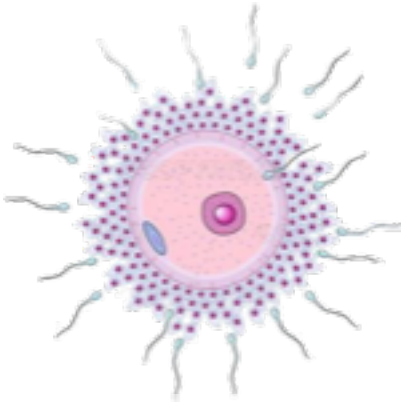
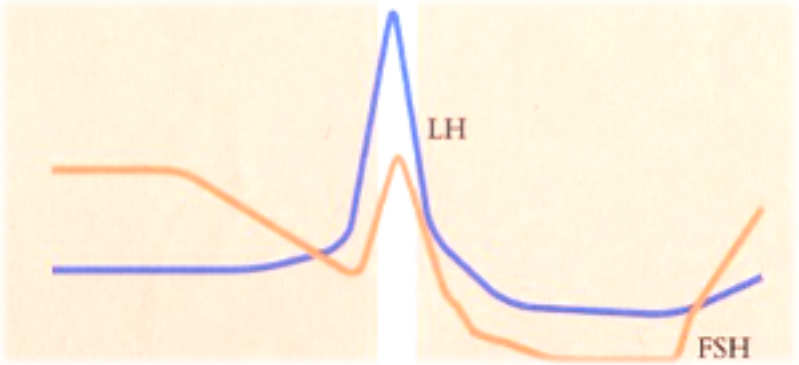
Drugs In OVULATION INDUCTION





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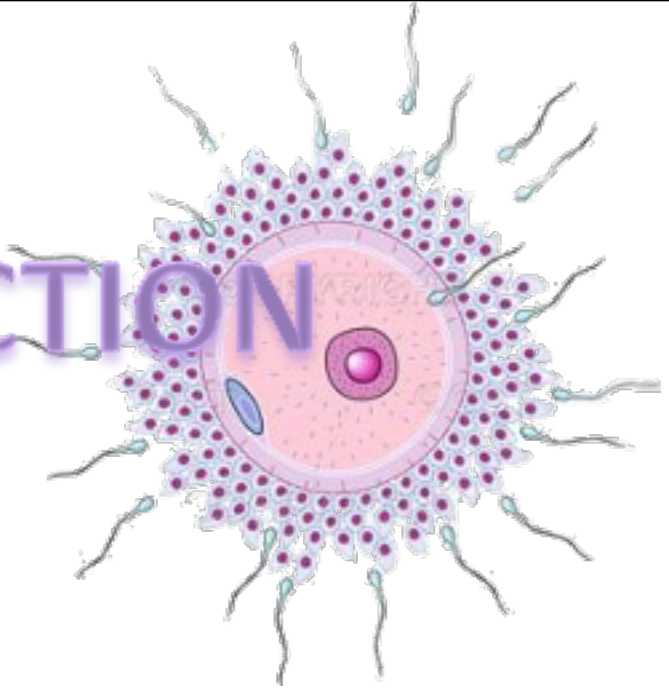
(Slides are adopted and modified from Prof. Mohamad Alhumayyd)

Drugs In OVULATION INDUCTION



ILOs

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

- 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

1. Antiestrogens

SERMs;
Clomiphene
Tamoxifen

2. GnRH

GnRH-agonists
Leuprolin
Goserelin

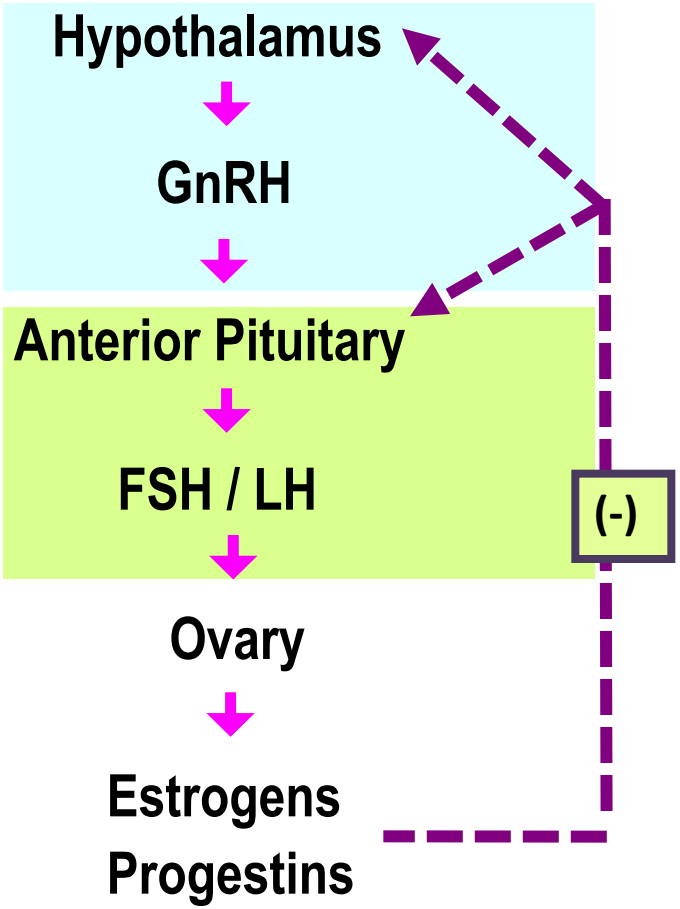
3. Gonadotrophins

HMGs; Menotropin
HCGs; Pregnyl

4. Hyperprolactinaemia

D_2 R agonists

Bromocreptine



5. POLYCYSTIC OVARIAN SYNDROME (PCOS)

Clomiphene, Tamoxifen
Metformin

Normogonadotrophic ☑

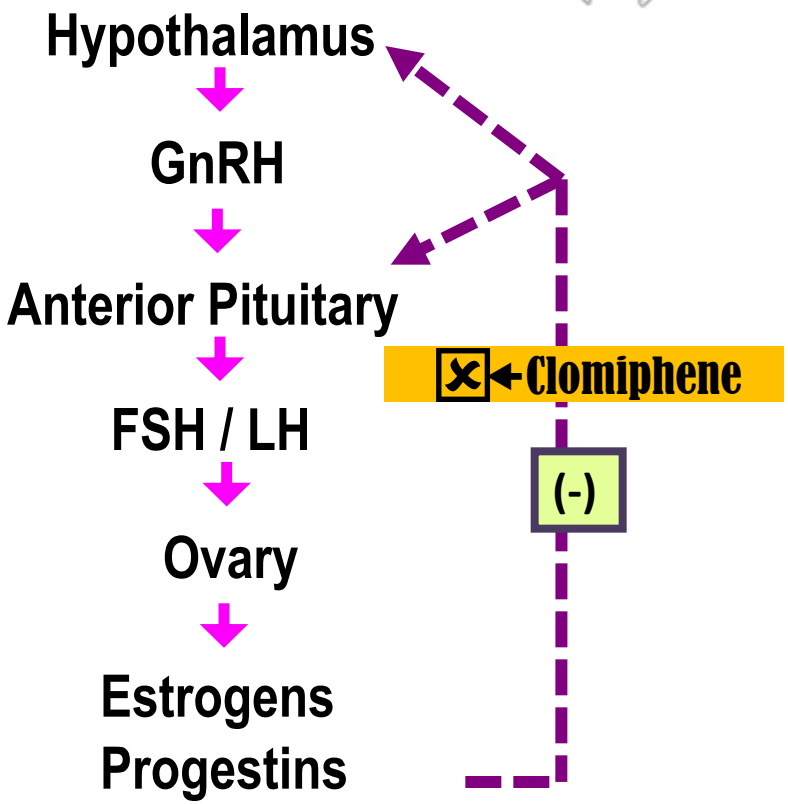
hMG, Human Menopausal Gonadotrophin; hCG, Human Chorionic Gonadotrophin

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 to10th day

Each dose can be repeated not more than 3 cycles .

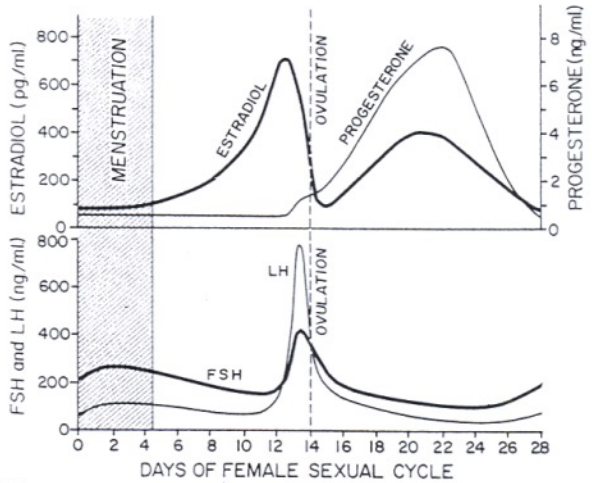


Figure 81–2. Plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle.

ADRs

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

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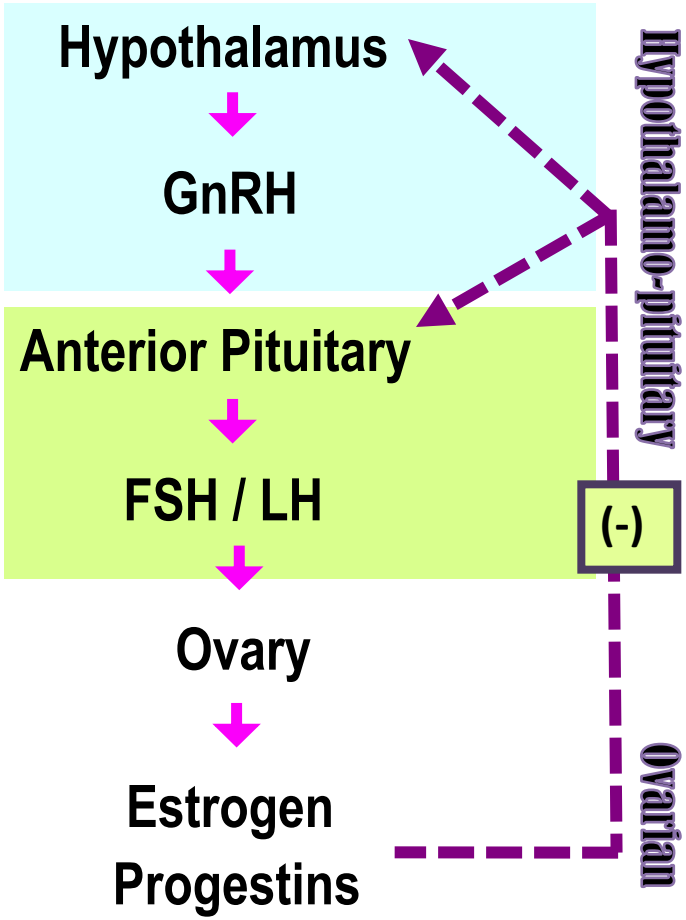
Goserelin



2. GONADOTROPIN RELEASING HORMONE (GnRH)

Uses:

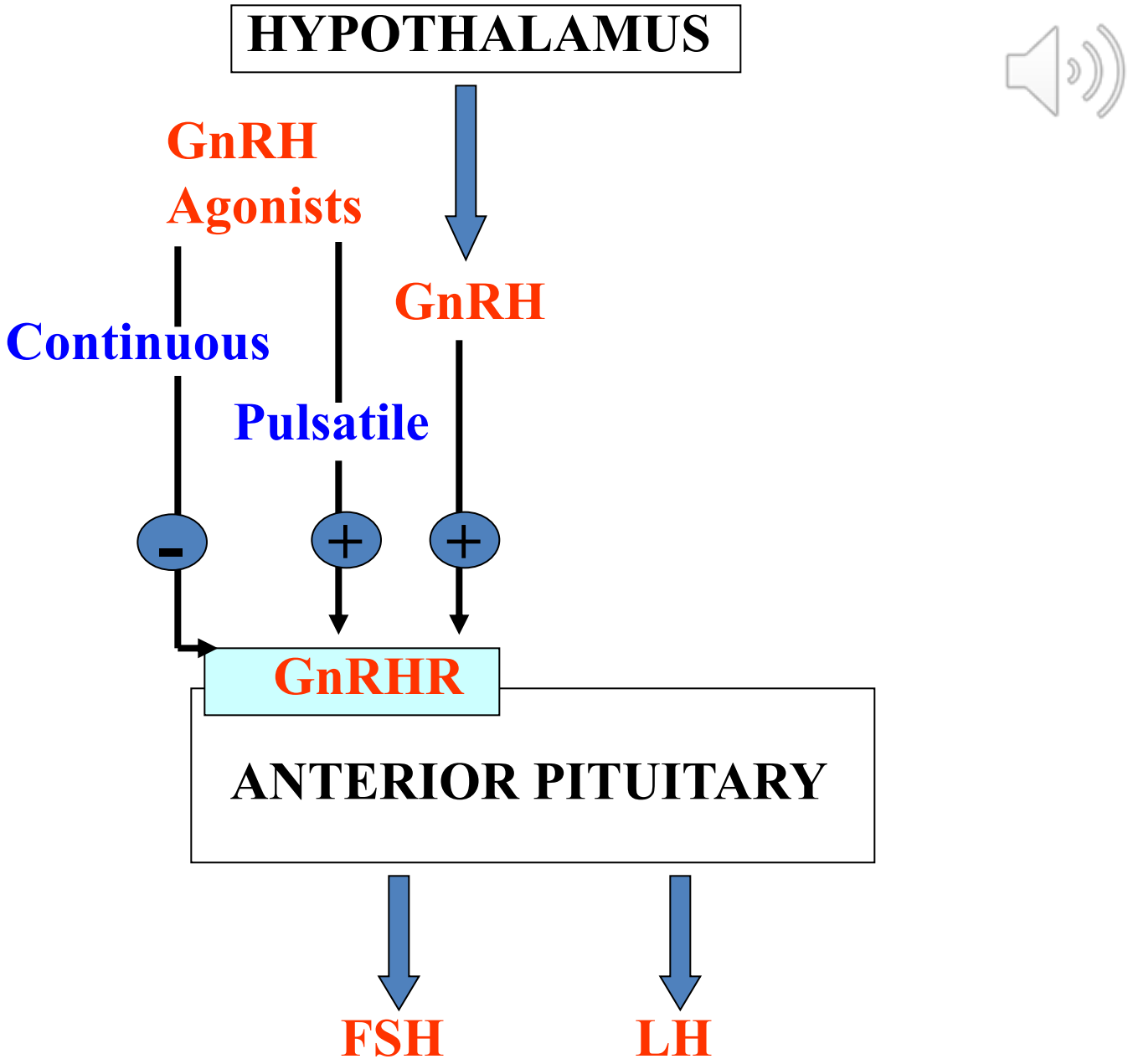
Induction of ovulation in patients with hypothalmic amenorrhea (GnRH deficient)

Analgoues 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.


HYPOTHALAMUS
GnRH
Agonists
GnRH
Continuous
Pulsatile
-
+
+
GnRHR
ANTERIOR PITUITARY
FSH
LH

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

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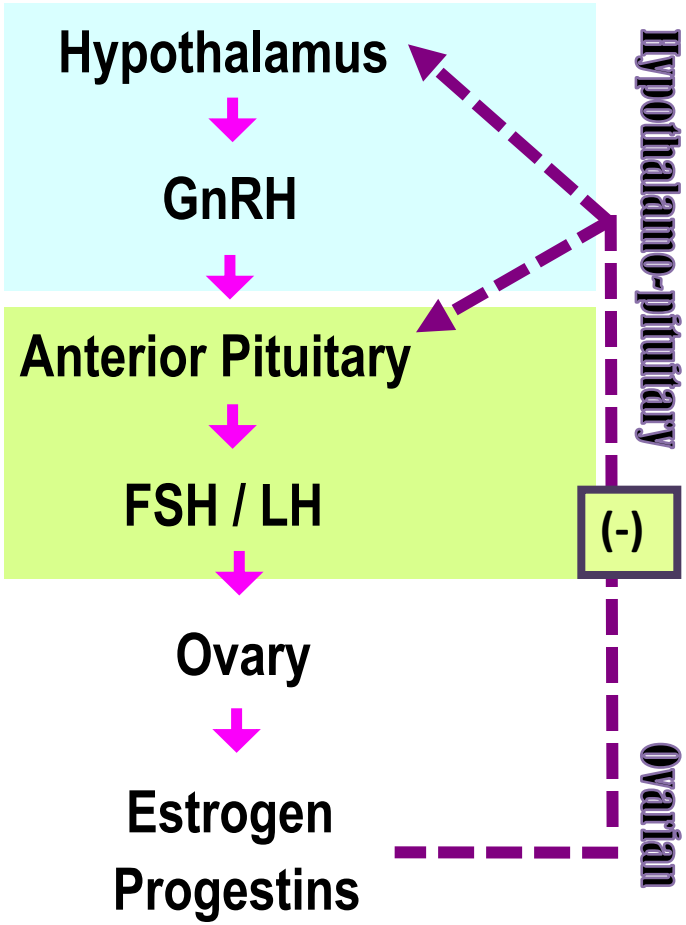


3.GONADOTROPHINS → [FSH & LH]

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 2^{ndry} to gonadotropin deficiency (pituitary insufficiency)

Success rate for inducing ovulation is usually ≥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 retreival .

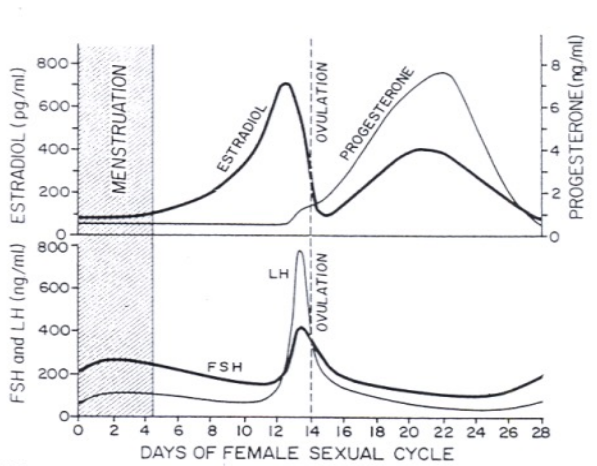


Figure 81–2. Plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle.

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

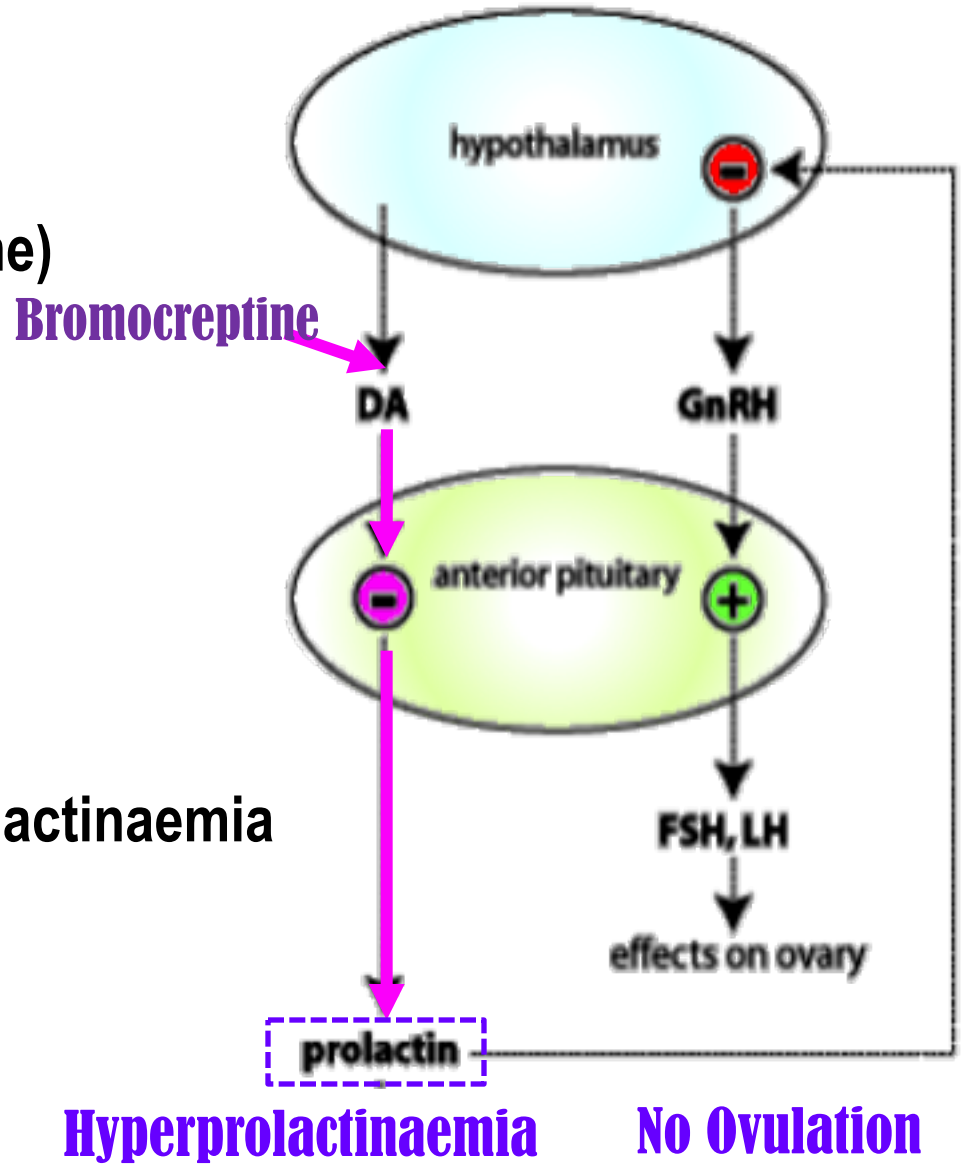
4. Hyperprolactinaemia

D_2 R Agonists

BROMOCREPTINE

Is an ergot derivative (not a hormone)

Mechanism D_2 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

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