SAWA UNIVERSITY

Clinical Endocrinology

Gonadal Gland

Sawa University

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Department of Medical Laboratories

جامعـــــة ســـــاوة الاهلية

كليـــة التقنيـــات الصحيـة والطبيـة

قسم تقنيات المختبرات الطبية

المرحلـــــــــــة الثالـثة

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تدريسي المادة : م.م عقيل محمد رسول

Gonadal Hormones

The gonads (**testes** in males, **ovaries** in females) perform closely related **dual functions**.

1. Synthesize sex hormones;

2. Produce germ cells.

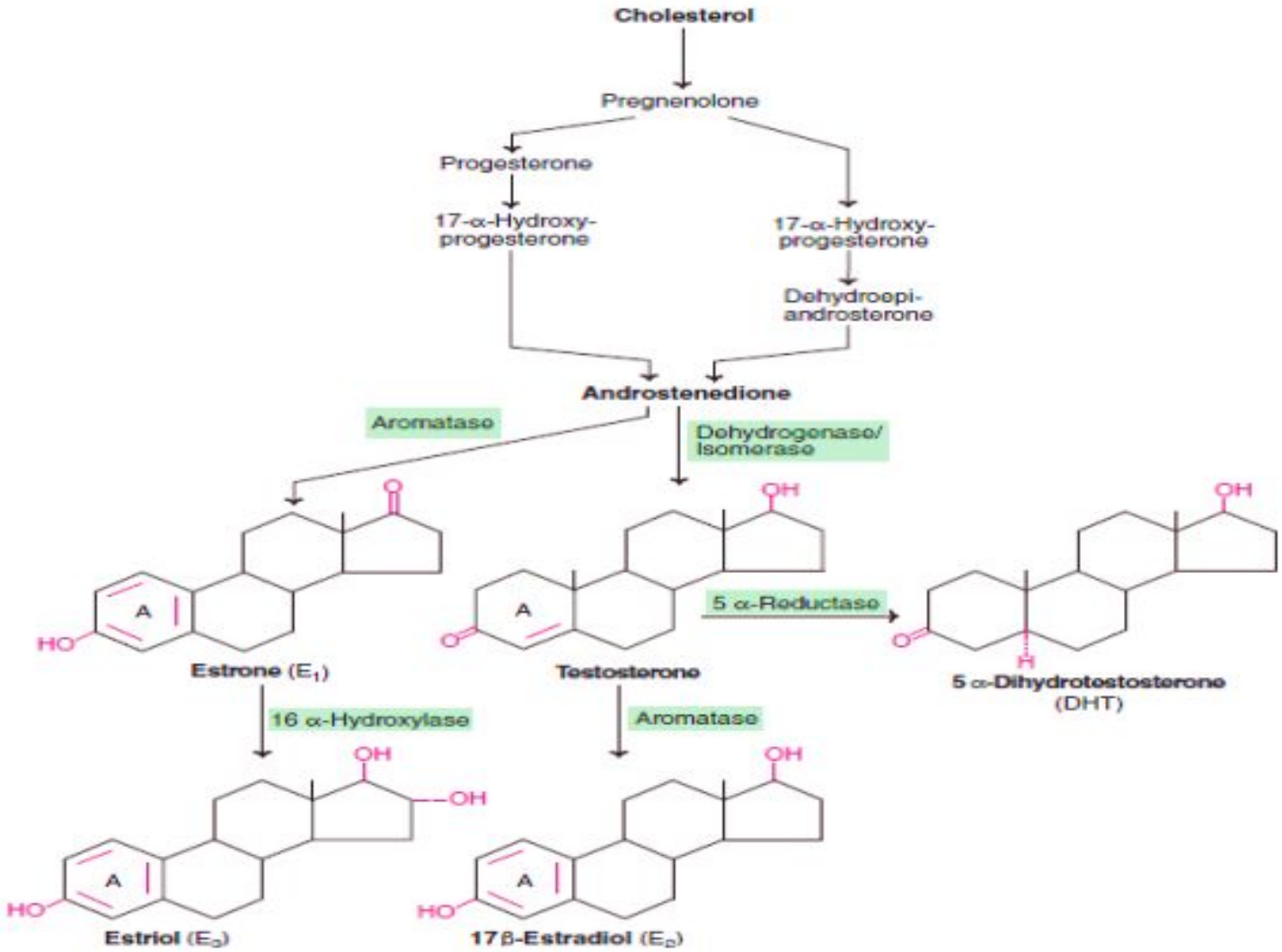
The steroid **sex hormones** are responsible for growth, development, maintenance and regulation of reproductive system. **Sex hormones** are essentially **required** for the **development of germ cells.**

The sex hormones are categorized into **three groups**

A. Androgens or **male sex hormones** which are C-19 steroids.

B. Estrogens or **female sex hormones** which are C-18 steroids. **Ring A** of steroid nucleus is **phenolic in nature** and is devoid of C-19 methyl group.

C. Progesterone is a C-21 steroid **produced** during **the luteal phase** of menstrual cycle **and** also during **pregnancy**.


Cholesterol
Pregnenolone
Progesterone
17-α-Hydroxy-progesterone
17-α-Hydroxy-progesterone
Dehydroepi-androsterone
Androstenedione
Aromatase
Dehydrogenase/ Isomerase
Estrone (E1)
Testosterone
5 α-Reductase
5 α-Dihydrotestosterone (DHT)
16 α-Hydroxylase
Aromatase
Estriol (E3)
17β-Estradiol (E2)

A- Androgens

The male sex hormones or androgens are **produced by** the **Leydig cells of the testes and** to a **minor extent by the adrenal glands** in both the sexes. Ovaries also produce small amounts of androgens.

Biosynthesis of androgens

Cholesterol is the **precursor** for the **synthesis of androgens**. It is first **converted to pregnenolone** which then forms **androstenedione** by **two pathways**—

- **either through** progesterone
- **or through** 17- hydroxypregnenolone.

Testosterone is **produced** from **androstenedione.** The **production of androgens** is *under the control of LH and FSH*.

Active form of androgen: The primary **product of testes is testosterone**. However, the active hormone in many tissues is **not** testosterone but its metabolite **dihydrotestosterone (DHT**). **Testosterone**, on **reduction** by the **enzyme 5 α-reductase**, forms **DHT.** This **conversion** mostly occurs in the peripheral tissues. Some workers consider testosterone as a prohormone and dihydrotestosterone, the **more potent form** as the hormone.

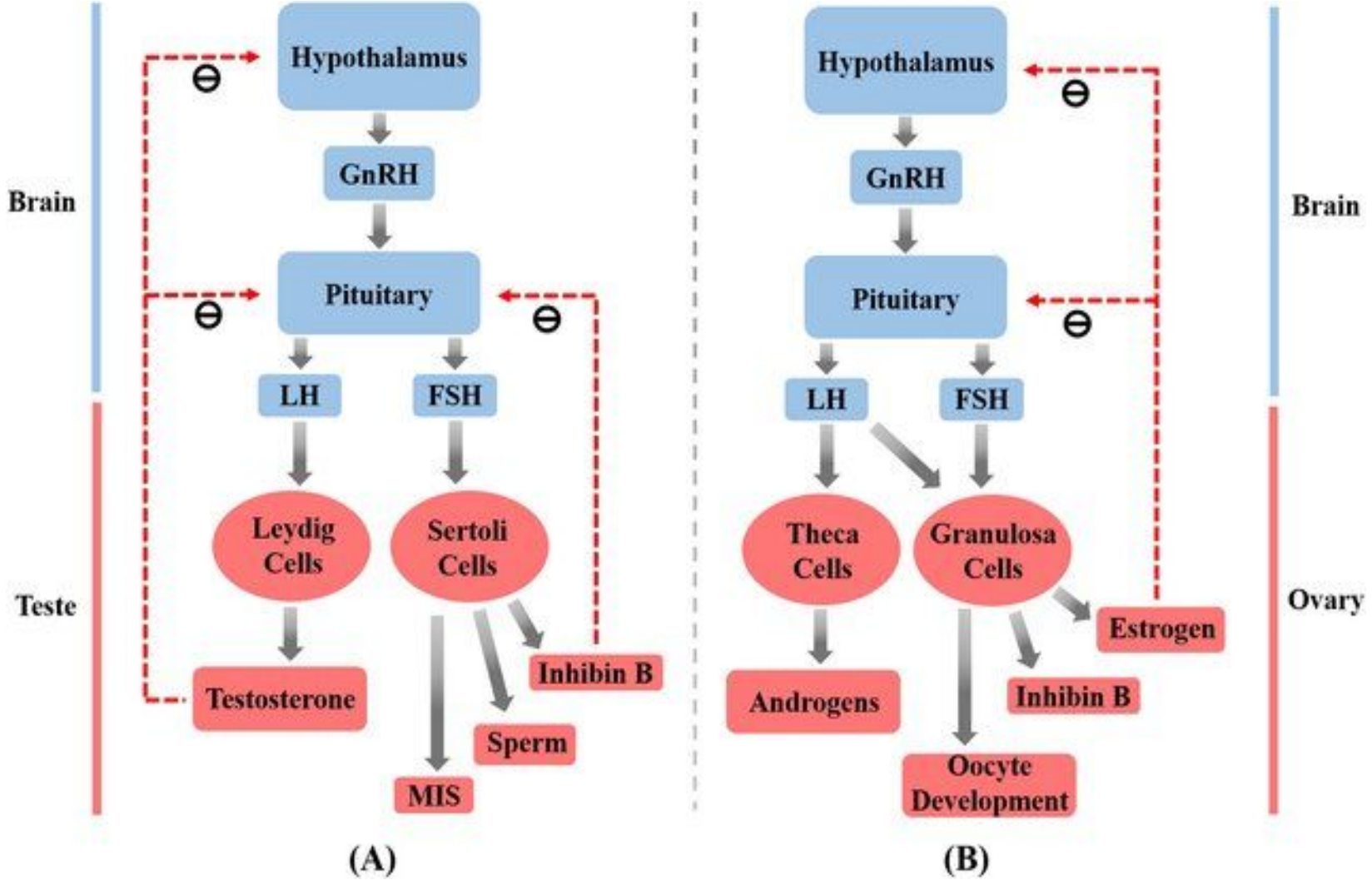
Physiological and biochemical functions of androgens

1. Sex-related physiological functions: The androgens, primarily DHT and testosterone, **influence**:

- * Growth, development **and** maintenance of **male reproductive organs.**
- * Sexual differentiation **and** secondary sexual characteristics.
- * Spermatogenesis.
- * Male pattern of aggressive behavior.

2. Biochemical functions: Many specific biochemical effects of androgens that ultimately influence the physiological functions stated above are identified. **Androgens are anabolic in nature.**

- **Effects on protein metabolism**: Androgens **promote** RNA synthesis (transcription) and protein synthesis (translation). Androgens **cause** *positive nitrogen balance and increase the muscle mass.*
- **Effects on carbohydrate and fat metabolisms**: Androgens increase glycolysis , fatty acid synthesis and citric acid cycle.
- **Effects on mineral metabolism**: Androgens **promote** mineral deposition **and** bone growth before the closure of epiphyseal cartilage.


Brain
Teste
Hypothalamus
GnRH
Pituitary
LH
FSH
Leydig Cells
Sertoli Cells
Testosterone
Inhibin B
Sperm
MIS
(A)
Hypothalamus
GnRH
Pituitary
LH
FSH
Theca Cells
Granulosa Cells
Androgens
Estrogen
Inhibin B
Oocyte Development
Brain
Ovary
(B)

B- Estrogens

Estrogens are predominantly **ovarian hormones**, **synthesized** by the **follicles and corpus luteum of ovary.** These hormones are responsible for *maintenance of menstrual cycle and reproductive process in women.*

Synthesis of estrogens

Estrogen synthesis occurs from the **precursor cholesterol.** Estrogens are **produced** by **aromatization** *(formation of aromatic ring*) **of androgens**. The **ovary produces** estradiol (E2) and estrone (E1) while the **placenta synthesizes** these two steroid hormones and estriol (E3). The synthesis of estrogens is under the control of LH and FSH.

Physiological and biochemical functions of estrogens

1. Sex-related physiological functions: The estrogens are primarily concerned with

- * Growth, development and maintenance of female reproductive organs.
- * Maintenance of menstrual cycles.
- * Development of female sexual characteristics.

2. Biochemical functions: Estrogens are involved in many metabolic functions.

* **Lipogenic effect:** Estrogens **increase lipogenesis** in adipose tissue and, for this reason, *women have relatively more fat (about 5%) than men.*

* **Hypocholesterolemia effect:** **Estrogens lower** the plasma total **cholesterol.** The LDL fraction of lipoproteins is decreased while the HDL fraction is increased. This explains the **low incidence of atherosclerosis** and coronary **heart diseases** .

***Anabolic effect:** Estrogens in general **promote transcription and translation**. The synthesis of many proteins in liver is elevated **e.g. transferrin.**

* **Effect on bone growth:** Estrogens like androgens **promote calcification and bone growth.** It is believed that decalcification of bone in the postmenopausal women leading to osteoporosis is due to lack of estrogens.

* **Effect on transhydrogenase:** Transhydrogenase is an enzyme activated by estrogen. It is capable of **transferring reducing equivalents** from NADPH to NAD+. It is explained that in the women after menopause, due to deficiency of estrogens, the ***transhydrogenase activity is low***. This **results** in the of NADPH **towards lipogenesis—causing obesity**

C- Progesterone: **is synthesized and secreted** by corpus luteum and placenta. Progesterone, as such, is **an intermediate** in the *formation of steroid hormones from cholesterol*. **LH controls the production of progesterone.**

Biochemical functions of progesterone

1. Progesterone is essentially **required** for the implantation of fertilized ovum and maintenance of pregnancy.
2. 2. It **promotes the growth** of glandular tissue in uterus and mammary gland.
3. Progesterone increases the body temperature by **0.5–1.5 F°**. The exact mechanism of this **thermogenic effect** is not clearly known. The measurement of temperature was used as an indicator for ovulation.

Relaxin

Relaxin is a hormone concerned with the **relaxation of pelvic tissues and cavity** operating in conjunction with other factors. **Relaxin** is **produced**, during pregnancy, in *tissues of the reproductive system*, e.g. principally by **corpus luteum** and also **by placenta**. *Its production is stimulated by progesterone*, *pregnenolone and related adrenocortical steroids*, **e.g.** *deoxy corticosterone.*

Chemistry: Porcine relaxin is made up of **two peptide chains**, consisting **of 22 and 26 amino acid** residues. It has **two S–S bonds linking** its two chains and one intra-chain **S–S bond** in the A-chain. Approximate mol. wt. = 9000. It is **inactivated** by proteolytic enzymes or by reagents which ***breaks the S– S bond.***

Metabolic Role

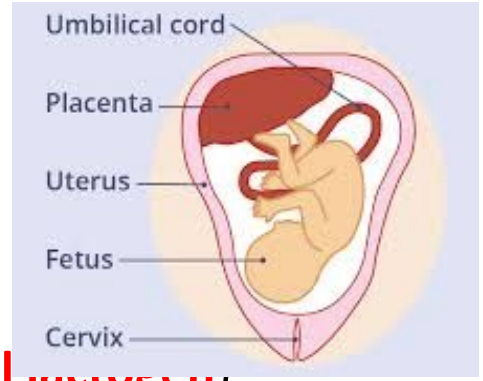
The specific effect of relaxin consists of:

- Increased vascularity of the connective tissue of the symphysis.
- Followed by imbibition of water, dissolution and splitting of collagen fibres, and disorganization of the fibrous structures. There is depolymerization of MPS of ground substance.
- The above makes separation of the symphysis pubis and, a dilatation .

Placental Hormones

Pregnancy activates the placental hormones. The implanted blastocyst forms the trophoblast which is subsequently organised into the placenta. **The placenta provides** the nutritional connection between the embryo and the maternal circulation. **Human placenta produces and secretes:**

[(a) Peptide hormones and (b) Ovarian steroid hormones]



(a) Peptide hormones:

1. Human chorionic gonadotropin hormone (hCG) and

2. Chorionic somatomammotropin (CS) (also called **placental lactogen**).

1. Human Chorionic Gonadotropin (hCG):

Origin: It is formed by the syncytiotrophoblast of chorionic villi within 12 to 14 days of fertilization.

Mechanism of Action: The hormone binds to "**specific receptor**" on the cell membrane of target tissues like **ovaries and testes**, **activates adenyl cyclase**, which in turn **increases cyclic AMP level ↑**. Cyclic AM Pacts as "**second messenger**" to produce the biological effects.

Metabolic Role

- **Luteotrophic effect**: The hormone produces enlargement of corpus luteum and stimulates its secretion.

It maintains a secretory corpus luteum in first three months of pregnancy.

- **Testosterone secretion**: Like LH, the hormone stimulates the growth of interstitial cells (Leydig cells) of embryonic testes and produces testosterone. This helps in verification of the reproductive system of male embryo.

2. Chorionic Somatomammotropin (CS):(Placental Lactogen)

The hormone **has biologic properties** of prolactin and growth hormone of anterior pituitary. It is a peptide hormone and amino acid sequences **are similar** to GH and prolactin (**85% homology**). The hormone is **secreted by the syncytiotrophoblast** from about *the second week of pregnancy*, *rises slowly and reaches a peak approximately by 36 weeks of pregnancy*.

Metabolic Role

The exact role of this hormone is **not clear**, because *pregnant women lacking this hormone have normal pregnancies and deliver normal babies*. But as the hormone has similar structure to anterior pituitary GH and prolactin, **it exerts similar effects:**

- **Somatotrophic effect**: May **promote** growth of maternal tissues.
- **Luteotrophic effect: Stimulates** the enlargement, growth and secretion of corpus luteum and helps to maintain a secretory corpus luteum.

- **Mammotrophic effect:** Stimulates alveolar growth of mammary glands during pregnancy.
- **Lactogenic effect:** Also **stimulates** lactation.
- **Anabolic effect: Stimulates** foetal and maternal tissue growth. Promotes retention of N, Ca++ and inorganic P.
- **Anti-insulin effect:** May decrease glucose utilization, decreased carbohydrate tolerance and hyperglycaemic effect.

(b) Ovarian steroid hormones

1. Progestins

2. Estrogens, chiefly Estriol.

1. Progestins: The corpus luteum is the **major source of progesteron**e for the first **6 to 8 weeks of pregnancy** and **then placenta takes over this function**. The corpus luteum though continues to function, but in third trimester onwards, the placenta produces 30 to 40 times more progesterone than the corpus luteum. **Placenta cannot synthesize cholesterol from 'active' acetate**, hence for cholesterol it has to **depend on maternal supply.**

2. Estrogens: *Plasma concentrations of estradiol, estrone and estriol gradually increase throughout pregnancy*. **Estriol** is **produced in the largest amount**. Adrenal cortex of **foetus produces DHEA and DHEA SO4,** which are converted to 16 α-OH derivatives by the foetal liver, and these are subsequently converted to estriol by the placenta. After its formation, **travels via** the placental circulation to the maternal liver, where they are conjugated to **glucuronides**, and then **are excreted in the urine**.

Clinical Significance

1. Feto-placental function: As estriol is **formed by placenta**, the measurement of urinary estriol levels **has been used as a test** of feto-placental function. **Failure of urinary estriol** or **total estrogens to rise in late pregnancy reflects** the integrity of the **feto-placental unit** and may **indicate** imminent **fetal death** or **placental insufficiency**, e.g **preeclamptic toxaemia.**

Note: **Urinary pregnanediol** (**or plasma progesterone**) **reflects** placental function only as does estimation of **plasma placental lactogen**. **A falling titre** of urinary estrogens **or** plasma placental lactogen is serious.

2. Pregnancy tests: Increased **urinary excretion of HCG** which **occurs in early pregnancy** (as early **as 10th day of gestation**) forms the basis for pregnancy tests.

Questions :

1. Which part of the adrenal gland produces glucocorticoids?
2. What is the primary function of mineralocorticoids?
3. Which of the following is the most important glucocorticoid in humans?

Learning Resources for Hormone Mechanisms

Here are excellent sources to deepen your understanding of this topic:

Medical Textbooks:

"Harper's Illustrated Biochemistry" (Chapter on Hormones & Signal Transduction): Provides a detailed, yet clear, biochemical perspective on second messenger systems.

"Guyton and Hall Textbook of Medical Physiology" (Chapter 74: Introduction to Endocrinology): Excellent for understanding the physiological principles of hormone-receptor interactions and signaling.

"Greenspan's Basic & Clinical Endocrinology": A comprehensive resource that links basic mechanisms to clinical practice.

YouTube Channels:

Armando Hasudungan: His detailed drawings are fantastic for visualizing signal transduction pathways.

Dr. Najeeb Lectures: Provides extremely detailed lectures on the entire process.