

FISIOLOGI ANDROGEN

Kuliah 2

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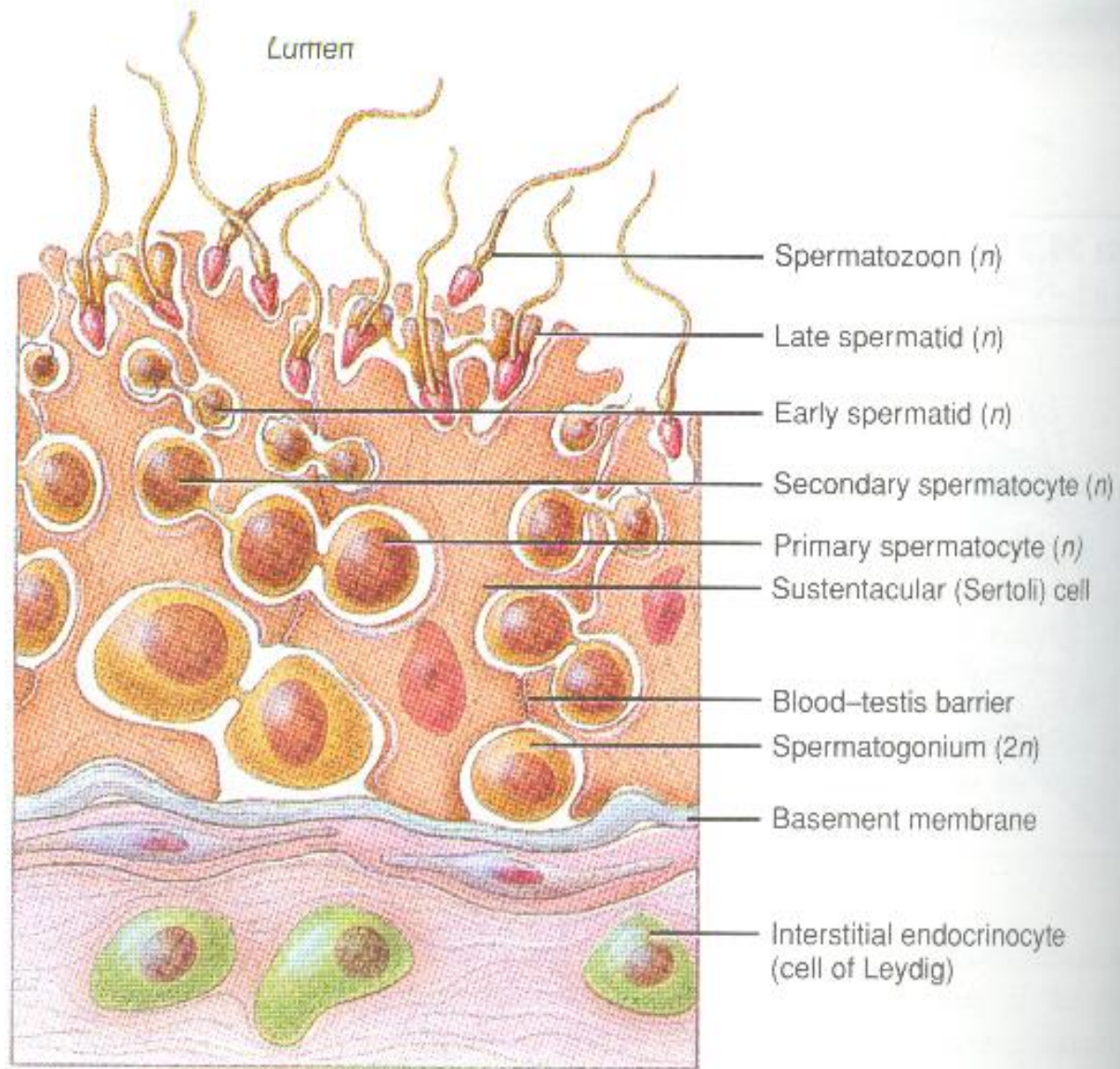
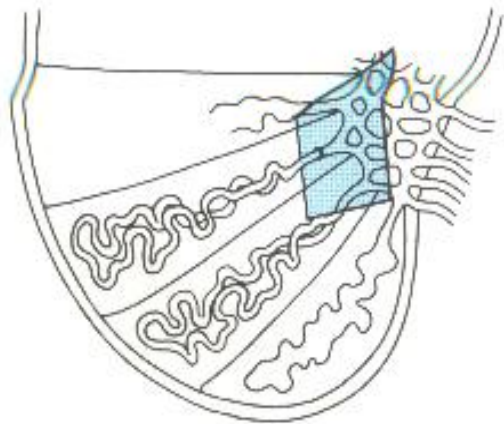
Bagian Fisiologi

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Testes

- Perform dual function of producing sperm and secreting testosterone
- \pm 80% of testicular mass consists of highly coiled seminiferous tubules \rightarrow spermatogenesis
- **Leydig cells/ interstitial cells**
 - in connective tissue between seminiferous tubules
 - are endocrine cells that **produce testosterone**
 - Less easily destroyed (by x-ray, excessive heat)

Thus, portion of testes that produce sperm and portion that secrete testosterone are **distinct structurally and functionally**



(c) Cross section of a portion of a seminiferous tubule

Androgen

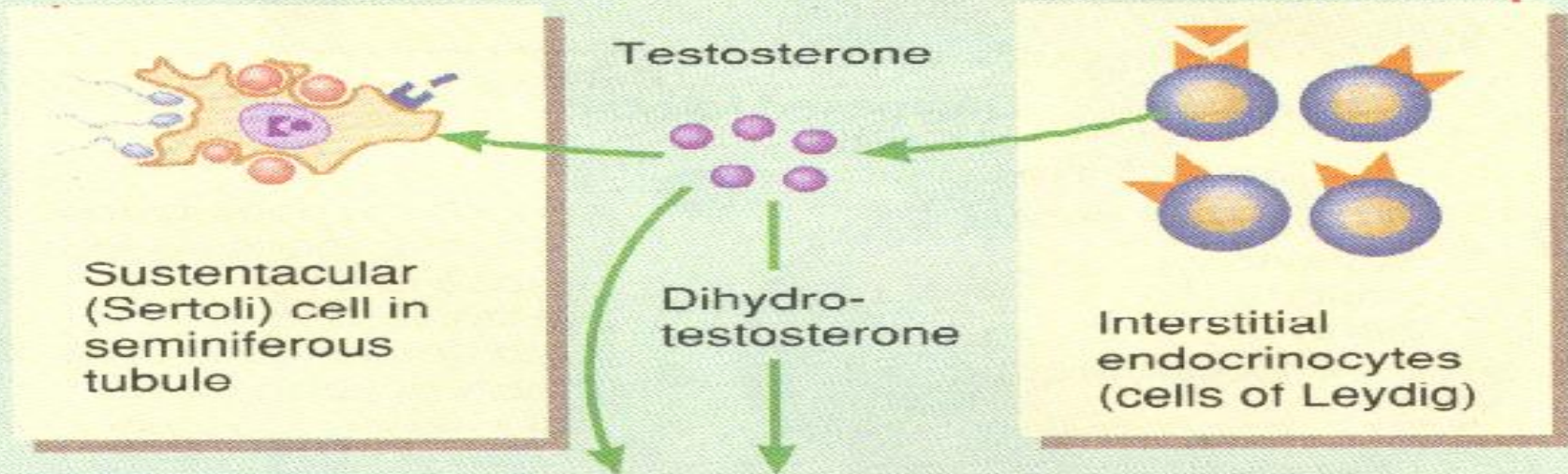
- **Steroid hormones**
- **Derived from cholesterol precursor molecule**
- **Masculinizing effects**
- **Produced by:**
 - **Testes**
 - **Adrenal glands**
 - **Ovary**
- **Consists of:**
 - **Testosterone**
 - **Dihydrotestosterone**
 - **Androstenedione**

Testosterone

■ Once produced:

- **Some of testosterone is secreted into circulation, where it is transported to its target sites of action**
- **A substantial portion goes into the lumen of seminiferous tubules, where it plays an important role in sperm production**

.....Testosterone



- Male pattern of development (before birth)
- Enlargement of male sex organs and expression of male secondary sex characteristics (starting at puberty)
- Anabolism (protein synthesis)

Key:

 LH	 FSH	 Testosterone
 LH receptor	 FSH receptor	 Testosterone receptor

.....Testosterone

- In circulation, testosterone primarily bound to plasma protein:
 - Loosely bound with plasma albumin
 - More tightly bound with a beta globulin: sex hormone-binding globulin
- Become fixed to the tissues (converted into dihydrotestosterone) especially target organs:
 - prostate gland
 - external genitalia of fetal male

.....Testosterone

■ The testosterone that dose **not become fixed** to the tissues is ***rapidly converted*** (mainly by the **liver**) into:

- androsterone
- dehydroepiandrosterone



conjugated as glucoronide or sulfate



excreted into - gut in the liver bile

- urine through the kidney

Functions of Testosterone

- Responsible for the distinguishing characteristics of the masculine body
- Most of testosterone's actions ultimately function to ensure delivery of sperm to the female
- The effects can be group into 5 categories:
 1. Effects on reproductive system **before birth**/ during fetal life
 2. Effects on sex-specific tissues **after birth**
 3. Other reproduction-related effects
 4. Effects on secondary sexual characteristics
 5. Non reproductive actions

Effects of Testosterone

1. Before birth/ During fetal life

- Secreted by genital ridges/ fetal testes
- Stimulated by **placental chorionic gonadotropin/ human chorionic gonadotropin (HCG)**
- Responsible for:
 - > Development of male characteristics:
Masculinizes reproductive tract and external genitalia
 - > Promotes descent of testes into scrotum

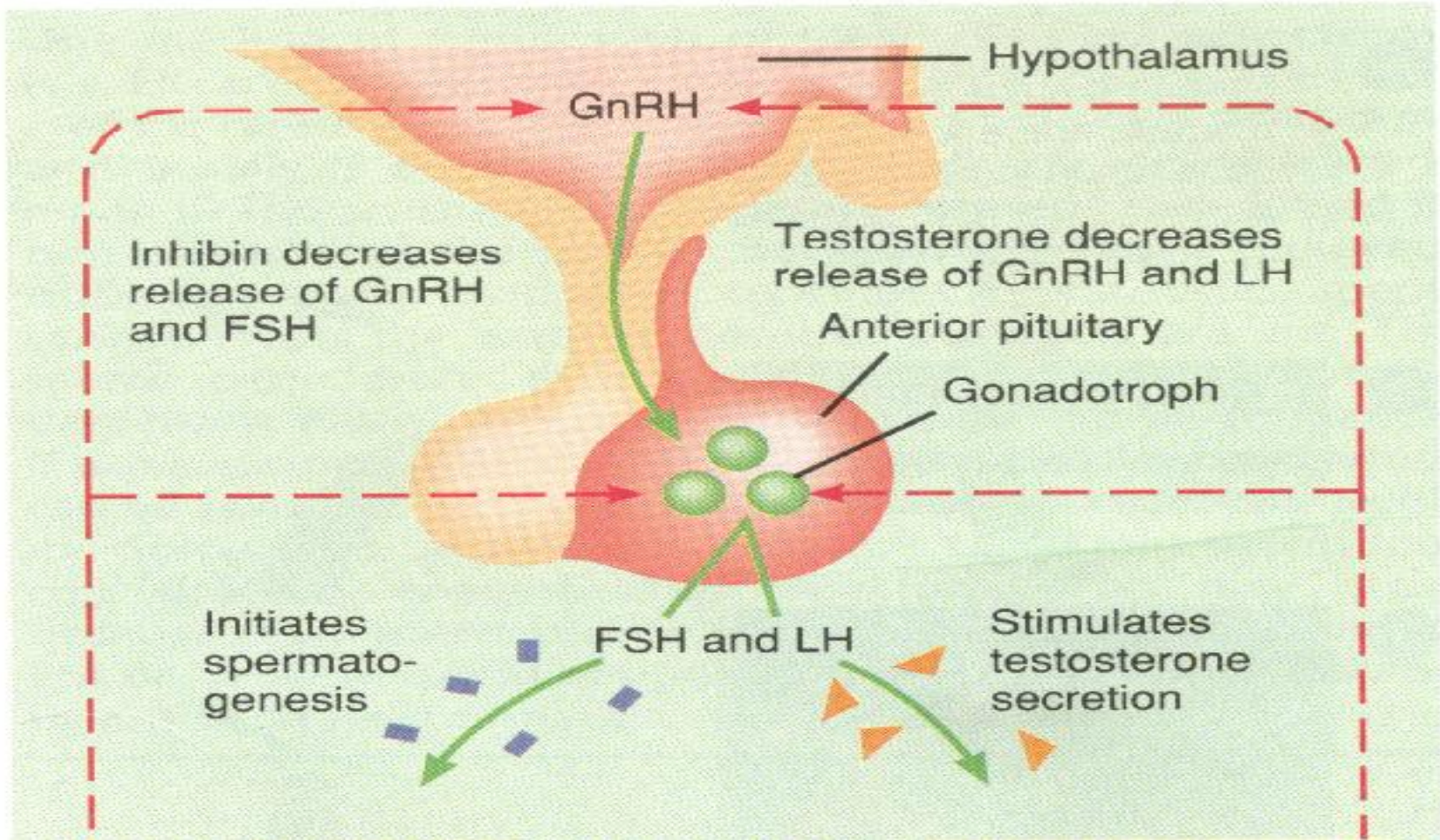
....Effects of Testosterone

2. After birth

- **Until puberty:**
 - > Testosterone secretion ceases
 - > Reproductive system remain small and nonfunctional
- **At Puberty:**
 - > Leydig cells start secreting testosterone once again, stimulated by **pituitary gonadotropin hormone** through **the brain-testicular axis**
 - > Testosterone is responsible for growth and maturation of entire male reproductive system

....Effects of Testosterone

The Brain – Testicular Axis



....Effects of Testosterone

2. After birth.....

- At Puberty:

- > Promotes growth and maturation of reproductive system: testes , penis, scrotum enlarge 8 X before the age of 20 years
- > Essential for producing sperm (spermatogenesis)
- > Maintains reproductive tract throughout adulthood

Once initiated at puberty, testosterone secretion and spermatogenesis occur continuously throughout the male's life

....Effects of Testosterone

2. After birth.....

- Puberty:

- > Usually begin between 10 - 14 years of age (2 years earlier in female)
- > Lasting 3 - 5 years
- > Period of arousal and maturation of previously nonfunctional reproductive system
- > Culminating in sexual maturity & ability to produce
- > Encompasses a complex sequence of endocrine, physical, and behavioral events

Adolescence is a broader concept that refers to entire transition period between childhood and adulthood not just to sexual maturation

....Effects of Testosterone

2. After birth.....

- Testicular efficiency gradually declines after 45 – 50 years of age, even though men in their 70s and beyond may continue to enjoy an active sex life, and some even father a child at this late age
- The gradual reduction in circulating testosterone levels and in sperm production:
 - > is not caused by a decrease in testes stimulation
 - > probably arises from **degenerative changes** that occur **in small testicular blood vessels**
- This gradual decline is termed “male menopause”/ “andropause”, recently has been more aptly termed **androgen deficiency in aging males (ADAM)**

....Effects of Testosterone

3. Other reproduction-related effects

- Develop **sexual libido** and **sex drive**
 - > Important for facilitating delivery of sperm to females
 - > In humans, libido is also influenced by many interacting social and emotional factors
 - > Once libido has developed, testosterone is no longer absolutely required for its maintenance
In castrated males: often remain sexually active, but at a reduced level, even though sex organ regress in size and function
- Control gonadotropin hormone secretion through negative-feedback mechanism

....Effects of Testosterone

4. On secondary sexual characteristic.....

- Effect on skin:

- > Increases the thickness of the skin
- > Increases the ruggedness of the subcutaneous tissues

- Effect on muscle:

- > Promotes muscle growth responsible for male body configuration
- > 50% increases in muscle over in the female
- > as a result of protein deposition

....Effects of Testosterone

- **Effect on hair:**

Induces male pattern of hair growth:

- > on face: beard**
- > chest hair: over the pubis and upward to linea alba**
- > on the back**
- > in genetically predisposed men: baldness**

- **Effect on voice:**

Causes voice to deepen: typical adult masculine bass voice

- > as results of hypertrophy of the laryngeal mucosa; enlargement of larynx; and thickening of vocal folds**

....Effects of Testosterone

5. Non reproductive actions

- **Exerts a protein anabolic effect**
 - > Increases basal metabolism (15%)
 - > Increases the number of red blood cells (15 - 20%)
- **Promotes bone growth**
 - > Increases total quantity of bone matrix and deposition of calcium salts
 - > Deposit additional calcium salts → thickness
 - > Specific effect on the pelvis
- **Closes the epiphyseal plates**
 - > after being converted to estrogen by aromatase

....Effects of Testosterone

- **Effect on electrolyte & water balances:**
 - > Increases the reabsorption of Na in the distal tubules of the kidneys (only the minor degree in comparison with adrenal mineralocorticoids) → increases volumes of extracellular fluid
- **Effect on sebaceous glands:**
 - > Increases the rate of sebaceous secretion → acne
- **May induced aggressive behavior**
 - > It is unclear to what extent general behavioral differences between the sexes are hormonally induced or result from social conditioning

Basic Intracellular Mechanism of Action

■ Increases the rate of protein formation in target cells

- Studied extensively in the prostate glands

Testosterone enter the cells

↓ Intracellular 5 α -reductase

Dihydrotestosterone

Binds with a cytoplasmic receptor protein



Migrates to the nucleus

Binds with a nuclear protein



Induces the DNA – RNA transcription process

.....Basic Intracellular Mechanism of Action

Induces the DNA – RNA transcription process



RNA polymerase become activated



Increases the concentration of RNA



Progressive increased in cellular protein



Increases the quantity of DNA



Increases number of cells

....Basic Intracellular Mechanism of Action

- Some target tissues that do not have the reductase enzyme



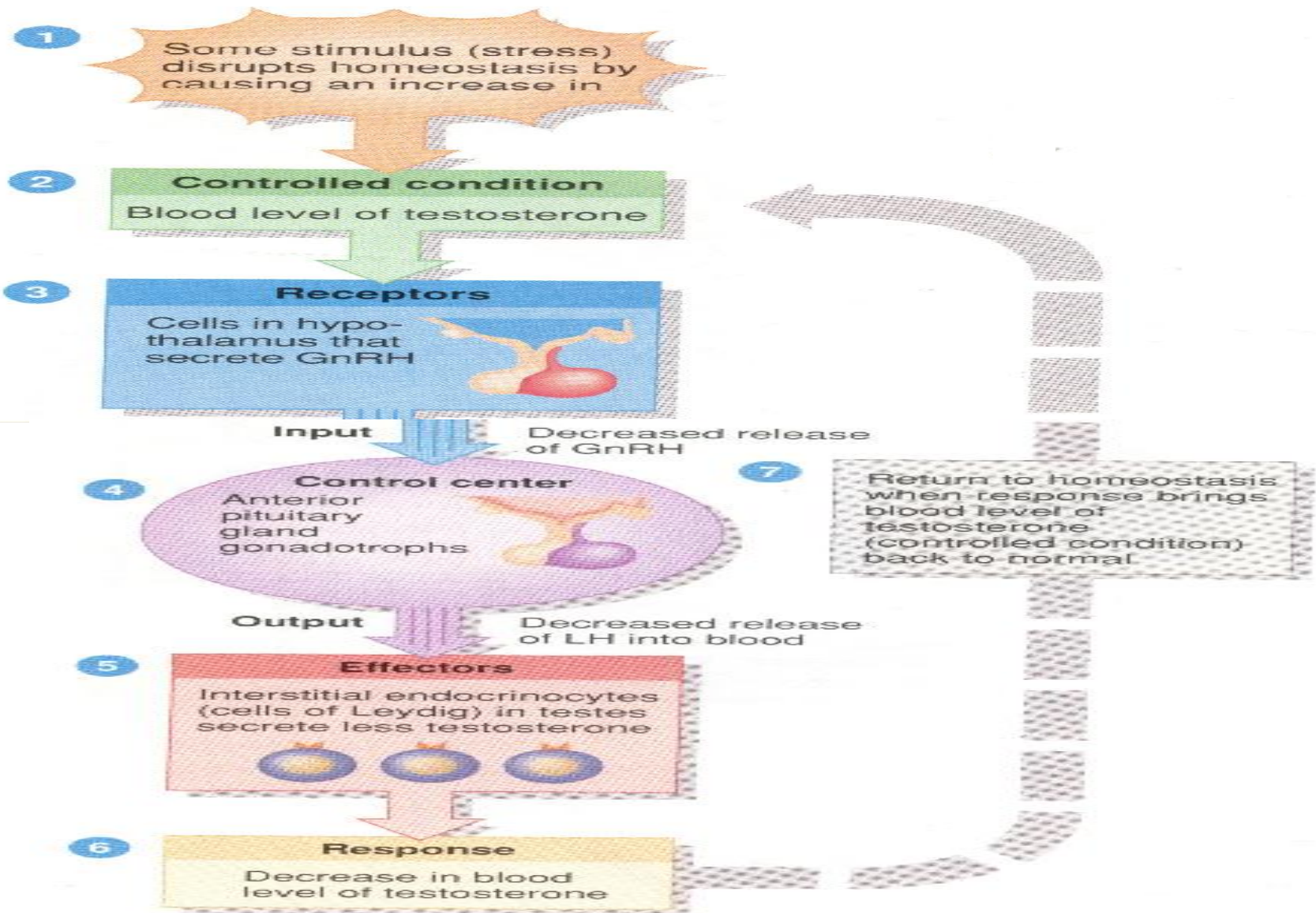
Testosterone cannot be changed into dihydrotestosterone



Testosterone functions directly

The potency to induce cellular protein formation **only half**

FIGURE 28.7 Negative feedback control of blood level of testosterone.



Question: Which hormones inhibit secretion of FSH and LH by the anterior pituitary gland?

Estrogen in Males

- **Small amount of estrogen produced by adrenal cortex and in adipose tissue**
- **A portion of testosterone secreted by testes is converted to estrogen outside testes by enzyme aromatase, which is widely distributed**
 - **because of this conversion, sometimes difficult to distinguish effects of testosterone itself and testosterone-turned-estrogen inside cells**
 - > **scientists recently learned that closure of epiphyseal plates in males is induced not by testosterone per se but by testosterone-turned-estrogen**

.....Estrogen in Males

- **Estrogen receptors have been identified in:**
 - testes
 - prostate
 - bone, and elsewhere
- **Recent findings suggest that estrogen plays an essential role in male reproductive health**
 - important in spermatogenesis
 - surprisingly contributes to male heterosexuality
- **Likely contributes to bone homeostasis**

The depth, breadth, and mechanisms of action of estrogen in males are only beginning to be explored

Thank You

Tugas

Hiperaktivitas:

- **Hormon seks pria pada pria**
- **Hormon seks wanita pada pria**