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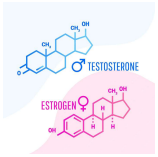
Reproduction Module

2nd Year MBBS (SGD)

Reproductive Hormones



H.O.D
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Presenter: Dr. Sana Latif
(Senior Demonstrator)

Updated Date: 25-02-25

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Motto, Vision, Dream

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

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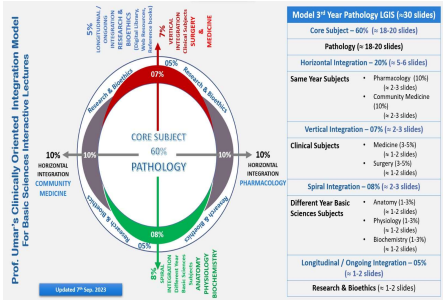
Professor Umar Model of Integrated Lecture



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SGD- MCQ Assessment

1. **Which steroid hormone serves as the precursor for both androgens and estrogens?**
   A. DHEA
   B. Progesterone
   C. Cortisol
   D. Estradiol
   E. ACTH
2. **The main source of progesterone during the luteal phase is the:**
   A. Adrenal medulla
   B. Corpus luteum
   C. Anterior pituitary
   D. Granulosa cells
   E. Theca interna
3. **Which hormone is directly responsible for the development of male external genitalia in utero?**
   A. Testosterone
   B. Estradiol
   C. Androstenedione
   D. DHT
   E. DHEA
4. **Estradiol is mainly synthesized in ovarian granulosa cells via conversion of:**
   A. DHEA
   B. Progesterone
   C. Testosterone
   D. Cortisol
   E. DHT

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SGD- MCQ Assessment

5. **Which enzyme converts progesterone to 17-hydroxyprogesterone?**
   A. 5α-reductase
   B. 17α-hydroxylase
   C. Aromatase
   D. 11β-hydroxylase
   E. 3β-HSD
6. **The strongest natural estrogen in premenopausal women is:**
   A. Estriol
   B. Estrone
   C. Estradiol
   D. Testosterone
   E. DHEA
7. **In males, which hormone is produced in the highest quantity in the adrenal cortex and serves as a weak androgen?**
   A. DHEA
   B. Estradiol
   C. Progesterone
   D. DHT
   E. Testosterone
8. **What is the role of aromatase in reproductive hormone metabolism?**
   A. Converts progesterone to cortisol
   B. Converts androgens to estrogens
   C. Converts DHEA to progesterone
   D. Converts DHT to estradiol
   E. Inactivates testosterone

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SGD- MCQ Assessment

9. **Androstenedione is converted into testosterone by which enzyme?**
   A. 5α-reductase
   B. Aromatase
   C. 17β-hydroxysteroid dehydrogenase
   D. 21-hydroxylase
   E. CYP11A1
10. **Which of the following increases significantly during the luteal phase of the menstrual cycle?**
    A. Estradiol
    B. DHEA
    C. Testosterone
    D. Progesterone
    E. LH

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SGD- MCQ Assessment

1. B
2. B
3. D
4. C
5. B
6. C
7. A
8. B
9. C
10. D

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Learning Objectives

- Biochemical aspects of Male and Female Reproductive Hormones.
- Outline of the Reproductive Anatomy.
- Mechanism of Regulation of Reproductive Hormones.
- Clinical Implications of Hormone imbalances.
- Management of related disorder.
- Role Of AI and Bioethics in Reproductive Endocrine Imbalance

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Interactive Session

A female XYZ, unmarried, age 25 years, comes to the OPD asking for information about how to manage the hair growth and acne on her face.

She explains that she has **polycystic ovary syndrome** and started taking the combined oral contraceptive pill three months ago. She is worried that although the treatment has helped with most of her symptoms (her periods are more regular and less painful), the acne on her face and the hair on her chin are still present. The patient confirms there is no family history of cardiovascular disease and she has recently joined a running club to help her maintain a fit and healthy lifestyle.

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Core Knowledge

Main Hormones of the Reproductive System

MALE
- **Testosterone**
- **Dihydrotestosterone (DHT)**

FEMALE
- **Estrogen**
- **Progesterone**

- Androgens:
  Androstenedione
  DHEA
- Follicle Stimulating Hormone
- Luteinizing Hormone
- Inhibin

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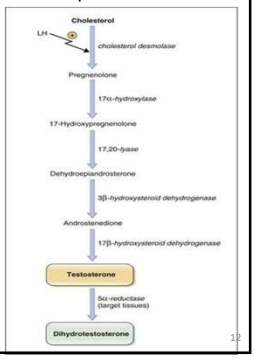
Core Knowledge

Male Reproductive Hormones

Testosterone

- **Production**: Leydig cells of the testes.
- **Regulation**: Hypothalamic-Pituitary-Gonadal (HPG) axis.
- **Enzyme**:17β-Hydroxysteroid dehydrogenase (17β-HSD).
- **Functions**
- **Primary Sexual Characteristics** (Fetal Life)
- **Secondary Sexual Characteristics** (Puberty)
- **Spermatogenesis** i.e production and maturation of sperm.
- **Anabolism :** protein synthesis and muscle growth.
- **Behavioral Effects**: Influences libido and aggression.



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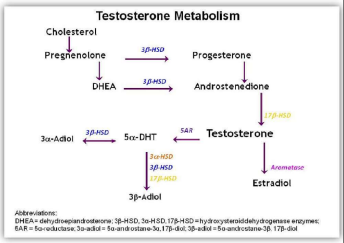
Core Knowledge — Male Reproductive Hormones

Dihydrotestosterone (DHT)

More potent than testosterone.

- ❖**Production**: Prostate, skin, liver
- ❖**Regulation**: Hypothalamic-Pituitary-Gonadal (HPG) axis.
- ❖**Enzyme**: 5 α Reductase
- ❖**Functions**
  - Development of the prostate.
  - Formation of external genitalia during fetal development.
  - Secondary sexual characteristics: facial/body hair, and sebaceous gland activity



Clinical Relevance:

- Conditions like benign prostatic hyperplasia (BPH) and androgenic alopecia (male pattern baldness) are influenced by DHT levels.

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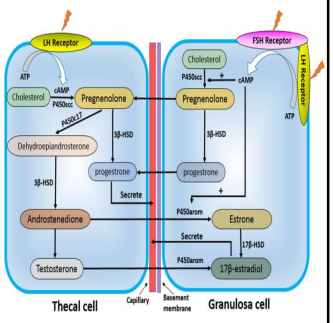
Core Knowledge — Female Reproductive Hormones

Estrogen

Most potent form: Estradiol

- ❖**Production**: Granulosa Cell of the Ovary, Adrenal Gland, Adipose Tissue.
- ❖**Regulation**: Hypothalamic-Pituitary-Ovarian (HPO) axis.
- ❖**Enzyme**:17β-HSD, P450 aromatase
- ❖**Functions**
  - development of female secondary sexual characteristics
  - regulation of the menstrual cycle, and maintenance of the reproductive tissues.
  - systemic effects on bone density, cardiovascular health, and skin integrity.



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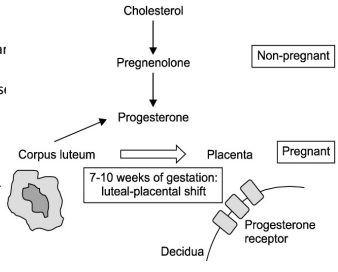
Core Knowledge — Female Reproductive Hormones

Progesterone

- ❖**Production**: corpus luteum in the ovaries and the placenta during pregnancy
- ❖ **Regulation**: Hypothalamic-Pituitary-Ovarian (HPO) axis.
- ❖**Enzyme**: 3 β- Hydroxysteroid dehydrogenase
- ❖**Functions**
  - to prepare the endometrium for implantation and maintain pregnancy.
  - Regulation of menstrual cycle by inhibiting LH and FSH release, thus preventing further ovulation during the luteal phase.
  - The development of mammary glands for lactation.
  - Uterine smooth muscle relaxation for preventing preterm labor.



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Core Knowledge — Common Reproductive Hormones

Androgens: Androstenedione and DHEA

- **Androstenedione**:
  - Produced in the adrenal glands and gonads.
  - Intermediate in the biosynthesis of testosterone and estrogen.
- **DHEA**:
  - Produced mainly by the adrenal cortex.
  - Functions as a precursor to male and female sex hormones.
  - Levels peak in early adulthood and decline with age.
- **Role in Puberty**:
  - Contributes to the growth spurt and development of secondary sexual characteristics.

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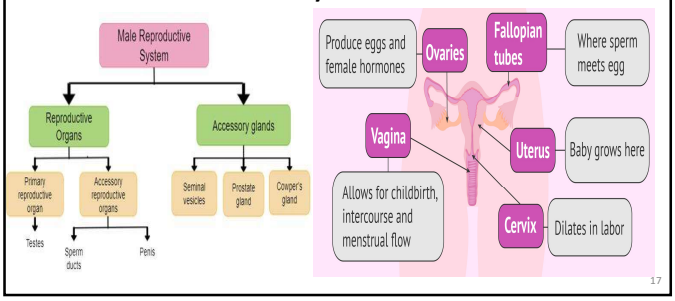
Horizontal Integration

Anatomy of the Male And Female Reproductive System



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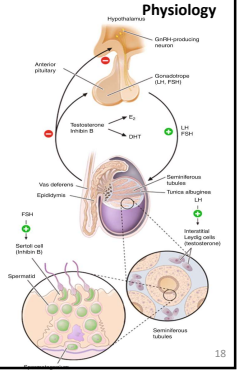
Horizontal Integration

Physiology

Hypothalamic-Pituitary-Gonadal Axis

The Regulator of Testosterone Level

- **Hypothalamus**:
  - Releases Gonadotropin-Releasing Hormone (GnRH) in a pulsatile manner.
- **Pituitary Gland**:
  - Releases Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) in response to GnRH.
- **Testes**:
  - **LH**: Stimulates Leydig cells to produce testosterone.
  - **FSH**: Supports Sertoli cells and spermatogenesis.
- **Negative Feedback**:
  Inhibition of GnRH and LH secretion.
- **Positive Feedback**:
  Conversion of testosterone to estradiol by the enzyme aromatase.



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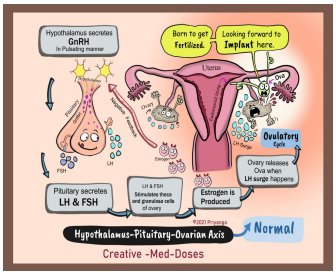
Horizontal Integration

Physiology

Hypothalamic-Pituitary-Ovarian Axis

- **Hypothalamus**:
  - Releases Gonadotropin-Releasing Hormone (GnRH) in a pulsatile manner.
- **Pituitary Gland**:
  - Releases Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) in response to GnRH.
- **Ovaries**:
  - **LH**: Triggers ovulation (LH Surge), Production of Progesterone by Corpus Luteum
  - **FSH**: Follicular Growth, Production of Estrogen
- **Negative Feedback**:

Estrogen and progesterone exert negative feedback on the hypothalamus and pituitary to regulate the secretion of GnRH, FSH, and LH, maintaining hormonal balance.



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Vertical Integration

Clinical Correlation
Male Hormonal Imbalances and Treatment

- **Hypogonadism**:
  - **Causes**: Klinefelter syndrome, testicular injury, pituitary disorders.
  - **Symptoms**: Reduced libido, erectile dysfunction, infertility, decreased muscle mass, fatigue.
  - **Treatment**: Testosterone replacement therapy (TRT).
- **Hypergonadism**:
  - **Causes**: Androgen-secreting tumors, anabolic steroid use.
  - **Symptoms**: Early puberty in boys, aggressive behavior, increased muscle mass.
  - **Treatment**: Address underlying cause, potential use of anti-androgens.
- **Androgen Insensitivity Syndrome**:
  - **Description**: Genetic condition where individuals have male XY chromosomes but develop female characteristics due to androgen receptor dysfunction.
  - **Management**: Psychological support, hormone therapy.
- **Benign Prostatic Hyperplasia (BPH)**:
  - **Description**: Enlargement of the prostate gland, common in older men.
  - **Symptoms**: Urinary frequency, urgency, weak stream.
  - **Treatment**: 5-alpha-reductase inhibitors, alpha-blockers, surgery.

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Vertical Integration

Clinical Correlation
Female Hormonal Imbalances and Treatment

- **Polycystic Ovary Syndrome (PCOS):**
  - ✓Hormonal imbalances, including elevated levels of androgens.
  - ✓Clinical features include irregular menstrual cycles, hirsutism, acne, weight gain, and infertility.
  - ✓Hormonal therapies for PCOS include combined oral contraceptives, anti-androgens, metformin, and clomiphene citrate.
- **Amenorrhea:**
  - ✓Amenorrhea is the absence of menstrual periods and can be primary or secondary.
  - ✓Causes include hormonal imbalances, hypothalamic dysfunction, pituitary disorders, PCOS, or thyroid dysfunction.
  - ✓Hormonal therapies depend on the underlying cause and may include hormone replacement therapy (HRT) in menopause-related cases.
- **Premature Ovarian Failure (POF):**
  - ✓ovaries stop functioning before the age of 40, leading to decreased estrogen production.
  - ✓Clinical features include irregular or absent menstrual periods, hot flashes, vaginal dryness, and infertility.
  - ✓Hormone replacement therapy (HRT) and combined oral contraceptives for symptoms management.
- **Hormonal Therapies and Their Uses:**
  - ✓Hormone Replacement therapy (HRT)
  - ✓Contraceptive hormonal therapy includes various forms such as combined oral contraceptives, progestin-only pills, patches, injectables, and hormonal IUDs.
  - ✓treatment of endocrine disorders like hypothyroidism, hyperthyroidism, adrenal insufficiency, and diabetes mellitus.

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Spiral Integration — Family Medicine

Management of PCOS

Family Medicine plays important role in following manner:

- Diagnosis
- Education
- Dietary Guidance
- Monitoring
- Refer to Specialists

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Spiral Integration — Family Medicine

Management of PCOS

- Since she has only been taking the pill for three months and has seen an improvement in her symptoms, she does not need to go to her GP for referral to a dermatologist. To see the full benefit of the pill, **up to six months of treatment is needed**; therefore, she should be **reassured** that it might take another three months for the full effects of treatment to be achieved. She should also be advised to maintain a balanced diet and continue with her running club.
- The patient can be advised to buy **over-the-counter benzoyl peroxide** as a 5% gel or as a 10% wash for her acne. For better efficacy, she should apply it to her face using a cleanser and sun protection moisturizer rather than applying to individual lesions. The treatment can be completed for six weeks and be assessed thereafter. Johanna should also be advised that non-comedogenic make up is available.
- **If after six months of treatment, Miss XYZ still has acne and facial hair, she should be referred to her Dermatologist/Endocrinologist** for a prescription. However, it is important to advise her that a common side effect of facial hirsutism cream is acne; therefore, hair removal may be a good option for this patient. Laser removal of facial hair may also be considered.

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Spiral Integration — Artificial Intelligence

Role Of AI in Management

Artificial Intelligence plays role in following aspects:

- Personalized Nutrition
- Diagnostic Tools
- Food Recommendations
- Drug Development

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Spiral Integration | Bioethics

Ethical Consideration

- **Informed Consent**:

Ensuring that individuals fully understand the risks and benefits of hormone treatments, particularly when used for purposes such as fertility treatments or gender transition.

- **Equity and Access**:

Ethical concerns arise when certain groups face barriers to accessing reproductive health care or when treatments are unaffordable.

- **Reproductive Rights**:

Balancing the rights of individuals to make decisions about their own reproductive health with societal concerns about the potential consequences of certain hormone therapies, such as the implications for future generations or the environment.

- **Risk and Safety**:

Assessing the risks and benefits of hormone therapies, including potential long-term health effects, and ensuring that patients are adequately informed about these risks. the responsibility of healthcare providers and researchers is to minimize risks and prioritize patient safety.

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Spiral Integration | Research Article

Quantifying The Variability In The Assessment Of Reproductive Hormone Levels.

Ali Abbara [1], Sophie Adams [2], Maria Phylactou [1], Chioma Izzi-Engbeaya [1], Edouard G Mills [1], Layla Thurston [1], Kanyada Koysombat [1], Simon Hanassab [3], Thomas Heinis [3], Tricia M-M Tan [3], Krasimira Tsaneva-Atanasova [3], Alexander N Comninos [1], Margaritis Voliotis [3], Waljit S Dhillo [1]

Fertil Steril. 2024 Feb;121(2):334-345. doi:10.1016/j.fertnstert.2023.11.010. Epub 2023 Nov 15.

- To quantify how representative a single measure of reproductive hormone level is of the daily hormonal profile using data from detailed hormonal sampling in the saline placebo-treated arm conducted over several hours.
- The initial morning value of reproductive hormone levels was typically higher than the mean value throughout the day (percentage decrease from initial morning measure to daily mean: luteinizing hormone level 18.4%, follicle-stimulating hormone level 9.7%, testosterone level 9.2%, and estradiol level 2.1%). Luteinizing hormone level was the most variable (CV 28%), followed by sex-steroid hormone levels (testosterone level 12% and estradiol level 13%), whereas follicle-stimulating hormone level was the least variable reproductive hormone (CV 8%). In healthy men, testosterone levels fell between 9:00 am and 5:00 pm by 14.9% (95% confidence interval 4.2, 25.5%), although morning levels correlated with (and could be predicted from) late afternoon levels in the same individual ($r^2 = 0.53$, P<.0001). Testosterone levels were reduced more after a mixed meal (by 34.3%) than during ad libitum feeding (9.5%), after an oral glucose load (6.0%), or an intravenous glucose load (7.4%).
- **Conclusion:** Quantification of the variability of a single measure of reproductive hormone levels informs the reliability of reproductive hormone assessment.

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How To Access Digital Library

- **Steps to Access HEC Digital Library**

a) Go to the website of HEC National Digital Library
b) On Home Page, click on the INSTITUTES
c) A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL
d) Select your desired Institute
e) A page will appear showing the resources of the institution
f) Journals and Researches will appear
g) You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal

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Learning Resources

- Textbook of Biochemistry, Lippincott 8th edition, chapter no.28 , pages no. 432-436
- Google scholar
- Google images

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