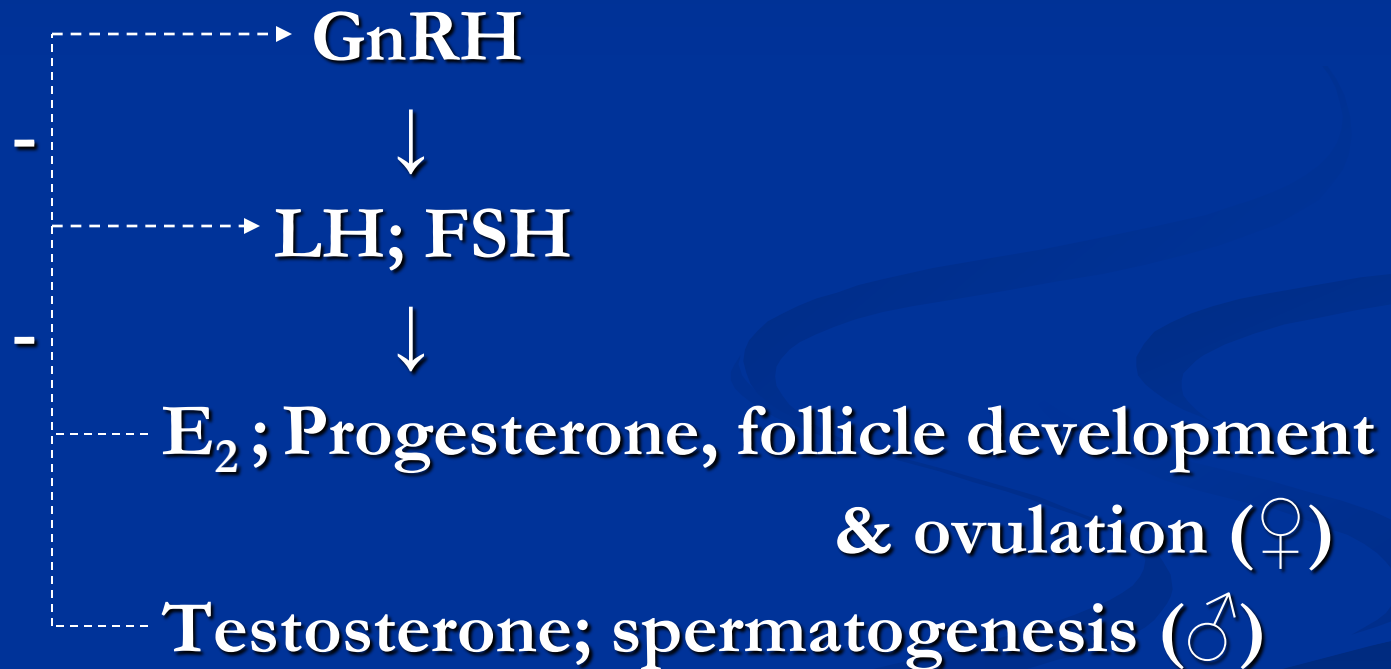


GnRH, LH, FSH

- **GnRH (Gonadotropin Releasing Hormone; Gonadorelin)** A decapeptide



**** Structure-activity relationship:**

Pro-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly

**** Pattern of release and MOA:**

- Pulsatile (Ca^{++} second messenger) \rightarrow \uparrow LH & FSH
- Large doses or continuous administration
(downregulation of pituitary GnRH receptors) \rightarrow \downarrow LH & FSH

■ GnRH synthetic preparations:

Leuprolide acetate, Triptorelin, Goserelin, Histrelin, Nafarelin, Busereline...

Could be given S.C, I.M, I.V

Mainly given S.C

Ineffective orally

Available in intranasal, suppositories, subdermal implants and vaginal pessaries dosage forms

■ GnRH clinical uses:

a. Pulsatile administration

- Diagnostic use
- GnRH deficiency (Kallman's syndrome)

R_x of ♂ & ♀ hypogonadism; induction of ovulation (infertility), delayed puberty, amenorrhea, cryptorchidism...

b. Continuous administration or large doses or the use of a GnRH superagonists:

- **Ca prostate; Ca breast**
- **Endometriosis**
- **IVF**
- **Precocious puberty**
- **Uterine fibroids or uterine leiomyomas, polycystic ovarian syndrome (PCOS)**
- **?? Contraceptive**

■ Side effects to GnRH:









- Production of GnRH Abs → resistance to treatment
- Headache and abdominal pain (tolerance develops to these side effects)
- Sweating, facial flushing, hot flushes
- Osteoporosis

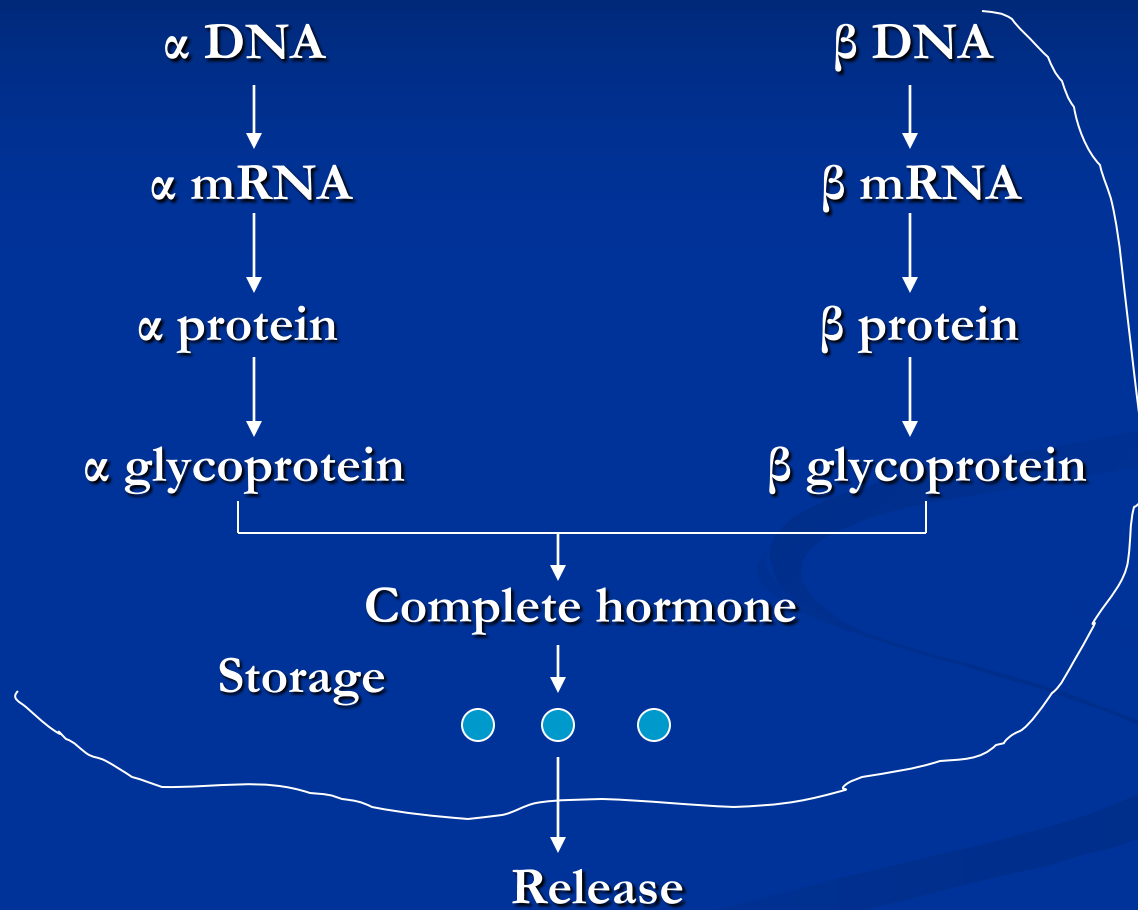
■ GnRH specific antagonist:

Ganirelix (IVF)

Gonadotropins: LH & FSH

Glycoproteins; under regulation by GnRH

	LH	FSH	TSH	hCG
α				
β				



■ MOA of LH & FSH:

- Surface receptors; cAMP 2nd messenger
- LH stimulates desmolase enzyme $\rightarrow \uparrow$ steroidogenesis in gonads
- LH helps in the descent of testes during fetal life

■ Source of LH & FSH:

- Natural human source. Human menopausal gonadotropins (HMG; Menotropin) (Mainly FSH)
- rDNA preparations (r β -FSH)

■ Human Chorionic Gonadotropin (hCG)

A product of the placenta

Has similar pharmacological properties to LH

Obtained from the urine of pregnant ladies

■ Clinical uses to gonadotropins:

- Infertility in ♂'s and ♀'s due to LH & FSH deficiency
- I.V.F
- Cryptorchidism (hCG; I.M)

■ Side effects to gonadotropins:

- Allergy
- Ovarian hyperstimulation syndrome (fever; abdominal pain, ovarian enlargement, ascites, pleural effusion, arterial thrombosis, hemoperitoneum, shock...)
- Multiple births
- Production of specific antibodies
- Precocious puberty and gynecomastia
- ? Ovarian tumors
- Failure of Rx (abortion)

*** If the problem is sexual function

Give estrogen or testosterone

*** If the problem is infertility:

- GnRH in pulses
- LH, FSH, hCG
- Estrogen (♀'s); testosterone (♂'s)
- Bromocriptine
- Clomiphene citrate or Tamoxifen (estrogen antagonists) in ♀'s & ♂'s

- E-antagonists (Clomiphene citrate or Tamoxifen) are highly effective in inducing ovulation in ♀'s and restoring fertility in ♂'s
- Also E-antagonists are used with HMG and hCG to regulate ovulation in IVF

- **MOA of estrogen antagonists as anti-infertility agents:**

