Sex hormones **Dr. Entisar Al-Mukhtar**

Progestogens

Progesterone, is the natural progestogen, produced in response to LH by both females (secreted by corpus luteum & placenta) & males (secreted by the testes). It is also synthesized by the adrenal cortex in both sexes.

Mechanism of action

- In females, **progesterone** promotes the development of a secretory endometrium.
- High levels of **progesterone** released during luteal phase of the menstrual cycle inhibit the production of gonadotropin & therefore, prevent further ovulation.
- If conception does not take place, the release of **progesterone** from the corpus luteum ceases abruptly. This decline stimulates the onset of menstruation.

Therapeutic uses of progestogens

1. Hormonal deficiency.
2. Contraception: progestogens are generally used with estrogens, either in combination or in a sequential manner.

- **Progesterone** by itself is not used widely as a contraceptive therapy because of its rapid metabolism.
- Synthetic progestogens (progestins) used in contraception are more stable to first-pass metabolism, they include **Desogestrel**, **Dienogest, Drospirenone, Levonorgestrel**, **Norethindrone**, **Norethindrone acetate**, **Norgestimate**, & **Norgestrel**.
- **Medroxyprogesterone acetate** is used as injectable contraceptive while its oral form is used in postmenopausal HT.
- Progestins are also used for the control of dysfunctional uterine bleeding, dysmenorrhea & management of endometriosis & infertility.

PROGESTOGENS

Desogestrel USED IN MANY COMBINATIONS
Dienogest (w/estradiol valerate) NATAZIA
Drospirenone (w/ethinyl estradiol) BEYAZ, YAZ, YASMIN
Etonogestrel (w/ethinyl estradiol) NUVA RING
Etonogestrel (subdermal) IMPLANON, NEXPLANON
Levonorgestrel MIRENA, NEXT CHOICE, PLAN B ONE-STEP
Medroxyprogesterone PROVERA
Norelgestromin (w/ethinyl estradiol) ORTHO EVRA
Norethindrone NOR-QD, ORTHO MICRONOR
Norethindrone acetate AYGESTIN
Norgestimate USED IN MANY COMBINATIONS
Norgestrel (w/ethinyl estradiol) LO/OVRAL
Progesterone USED IN MANY COMBINATIONS

PROGESTERONE AGONIST/ANTAGONIST

Ulipristal acetate ELLA

PROGESTERONE ANTAGONIST

Mifepristone MIFEPREX

Pharmacokinetics

- The micronized preparation of **progesterone** is rapidly absorbed after oral administration & has a short half-life in the plasma.

- Synthetic progestins are less rapidly metabolized.
- Oral **medroxyprogesterone acetate** has a half-life of 30 days, when injected IM or SC it has a half-life of about 40-50 days & provides contraception for approximately 3 months.
- The half-lives of other progestins are 1-3 days, allowing for once-daily dosing.

Adverse effects

- Headache, depression, weight gain & changes in libido.
- The 19-nortestosterone derivatives (e.g, **norethindrone**, **norethindrone acetate**, **norgestrel**, **levonorgestrel**), possess some androgenic activity & can cause acne & hirsutism. Less androgenic progestins, such as **norgestimate** & **drospirenone**, may be preferred in women e.g., with acne.
- **Drospirenone** has antimineralocorticoid effects, and its concurrent use with other drugs that increase serum potassium (e.g., ACEIs) may increase the risk of hyperkalemia.

Antiprogestin

Mifepristone

- A progesterone antagonist with partial agonist activity (note: **mifepristone** also has potent antiglucocorticoid activity), its administration in early pregnancy usually results in abortion due to interference with the **progesterone**.
- **Mifepristone** is often combined with the PGE1 analog **misoprostol** (orally or I.V) to induce uterine contractions.
- The major adverse effects are uterine bleeding & possibly an incomplete abortion.
- **Mifepristone** has also been investigated as an oral & an emergency contraceptive.