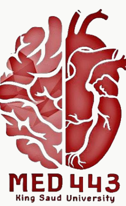
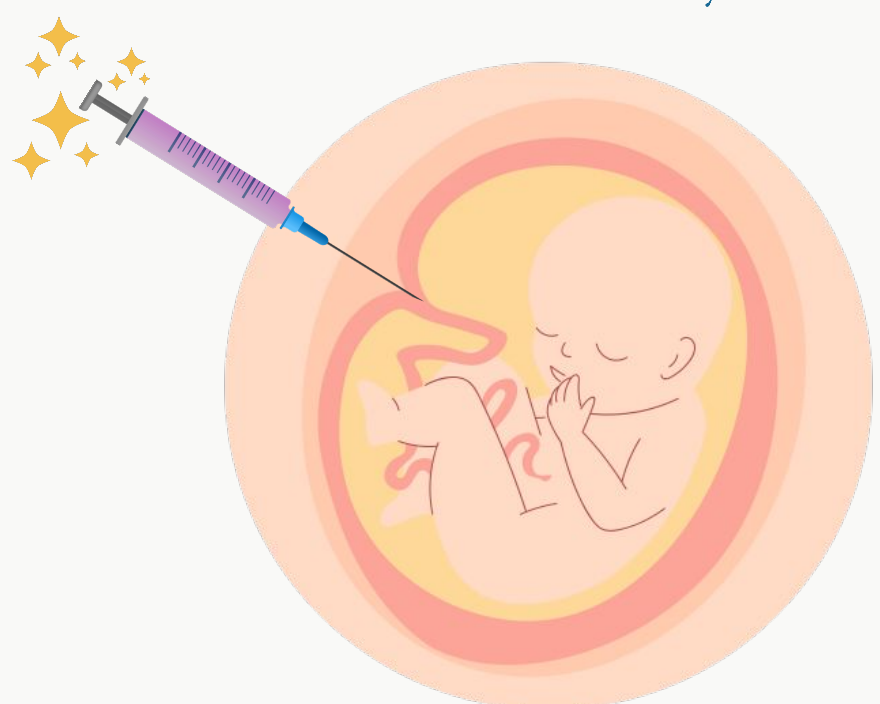


Drugs inducing ovulation

Dr. Alaa Alanteet | Dr. Sary Alsanea



- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

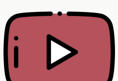
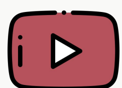
Objective

Recall how ovulation occurs and specify its hormonal regulation.

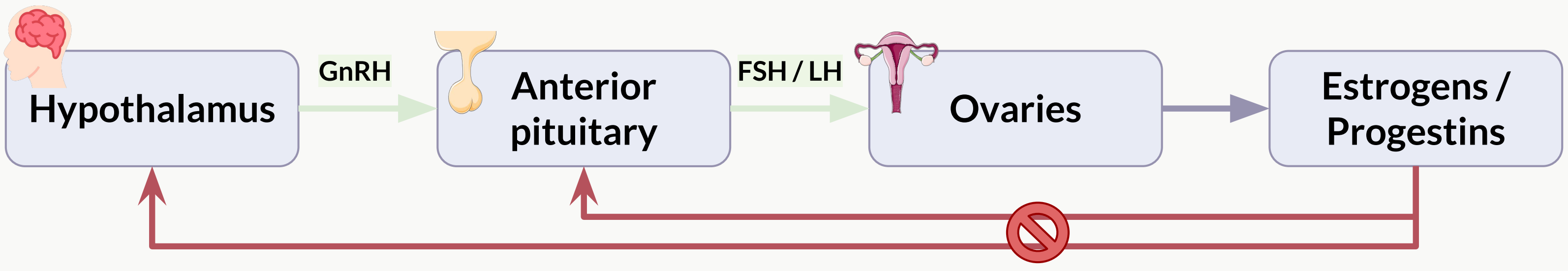
Classify ovulation inducing drugs in relevance to the existing deficits.

Expand on the pharmacology of each group with respect to mechanism of action, protocol of administration, indication, efficacy rate and adverse effects.

Overview

Normogonadotropic



Ovulation Induction

- **1- Antiestrogens (SERMs)**
  - Clomiphene
  - Tamoxifen
- **2- GnRH-agonists**
  - Leuprorelin (leuprolide)
  - Goserelin
- **3- Gonadotropins**
  - HMGs: Menotropin
  - HCGs: Pregnyl
- **4- Hyperprolactinemia**
  - **D_2 receptors agonists:** Bromocriptine

Drug of Polycystic Ovarian Syndrome (PCOS)

- Clomiphene
- Tamoxifen
- Metformin

HCG: Human Chorionic Gonadotropin
HMG: Human Menopausal Gonadotropin

1-Antiestrogens (SERMs)-Selective estrogen receptor modulator-

Drugs	Clomiphene	Tamoxifen
MOA	**Compete with estrogen on the hypothalamus and anterior pituitary gland:** ○ ↓ the negative feedback of endogenous estrogen →↑ GnRH → ↑ production of FSH & LH → ***Ovulation.*** Stops the -ve feedback of estrogen thereby gonadotropin will be high (disinhibition)	Hypothalamus GnRH Pituitary gland LH/FSH Ovaries Estrogens/Progestins - Clomiphene
P.K	•**Method of administration:** -Given 50 mg/d for 5 days from **5th day of the cycle to the 10th day.** As mentioned we need gonadotropin and this is the most imp time for it due to the development of follicle. -If no response give 100 mg for 5 days again from 5th to10th day. -Each dose can be repeated **not more than 3 cycles**.	Is similar & alternative to clomiphene.
Uses	• Female infertility **not** due to ovarian or pituitary failure →**Normogonadotropic.** • The success rate for ovulation is 80% and pregnancy is 40% .	• It is a good alternative to clomiphene in women with PCOS & **Clomiphene-resistant cases.** • Former use: in palliative treatment of **estrogen receptor-positive breast cancer.** • **But why not clomiphene ?** Because Tamoxifen has potent anti estrogen activity in breast cancer.
ADRs	• **Hyperstimulation of the ovaries & high** incidence of multiple birth(75% twins). Increased ovulation →↑ chance of twin birth. • Hot Flushes & breast tenderness. • Gastric upset (nausea and vomiting). • Visual disturbances (reversible). • ↑ nervous tension & depression. • Skin rashes. • Fatigue. • Weight gain. • Hair loss (reversible).	–

2- Gonadotropin Releasing Hormone (GnRH)

Drug: **Leuprorelin** (Leuprolide) , **Goserelin**

MOA: Analogues with agonist activity.

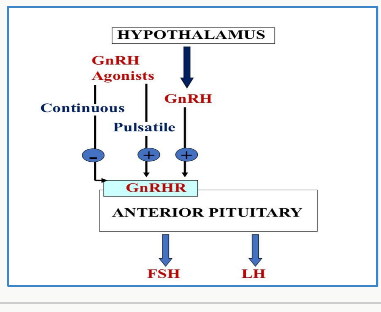
P.K:

Administration:

- GnRH and agonists, given S.C. in a pulsatile (drip) to stimulate gonadotropin release (1 – 10 μg / 60 – 120 min), start from day 2-3 of cycle up to day 10.
- Given continuously **(paradoxical opposite effect)**, when gonadal suppression is desirable e.g. precocious puberty and advanced breast cancer in women and prostatic cancer in men.

P.D:

Pharmacological effects
Hypothalamus
GnRH
GnRH Agonists
Pulsatile
Continuous
GnRHR in anterior pituitary
FSH / LH



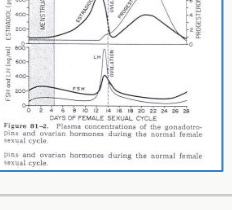
Uses: For ovulation in patients with hypothalamic amenorrhea (GnRH deficient).

ADRs:

- GIT disturbances, abdominal pain, nausea….etc
- Headache.
- **Hypoestrogenism** on long term use:

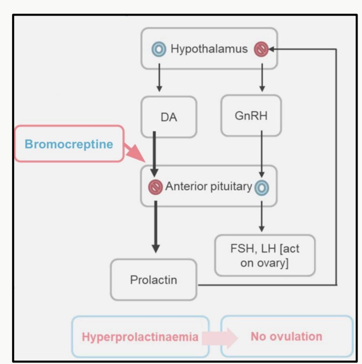
-Hot flashes. -↓ Libido. - Osteoporosis. -Rarely ovarian hyperstimulation → ovaries swell & enlarge.

3-Gonadotropins (FSH & LH)

Drug	Menotropin	Pregnyl
MOA	• **FSH** and **LH** are naturally produced by the pituitary gland. • For therapeutic use, extracted forms are available as: ***Menotropin* | *Pregnyl*.**	
	Human **Menopausal** Gonadotropin (hMG) extracted from **postmenopausal** urine contains **LH & FSH** . due to low estrogen in menopause they will be high .	Human **Chorionic** Gonadotropin (hCG) extracted from urine of **pregnant** women contains mainly **LH.**
P.K	**hMG** is given I.M every day starting at day 2-3 of cycle for 10 days as explained before. followed by **hCG** on (10th - 12th day) for ovum retrieval. to mimic the physiological LH surge for the follicular release. 	
Indications	• Stimulation & induction of ovulation in infertility **2^{ndry} to gonadotropin deficiency (pituitary insufficiency)** problems with hypothalamus = GnRH probleme with the AP = gonadotropin. • Success rate for inducing ovulation is usually ≥75 %.	
ADRs	• **LH** containing preparations: Headache & edema.	
	• **FSH** containing preparations: ○ Fever. ○ Ovarian enlargement *(hyperstimulation)*. ○ Multiple Pregnancy (approx. 20%).	–

4- Hyperprolactinemia

D_2 Receptor Agonists: Bromocriptine

MOA	• Is an ergot derivative (not a hormone) • D_2 receptor agonists bind to dopamine receptors in the anterior pituitary gland & **inhibits prolactin secretion.** 
Uses	Female infertility **2^{dry} to hyperprolactinemia.**
ADRs	• GIT disturbances: nausea, vomiting, constipation. • Headache dizziness & orthostatic hypotension cuz dopamine lower blood pressure • Dry mouth & nasal congestion. • Insomnia.

Polycystic Ovarian Syndrome - PCOS -

•Most common cause of infertility.

•The exact cause of PCOS is unknown, **Insulin resistance** (obese patient) **may play a role:** Hyperinsulinemia decrease serum sex hormone - binding globulin (SHBG) concentrations and increase free testosterone.

•**Treatment: Metformin** (first choice 442 Dr) [1] | **Clomiphene also used.**

(1)442:Why metformin? Several effect needed for pcos pt such as, restoring ovulation, reducing weight, reducing circulating androgen levels, reducing the risk of miscarriage and reducing the risk of gestational diabetes mellitus (GDM) and as we know pcos cause insulin resistance (dm2).

Extra Summary:

Normogonadotropic State: *Anovulation or Oligoovulation e.g: PCOD*	**Antiestrogens (SERMS):** Clomiphene & Tamoxifene
Hypothalamic Amenorrhea	**GnRH:** Leuprorelin & Goserelin
Pituitary Insufficiency: *Infertility 2^{dry} to gonadotropin deficiency*	**HCG:** Pregnyl (LH) **HMG:** Menotropin (LH & FSH)
Hyperprolactinemia	**D_2 receptors agonists:** Bromocriptine

Team leaders

Sarah Alajaji **Maryam Alghannam**

Team members

Sarah Aldossary
Sultan Almishrafi
Lama Hazzaa
Omar Banjar
Aroub Almahmoud
Fatimah Alghamdi
Layan Al-Ruwaili
Naif Alateeq
Mohammed Alhudaithi
Rahaf Alslimah
Mansour Alotaibi
Wasan Alanazi
Lama Alotaibi
Sultan Albaqami
Ghaida Aldossary
Fahad Aldhafian
Zeyad Alotaibi
Alanoud Alolaywah

Special thanks to Norah Almania for the amazing logo