

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

The image features a sunset over a body of water, with the sun low on the horizon and its light reflecting on the water's surface. Overlaid on this scene is the Basmala (Bismillah) in Arabic calligraphy. The text is written in a bold, black, stylized script. The words are arranged in three lines: 'بِسْمِ' (Bism) on the top line, 'اللَّهِ' (Allah) on the middle line, and 'الرَّحْمَنِ الرَّحِيمِ' (The Most Gracious, The Most Merciful) on the bottom line. The calligraphy is highly decorative, with thick, flowing lines and intricate flourishes. A faint watermark 'www.istiqomah.com' is visible in the background of the calligraphy.

وَخَلَقْنَاكُمْ أَزْوَاجًا

And We created you in pairs

The Noble Qur'an [78:8]

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Objectives

- Introduction of reproductive system.
- Genetic basis of sex
- Discuss the Chemical structure of sex hormones.
- Describe the Synthesis of sex hormones

Sex hormones chemistry and synthesis

By

Dr Gulnaz Begum

Reproductive system

Reproduction is needed for survival of species

so

- Reproduction means continuation of species.
- In case of human reproduction is bi-sexual ,i.e it is dependant on fusion of male & female gametes.



Reproductive system
consist of

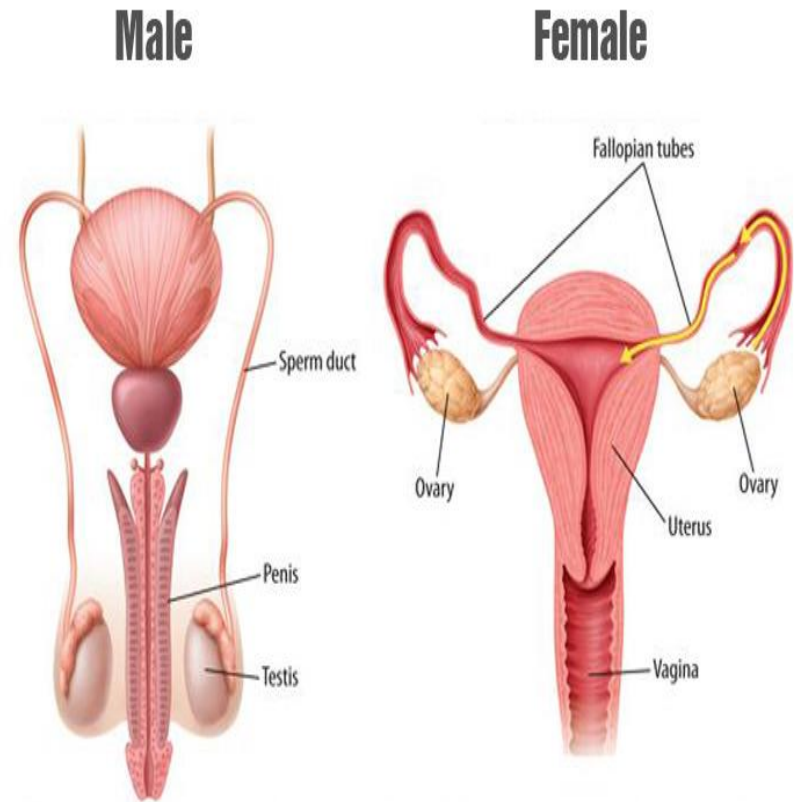
Primary sex organs.

These are gonads

- Testes in male & ovaries in female.

Gonads perform two
functions

1. Production of gametes
2. Production of hormones



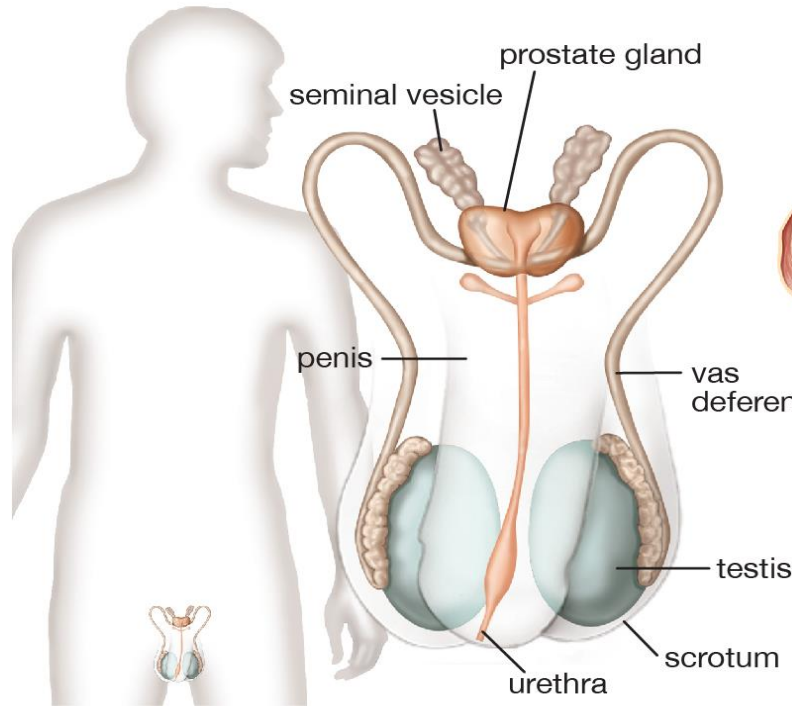
The organs of the male reproductive system produce sperm and deliver it to the female reproductive system.

The female reproductive system produces eggs and provides a place for a new human to grow and develop before birth.

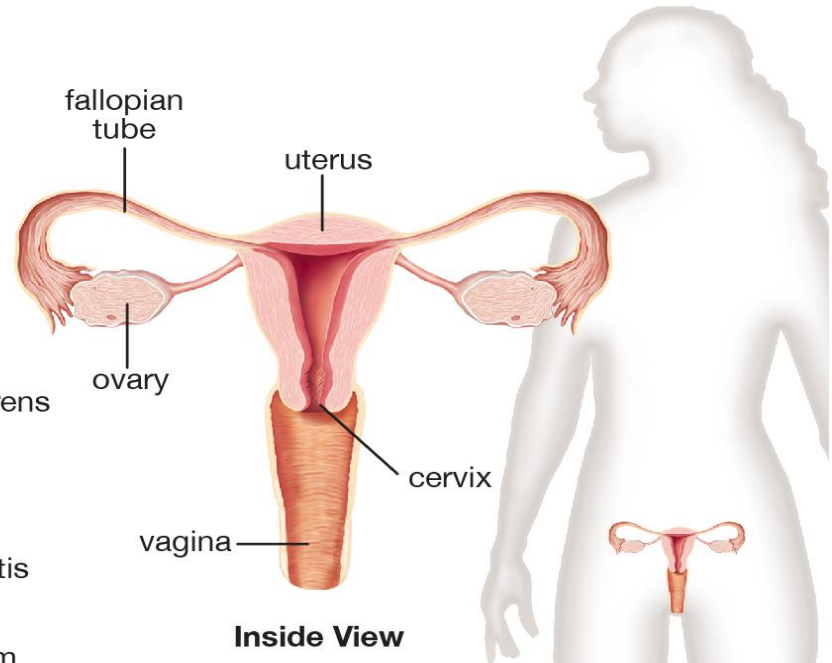
The accessory sex organs

- They are essential for normal reproduction.
- These are
- External genitalia of both sexes.
- Vagina ,uterus, uterine tubes in female
- Seminal vesicles ,vas defrens , bulbouretheral gland & prostate in male

Male Reproductive System



Female Reproductive System



Puberty

This is the biological process through which a person becomes sexually mature.

It is affected by

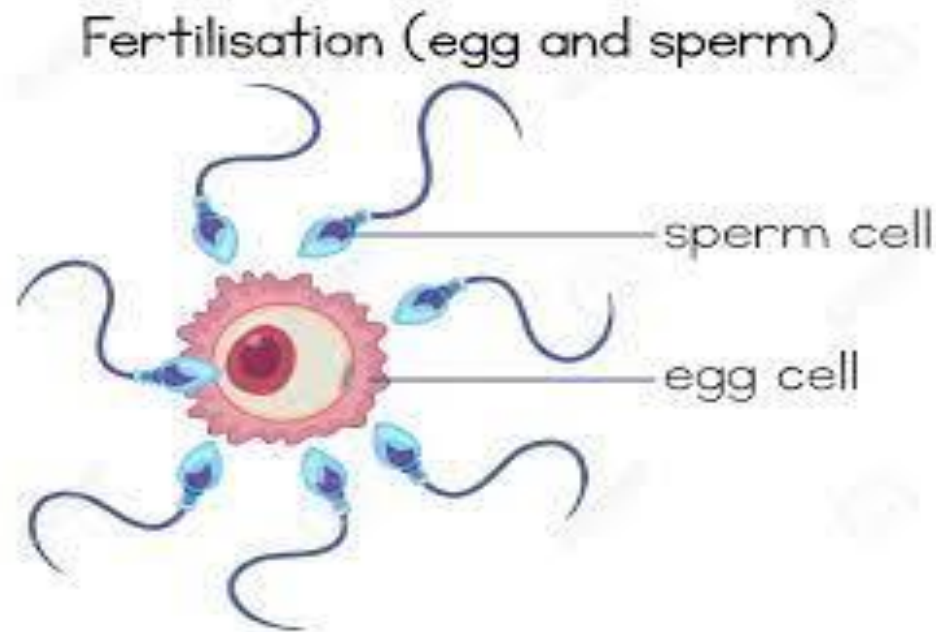
- Inheritance & genotype
- Socioeconomic factors
- General wellbeing of person

Secondary sex characters

- Physical changes that appear in both sexes at the time of puberty. These are
- Appearance of axillary & pubic hairs in both sexes.
- Facial hairs & deepening of voice in male.
- Development of breast & beginning of menstruation in female.

Genetic basis of sex

- The genetic sex of an individual is determined at the time of fertilization when an X & Y-chromosome bearing spermatozoa fuses with a normal X-chromosome bearing ovum, which produces a female (xx) or a male (xy) zygote.



Genetic determinants

- The X & Y –chromosomes are called the sex chromosomes.
- In male the Y chromosome normally carries the sex determining region of Y chromosome which causes the undifferentiated, bipotential gonad to become testis. Y chromosomes are lighter than X chromosome, so Y chromosome containing sperm reach earlier to ovum than X chromosome containing sperm.

- **Hormonal determinants**
- Fetal testes secretes hormones
 1. Anti mullerian hormone, which regresses mullerian duct.
 2. Testosterone ,which causes virilization of the wolffian duct.
 3. Differentiation of external genitalia is dependent upon 5 α -reductase ,which converts testosterone to 5 α - dihydrotestosterone.

Deficiencies of any one of these is responsible for abnormal sexual differentiation.

SEX HORMONES

Sex hormones

- Three types

- **Androgen**

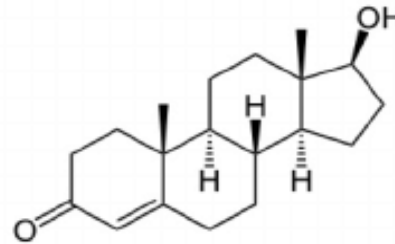
Male hormones

- **Estrogens**

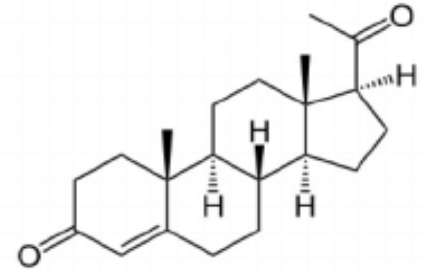
Female hormones

- **Gastogens**

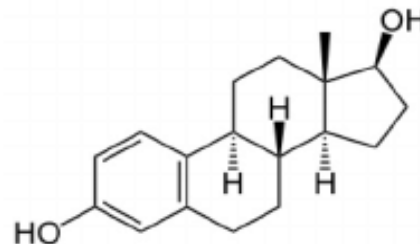
Progestational hormones



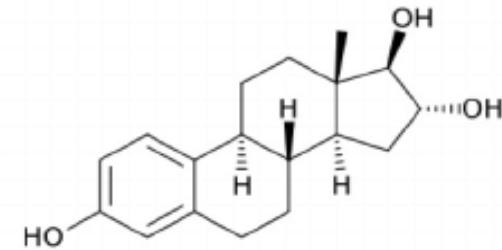
Testosterone (C₁₉H₂₈O₂)



Progesterone (C₂₁H₃₀O₂)



17-β-Estradiol
(C₁₈H₂₄O₂)

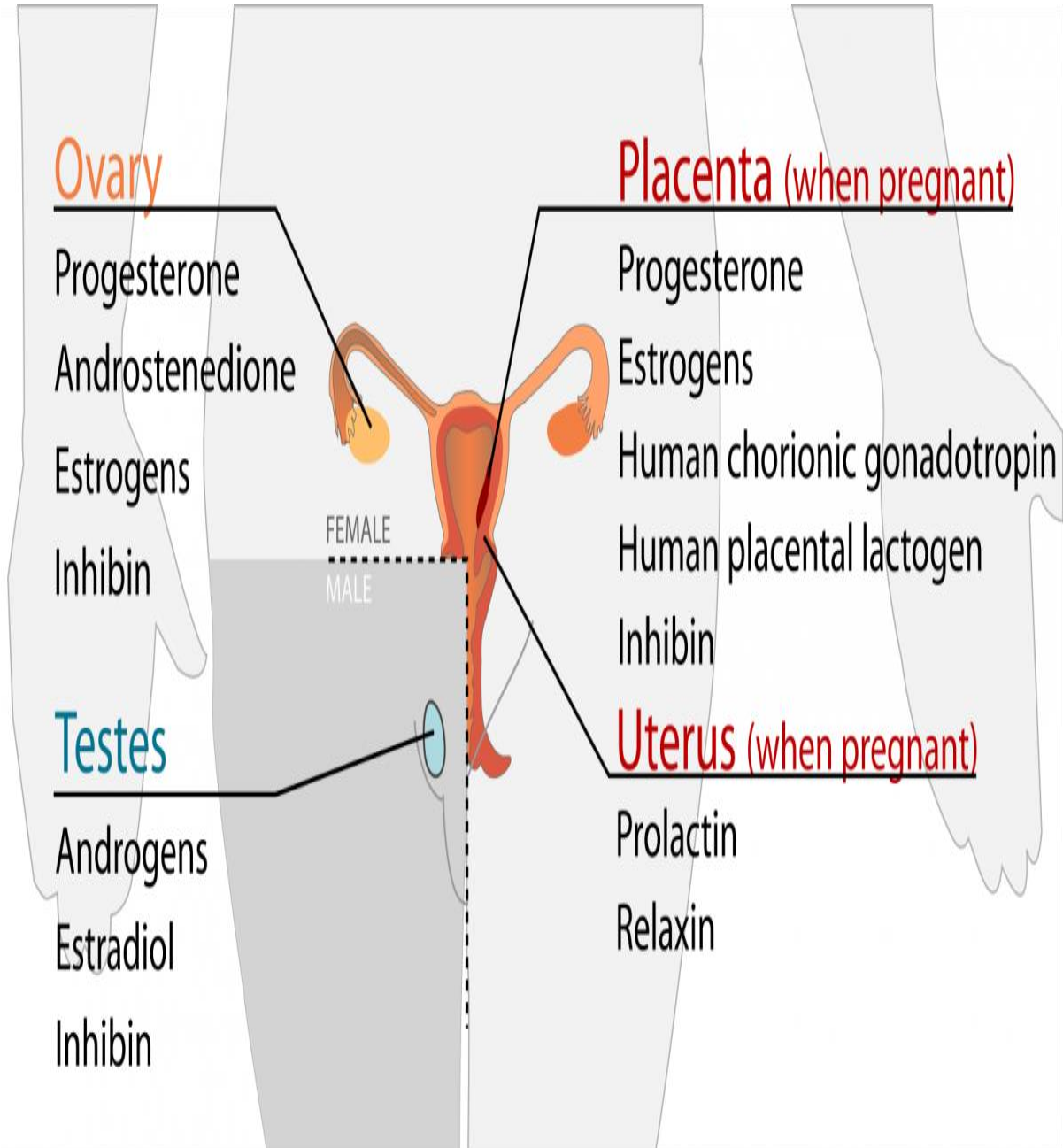


Estriol (C₁₈H₂₄O₃)

Secreted by testes in male and ovaries in female.

They are also secreted in small amount by placenta and adrenal cortex.

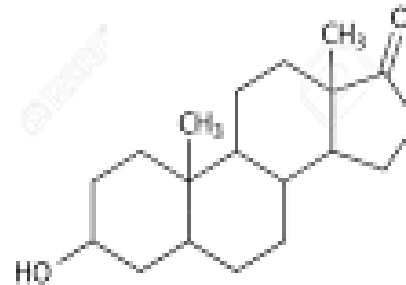
Steroid in nature.
Related to adrenal cortical hormones



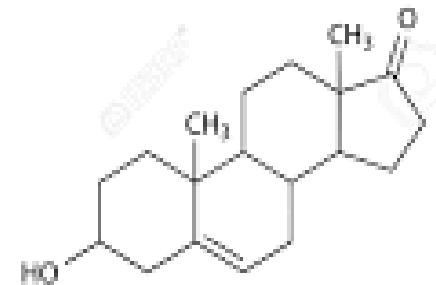
Male hormones

Androgens in man are

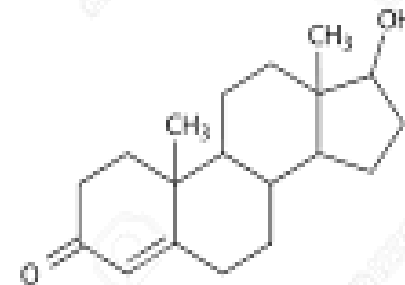
- Testosterones
- Epiandrosterone (3 β -androsterone)
- Androsterone
- Dehydroepiandrosterone



Androsterone



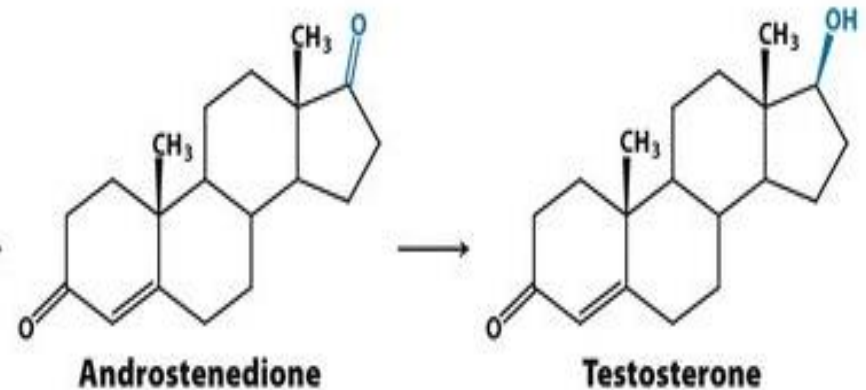
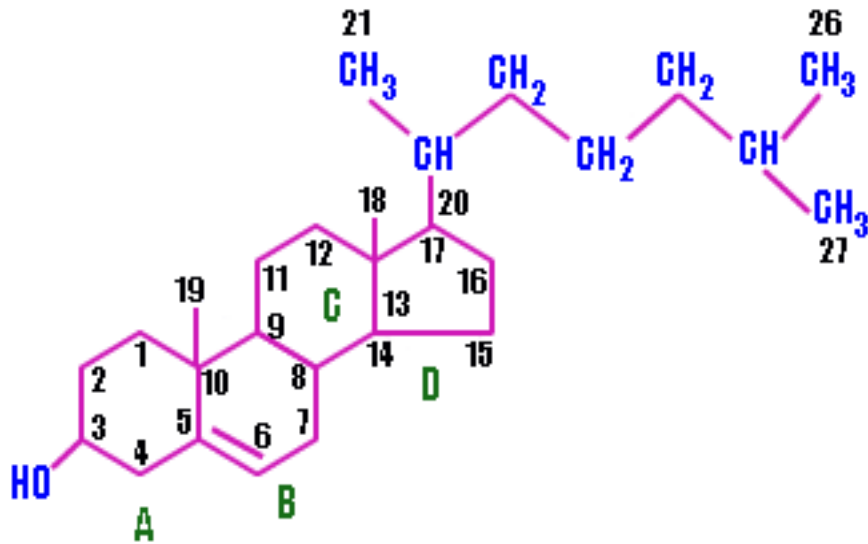
Dehydroepiandrosterone



Testosterone

Chemical structure of Androgens

- All contain C_{19} atoms.
- CH_3 group at C_{10} and C_{13} position.

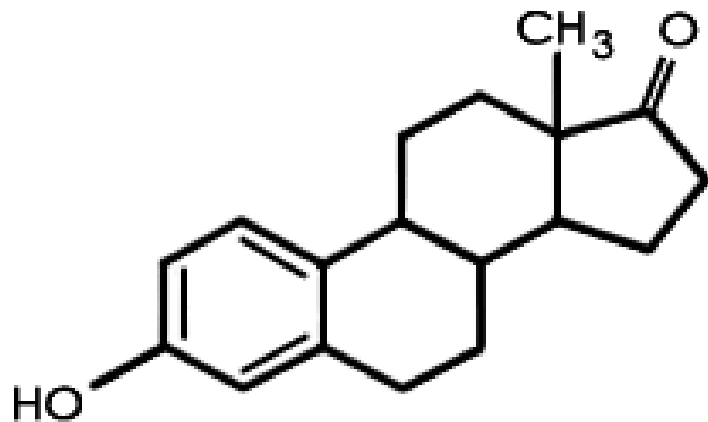


Female hormones

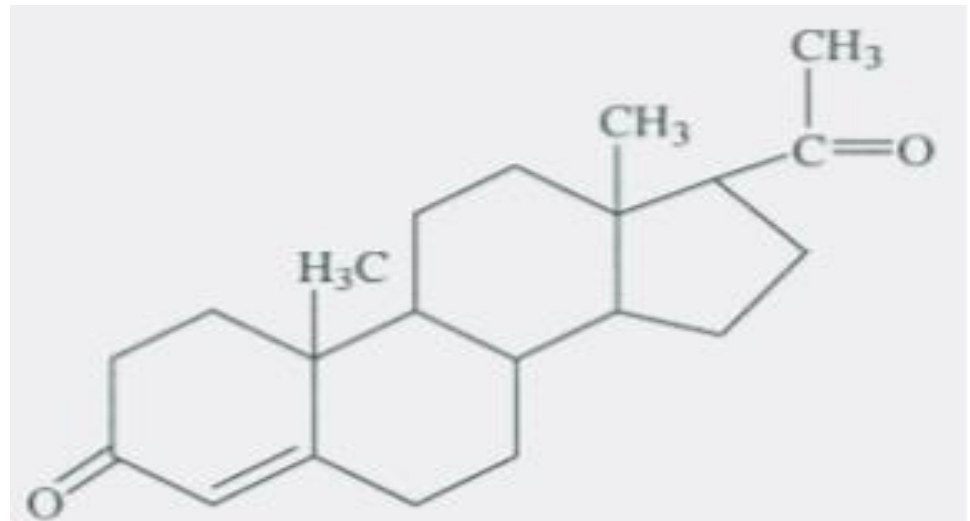
Two main types

Follicular or estrogenic hormones

Progestational hormones



Estrogen

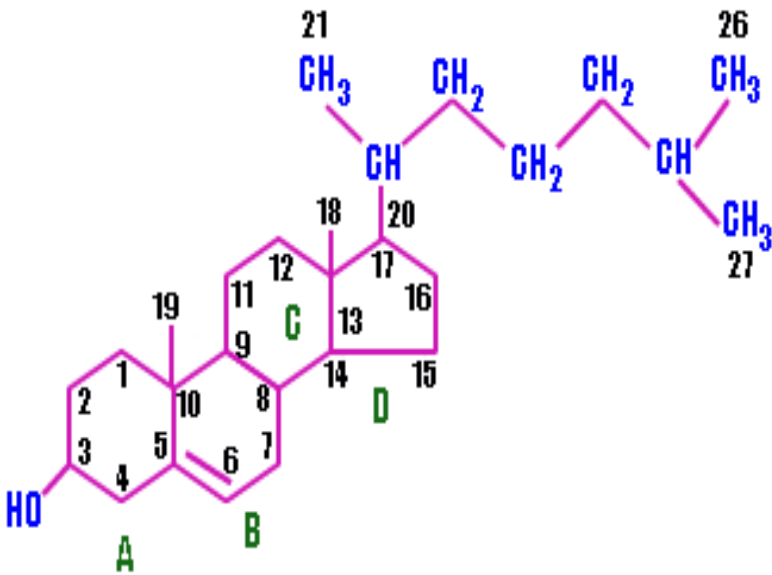


progesterone

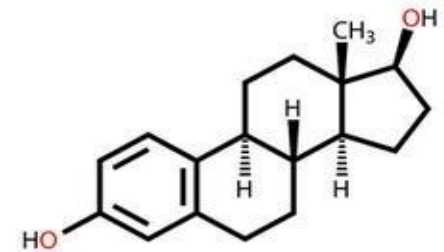
Female hormones

Oestradiol/estrogen

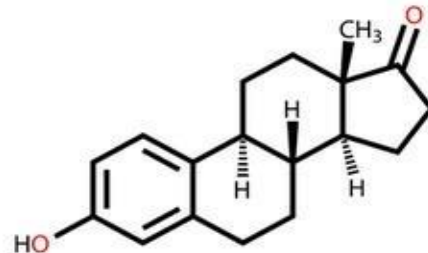
- All naturally occurring estrogens are C₁₈ steroids
- Ring A has aromatic nature.
- A methyl group is attached only at 13 position.
- OH group at C₃ position possess phenolic properties.



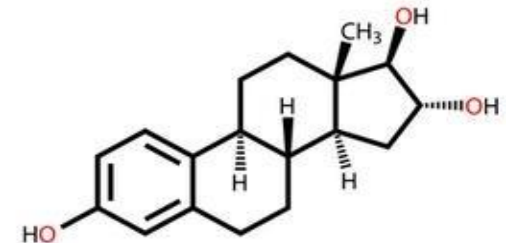
ESTROGENS



Estradiol



Estrone



Estriol

Estrogens classification

NATURAL

- **Beta Estradiol**

The principal estrogenic hormone in circulation and the most active form, and the principal estrogen secreted by the ovaries.

- **Estriol**

Principal metabolite found in urine of pregnant and non pregnant women.

Estriol is a weak estrogen , derived both from estradiol and estrone

- **Estrone**

Small amounts of estrone are also secreted but most of this is formed in the peripheral tissues. it is an oxidative product of estradiol

The estrogenic potency of beta-estradiol is 12 times that of estrone and 80 times that of estriol.

STEROID

SYNTHETIC

Ethinyle Estradiol

Mestranol

NON STEROID

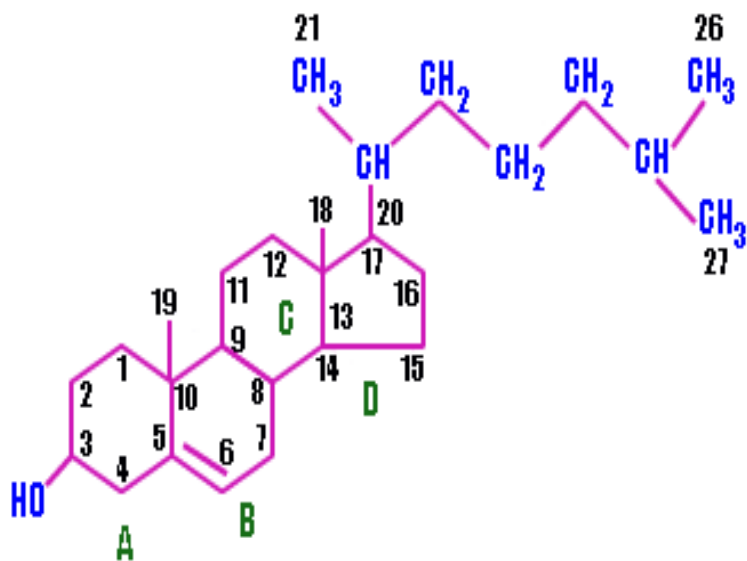
SYNTHETIC

Diethylstilbestrol

Progesterone

Chemically it is 4-pregnane-3,20-dione .

It is C_{21} steroid having methyl group at C_{10} & C_{13}



PROGESTINS CLASSIFICATION

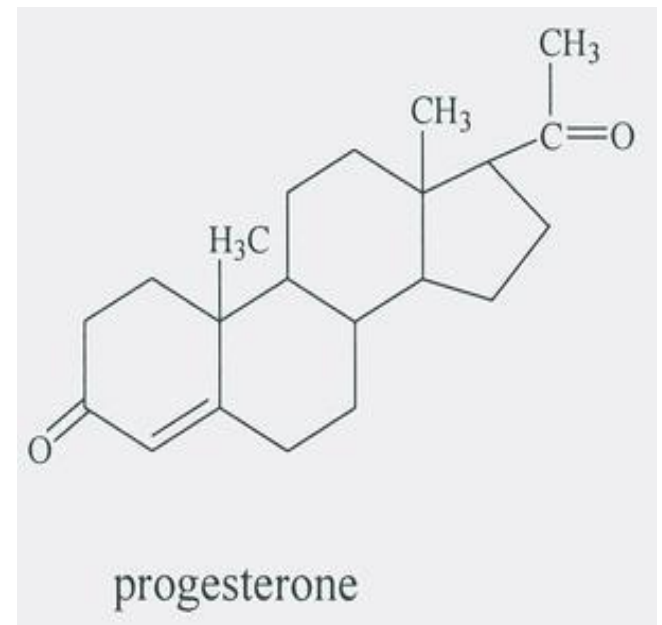
NATURAL

- PROGESTERONE

In the normal non-pregnant female , progesterone is secreted in significant amounts only during the latter half of each ovarian cycle , where it is secreted by the corpus luteum. Also formed in adrenal cortex & testes.

SYNTHETIC

- 17– HYDROXYPROGESTERONE
- MEDROXYPROGESTERONE ACETATE
- MEGESTROLE

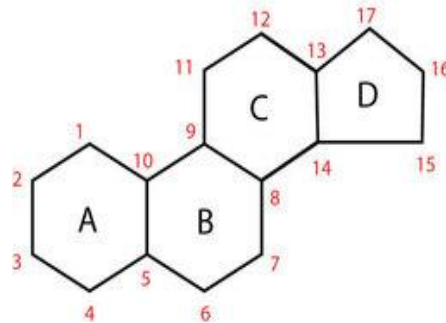


Synthesis of Androgens

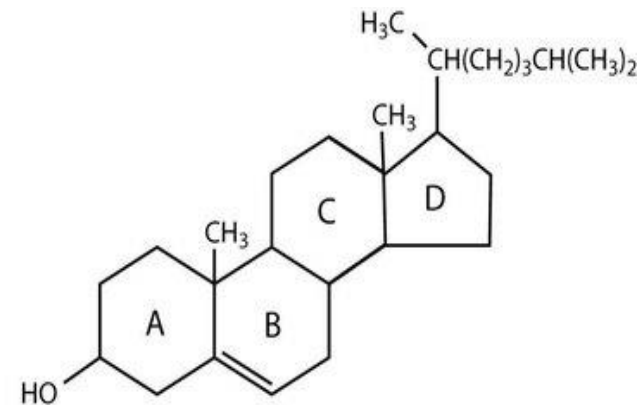
- Androgens are produced in testes(leyding cells),adrenal cortex and placenta.
- Synthesized in the interstitial tissues by the Leyding cells.
- The immediate precursor is cholesterol.

Synthesize from

- Acetate
- Cholesterol
- **Two pathways**
- Δ^4 - pathway
- Δ^5 - pathway



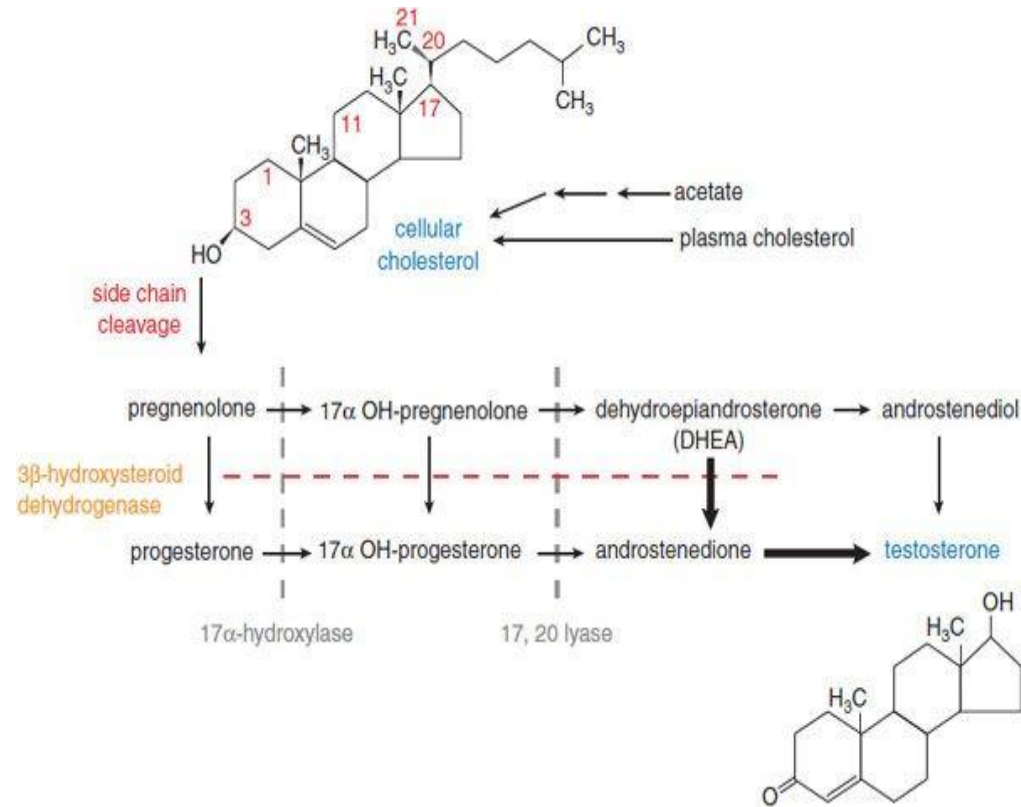
(a) Steroid skeleton



(b) Cholesterol

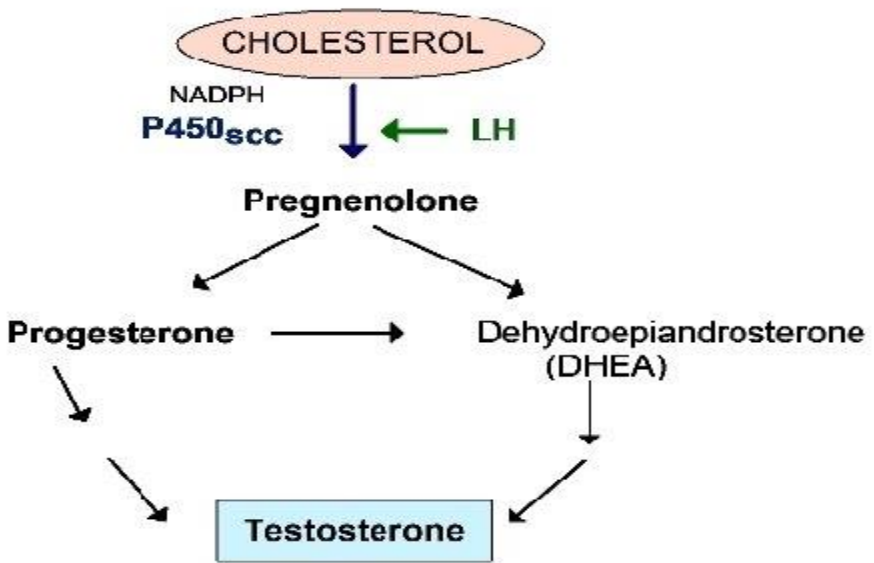
Biosynthesis of androgens

- Rate limiting step is delivery of cholesterol to the inner membrane of mitochondria by the transport protein(StAR) .
- Cholesterol is acted upon by side chain cleavage enzyme P450_{scc}.
- Cholesterol is converted to pregnenolone in the leydig cells mitochondria.

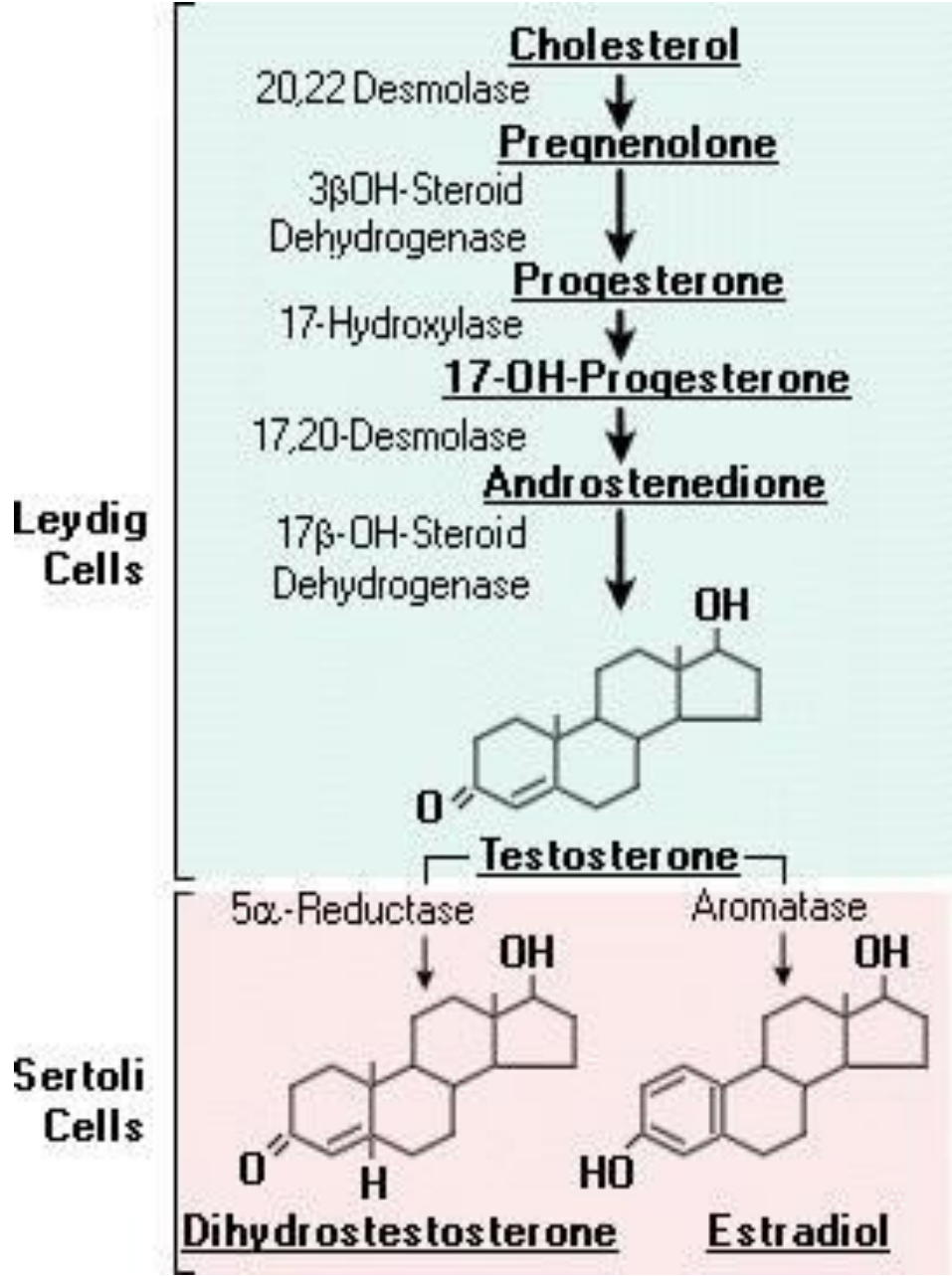


- Conversion of cholesterol to pregnanolone is similar in adrenal cortex, ovary and testes.
- The difference is that LH hormone promotes the synthesis in these organs instead of ACTH.

Androgens : Synthesis



- Pregnenolone is translocated to smooth endoplasmic reticulum, where testosterone is synthesized.
- Testosterone secretions are bi-urinal that is more in the morning than in the late afternoon.



Synthesis of androgens

- Five enzyme activities are present in three proteins.
- 3- β -hydroxy steroid dehydrogenase and Δ^{4-5} isomerase.
- 17- α -hydroxylase and 17-20-lyase.
- 17- β OH- steroid dehydrogenase

Δ^5 pathway

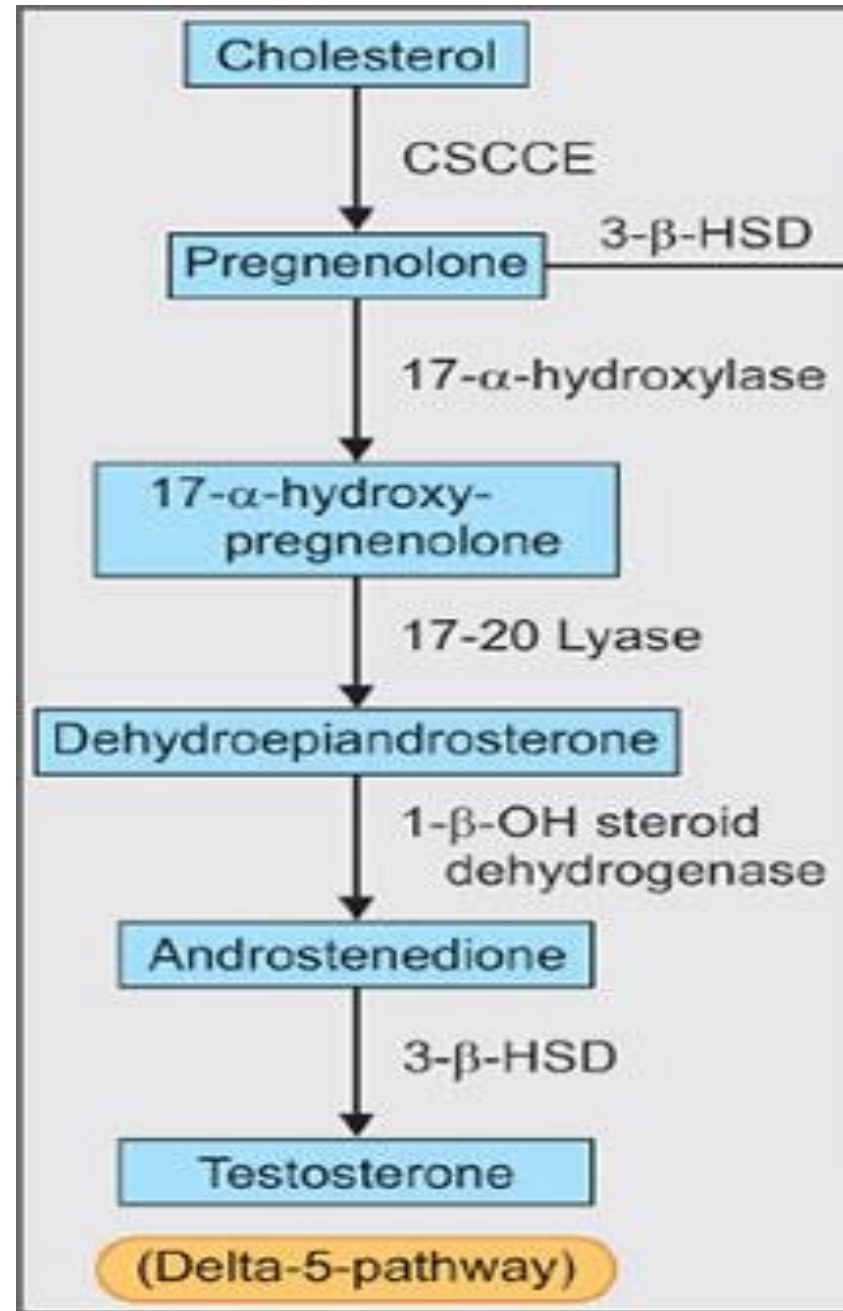
Predominates in human

Pregnenolone is converted to 17- α -OH-pregnenolone by the enzyme 17- α -hydroxylase.

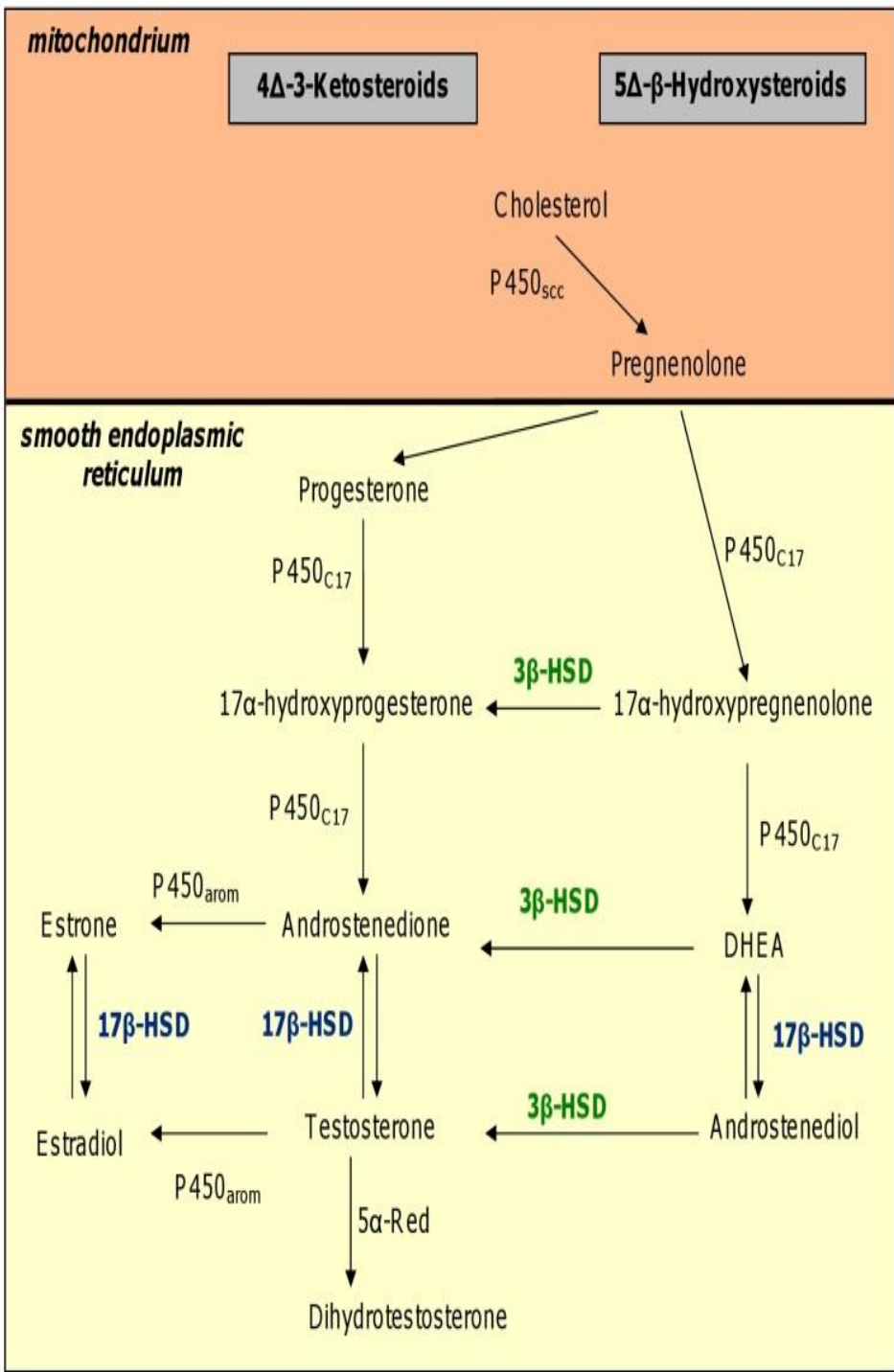
17- α -OH-pregnenolone is then converted to

Dehydroepiandrosterone (DHEA) by cleavage of side chain by enzyme lyase.

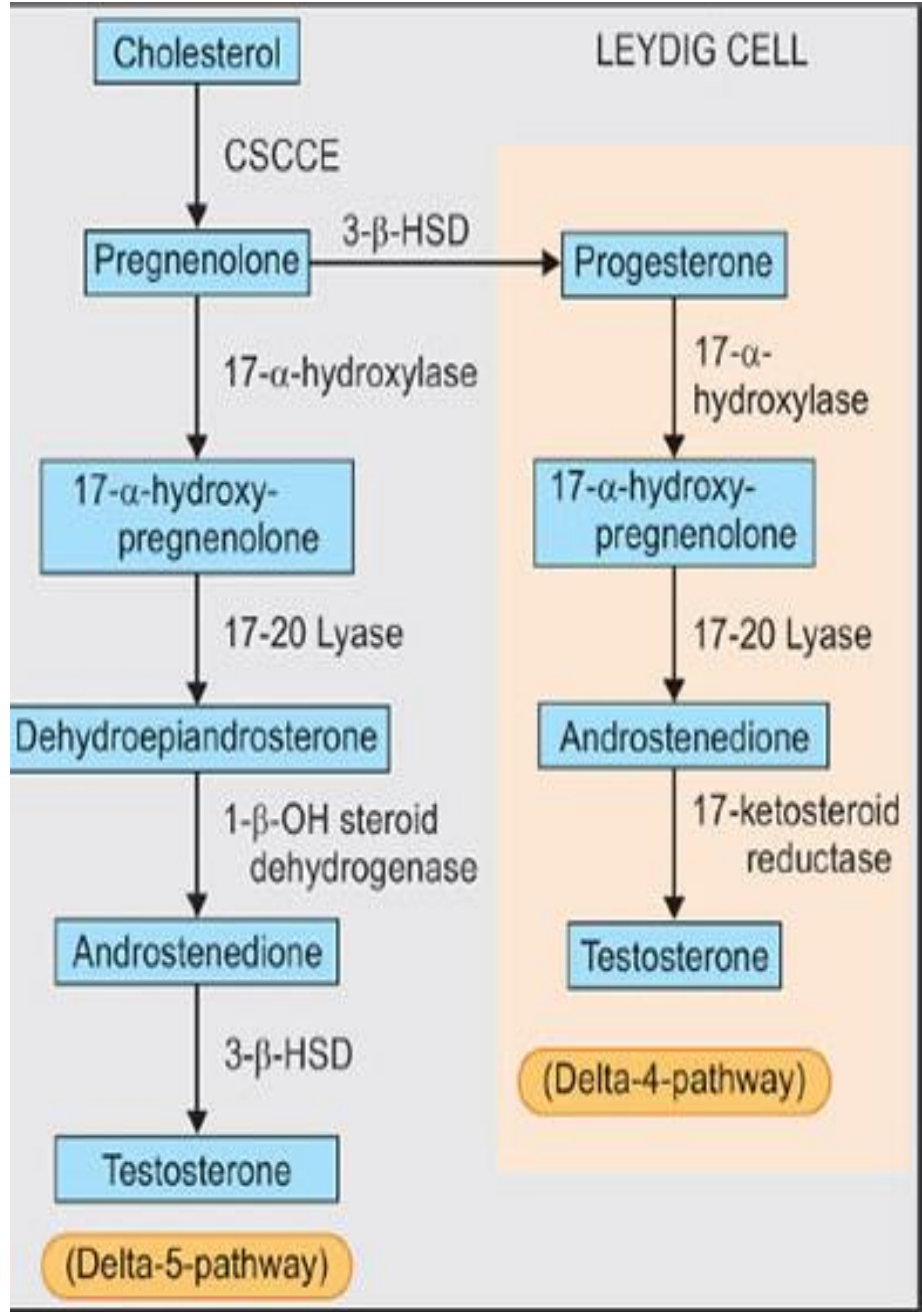
DHEA is first reduced to Δ^5 Androstendiol by 17- β -OH steroid dehydrogenase.



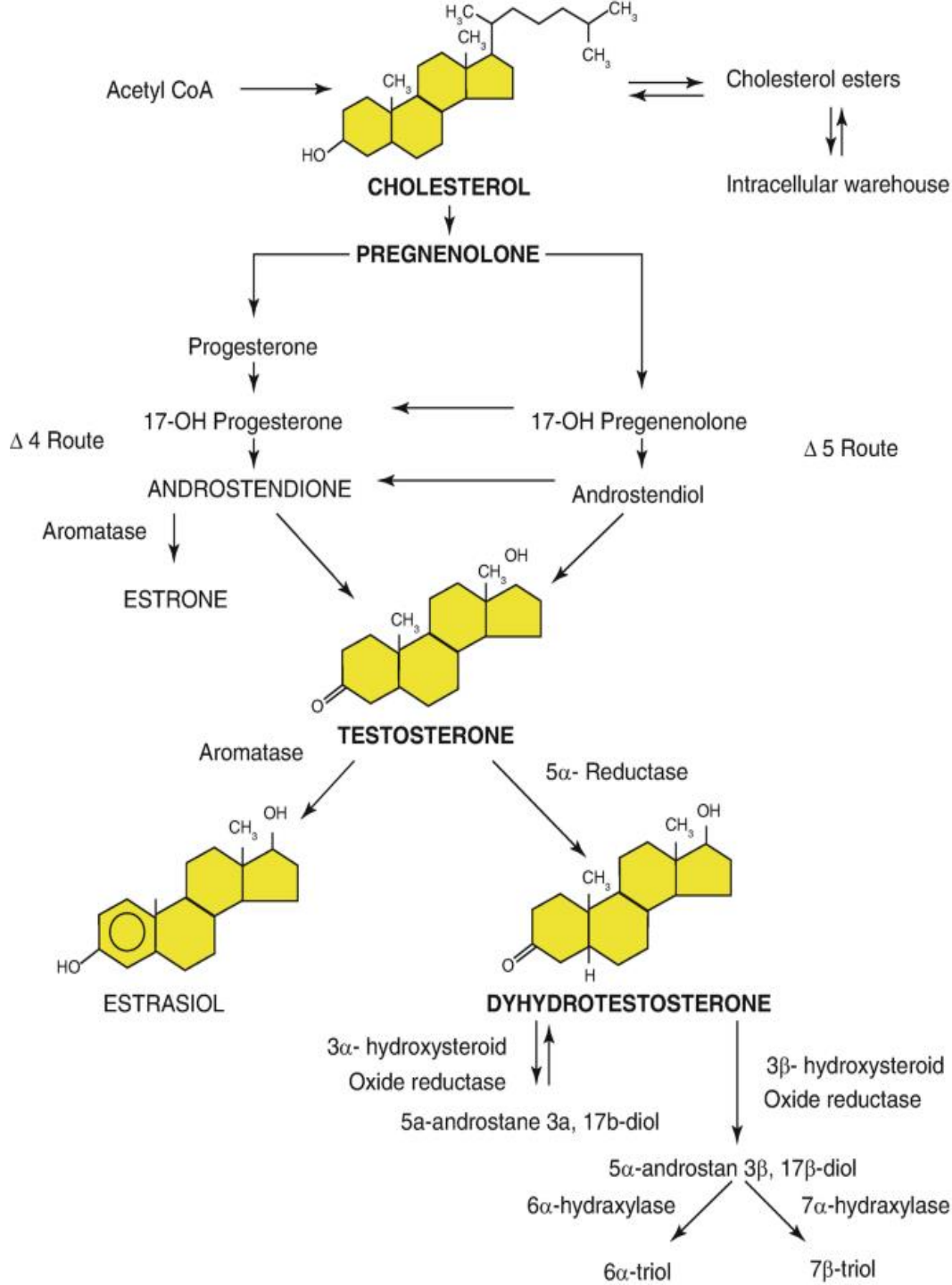
- Androstenediol further undergoes reduction & isomerization to form testosterone.
- DHEA alternatively converted to 'Androstenedione' by dehydrogenase which is reduced to form testosterone.



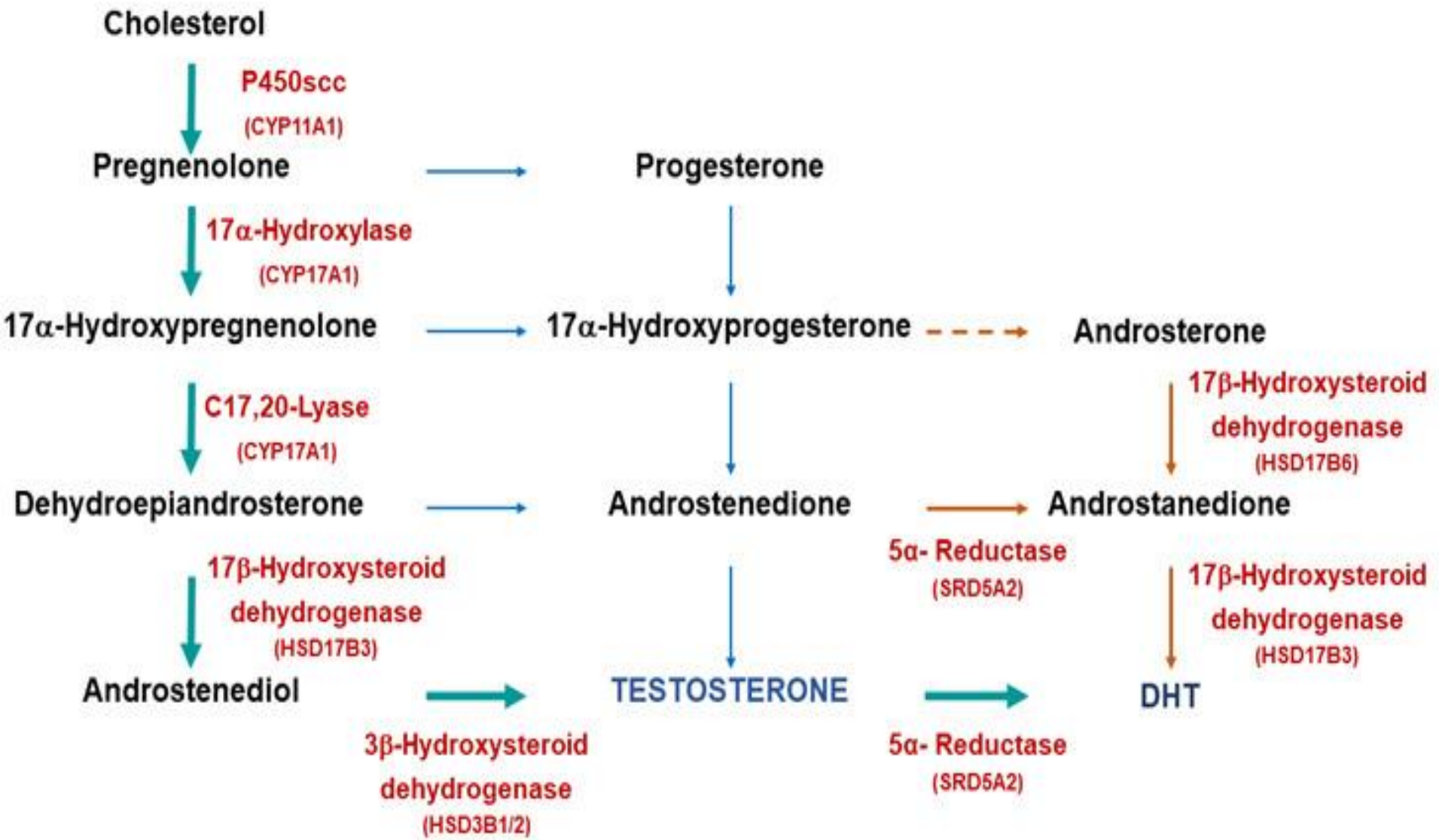
- Δ^4 pathway
- Pregnenolone is converted to progesterone catalyzed by enzyme 3- β -OH steroid dehydrogenase & isomerase.



- Progesterone is hydroxylated by
 - 17- α -hydroxylase to form
- 17- α -OH-progesterone, which loses its side chain to form 'androstendione' by the enzyme lyase.

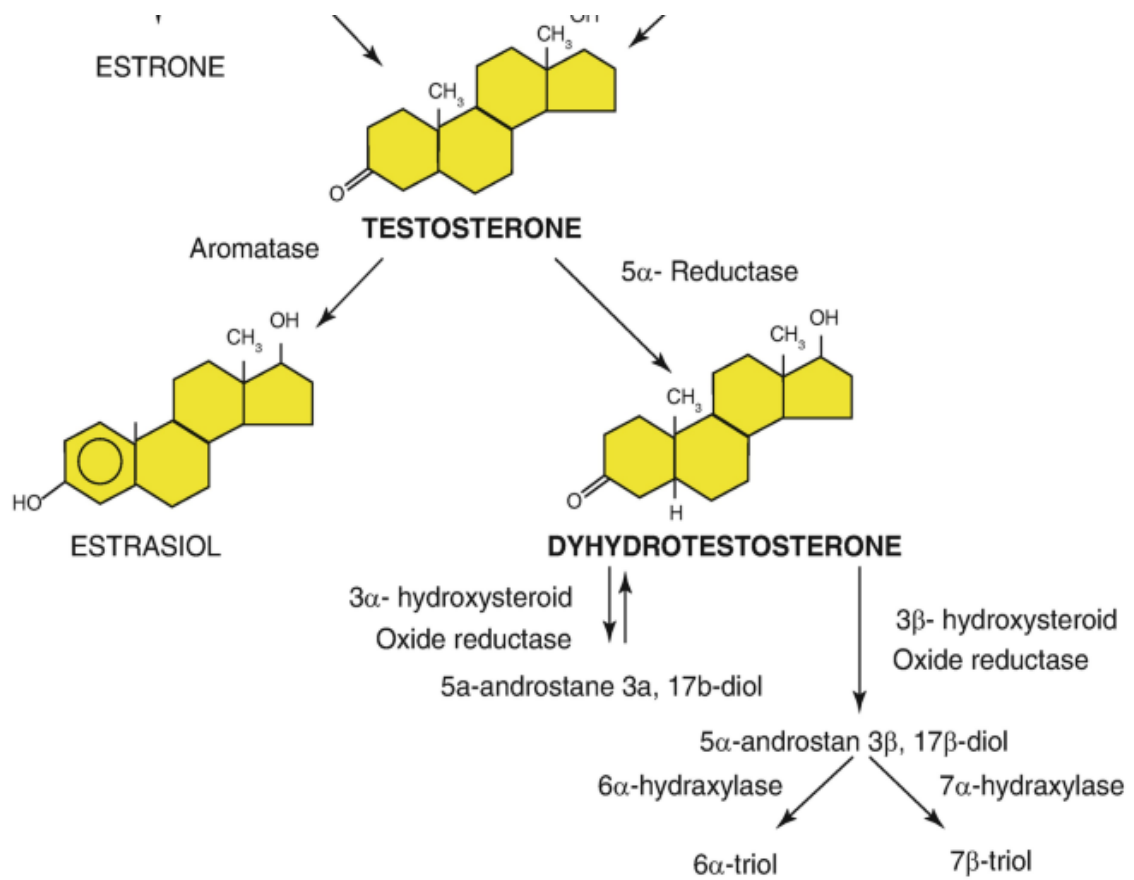


- It is reduced at C₁₇ position by enzyme 17-β-OH steroid dehydrogenase to form testosterone.



- Testosterone is metabolized in two ways
- 1. Oxidation at 17 position occur in many tissues including liver and produce 17-ketosteroids that are generally inactive or less active.

- 2. Reduction of ring A double bond and 3-ketone is less efficient occur primarily in target tissues and produce more active or potent form dihydrotestosterone by enzyme 5 α -reductase.



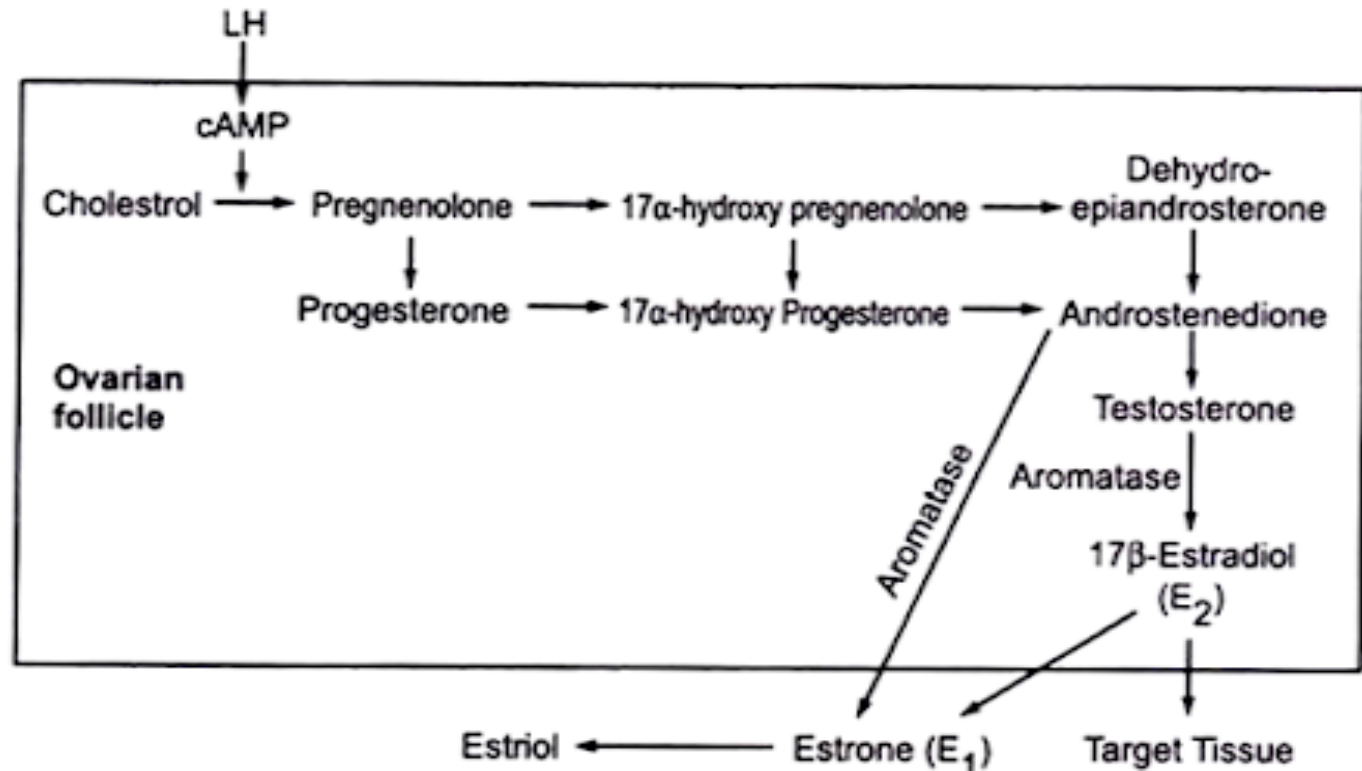
- DHT is active form in prostate, external genitalia and some areas of skin.
- Testosterone production in adult male is 5mg/day.
- DHT is 400 μ gm. 50-100 μ gm is secreted by testes the rest is produced peripherally by 5- α reductase.

SYNTHESIS OF ESTROGENS

Estrogen is synthesized by aromatization of androgens i.e testosterone & androstendione.

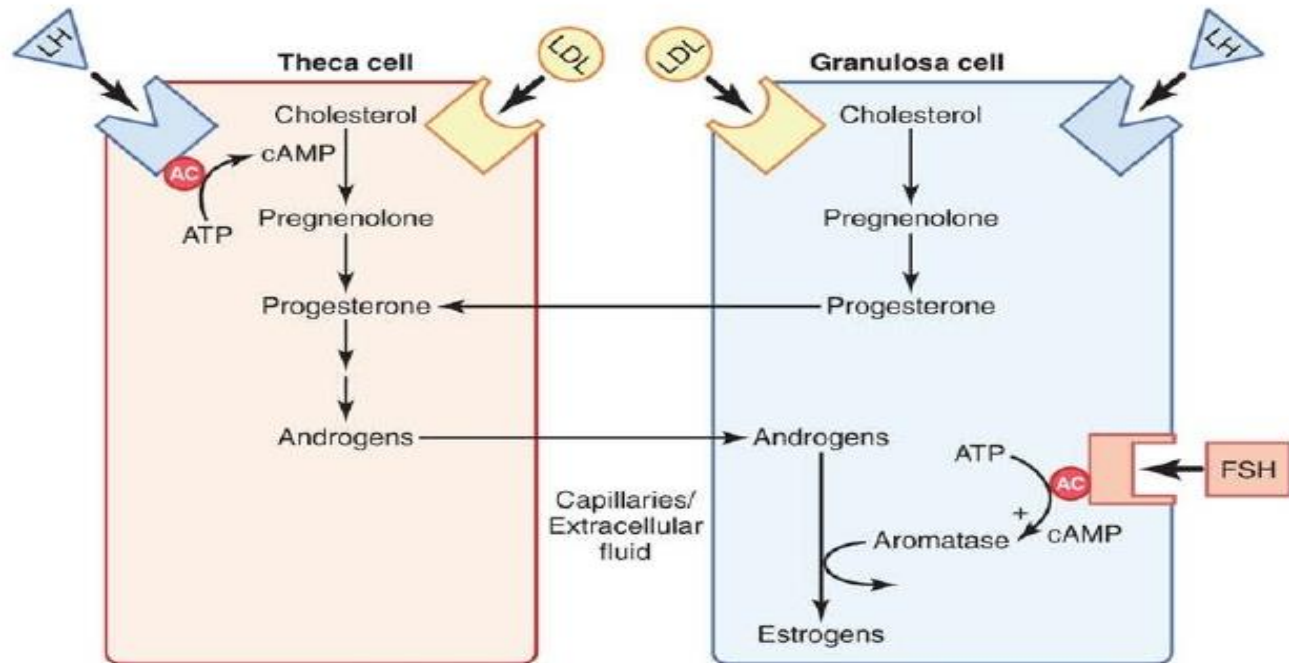
The process involves three hydroxylation steps, requiring molecular oxygen & NADPH.

Enzyme aromatase complex includes P450 monooxygenase.



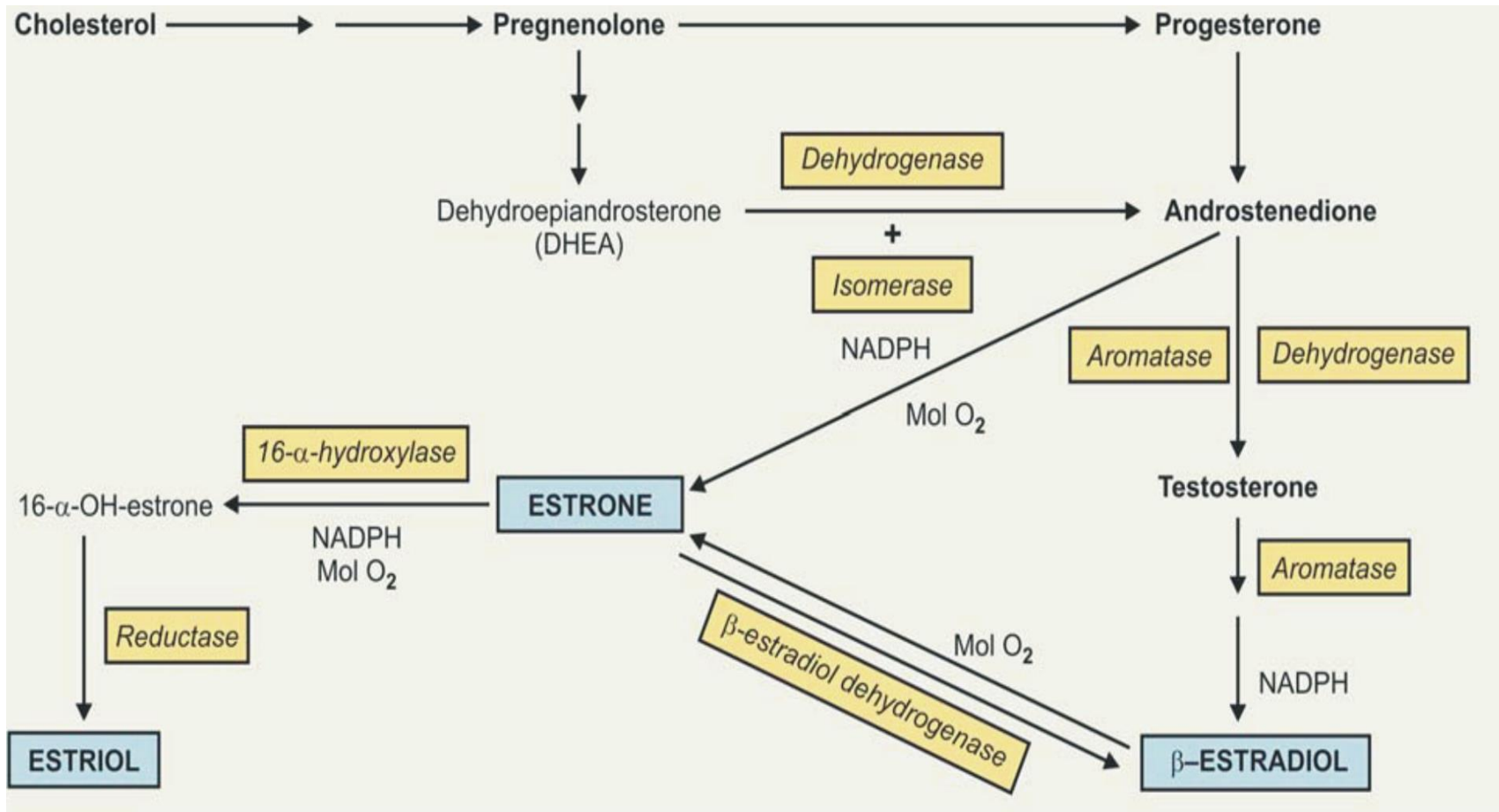
SYNTHESIS OF ESTROGENS

- Theca interna cells of graffian follicles are source of testosterone and androstendione.
- In granulosa cells testosterone is converted to estrone and β -estradiol by enzyme aromatase.



Synthesis of estrogen

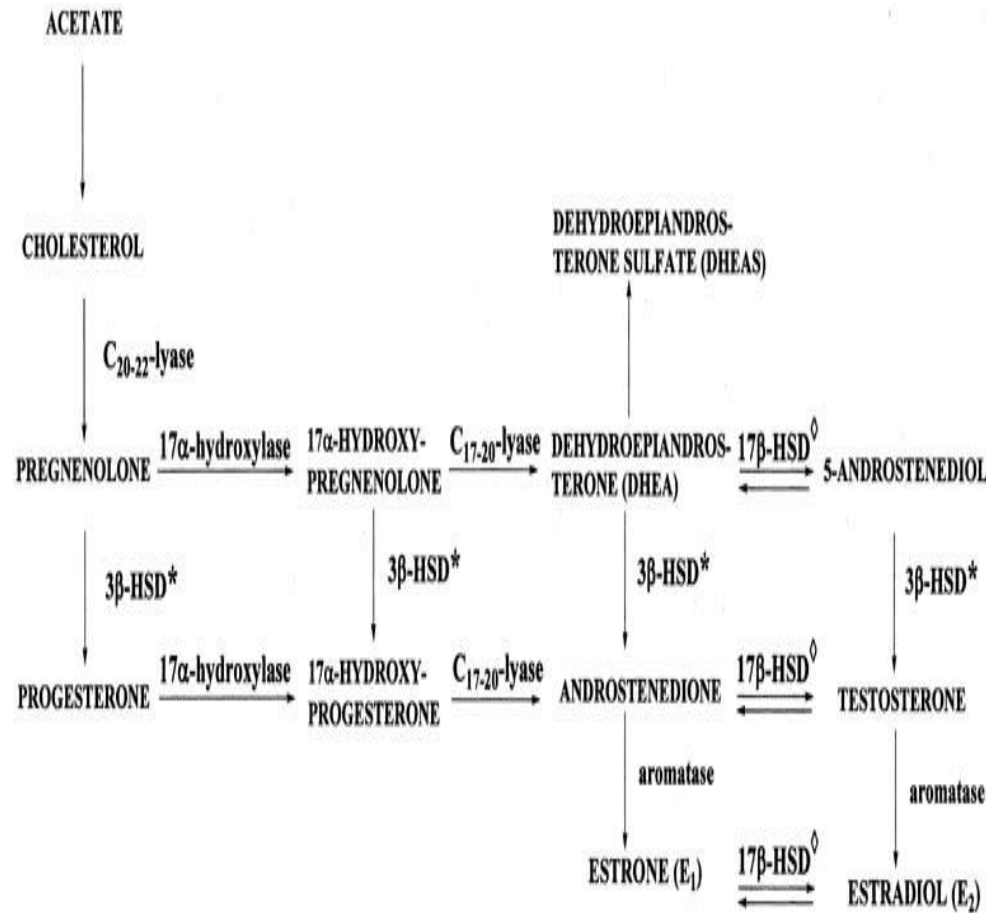
- Estrone is converted to 16- α -OH-estrone by enzyme 16- α -hydroxylase, which also require mol O₂ & NADPH.
- 16- α -OH-estrone is reduced to form estriol by enzyme reductase.



- Significant estrogen is produced by peripheral aromatization of androgens.
- In males peripheral aromatization accounts for 80% production of estradiol.
- In females 50% estradiol is produced by aromatization of adrenal androgens in pregnancy.
- Conversion of androstendione to estrone is the major source of estrogen in postmenopausal women.

Synthesis of progesterone

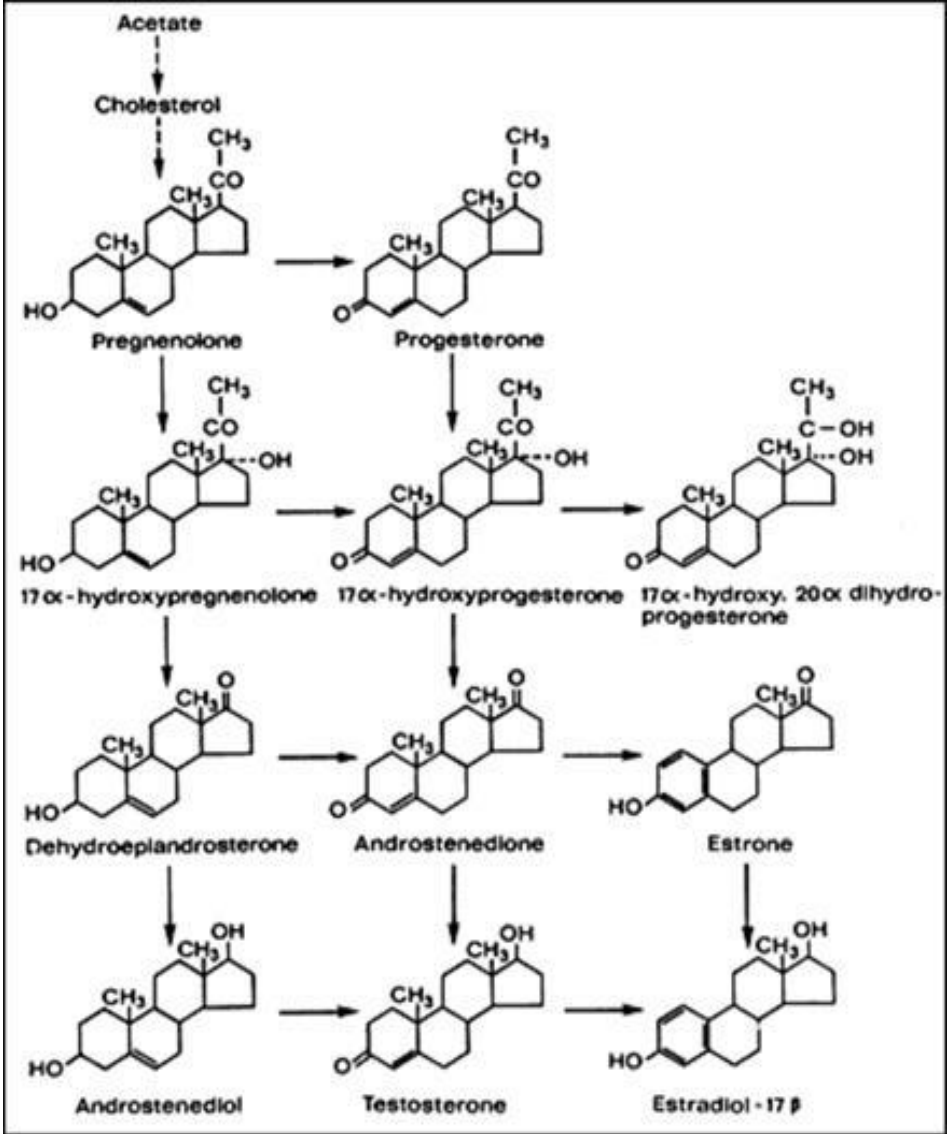
- Progesterone is an intermediate in the synthesis of corticosteroids, testosterone & estrogen.
- Pregnenolone is immediate precursor.



* 3β-HSD = 3β-hydroxysteroid dehydrogenase- $\Delta^{5,4}$ -isomerase

◊ 17β-hydroxysteroid dehydrogenase

- In the plasma it is transported in bound(98%) as well as in free(2%) form.
- 80% is bound to plasma albumin,18% to cortisol binding globulin.
- Metabolized in the liver to pregnandiol which is excreted in urine.



- Chatterjea
- Satiyanarayn
- Harper's illustrated biochemistry

A photograph of a small, rectangular, light-brown paper tag with a hole on the left side, tied with a black string. The tag is placed on a rustic, weathered wooden surface. The tag has the words "Thank you!" written in a black, cursive font. To the right of the tag is a single white daisy with a yellow center. In the background, two more daisies are visible, slightly out of focus. A faint "dreamstime" watermark is visible across the middle of the image.

Thank
you!