

This summary includes all what's written in the slides, some notes are added from the record to make things clear, what's written in italics is added by the editor. Good luck all

Estrogens & Antiestrogens

- Menstrual cycle... Changes and hormonal events

- **Natural estrogens:**

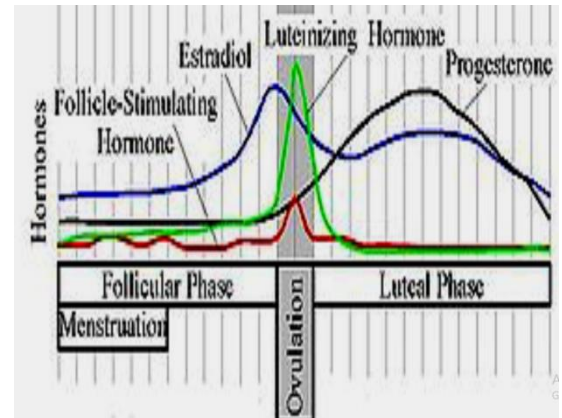
Estradiol >> Estrone > Estriol

-Ineffective orally

- **Synthesis:**

-From cholesterol.

- aromatase enzyme converts androgens (testosterone & androstenedione) to estrogen



- **Estrogen synthesis:**

Cholesterol → Pregnenolone → Progesterone → Hydroxyprogesterone →

Androstenedione → Testosterone $\xrightarrow{\text{Aromatase}}$ Estradiol → Estrone

- **Transport:**

SHBG (sex hormone binding globulin)

- **M.O.A:**

Estrogen receptors (ER- α ; ER- β) ,nuclear receptors → Modulation of gene transcription .

Stimulation of endometrial nitric oxide synthase → nitric oxide production →

vasodilatation → cardioprotection (so estrogen is protective to women).

- **Estrogen actions:**

1- 1^o & 2^o sexual characteristics of females.

2- Proliferation of the endometrium & follicular maturation

3- ↑ elasticity of skin

4- ↑ synthesis of certain globulins by the liver (SHBG, corticosteroid binding globulin & thyroid binding globulin)

5- ↑ synthesis of certain clotting factors (fibrinogen, factors 7;9 & 10) and ↓ activity of antithrombin III

6- ↓ cholesterol, ↑ HDL & ↓ LDL blood levels

7- Salt & water retention

- **Absorption & metabolism of estrogens:**

Conjugation → enterohepatic circulation (excretion by the liver)

• **Estrogens clinical uses:**

1- HRT (Hormone Replacement therapy) يعنى لتعويض غياب الاستروجين بعد سن اليأس

Postmenopausal syndrome & osteoporosis,

prevention of heart attacks

2- Components of OCP's (oral contraceptive pills)

3- Prostate, breast, endometrial cancer , used along with **progesterone**

4- Dysmenorrhea(symptoms of painful menstruation)

5- Infertility

6- Acne, hirsutism(male hair pattern growth in women)

• **Estrogen preparations:**

1- Synthetic steroidal

Estradiol benzoate; Estradiol valarate

Ethinylestradiol; Mestranol..

2- Synthetic non steroidal estrogens : Diethylstilbesterol

3- Conjugated estrogens :Estrone sulfonate

• **Estrogen side effects:**

1- Nausea & vomiting

2- Headache, migrainous headache

3- Dizziness, weight gain

4- Salt & water retention →
↑ BP

5- ↑ risk of
thromboembolism and
endometrial cancer

6- Teratogenic effect

• **Antiestrogens:**

-Competitive antagonists at estrogen receptors: **Tamoxifen & clomiphene citrate**

-**Tamoxifen is considered an estrogen agonist on bone and endometrium**; long term use of tamoxifen could lead to endometrial cancer

Tamoxifen acts also as an estrogen agonist in breast; so used in certain cases of breast cancer

Clomiphene citrate and tamoxifen act as estrogen antagonists at the level of the hypothalamus, so mainly used to manage infertility in ♂'s and ♀'s. (Remember the feedback loop)

Clomiphene citrate and tamoxifen are given **orally**.

• **Selective estrogen receptor modulators (SERM's):**

Nonhormonal pharmacological agents that bind estrogen receptors producing **agonistic activity in certain tissues (in bone)** and estrogen **antagonistic effect at other tissues (breast and endometrium)**

Note: The major physiological effect of estrogen is to inhibit bone resorption..

Raloxifene

-Orally effective SERM widely used in the management of osteoporosis (prophylactic and treatment) (so it inhibits bone resorption).

-Recently some researchers consider tamoxifen and clomiphene citrate as SERM

Aromatase inhibitors: (remember that aromatase catalyzes the transformation of testosterone into estradiol)

- Nonselective: Aminoglutithemide

- Selective: Anastrozole; Fadrozole (given orally)

Mainly used in the management of breast cancer.

.

Progesterone & Antiprogestins

• Biosynthesis:

From cholesterol

Cholesterol → Pregnenolone → Progesterone

Feedback effects

• Physiological & Pharmacological effects:

1- Endometrial differentiation, growth and development.

Sudden withdrawal → bleeding (menses)

2- Maintenance of pregnancy

3- Breast development

4- Vagina: ↓ cornification (reduce the cornified epithelial cells), ↑ mucus content

5- Cervix: ↑ viscosity ↓ NaCl content

6- Thermogenic effect

7- Weak aldosterone-like effect

• Absorption & metabolism:

Progesterone is available in oral; depot injection (I.M), injectable and subdermal implants dosage forms

• Preparations:

Medroxyprogesterone; Norethindrone acetate; Norethindrone; Norgestrel; Megesterol acetate; Hydroxyprogesterone caproate; **Cyproterone acetate (Cancer of prostate);**

Dydrogesterone (IVF)

• Progesterone clinical uses:

1- Components of OCP's

2- Dysfunctional uterine bleeding (*abnormal **bleeding** from the **vagina** that is due to changes in hormone levels. It is **bleeding** that is NOT caused by: Pregnancy or miscarriage.*)

3- Endometrial; breast & prostate cancer

4- Abortion or maintaining pregnancy

5- Endometriosis

• Progesterone side effects:

Depression; weight gain; salt-water retention

• Antiprogestins:

Mifepristone

• Clinical uses:

1- Abortifacient + PG (prostaglandins) (*to terminate pregnancies*) 2- Induction of labor +

PG 3- Progesterone-dependent cancer 4- Cushing's syndrome

Contraception:

I. Male contraception:

1. Behavioral
2. Mechanical (e.g. condoms) ± spermicidal agent (**nonoxynol-9**)
3. Drugs Estrogens; progestins; danazol; GnRH agonists & antagonists; spermicidal agents; gossypol(*acts as an inhibitor for several dehydrogenase enzymes*)
4. Surgical procedures e.g. vasectomy

II. Female contraception:

1. Behavioral
2. Mechanical Diaphragms; condoms ± spermicidal agents
IUD's (intra-uterine devices) ± progestins (progestasert)
3. Drugs
 - Estrogen alone Morning after pill or postcoital pill
Ethinylestradiol; DES(Diethylstilbestrol); mestranol..... ×5
 - Progesterone alone: The minipill
 - * Norethisteron... Tab
 - * I.M medroxyprogesterone
Depo-provera (effect lasts in 3-6 months)
 - * Subdermal progesterone implants
Levonorgesrel (effect lasts in 5-6 years)
4. Sequential
Estrogen followed by progesterone
5. Combined oral contraceptive pills (COCP's)
 - ethinylestradiol or mestranol + Norgestrel
 - ethinylestradiol or mestranol + Norethisterone
 - * Estrogen + progesterone in different ratios (lowest E highest P to achieve the lowest or zero failure rate)

• MOA of OCP's:

- 1- **Inhibition of ovulation (major mechanism)** At the level of the pituitary
- 2- ↑ viscosity of cervical mucus
- 3- Change in Fallopian tube motility

• OCP's side effects:

- 1- Nausea, vomiting, dizziness, headache, migraine, nervousness, depression
- 2- Salt & water retention → ↑ BP
- 3- Thromboembolic disease, embolism, MI
- 4- Vaginal yeast growth
- 5- Postpill amenorrhea and infertility

• OCP's contraindications:

- 1- History of thromboembolic disease
- 2- Severe headache
- 3- Severe nausea & vomiting
- 4- Liver dysfunction
- 5- Pregnancy
- 6- Abnormal menstrual cycles

• OCP's drug-drug interactions:

1- Drugs inhibiting enterohepatic circulation (because as we said, sex hormones are generally metabolized by the liver)

Ampicillin; cephalosporins; tetracyclines; sulfonamides; co-trimoxazole

2- Drugs ↑ metabolism

Phenobarbitone; phenytoin; ethosuximide; rifampicin; griseofulvin...

3- Miscellaneous interactions

+ anticoagulants → ↓ activity of anticoagulants + insulin → ↑ insulin need

يعني اذا استخدمناهم مع مضادات التخثر يقللوا تأثيرهم و يقللوا تأثير الانسولين و يزيديا الحاجة للانسولين.

أنا ما And since this is my last summary for the basic years, I would like you all to know that
D: إلي عائلة



Good luck ..