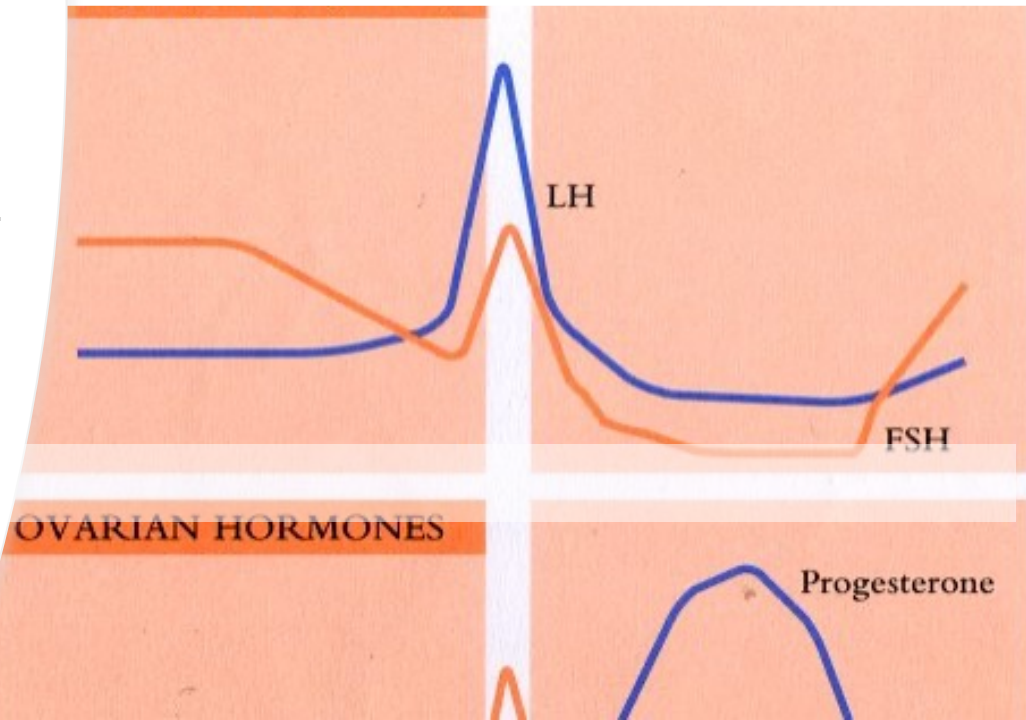
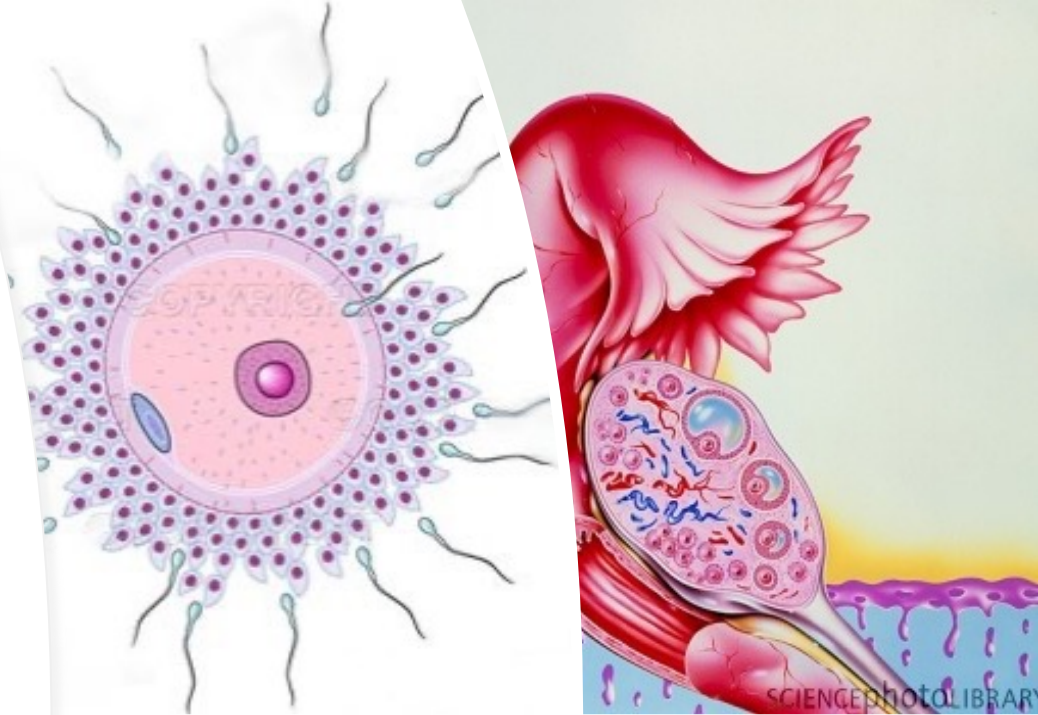
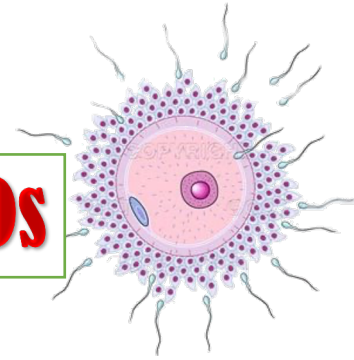


Drugs Used in OVULATION INDUCTION

(Slides are adopted and modified from Prof. Mohamad Alhumayyd)



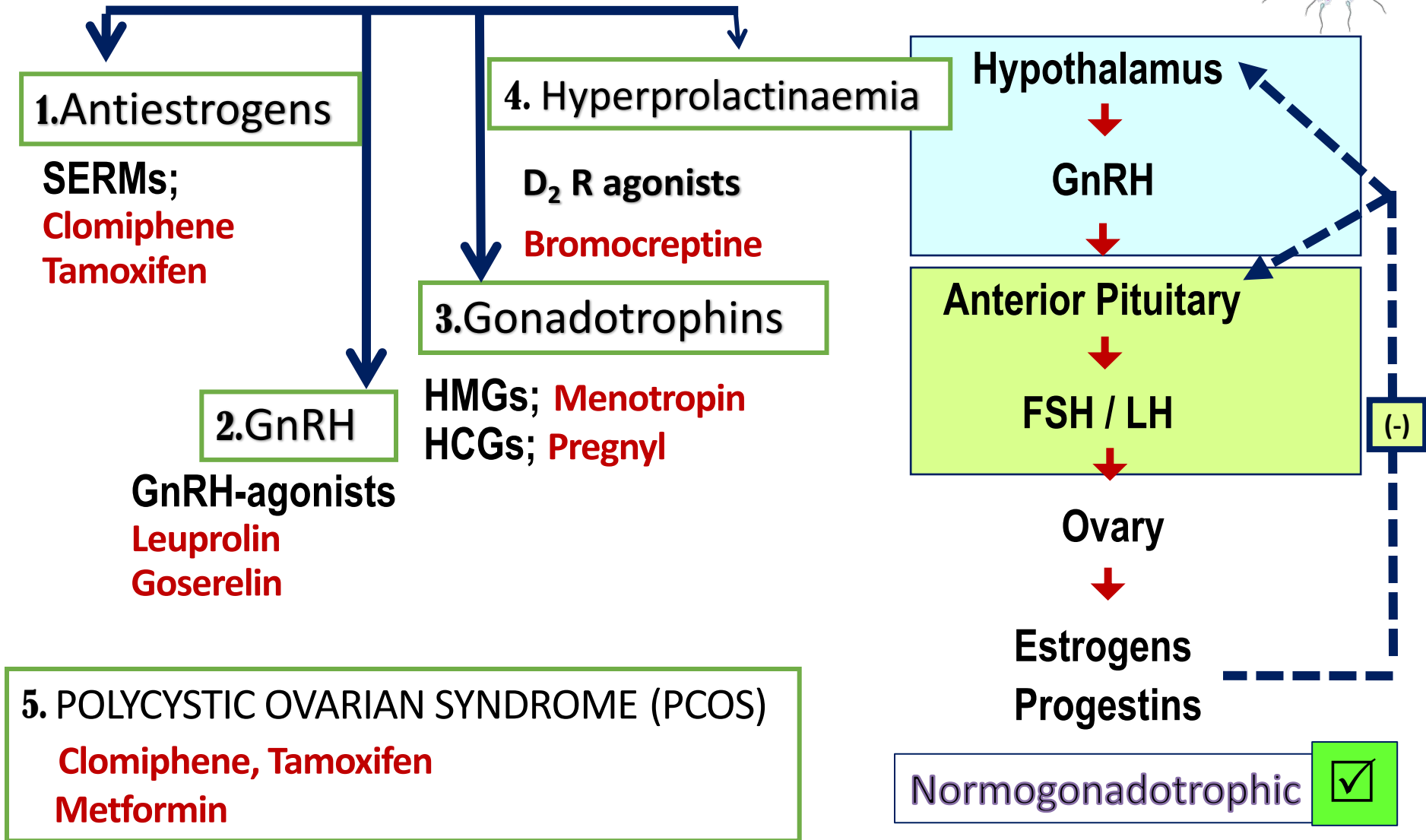
Drugs In OVULATION INDUCTION **ILOs**



By the end of this lecture you will be able to:

- 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.

Ovulation Induction



hMG, Human Menopausal Gonadotrophin; hCG, Human Chorionic Gonadotrophin

ANTIESTROGENS

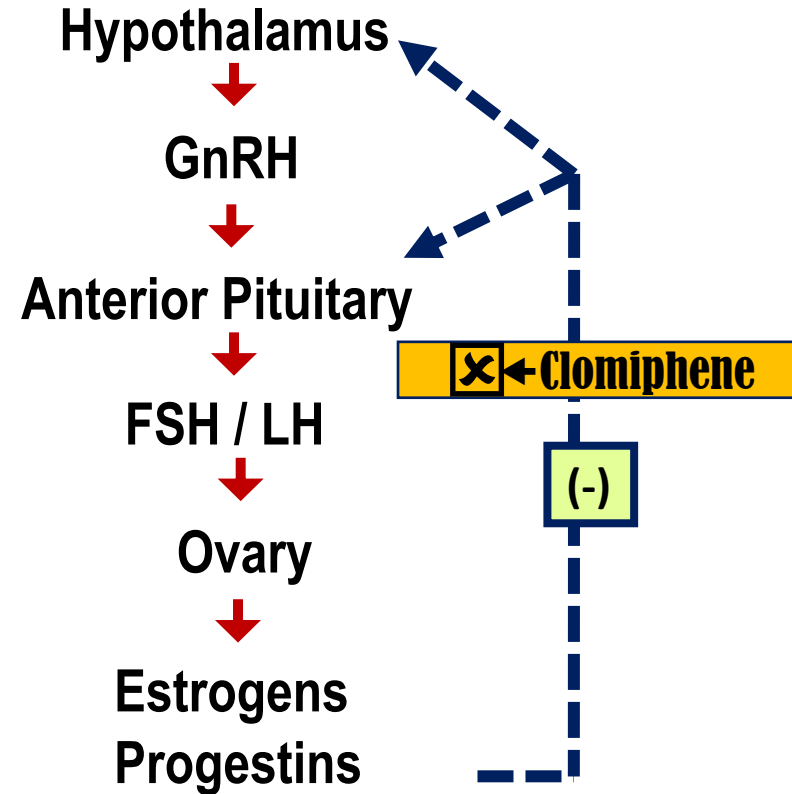
1. CLOMIPHENE

Pharmacological effects

- Compete with estrogen on the hypothalamus and anterior pituitary gland; ↓ negative feed back of endogenous estrogen → ↑GnRH →
- ↑production of FSH & LH → OVULATION

Indication

- Female infertility;
- not due to ovarian or pituitary failure → Normogonadotrophic
- The success rate for ovulation → 80% & pregnancy → 40% .



Method of administration

- Clomiphene given ➔ **50 mg/d** for 5 days from 5th day of the cycle to the 10th day.
- If no response give **100 mg** for 5 days again from 5th to 10th day
- Each dose can be repeated not more than 3 cycles.

ADRs

1. Hot Flashes & breast tenderness
2. Gastric upset (nausea and vomiting)
3. Visual disturbances (reversible)
4. ↑ nervous tension & depression
5. Skin rashes

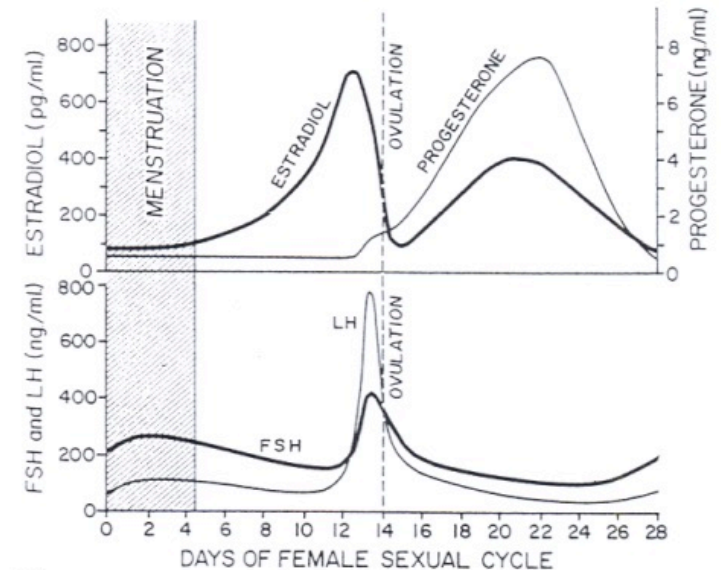


Figure 81-2. Plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle.

6. Fatigue
7. Weight gain
8. Hair loss (reversible)
9. Hyperstimulation of the ovaries & high incidence of multiple birth (75% twins).

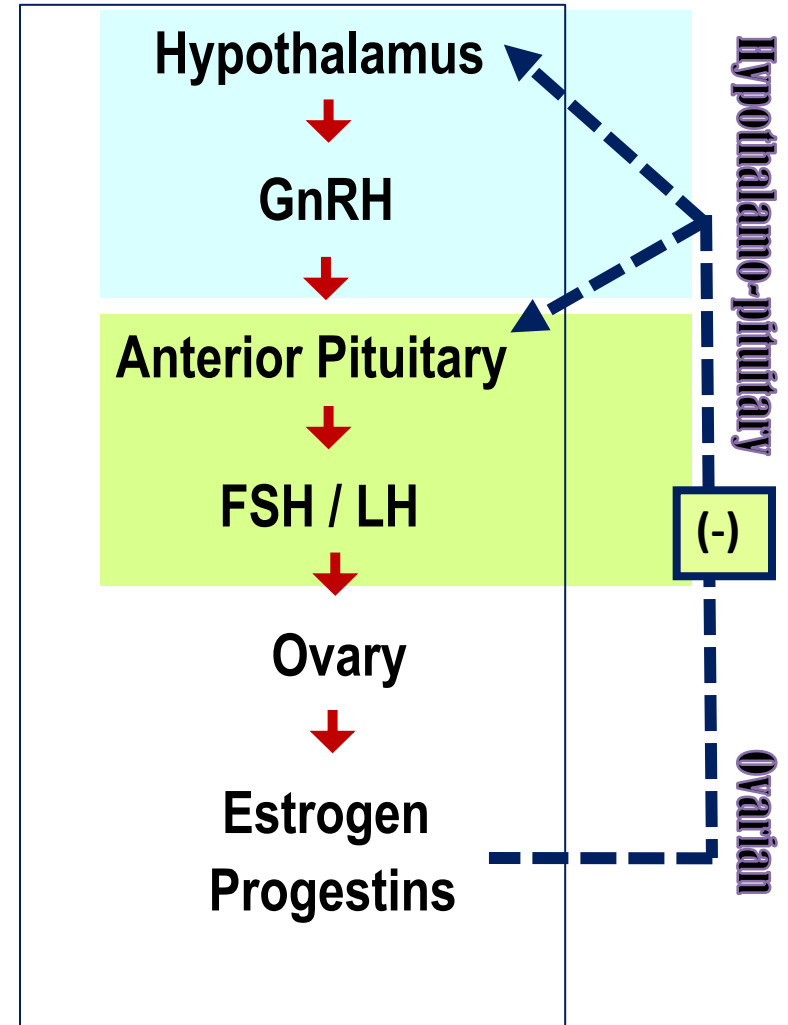
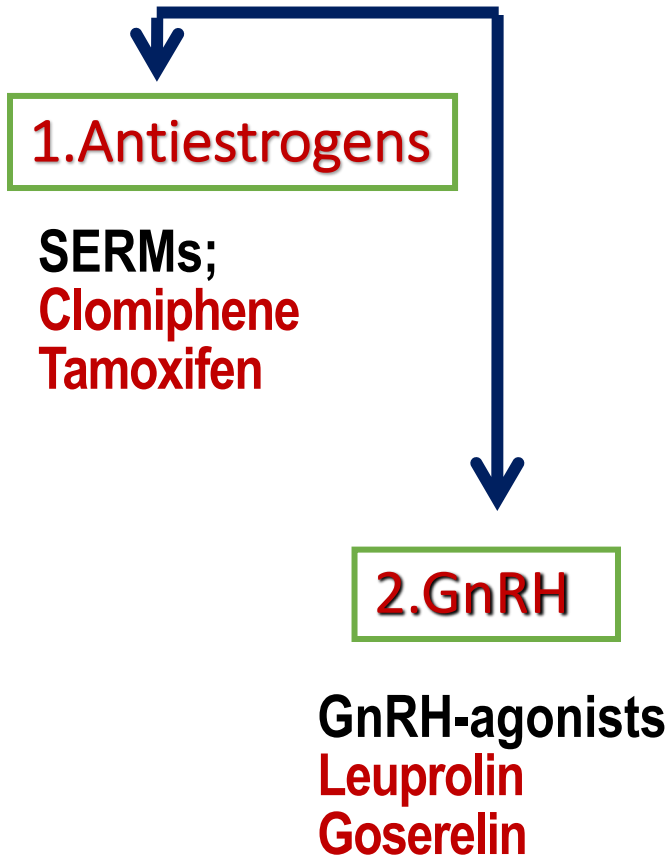
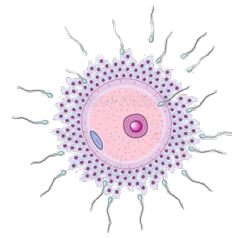
2. TAMOXIFEN

Is similar & alternative to clomiphene

- **It is a good alternative to clomiphene in women with PCOS and clomiphene- resistant cases.**
- **Used in palliative treatment of estrogen receptor- positive breast cancer.**

But why not clomiphene?

Ovulation Induction



2. GONADOTROPIN RELEASING HORMONE (GnRH)

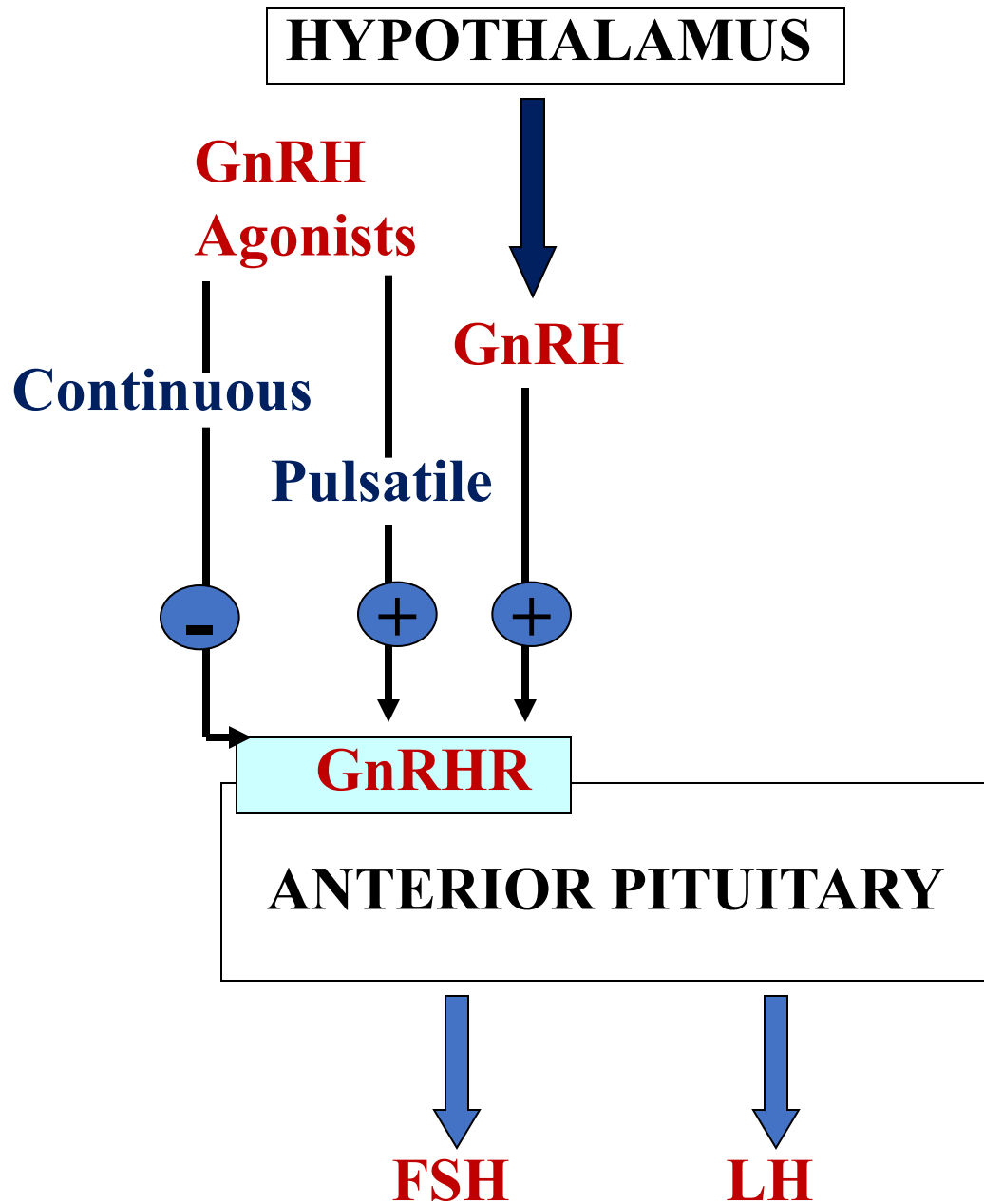
Uses: Induction of ovulation in patients with hypothalamic amenorrhea (GnRH deficient).

Analogues with agonist activity:

Leuprolin, Goserelin

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.

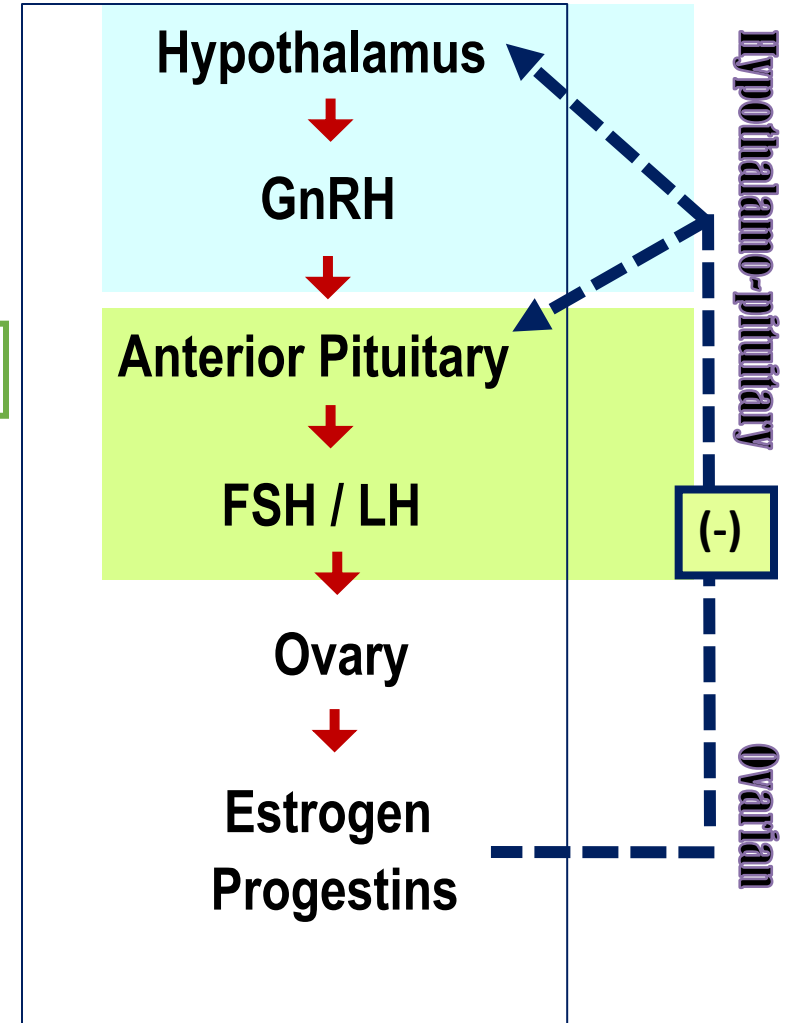
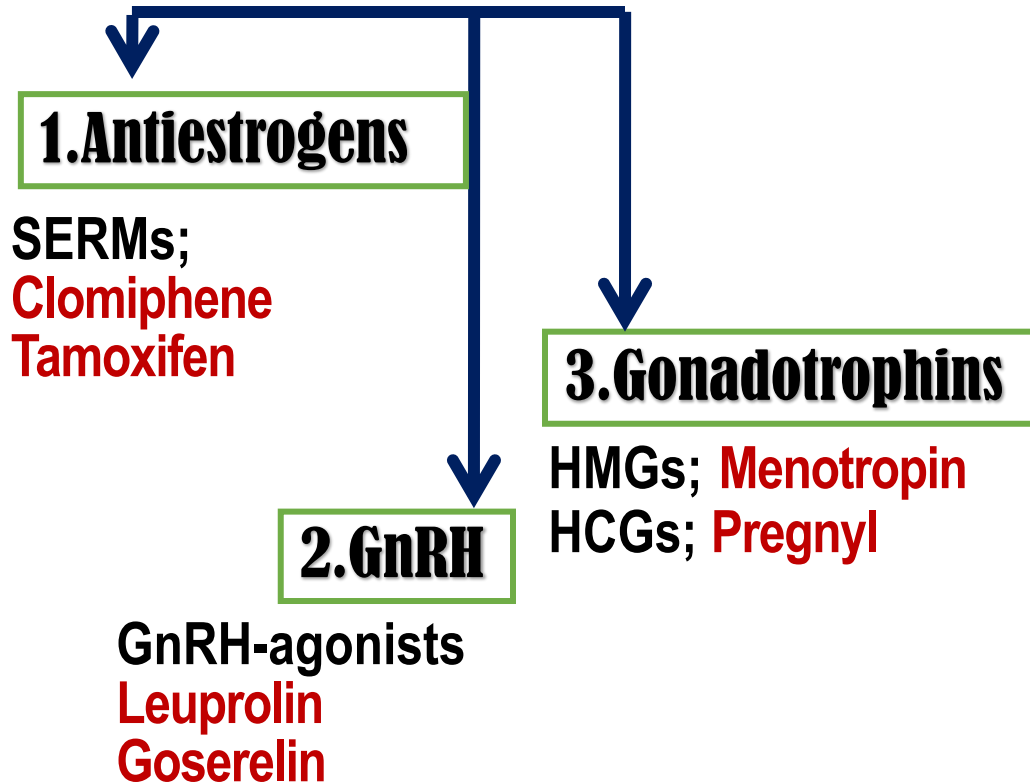
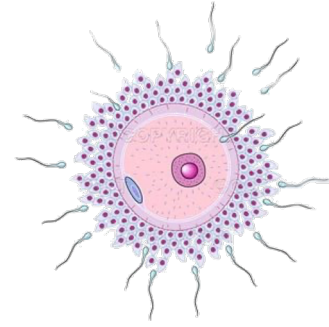
Given **continuously** (paradoxical opposite effect), when gonadal suppression is desirable e.g. precocious puberty and advanced breast cancer in women and prostatic cancer in men.



ADRs OF GnRH Agonists

- GIT disturbances, abdominal pain, nausea....etc
- Headache
- Hypoestrogenism *on long term use* ➔
 - Hot flashes
 - ↓ Libido
 - Osteoporosis
 - Rarely ovarian hyperstimulation ➔ (ovaries swell & enlarge).

Ovulation Induction



3.GONADOTROPHINS

[FSH & LH]

Are naturally produced by the pituitary gland

For therapeutic use, extracted forms are available as;

1. Human Menopausal Gonadotrophin (hMG) → extracted from postmenopausal urine → contains LH & FSH → **MENOTROPIN.**
2. Human Chorionic Gonadotrophin (hCG) extracted from urine of pregnant women → contains mainly LH → **PREGNYL.**

Indication

- Stimulation & induction of ovulation in infertility 2ndry to gonadotropin deficiency (pituitary insufficiency).

Success rate for inducing ovulation is usually $\geq 75\%$

GONADOTROPHINS

Method of administration

hMG is given *i.m* every day starting at day 2-3 of cycle for 10 days followed by **hCG** on (10th - 12th day) for ovum retrieval.

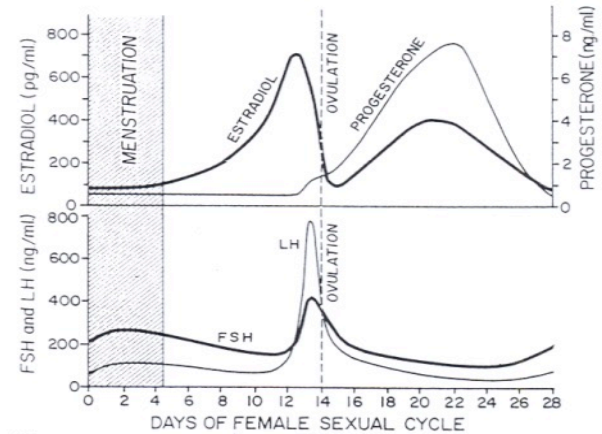


Figure 81-2. Plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle.

pins and ovarian hormones during the normal female sexual cycle.

ADRs

FSH containing preparations; Fever

Ovarian enlargement (hyperstimulation)

Multiple Pregnancy (approx. 20%)

LH containing preparations; Headache & edema

4. Hyperprolactinaemia

D₂ R Agonists **BROMOCREPTINE**

Is an ergot derivative (not a hormone)

Mechanism

D₂ R Agonists binds to dopamine receptors in the anterior pituitary gland & inhibits prolactin secretion .

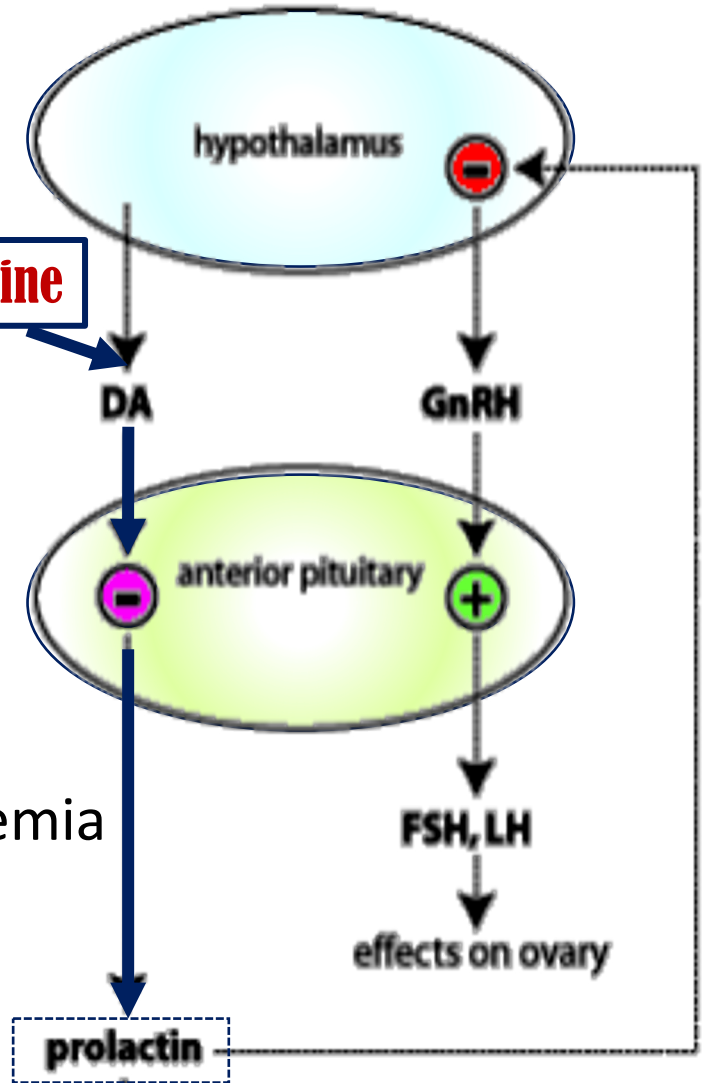
Indications

- Female infertility 2ndry to hyperprolactinaemia

ADRs

- GIT disturbances; nausea, vomiting, constipation
- Headache dizziness & orthostatic hypotension
- Dry mouth & nasal congestion
- Insomnia

Bromocriptine



Hyperprolactinaemia

**No
Ovulation**

5. POLYCYSTIC OVARIAN SYNDROME (PCOS)

Most common cause of infertility

The exact cause of PCOS is unknown

Insulin resistance may play a role ???

Metformin

Clomiphene also used

Thanks