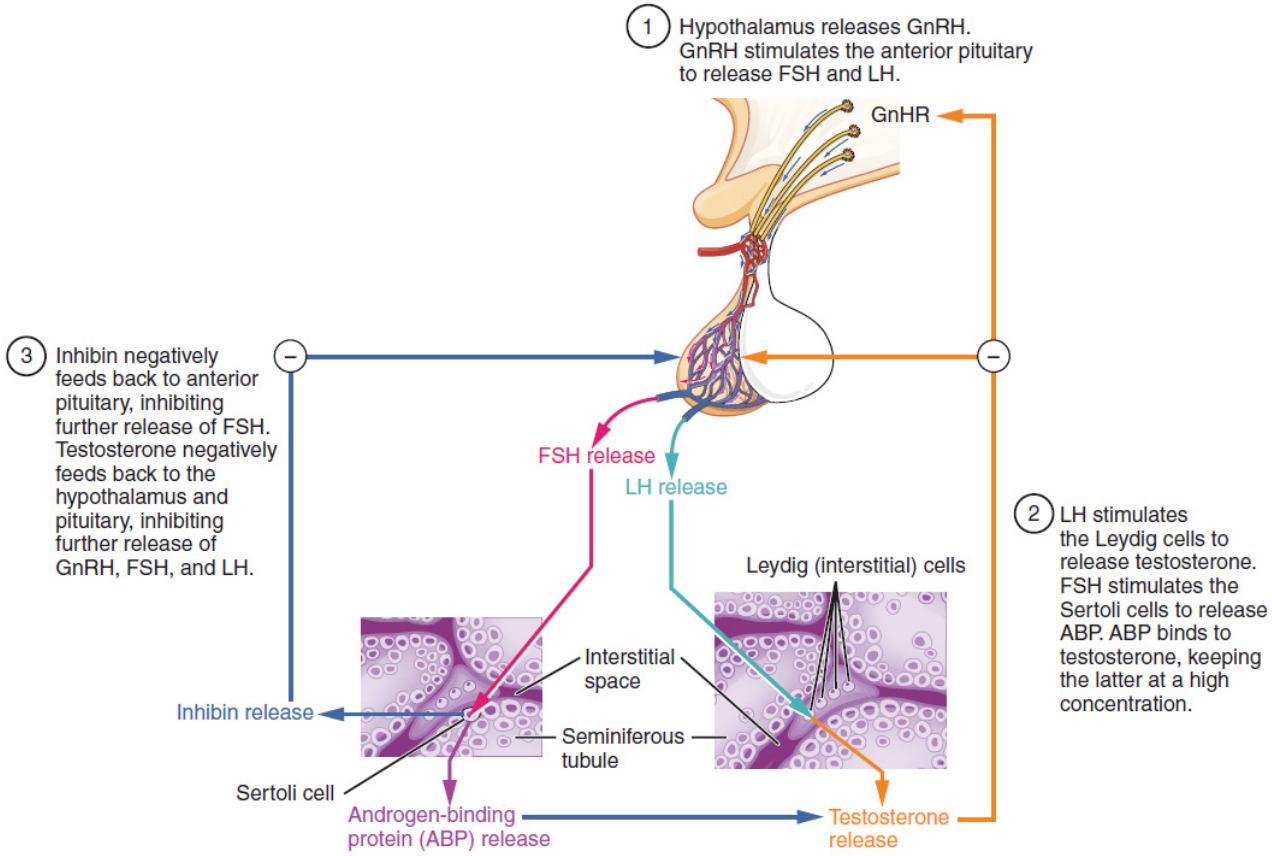
The male testes become fully grown and functionally mature during puberty. The exact combination of biological processes that initiate puberty is still a mystery but it is believed that as the brain matures, connections (synapses) are made in the hypothalamus which eventually lead to the onset of puberty. Stimulation of the hypothalamus causes the secretion of GnRH. GnRH travels through special blood vessels that make up the hypothalamo hypophysial portal system to the anterior pituitary gland. Gonadotrophic cells in the anterior pituitary gland respond to GnRH by producing and releasing LH and FSH. FSH and LH circulate in the blood until they contact the tissues of the testes. LH binds to receptors on the Leydig cells and stimulates the secretion of Testosterone, the male sex steroid. FSH binds to receptors on the Sertoli cells.

In response to FSH, the Sertoli cells produce several proteins including: growth factors that initiate and support spermatogenesis; androgen-binding protein that helps keep the levels of testosterone high in the seminiferous tubules; an enzyme that converts testosterone to estrogen (ironically estrogen is thought to be very important in spermatogenesis); and inhibin which selectively inhibits FSH secretion. All of this is regulated by negative feedback of testosterone on the hypothalamus and pituitary to inhibit GnRH, FSH and LH secretion. Therefore, if testosterone levels increase, GnRH secretion decreases (negative feedback) resulting in reduction in FSH and LH secretion. Reduction in LH results in decreased testosterone secretion and levels come back to normal. The reverse would happen if testosterone dropped below normal.

Inhibin from the Sertoli cells selectively inhibits the release of FSH from the anterior pituitary and allows for differential secretion of FSH and LH (GnRH stimulates both FSH and LH, therefore if inhibin is present LH secretion can continue while FSH secretion is slowed). It is of interest that prior to puberty the hypothalamus is extremely sensitive to testosterone and tiny amounts are sufficient to inhibit GnRH secretion. At puberty the hypothalamus becomes much less sensitive and much higher concentrations of testosterone are required to turn off GnRH, hence the sudden increase in testosterone levels at puberty. However, as mentioned above we still don't know the exact cause of this change.



Regulation of Male Testosterone Production.

Actions of Testosterone

As described above, testosterone is secreted by the Leydig cells and is the primary sex hormone in males and as such has a number of important actions. During fetal development it is testosterone that is responsible for descent of the testes into the scrotum. Interestingly, Human Chorionic Gonadotropin (hCG), a hormone secreted by the placenta, is nearly identical to LH. During fetal development hCG stimulates the Leydig cells to secrete testosterone which is then responsible for testicular descent. Once the baby is born it is no longer exposed to hCG and testosterone secretion essentially ceases until puberty.

Most of the changes associated with puberty can be ascribed to increased testosterone production. Listed below are the known effects of Testosterone.

1. Stimulation of growth of the genitalia and the male duct system.
2. With FSH it is required for spermatogenesis.
3. Stimulation of growth of pubic and axillary hair.
4. It is also responsible for the male secondary sexual characteristics, including:

- Growth of hair on the face, arms, chest, legs and back
- Hypertrophy of the larynx and voice change
- Increased melanin production
- Thickening of the skin
- Increased protein synthesis resulting in increased muscle mass
- Increased secretion of the sebaceous glands
- Increased metabolism (male basal metabolic rate is slightly higher than females)
- Rapid bone growth and closing of the growth plates
- Increased production of red blood cells (male hematocrit is about 10% higher than females)
- Male pattern baldness in genetically predisposed men.