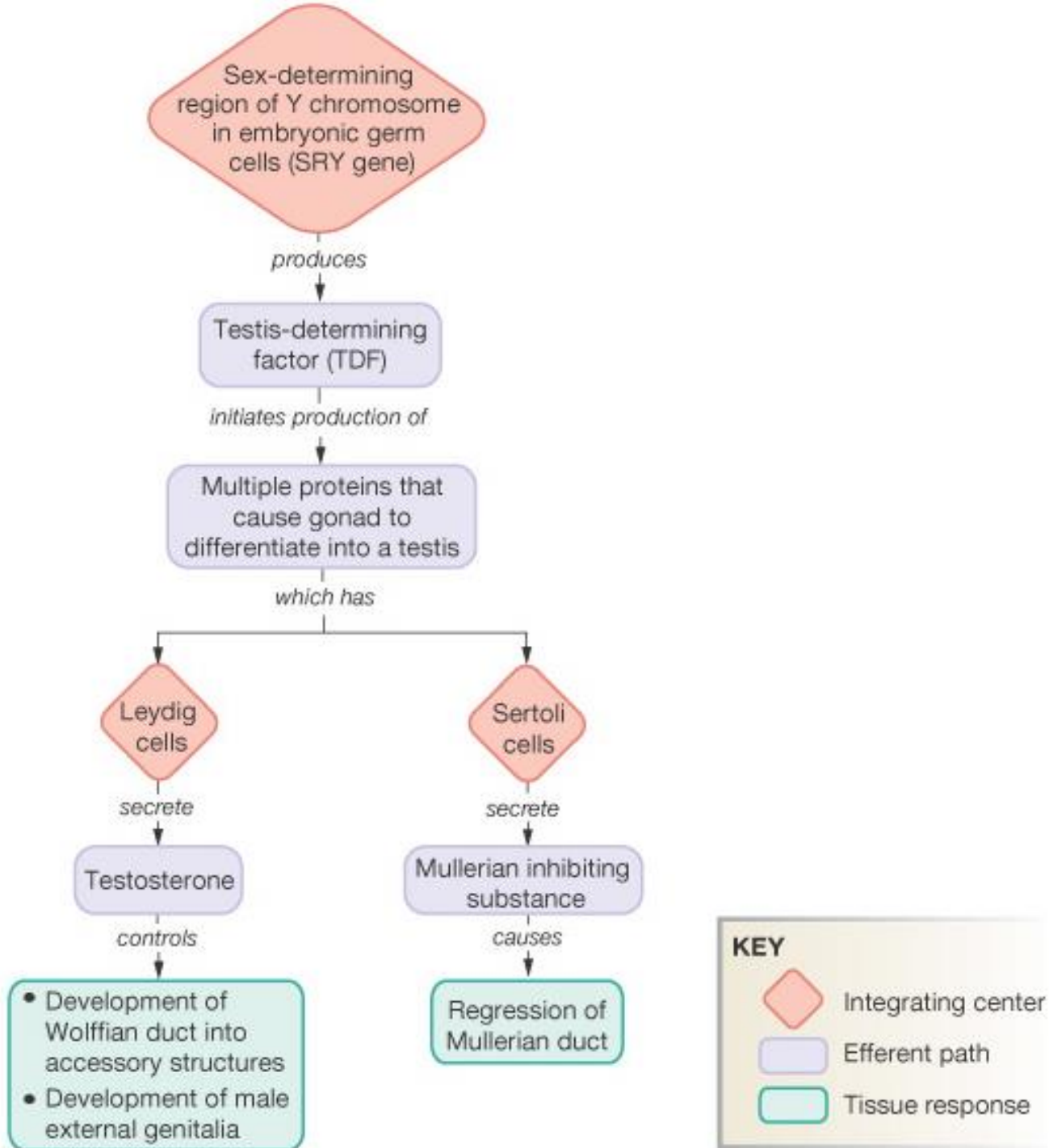


# **Reproductive Physiology**

## **Lecture 1**

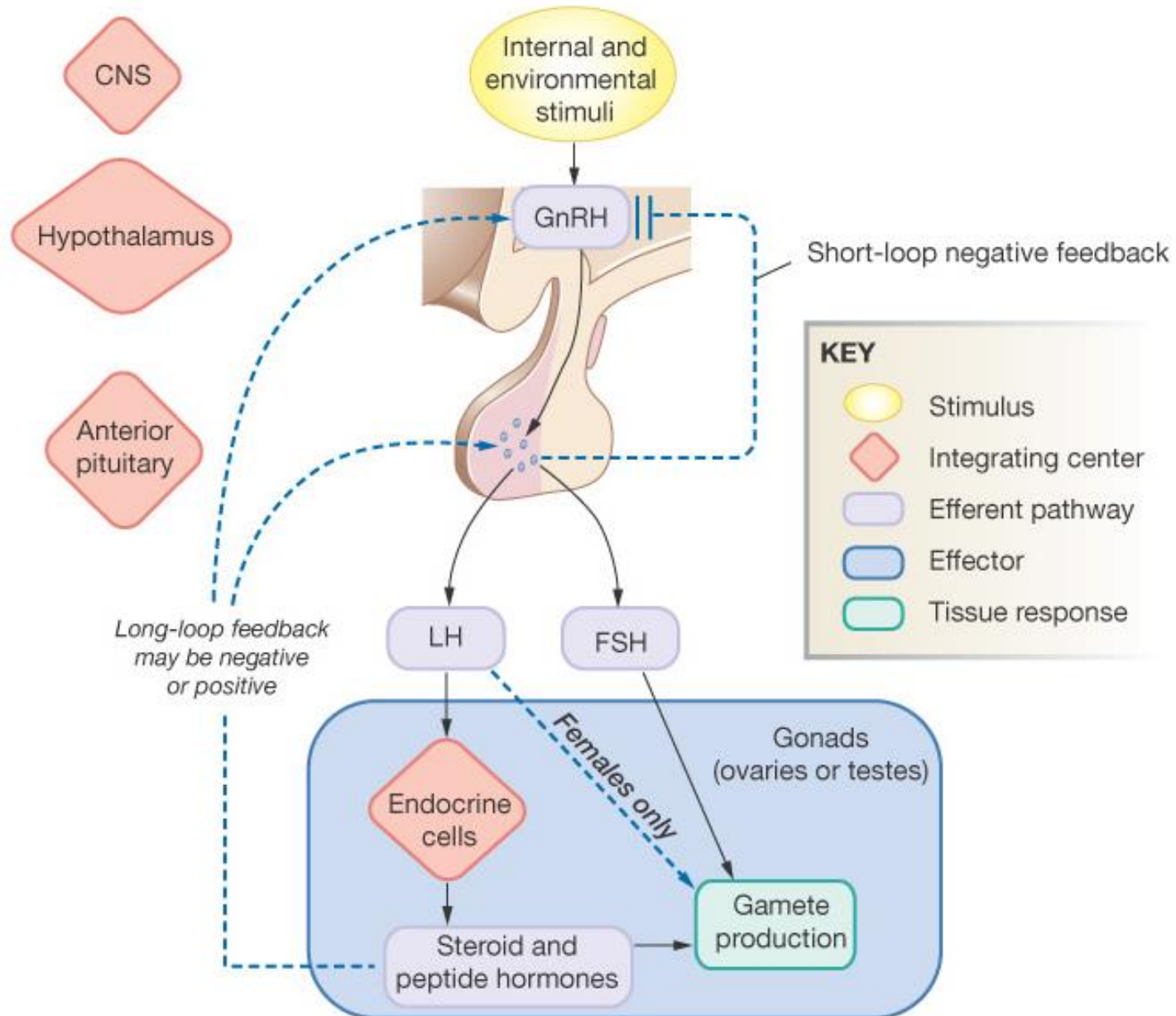
# **Hypothalamic-Pituitary-Gonadal axis**



# Regulation of Reproduction: General Pathways

- **Hypothalamus:**
  - Gonadotropin releasing H (GnRH)
- **Anterior Pituitary**
  - Lutenizing H (LH)
  - Follicle stimulating H (FSH)
- **Ovary:**
  - Estrogen, progesterone, Inhibin
- **Testis:** testosterone, Inhibin

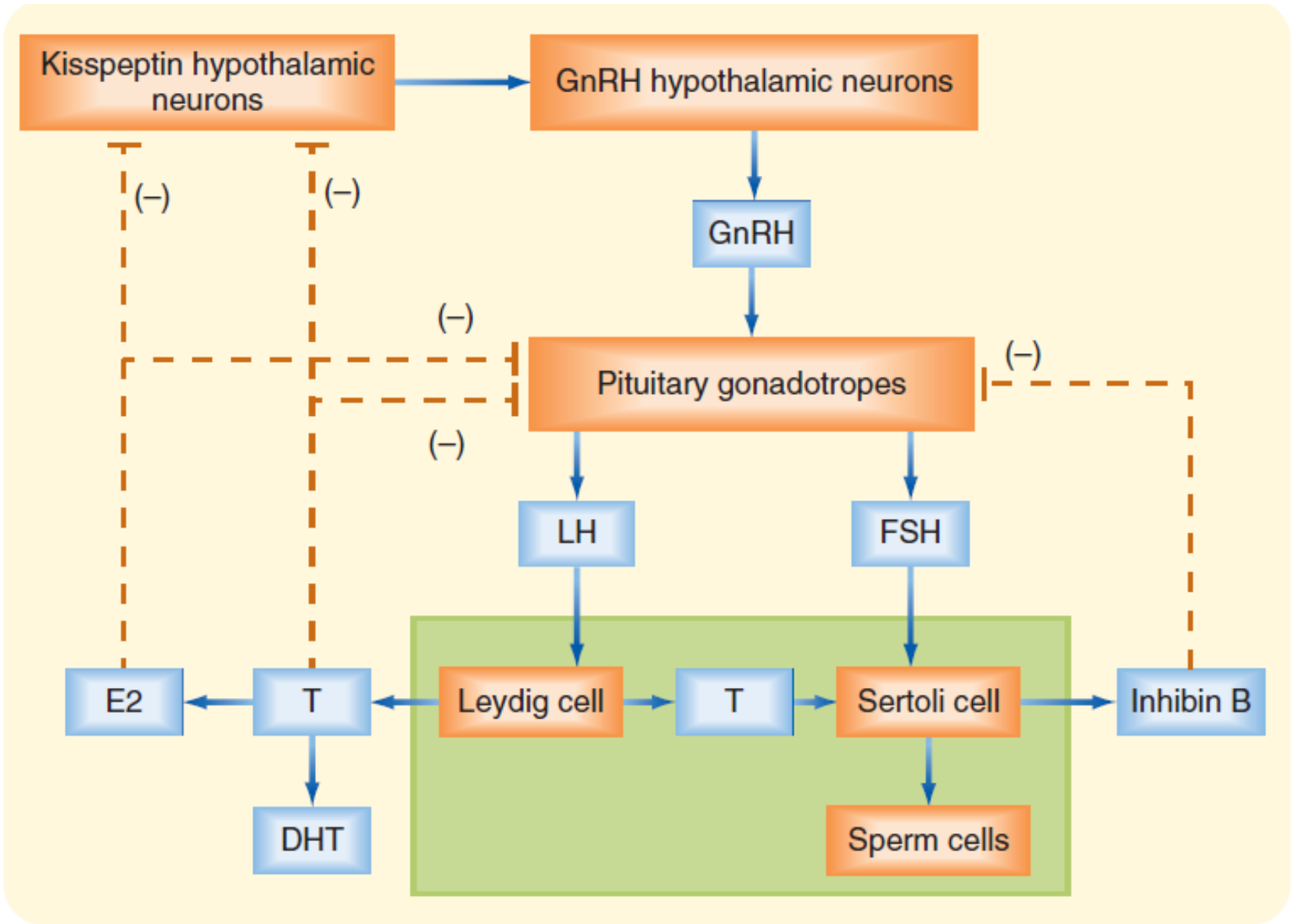
# Regulation of Reproduction: General Pathways



# Control of male sexual functions by hormones from the hypothalamus and anterior pituitary gland:

**GnRH** and its effect in increasing the secretion of LH and FSH: GnRH peptide secreted by the arcuate nuclei of the hypothalamus through the hypothalamic-hypophysial portal system to the anterior pituitary gland and stimulates the release of gonadotropins (LH and FSH).

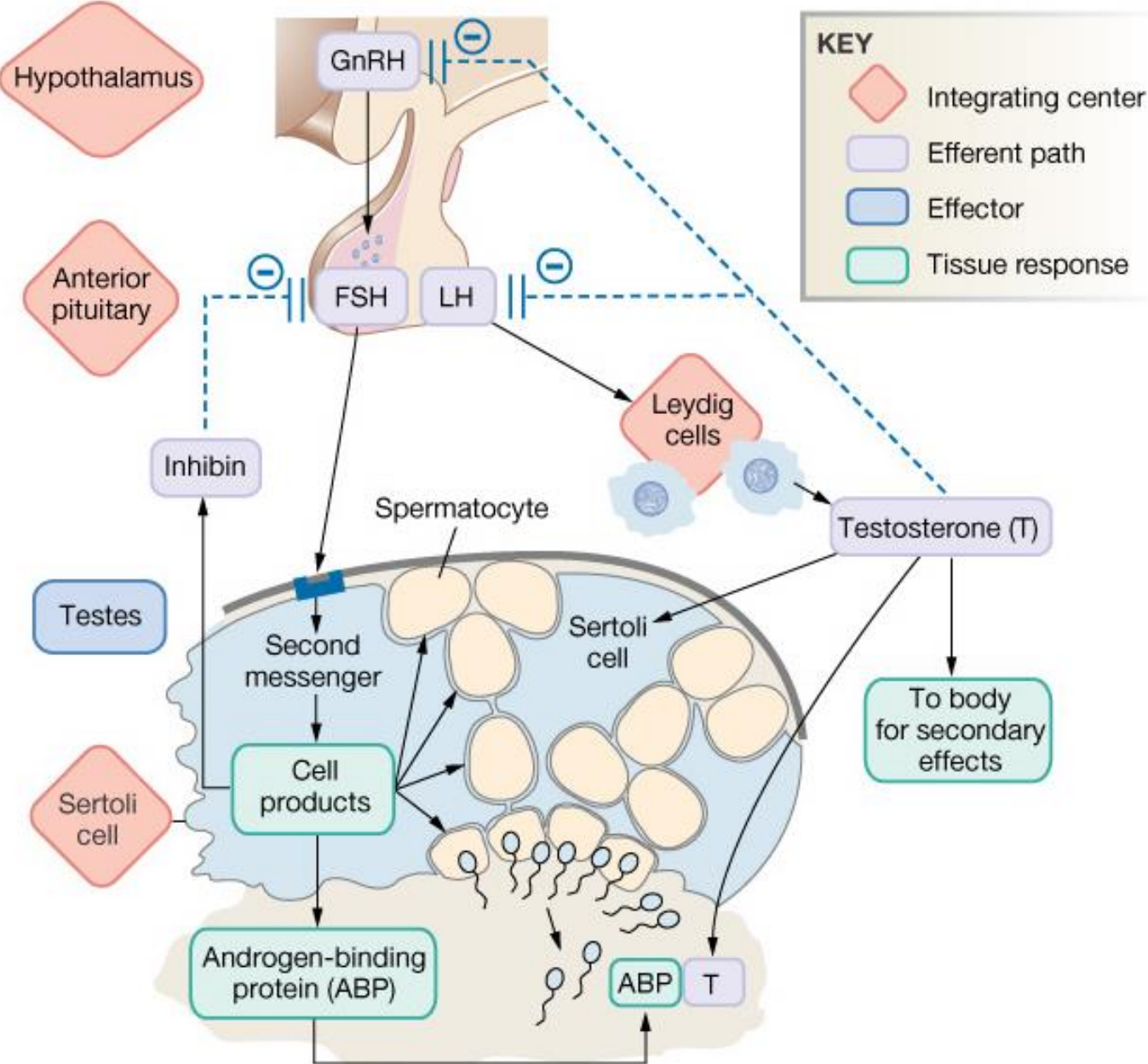
**GnRH** is secreted intermittently for few minutes every 1 to 3 hrs. The secretion of LH and FSH by the anterior pituitary is also cyclical following the **pulsatile** release of GnRH.



# Hormonal Regulation of Testicular Function

- The hypothalamus releases gonadotropin-releasing hormone (GnRH)
- GnRH stimulates the anterior pituitary to secrete FSH and LH
  - **FSH** Binds to its receptors on Sertoli cells to induce:
    1. Production of androgen-binding protein (ABP),
    2. growth factors important for spermatogenesis,
    3. the synthesis of the aromatase enzyme that converts androgens to estrogens,
    4. production of inhibin which inhibits FSH secretion.
  - **LH** stimulates interstitial (Leydig) cells to release **testosterone**

# HPG Axis





## **Testosterone regulation of its production by LH:**

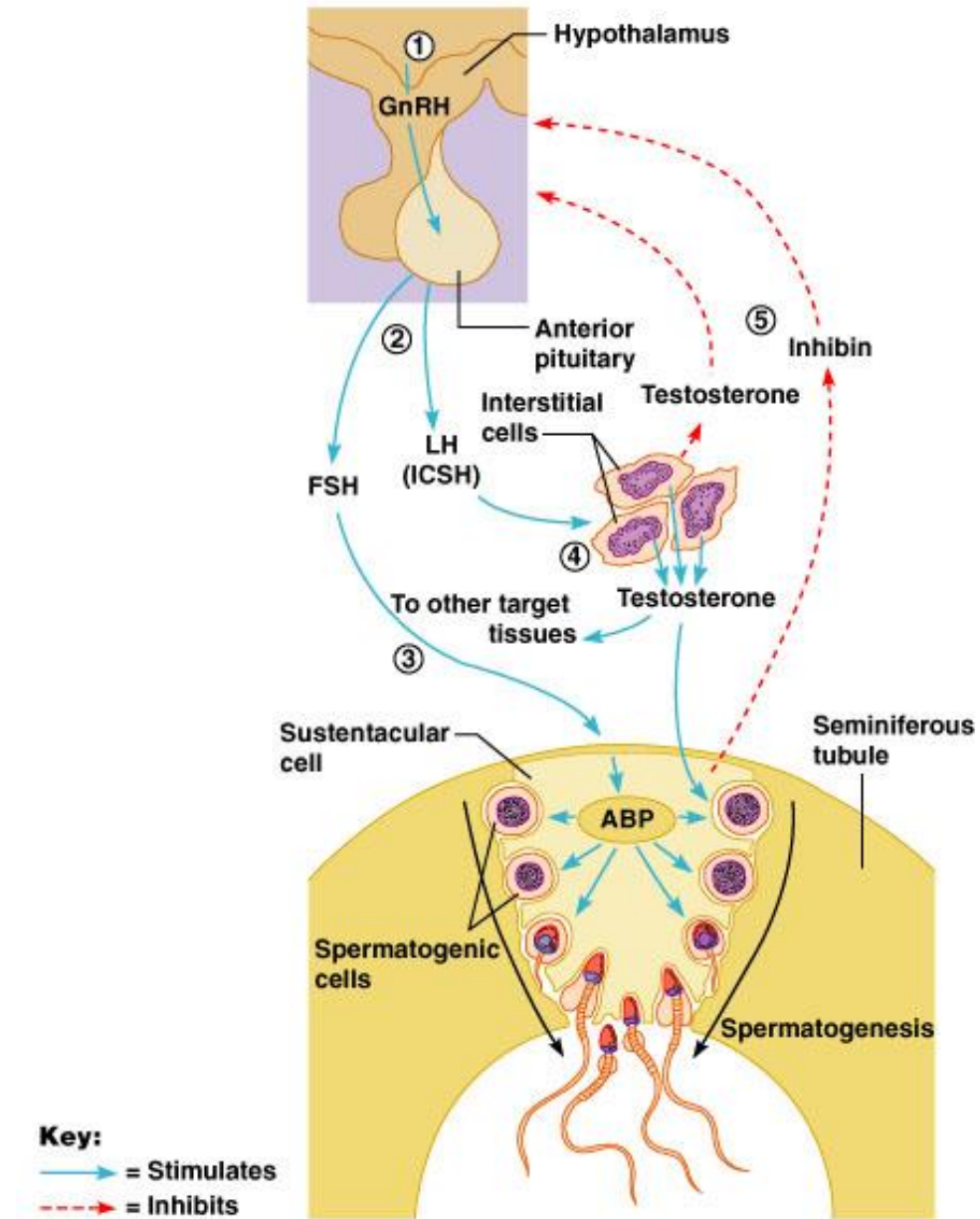
**Testosterone** is secreted by **leydig cells**, in the interstitium of the testis in response to **LH** stimulation.

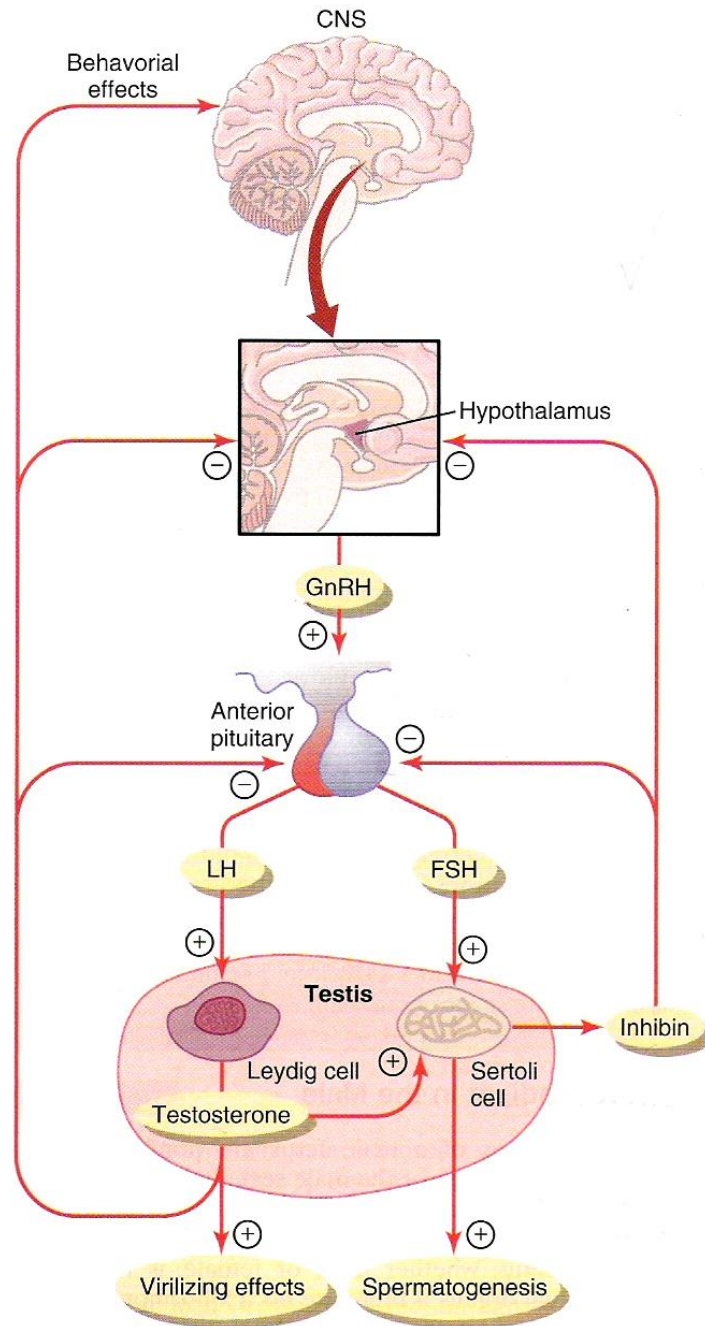
## **Inhibition of anterior pituitary secretion of LH and FSH by testosterone – negative feedback control of testosterone secretion:**

Testosterone is secreted by the testes in response to LH stimulation and has reciprocal effect of inhibiting the AP secretion of LH. Most of the inhibitory effects result from a direct effect of testosterone in the hypothalamus to decrease secretion of GnRH which causes decreased secretion of both LH & FSH.

# Hormonal Regulation of Testicular Function

- Feedback inhibition on the hypothalamus and pituitary results from:
  - Rising levels of testosterone
  - Increased inhibin





## **Regulation of spermatogenesis by FSH and testosterone:**

- **FSH** binds with specific FSH receptors on Sertoli cell in the seminiferous tubules, which causes these cells to grow & secrete spermatogenic substances. Also testosterone & dihydrotestosterone diffuses into the seminiferous tubules from the Leydig cells affect the spermatogenesis, so both FSH & testosterone are necessary to initiate spermatogenesis.

## **Negative feedback control of seminiferous tubule activity – role of the hormone inhibin:**

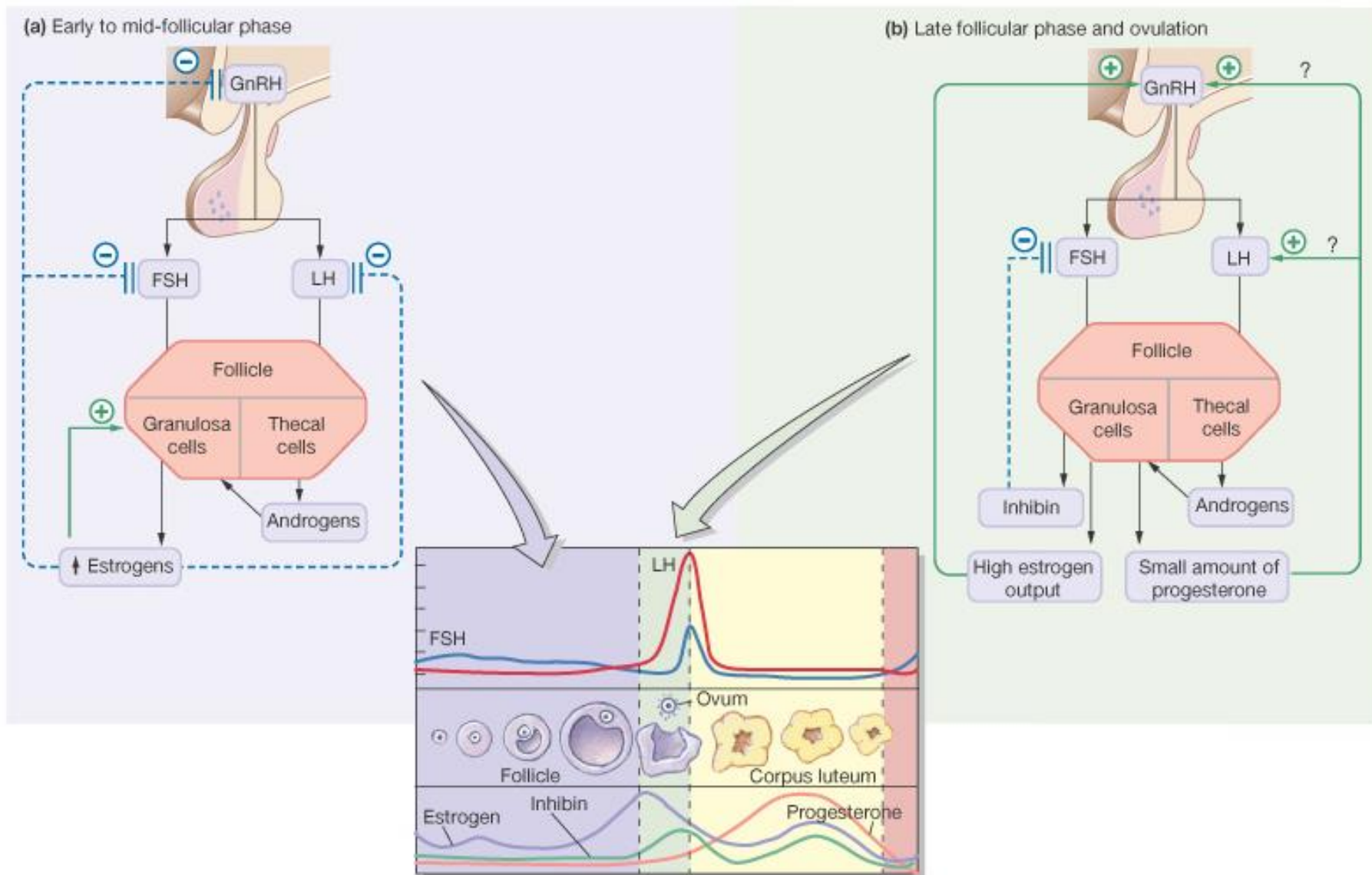
- When the seminiferous tubules fail to produce sperm secretion of FSH from the AP increases. Conversely, when spermatogenesis proceeds rapidly pituitary secretion of FSH diminishes. This is due to the secretion of inhibin hormone from Sertoli cells which strongly inhibits the AP- FSH and has a slight inhibitory effect on the hypothalamus to inhibit GnRH secretion.

## **Regulation of the female monthly rhythm, interplay between the ovarian and hypothalamic-pituitary hormones:**

- Secretion of AP hormone is controlled by the hypothalamic GnRH.
- Intermittent, pulsatile secretion of GnRH by the hypothalamus stimulates pulsatile release of LH from the AP

GnRH is secreted in pulses lasting 5 to 25 minutes every 1 to 2 hrs. The pulsatile release of GnRH cause intermittent output of LH secretion about every 90 minutes.

# Endocrine Control of the Female Reproduction



## **Negative feedback effects of estrogen and progesterone in decreasing both LH and FSH secretion:**

○ Estrogen in small amounts has strong effect to inhibit the production of LH & FSH. This inhibitory effect of estrogen is increased when progesterone is available. This inhibitory effects more on the AP directly & to lesser extent on the hypothalamus to inhibit the secretion of GnRH.

## **Hormone inhibin from the corpus luteum inhibits FSH & LH secretion:**

○ The hormone inhibin secreted by the granulosa cells of the ovarian corpus luteum inhibit the secretion of FSH & to lesser extent LH.

## **Positive feedback effect of estrogen before ovulation – the pre-ovulatory LH surge:**

- AP secretes increased amount of LH for 1 to 2 days before ovulation. FSH surge is much smaller in the pre-ovulatory than LH surge.
- estrogen has special **positive feedback** effect of stimulating pituitary secretion of LH & to a lesser extent FSH
- the granulosa cells of the follicle begin to secrete small increasing amount of progesterone about 1 day before ovulation which stimulate LH secretion



## **Feedback oscillation of the hypothalamic-pituitary-ovarian system:**

## **Postovulatory secretion of the ovarian hormones, and depression of the pituitary gonadotropins:**

During the postovulatory phase (between ovulation & beginning of menstruation) the corpus luteum secrete large quantities of both progesterone & estrogen & inhibin which all together cause negative feedback effect on AP & hypothalamus to inhibit both FSH & LH secretion. (lowest level 3-4 days before the onset of menstruation)

## **Follicular growth phase :-**

- 2 to 3 days before menstruation, corpus luteum regress & secretion of estrogen, progesterone & inhibin decrease.
- This decrease remove the negative feedback effect on AP hormones. Therefore a day after menstruation FSH secretion begins to increase (2 folds) while LH secretion is slightly. These hormones causes growth of the follicle. During the first 11 to 12 days of this follicle growth the rate of secretion of FSH & LH decrease slightly because of the negative feedback effect of estrogen on the AP.

## **Pre ovulatory surge of LH & FSH causes ovulation:**

- About 12 days of the monthly cycle, the high secretion of FSH & LH start to increase due to high level of estrogens causes positive feedback on the anterior pituitary which leads to pre-ovulatory LH surge & FSH surge.