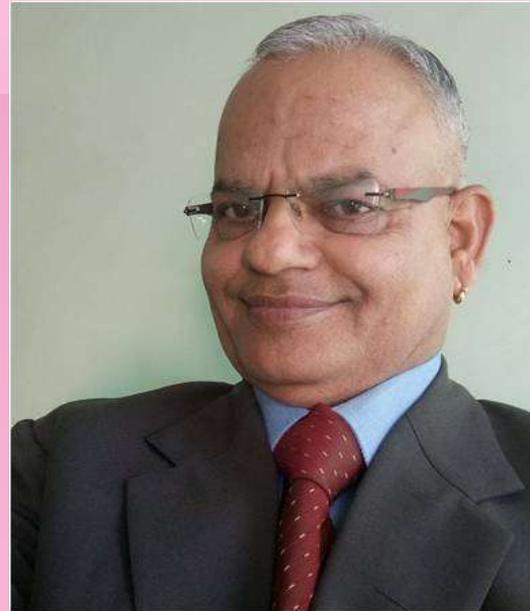
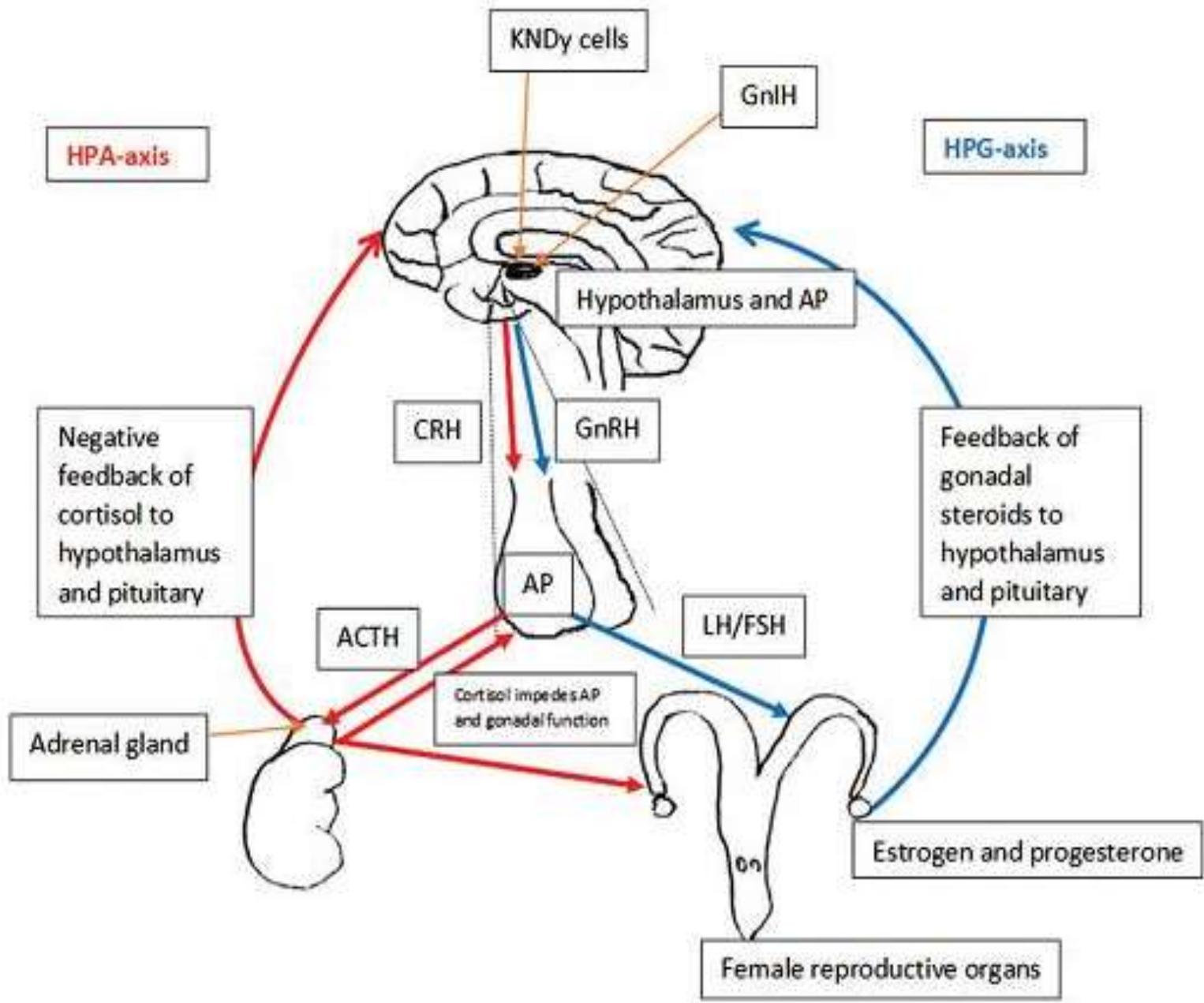


HORMONES OF REPRODUCTION IN DOMESTIC ANIMALS

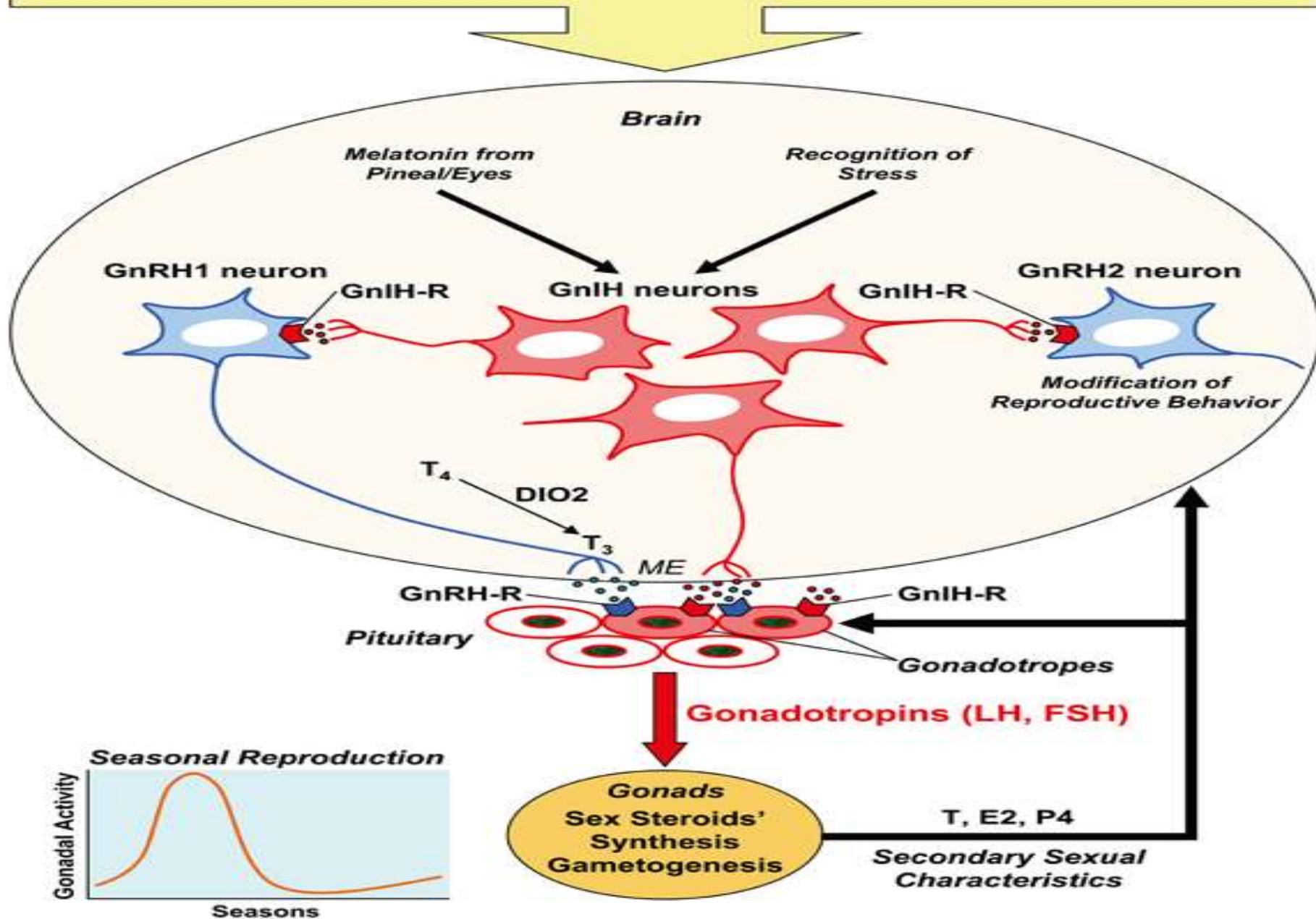


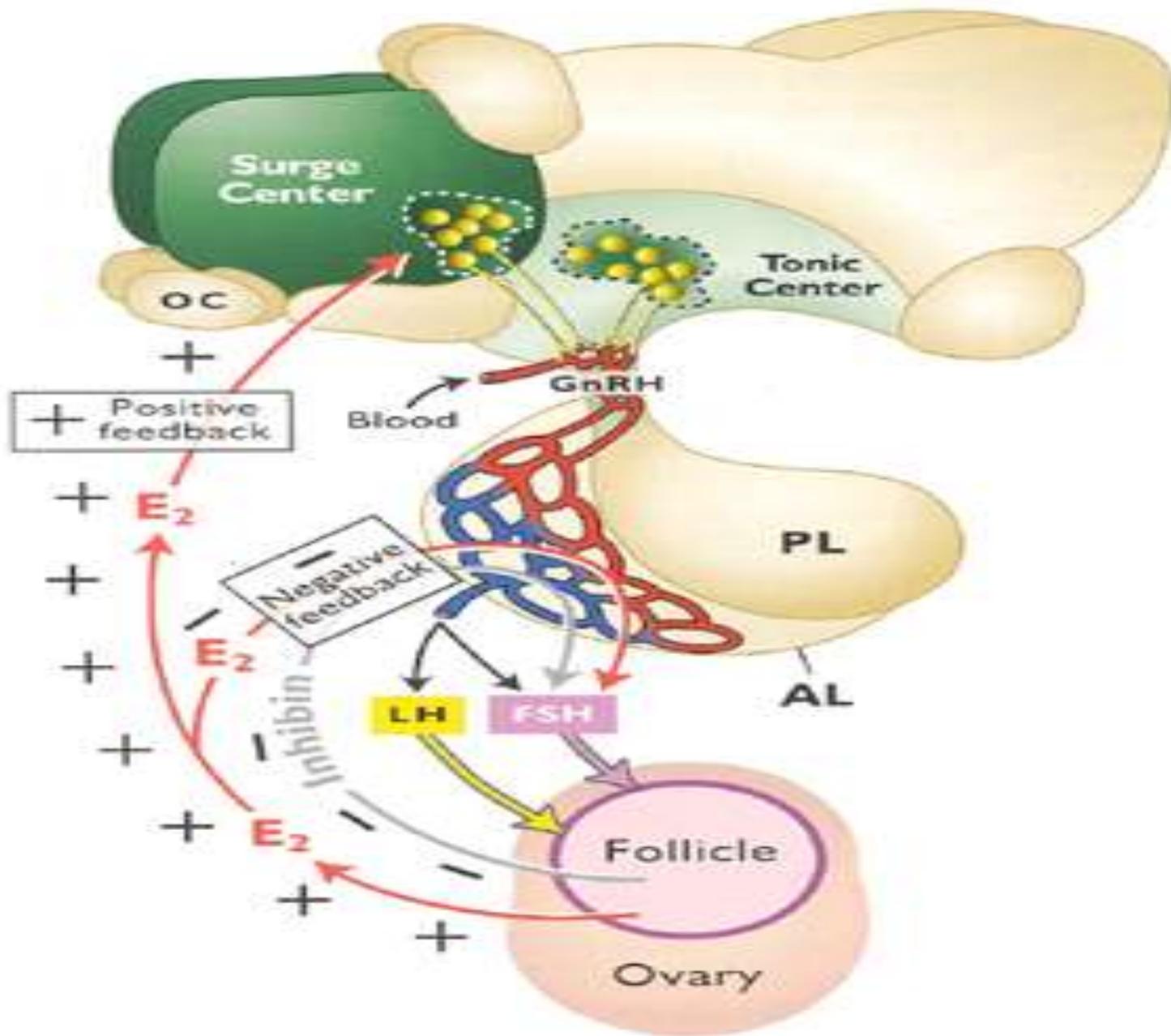
Prof G N Purohit



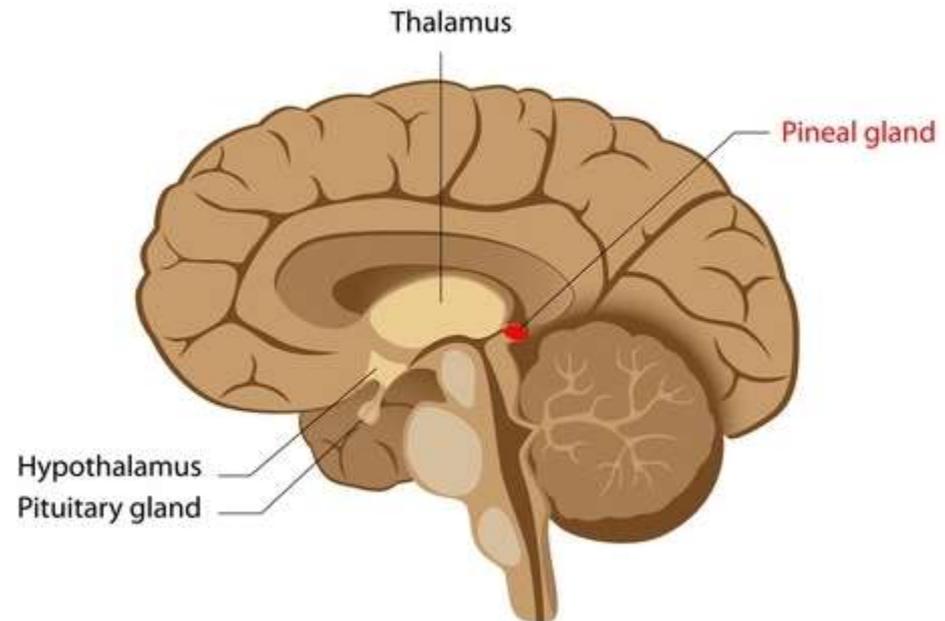
Environmental Signals (Light, Temperature, Water, Food, Predator, etc.)

Social Interactions (Sound, Sight, Contact, etc.)





- **Pineal gland** → **Melatonin**
- **Liver** → **Insulin like growth factors (IGF I & IGF II)**



HORMONES SECRETED BY HYPOTHALAMUS

- ◉ **Gonadotropin releasing hormone
(GnRH)**

Dopamine

**Corticotropic releasing hormone
(CRH)**

Growth hormone- releasing hormone

Oxytocin

Hormones secreted by pituitary gland

- ◉ **Anterior Pituitary**



- ◉ **Follicle stimulating hormone**

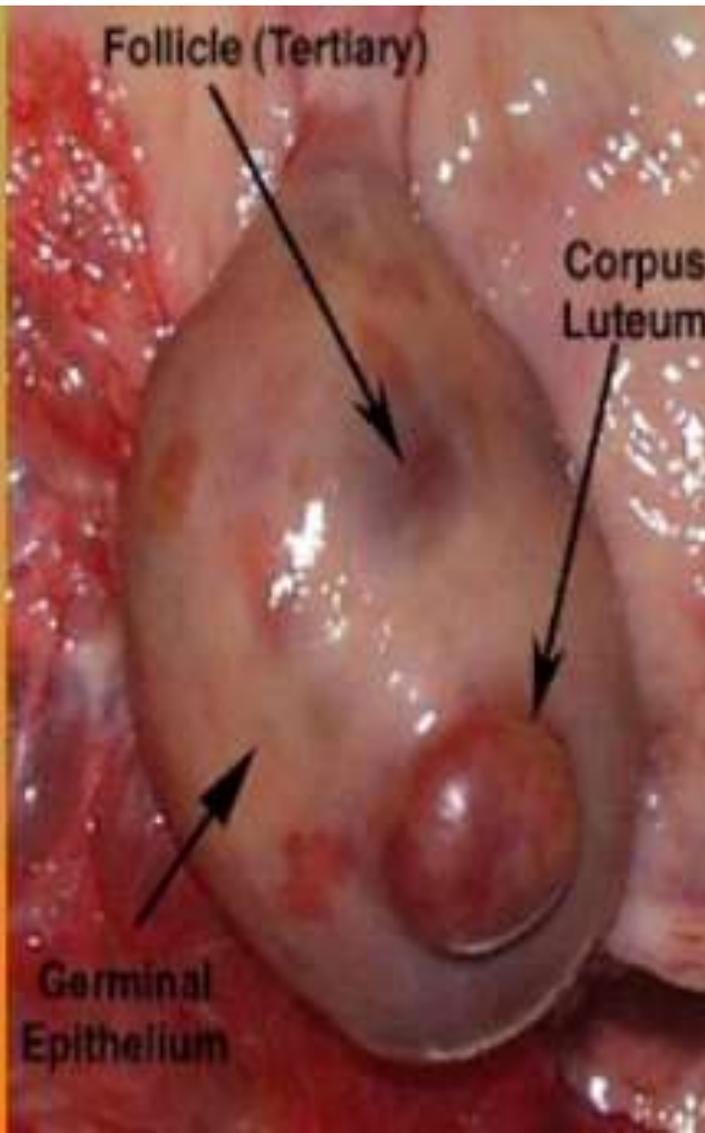
- ◉ **Luteinizing hormone**

- ◉ **Prolactin**

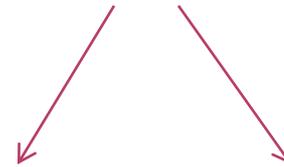
- ◉ **Adrenocorticotrophic hormone**

- ◉ **Posterior pituitary** \longrightarrow **Oxytocin**

HORMONES SECRETED BY OVARY



Graafian Follicle



Estrogen

Inhibin

Corpus Luteum



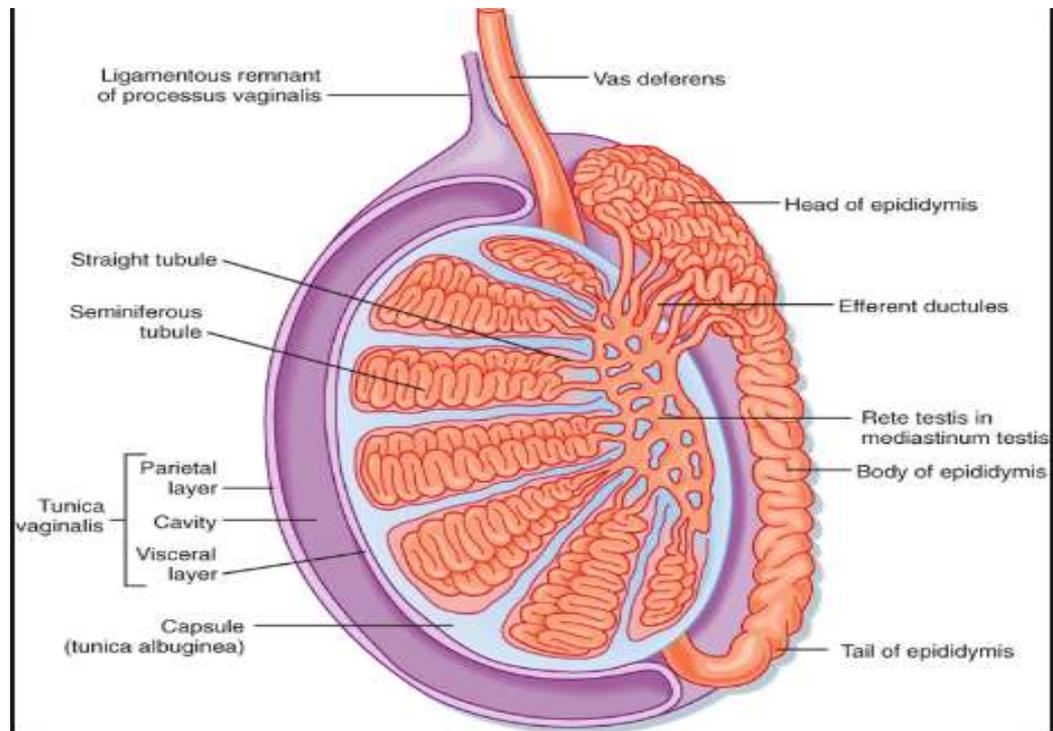
Progesterone

Relaxin

HORMONES SECRETED BY TESTIS

○ **Leydig cells** → **Androgens**

Sertoli cells → **Inhibin**

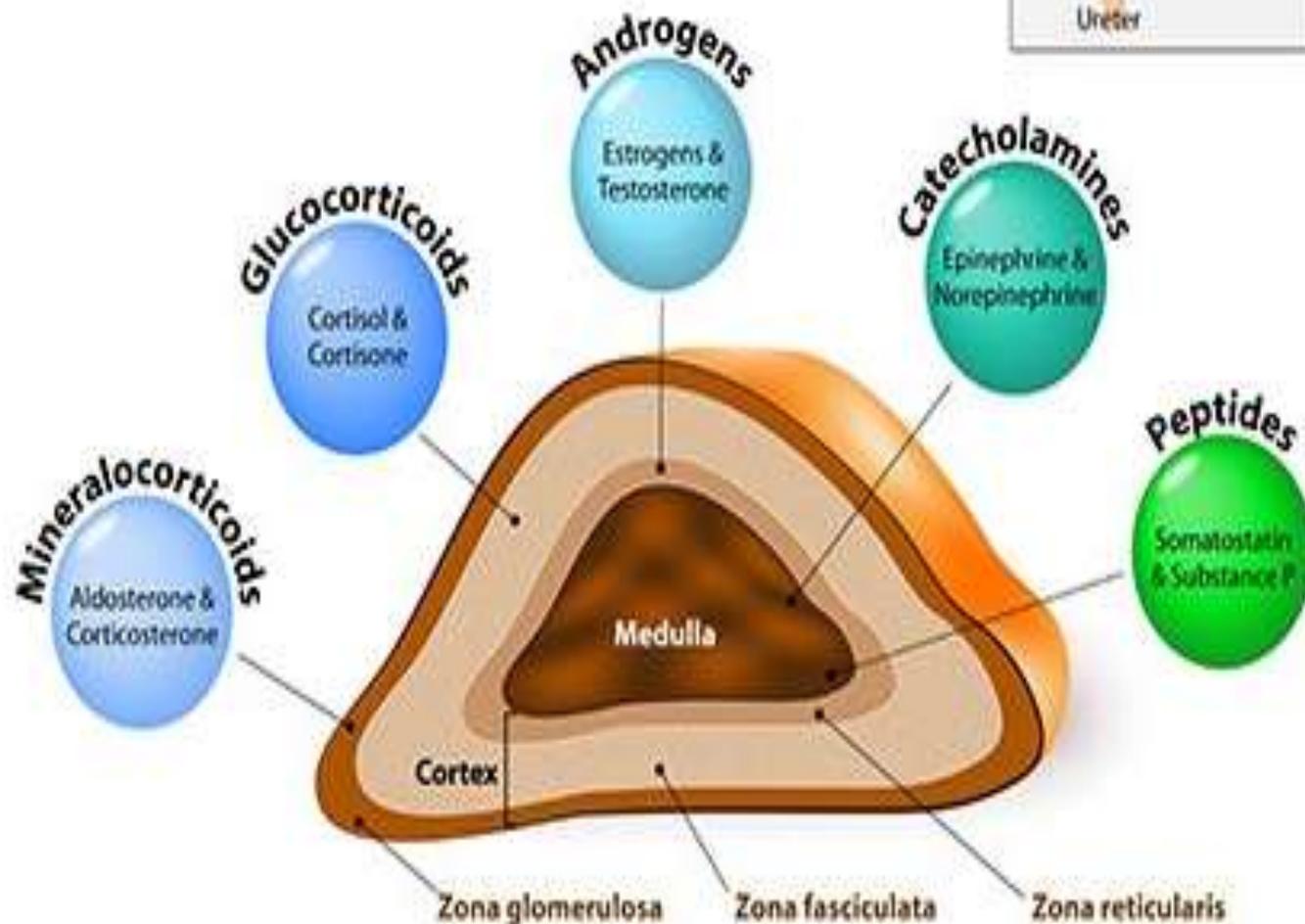
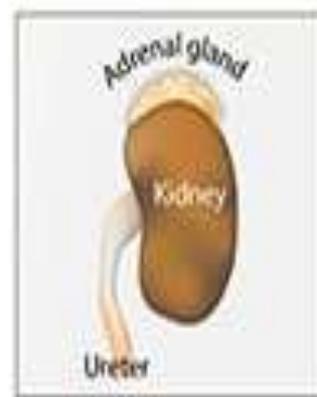


HORMONES SECRETED BY PLACENTA

- ◉ **Human chorionic gonadotropin hCG**
- ◉ **Equine chorionic gonadotropin eCG**
- ◉ **Estrogens/ Progestins**
- ◉ **Relaxin**
- ◉ **Placental Lactogens**

ADRENAL GLAND

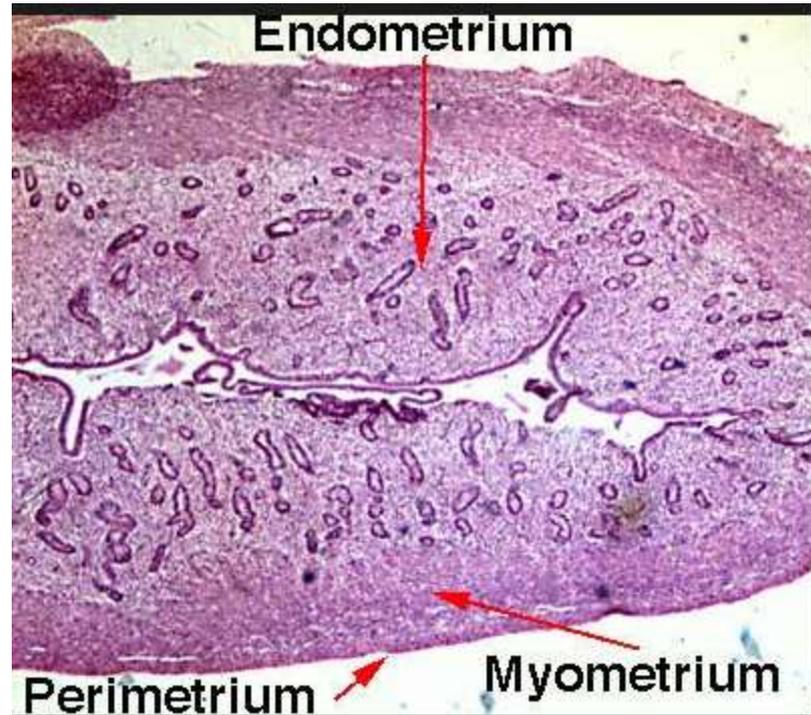
(hormones)



○ **Uterine Endometrium,
Seminal Vesicles,
Graafian Follicles**



**Prostaglandin F₂α
(PGF₂α)**



Histology of Bovine
Uterus

GnRH/FSHRH/LHRH/GONADOLIBERIN/ GONADORELIN

- Identified by Nobel Laureates Roger Guillemin and Andrew V Schally in 1977. GnRH is released from nerve endings at the median eminence of the hypothalamus, where it is stored in secretory granules; it then travels through portal vessels to reach the adenohypophysis where it binds to receptors on gonadotropes in the pars distalis of the hypothalamus
- Neuropeptide ---Arcuate nucleus—Tonic release
---Preoptic area—Surge like release

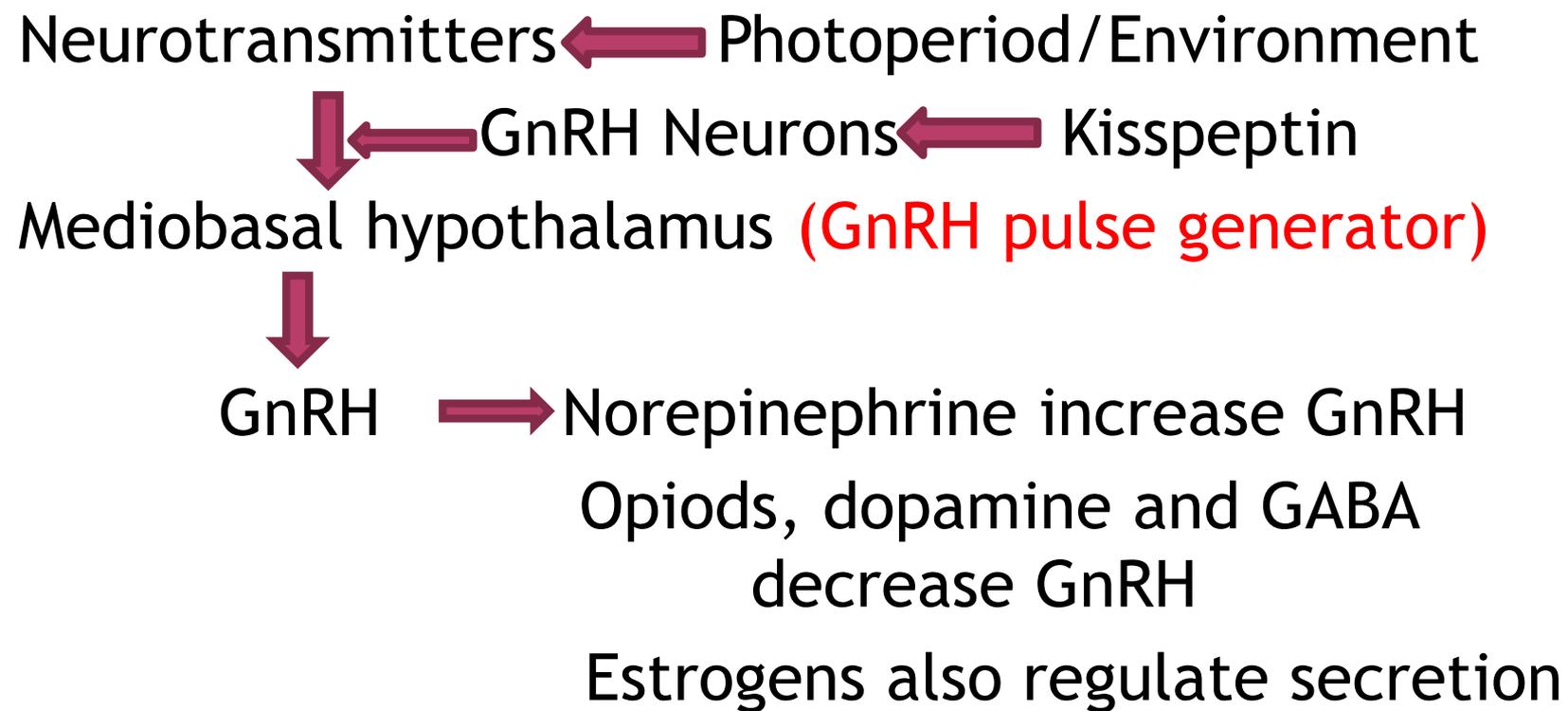
Transported and stored in median eminence and released into hypothalamo-hypophyseal portal system on stimulation

Reaches Anterior pituitary and causes the release of FSH and LH

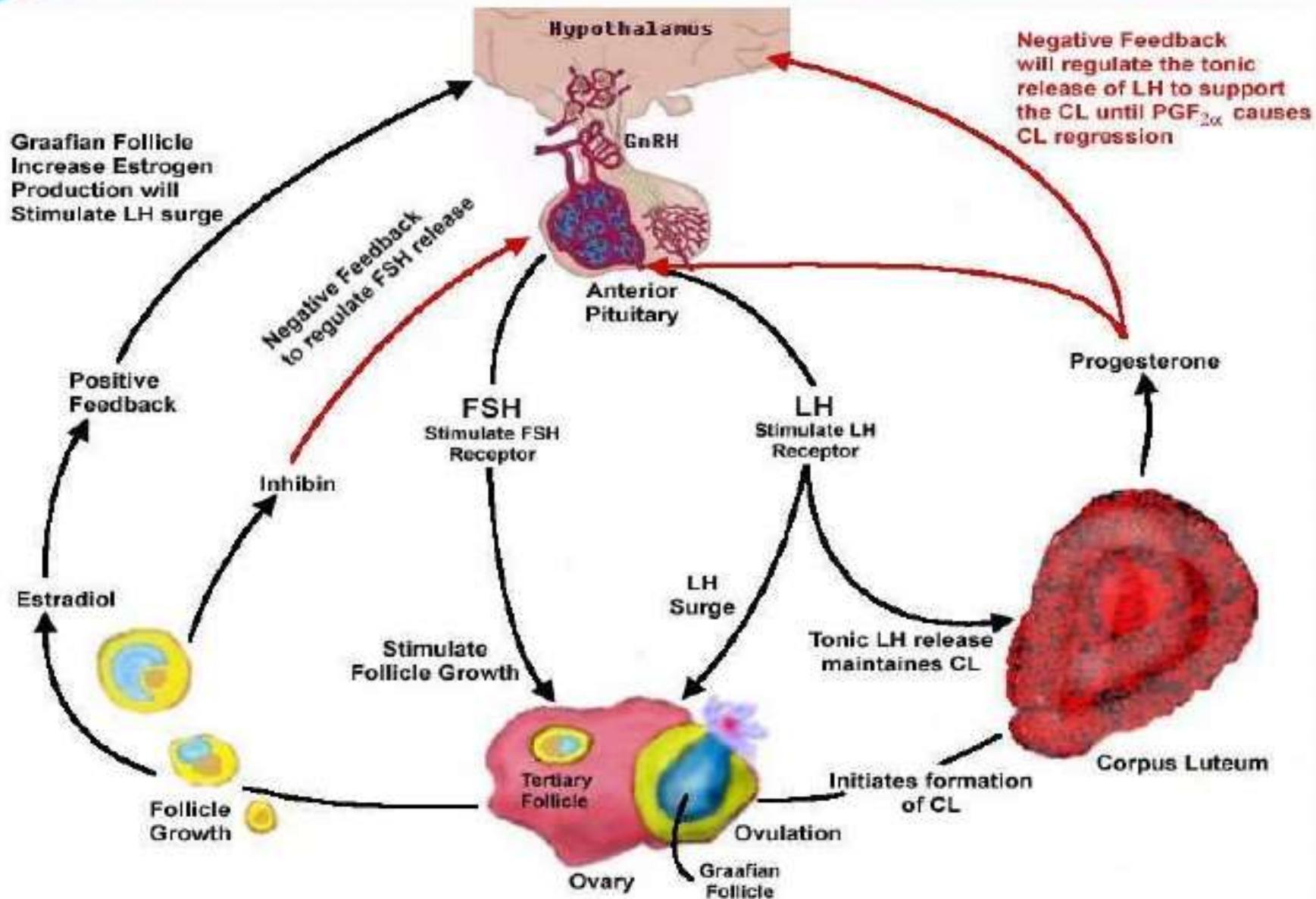
Has a short half life of 2-4 minutes

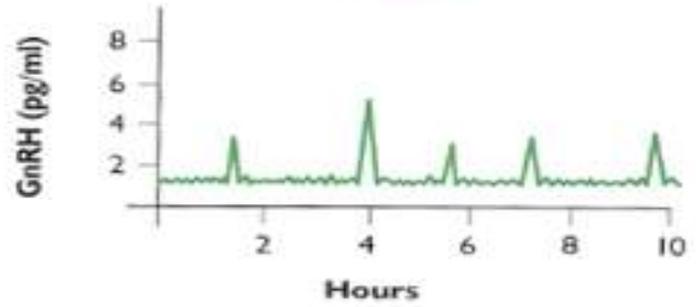
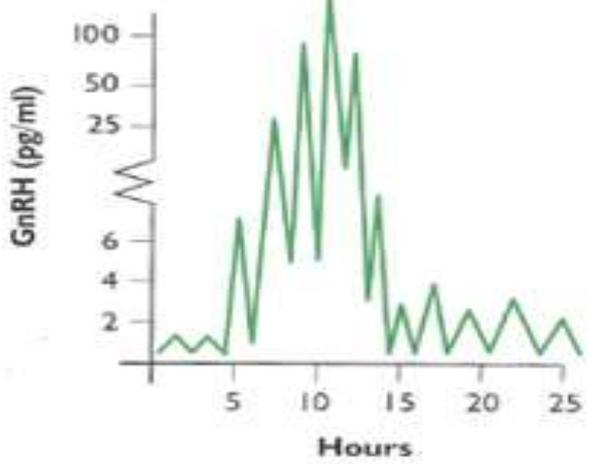
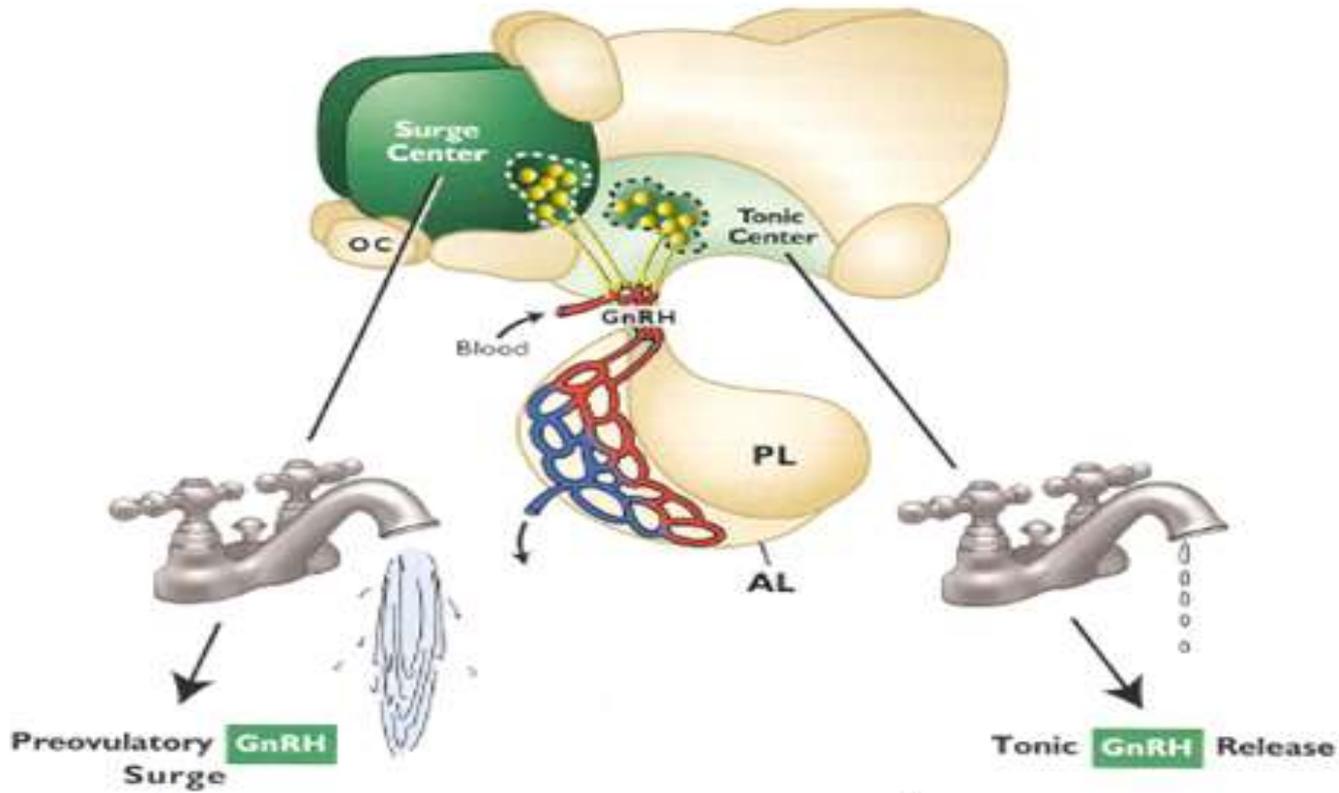
Target tissue is Gonadotroph cells (Anterior pituitary)

GNRH SECRETION



In females-

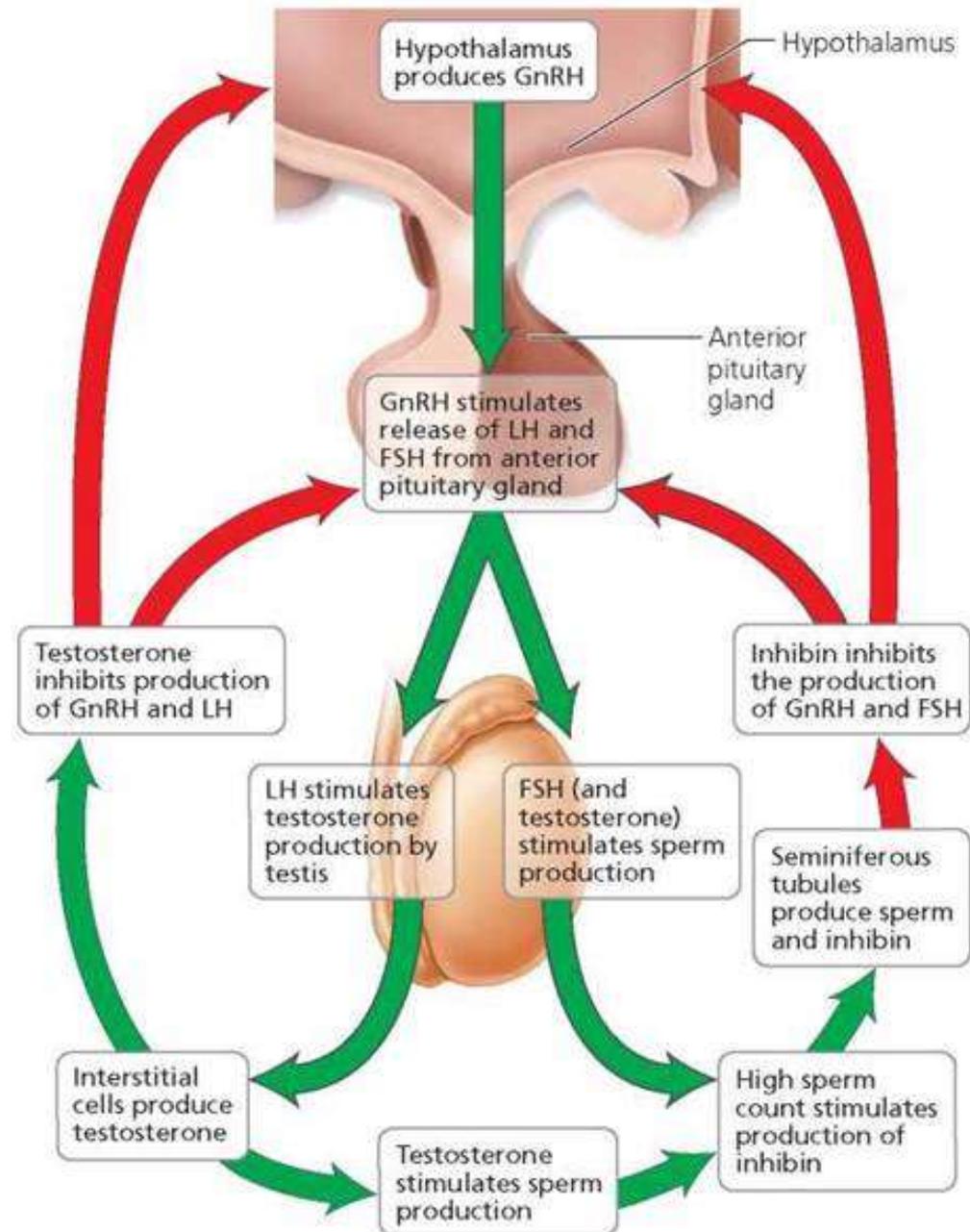




GnRH secretion IN MALES

In males the **surge centre** becomes inactivated during **fetal life**.

In males there are between **4-12 GnRH peaks** per day.



CLINICALLY GNRH ANALOGS AND AGONISTS ARE USED

Analogs/agonists cause an initial stimulation of pituitary gonadotrops that results in secretion of FSH and LH however, on prolonged use they cause a down regulation and inhibition of pituitary-gonadal axis.

Suppression of estrus with prolonged use have rendered them useful for estrus suppression in bitches.

Buserelin most potent analog

Fertirelin

Gonadorelin

Analogs -----Leuprolide and deslorelin

CLINICAL USES

Anestrus

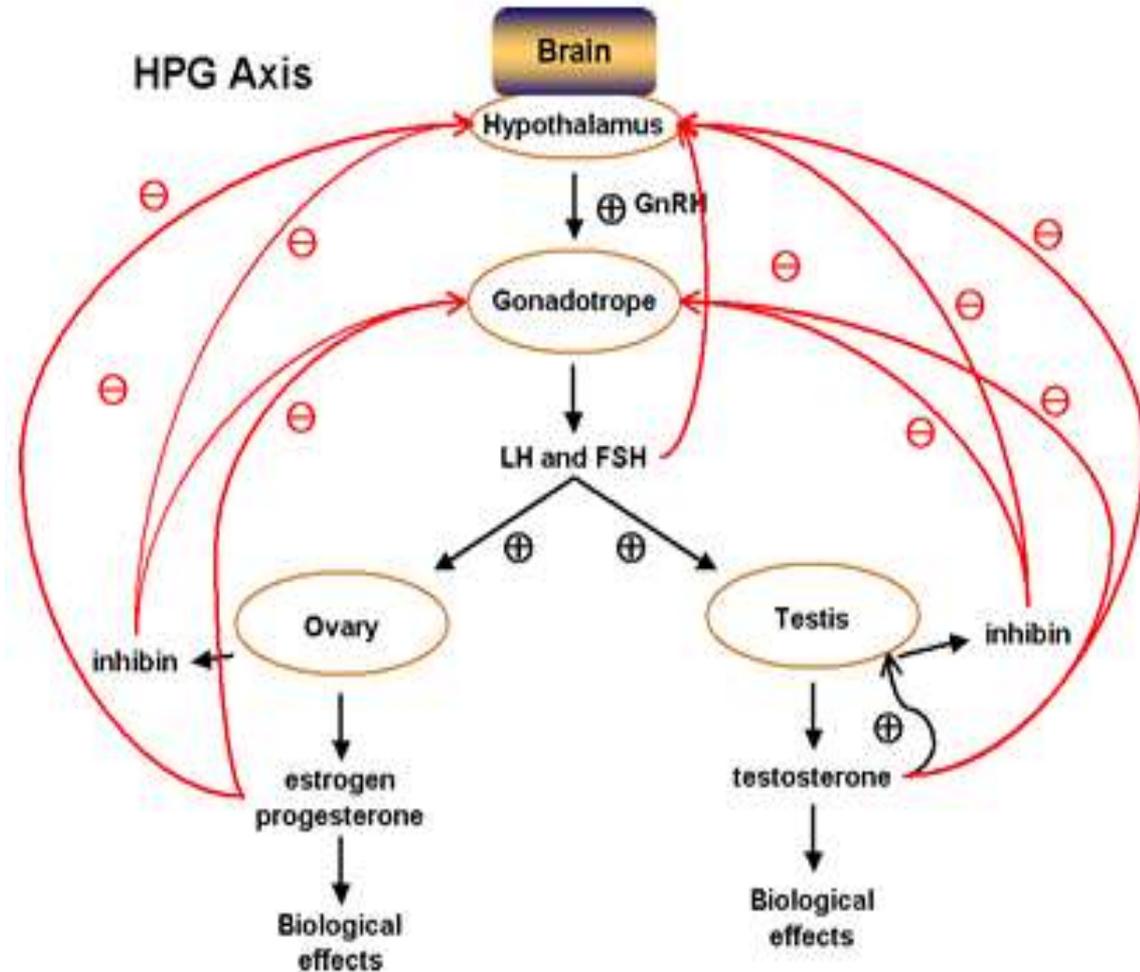
**Ovulation
induction**

Ovarian Cysts

Estrus

Synchronization

**Postpone estrus
in bitches**



COMMERCIALLY AVAILABLE PRODUCTS



(Buserelin acetate)

(Deslorelin)



(Leuprolide)

(Gonadorelin)



GnRH analog	Trade Name	Company	Dose and indications				
			Cattle/ Buffalo	Sheep and Goat	Mares	Bitches	Camels
Buserelin acetate	Receptal Pregulate	MSD Virbac	Anestrus 20 µg IM Ovarian cysts 20-40 µg IM Delayed ovulation 5-10 µg IM	Ovarian cysts 10 µg IM	Ovulation of mature follicle Cystic changes in ovaries 40 µg Anestrus 20 µg twice at 24 h interval		Ovarian cysts 40 µg IM
Fertirelin	Conceral	Takeda Chemicals Japan	50-200 µg IM				
Gonadorelin	Factrel 50 µg/mL Fertagyl Cystorelin	Zoetis MSD Forte Dodge	100 µg IM estrus synchronization and ovarian cysts				
Deslorelin	Sucromate Ovuplant Suprelorin	Thorn Zoetis Virbac	1.5 mg 2.1 mg 4.7 mg 9.4 mg		Ovulation induction 1.5 mg 48 h before planned ovulation when the follicle is 30-40mm	Prevention of breeding, estrus induction in females and chemical sterilization of male dogs	
Leuprolide	Lupride Lupron Depot	Sun Pharma India Abbvie Endocrine Inc	3.75 mg			0.10 mg/Kg SC once for estrus induction	

GnRH ANTAGONISTS

(under development)

Use

Pregnancy termination
Estrus suppression in Pets

- DETIRELIX
- CETRORELIX
- GANORELIX
- AZALINE
- ACYLINE

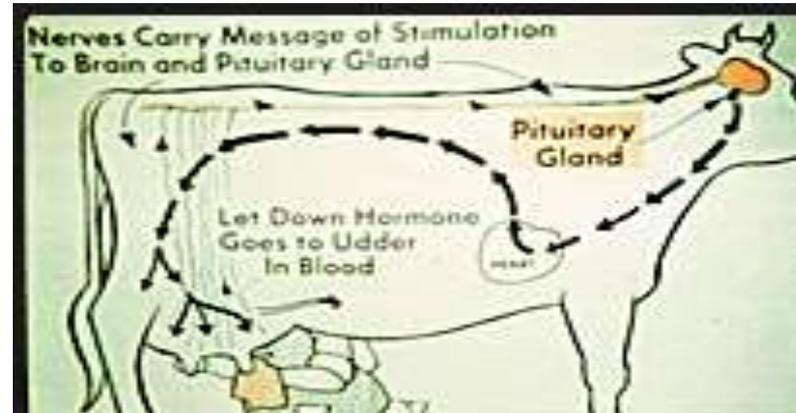


OXYTOCIN

- ◉ **Octapeptide (neuropeptide)**
- ◉ **Synthesized by neurons of supraoptic nucleus (small amount by CL)**
- ◉ **Acts only on a uterus pre-sensitized with estrogen**
- ◉ **Transported axonally to storage sites in posterior pituitary**
- ◉ It upregulates the activity of smooth muscle cells in the uterus and the smooth muscles surrounding the alveoli ducts of the mammary glands.

FUNCTIONS OF OXYTOCIN

- **Milk let down**



- **Transport of both sperms & oocytes in the tubular genitalia**



- **At parturition causes myometrial contractions**

- **Luteal regression in cow & ewe**

- ◉ **Induction of foaling in mare after 340 days of gestation**



Foaling in mare

- ◉ **Treatment of uterine inertia in bitches**
- ◉ **For uterine involution**
- ◉ **Expulsion of a retained placenta (ROP) in mare and bitch**

(ROP in Mare)



COMMERCIALLY AVAILABLE PREPARATIONS

◉ Suggested doses of oxytocin in Obstetrics cases (I/M)

Cattle & Mare	60 - 100 IU
Sow, ewe & doe	30 - 50 IU
Bitches	10 - 20 IU



5 IU / ml oxytocin

PROLACTIN (LACTOTROPHIC HORMONE LTH)

- ◉ **Secreted by lactotrops or mammatrops cells of anterior pituitary gland**
- ◉ **Lactotrophic hormone Suckling is a potent stimulus for prolactin secretion**
- ◉ **Luteotropic in rodents & bitch**
- ◉ **Maternal behavior**
- ◉ **Prolactin inhibitory hormone Dopamine**

Half life 20 minutes

CLINICAL USES

- ◉ **Prolactin suppress LH surge & ovulation thus antiprolactins can presumably stimulate LH and ovulation**
- ◉ **Antiprolactins (dopamine agonists)**
(Bromocryptine, cabergoline, metergoline)
Timely ovulation in cows, in bitches for estrus induction, pregnancy termination, pseudopregnancy.
Bromocryptine 30-100 µg/Kg for 6-10 days
Cabergoline 5 µg/kg for 5-7 days
- Domperidone (dopamine antagonist) & sulpiride for estrus & ovulation induction in mares (1 mg/kg) and probably for increase in milk production in cows (metoclopramide and domperidone)**

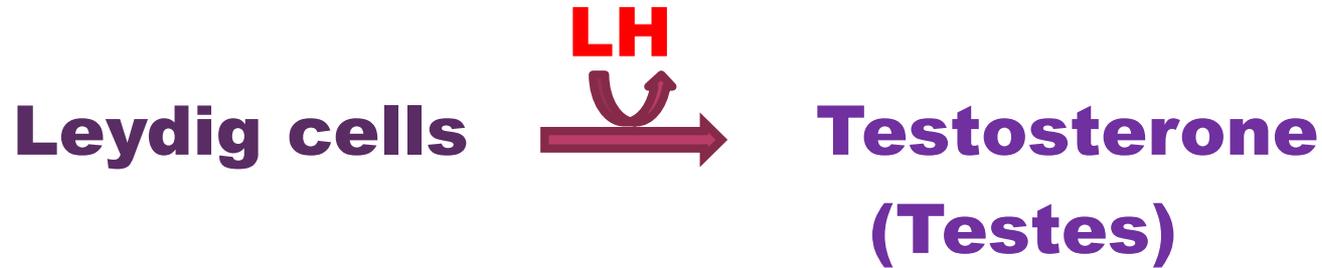
GLYCOPROTEIN HORMONES

- ◉ **Follicle stimulating hormone (FSH)**
- ◉ **Luteinizing hormone (LH)**
- ◉ **Human chorionic gonadotropin (hCG)**
- ◉ **Equine chorionic gonadotropin (eCG)**
- ◉ **Thyroid stimulating hormone (TSH)**
- ◉ **Inhibin and Activins**

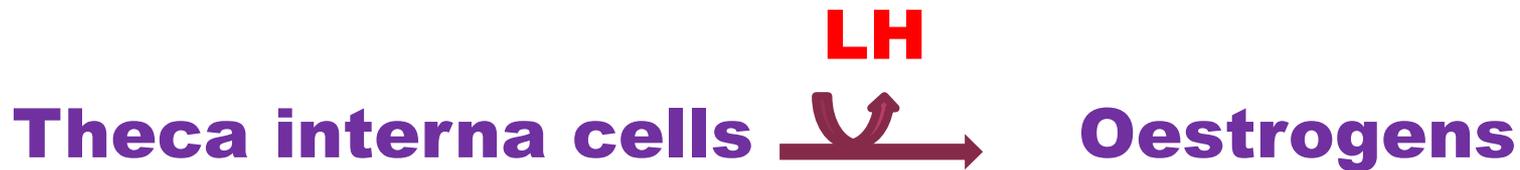
LUTEINIZING HORMONE (LH)

- ◉ **Also known as Lutropin or Interstitial Cell Stimulating Hormone in males**
- ◉ **Produced by basophilic gonadotroph cells of anterior pituitary gland**
- ◉ **LH surge around 6 h in cattle**
- ◉ **Heterodimeric glycoprotein**
- ◉ **Half life – 20 minutes**

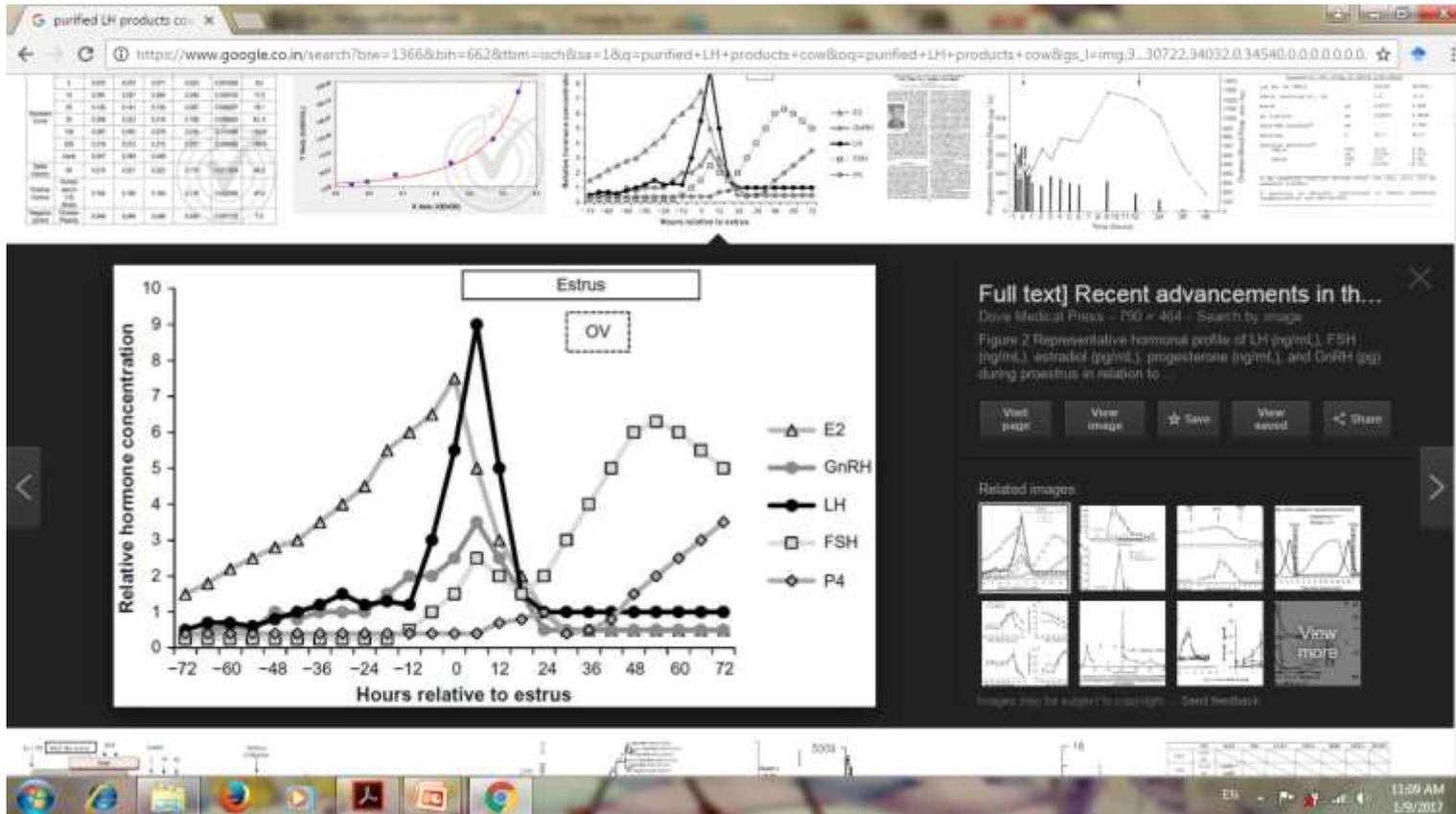
○ **In males**



In females



PREOVULATORY LH SURGE → OVULATION



CLINICAL USES

- ⦿ **Delayed Ovulation**
- ⦿ **Planned Ovulations**
- ⦿ **Ovarian Cysts**
- ⦿ **Corpus Luteum development**

FOLLICLE STIMULATING HORMONE (FSH)

○ Produced via gonadotroph cells (Ant. pituitary)

Target tissues

Sertoli cells (Testes)

Granulosa cells (ovary)

Inhibin,

Androgen binding protein

Estradiol synthesis & follicular development

Half life 3 – 4 hours

CLINICAL USES

- **Multiple ovulations in embryo transfer**
- **Anestrus**
- **Out of season breeding**
- **Estrus synchronization especially during non breeding season**



EQUINE CHORIONIC GONADOTROPIN

- ◉ **Secreted by fetal trophoblastic cells of endometrial cups of equines between day 35 and 150 of pregnancy**

Immunoprotection of fetus

Formation of accessory corpus luteum

FSH & eCG share a common receptor

CLINICAL USES

- ◉ **Anestrus**
- ◉ **Superovulation**
- ◉ **Out of season breeding**

COMMERCIALLY AVAILABLE PREPARATIONS



HUMAN CHORIONIC GONADOTROPIN

**Produced by syncytial trophoblast cells
of human placenta**

**LH like activity with little or no FSH
like effects**

Half life 24 hours

CLINICAL USES

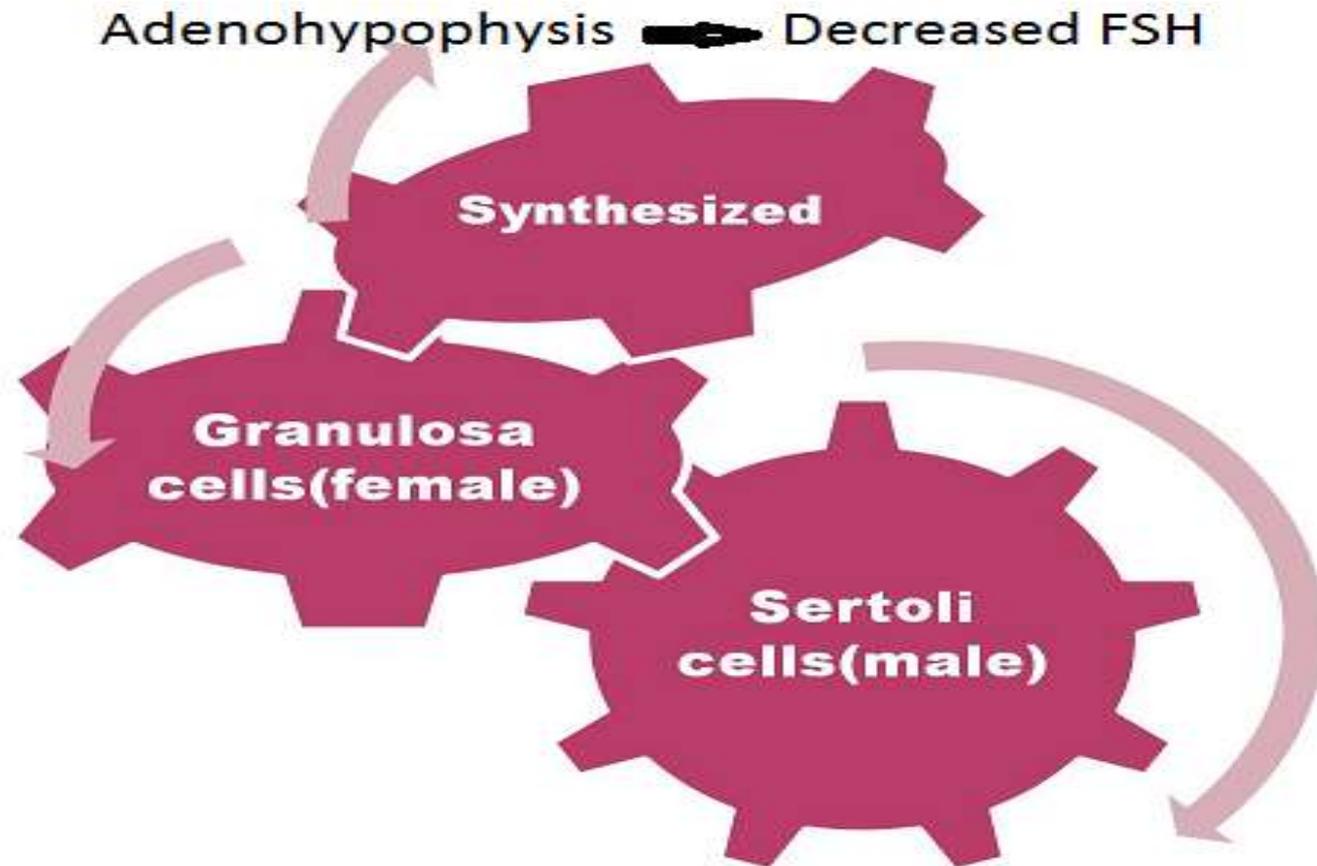
- ◉ **Induction of ovulation**
- ◉ **Treatment of ovarian cysts**
- ◉ **Delayed ovulation**

COMMERCIALLY AVAILABLE PREPARATIONS



hCG	Name	Company	Pack	Use, mode of administration and dose				
				Cows/buffalo	Mares	Sheep and goat	Sow	Bitches
	Chorulon	MSD	1500IU	Ovarian cysts 3000-5000 IU IM or IV Delayed ovulation/ Anovulation 1500-3000 IU	Inducing ovulation 2000-2500 IU when the follicle is above 35 mm	250-500 IU for ovulation induction	Inducing ovulation 500-1000 IU IM	500 IU for inducing ovulation in estrus induced by eCG (250 IU IM for 9 days)
eCG + hCG	PG 600	Merck	400 IU eCG + 200 IU hCG	-	-	-	Estrus induction	-
eCG								
	Folligon	MSD	1000IU	Anestrus/Out of the season breeding 800-1000 IU IM or SC Superovulation 2000-3000 IU	-do not respond	Out of season breeding 100-500 IU IM after progesterone	Estrus induction 1000-1500 IU 5-7 days after weaning	Inducing estrus 250 IU IM daily for 10 days

INHIBIN (PROTEIN COMPLEX)



Inhibin **×** **FSH**

GnRH **↓** **Inhibin**

Insulin like growth factor I **↑** **Inhibin**

ACTIVIN

- **Produced within granulosa cells in females & sertoli cells in males**

- **Stimulates**



FSH synthesis

Cell proliferation

Cell differentiation

Apoptosis

Homeostasis

Keratinocytes

FSH induced aromatization

STEROID HORMONES

- ◉ **Progestagens**

- ◉ **Androgens**

- ◉ **Estrogens**

- ◉ **Corticosteroids**

PROPERTIES

- **Lipophilic compounds**
- **Primary steroid producing tissues**
Testes, ovaries, adrenals, placenta
fetal gonads

Steroids bound to large carrier proteins

Albumin

Globulin

- ★ **Classical steroid sex hormones**
Oestradiol – 17 β , testosterone,
progesterone

Estrogen



- ◉ **Estrogen is primary female sex hormone**
- ◉ **Development of female reproductive system & secondary sex characteristics**
- ◉ **Natural estrogens: 17 β estradiol, estrone, estriol, conjugated equine estrogens: equilin, equilenin, estrone sulphate**
- ◉ **Synthetic estrogens:**
Estradiol valerate, estradiol cypionate, estradiol acetate, estradiol benzoate, ethinyl estradiol, Di ethyl stilbesterol
Phytoestrogens & mycoestrogens

ROLE OF ESTROGENS

- ◉ **Anabolic**
- ◉ **Mammary development**
- ◉ **Skin growth**
- ◉ **Follicular growth**
- ◉ **Estrus expression**
- ◉ **Receptivity to male**
- ◉ **Luteolytic in ruminants**
- ◉ **Luteotropic in sow & mare**
- ◉ **At parturition contraction of uterus**

CLINICAL USES NOT WIDELY USED DUE TO RESIDUES

- ◉ **Anestrus**
- ◉ **Fetal mummification**
- ◉ **Fetal maceration**
- ◉ **Pyometra**
- ◉ **Metritis**
- ◉ **Estrus synchronozation**
- ◉ **In bitches**
 - misalliance, estrus suppression, spayed bitches**



Side effects

COMMERCIALLY AVAILABLE ESTROGENS



ANTIESTROGENS

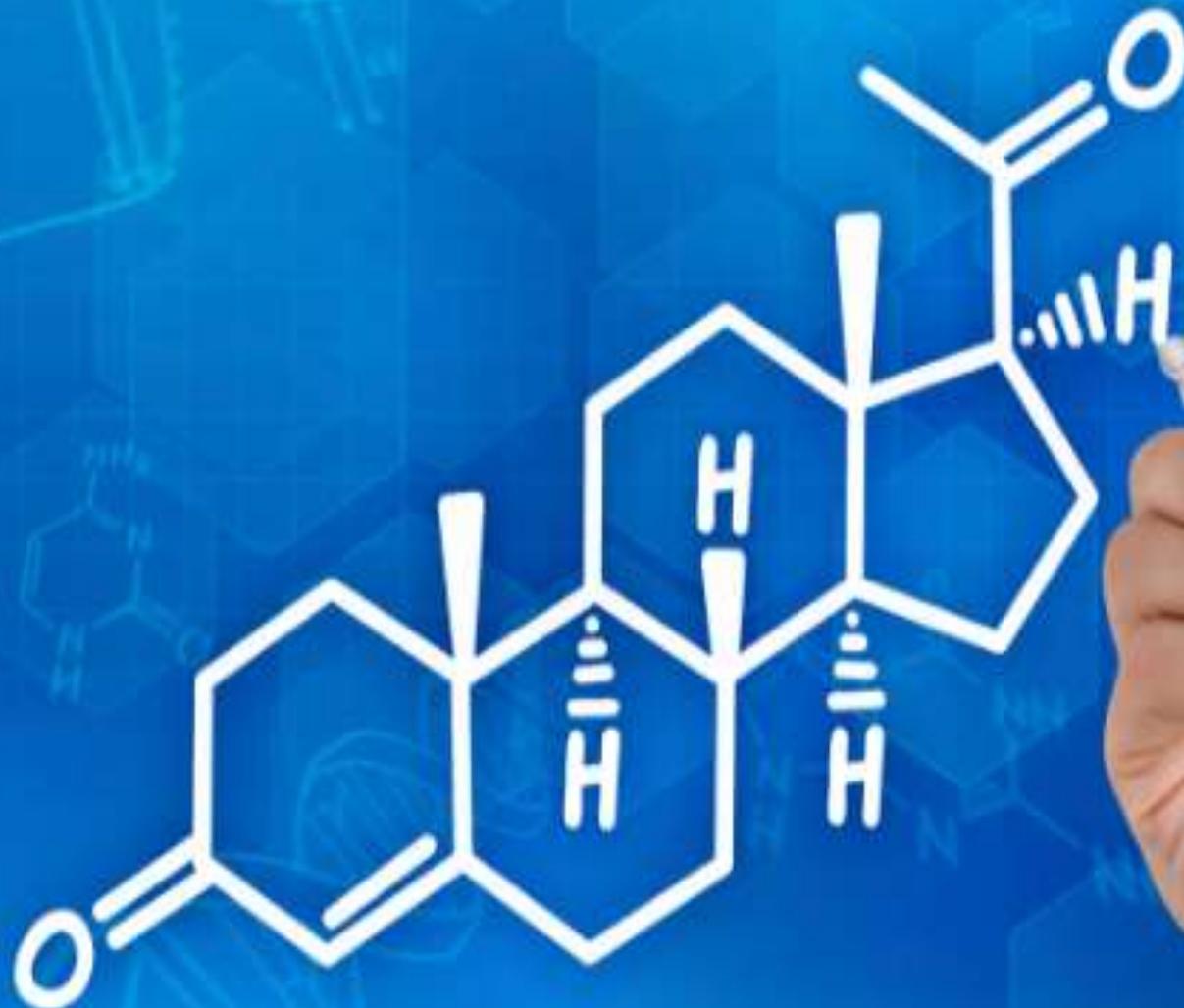


- **Tamoxifen**



- **Clomiphene
citrate 300 mg**

PROGESTERONE



◉ **Synthesized by**

corpus luteum, feto-placental unit, adrenal cortex. Secretion is controlled by LH, PG, prolactin and many other intermediaries

Role

Ovulation, implantation, pregnancy maintenance, lactation, initiation of follicular growth waves, development of dominant follicle.

Half life 22-36 min in cow

CL dependent species cow, doe, bitch, sow, buffalo, camel

CL independent species mare, ewe

PROGESTERONE AGONISTS

- ◉ **Medroxyprogesterone acetate (MPA)**
- ◉ **Megestrol acetate**
- ◉ **Melengestrol acetate MGA**
- ◉ **Proligestone**
- ◉ **Flurogestone acetate FGA**
- ◉ **Norgestomet**
- ◉ **Progesterone vaginal implants**
- ◉ **Altrenogest (Nor-testosterone derivative with progesterone like activity)**
- ◉ **Hydroxyprogesterone caproate**

CLINICAL USES

CLINICAL USE OF PROGESTOGENS

LIES IN THE ABILITY OF THE STEROID TO BLOCK ESTRUS AND OVULATION AND PROMOTE NEW FOLLICLE GROWTH ON LONG TERM USE. REDUCING UTERINE CONTRACTIONS IS ANOTHER FUNCTION OF PROGESTINS HELPFUL IN PREGNANCY MAINTENANCE.

- ◉ **Estrus suppression**
- ◉ **Estrus synchronization**
- ◉ **Pregnancy maintenance**
- ◉ **Induction of new follicular wave**
- ◉ **Anestrus**
- ◉ **Ovarian cysts**
- ◉ **Luteal insufficiency**
- ◉ **Vaginal prolapse**
- ◉ **Prevention of abortion**

MEDROXYPROGESTERONE ACETATE (MPA)

- ◉ Estrus suppression in the dog at the dose rate of 2 mg/kg every 3-4 months
- ◉ MPA(60 mg impregnated vaginal sponges) has been used for estrus synchronization in goats and sheep.
- ◉ Similarly it has been used (300 mg intravaginal sponge) in cows for estrus synchronization.

Megestrol acetate

Oral progestin for estrus suppression in dogs (0.5-2.0 mg/kg /day for 8 days)

Estrus synchronization (40-50mg/day for 14-20 days) in beef cows

Proligestone

- ◉ estrus suppression in the bitch by IM administration (50mg/kg SC every 3 weeks)

Flurogestone acetate

- ◉ intravaginal sponge preparation (containing 20 mg FGA) to synchronize estrus in sheep and goats.

Norgestomet (Synchromate-B)

ear implant for estrus synchronization in cattle

Progesterone vaginal implants

CIDR/PRID for estrus synchronization in cattle

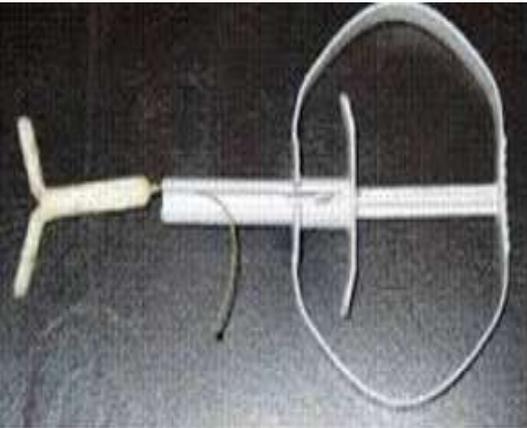
Altrenogest (allyl trenbolone) Regumate

Estrus control in mares (0.044mg/Kg) and pigs (15mg/day) for 7-10 days administered orally.

Hydroxyprogesterone caproate

Depot injection

COMMERCIALLY AVAILABLE P4 AGONISTS



CIDR with applicator

PRID



신크로메이트 (Synchronate) - 신한...

www.distrib.com - 1182 x 1172 - Search by image

Synchronate)

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Subject to copyright - Send feedback

Manual Manipulation

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ANTIPROGESTINS

- **Mifepristone**

- Pregnancy termination in the bitch 2.5 mg/kg BD for 4.5 days beginning at Day 32 of pregnancy

Aglepristone

The twice daily SC administration of 10mg/kg

Onapristone

Hormone

ANDROGENS

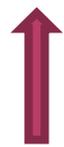
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ROLE OF ANDROGENS (ANDROS MEANING MASCULINE)

Anabolic

**Growth of muscle mass
& territorial marking**



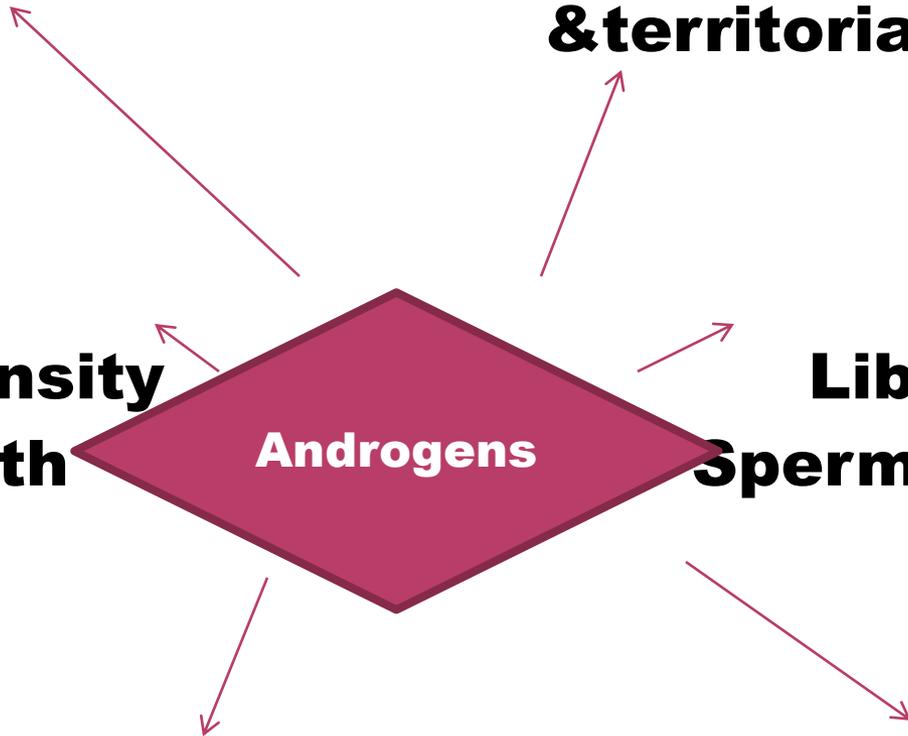
**Bone density
& Strength**

Androgens

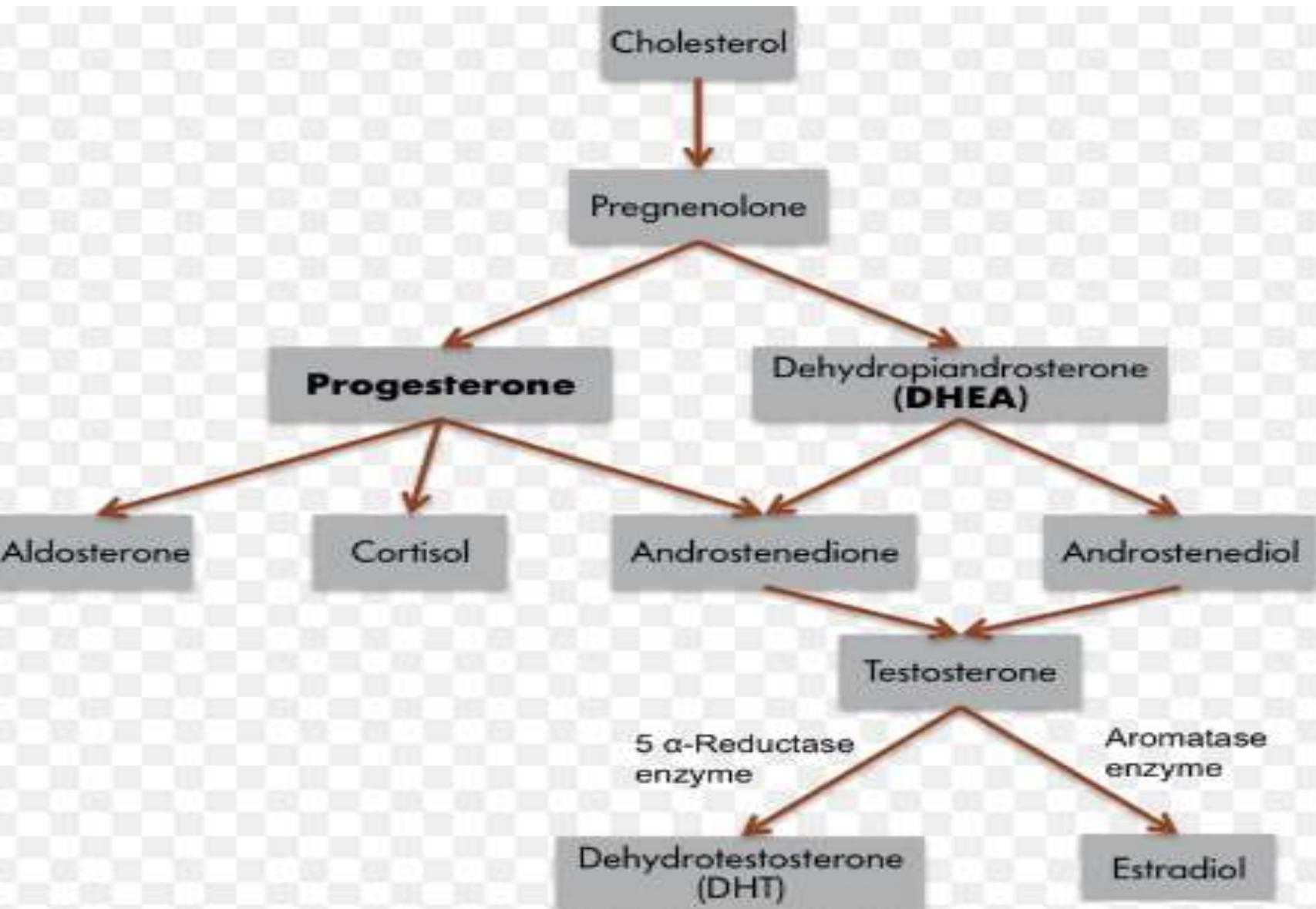
**Libido &
Spermatogenesis**

**Secondary Sex Characteristics
& deepening of voice**

**Growth
of hump**

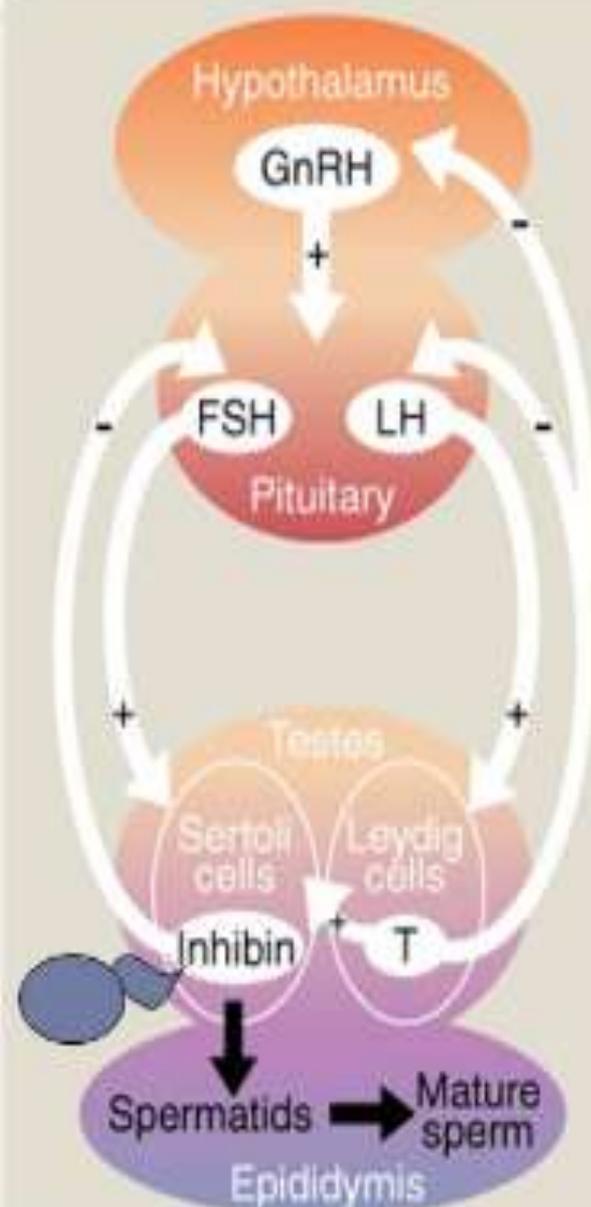


SYNTHESIS OF ANDROGEN



Male Hormone Loop

- ▶ Brain releases GnRH, which tells pituitary to release FSH, LH
- ▶ LH tells Leydig cells to release testosterone, which stimulates production of sperm.
 - *note negative feedback!*
- ▶ Testosterone also slows the release of LH (as does Inhibin for FSH)



ANDROGEN DERIVATIVES

- ◉ **Testosterone**
- ◉ **Hydroxytestosterone**
- ◉ **Testosterone propionate**
- ◉ **Dihydrotestosterone**
- ◉ **Trenbolone acetate**
- ◉ **Nandrolone (potent anabolic)**
- ◉ **Methyltestosterone**
- ◉ **Mibolerone (estrus suppression in the bitch 30-60 Ug daily orally)**
- ◉ **Norgestrel**

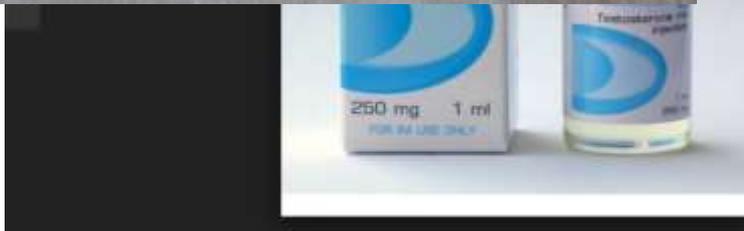
CLINICAL USES

- ◉ **Growth promoters**
- ◉ **Estrus suppression**
- ◉ **Cryptorchid bulls**
- ◉ **Delayed puberty in bulls**
- ◉ **Androgenized cows as teaser**



Side effects

COMMERCIALLY AVAILABLE PREPARATIONS



ANTIANDROGENS

Lower
production of
androgens

**Leuprolide, abarelix,
goserelin, triptorelin**

Receptor
blocker

**Flutamide, finasteride,
cyproterone acetate**

Others

**Ketoconazole
,Spironolactone,
medroxyprogesterone acetate**

**Benign prostatic hyperplasia –
finasteride 0.1-0.5 mg/kg for dogs**

FATTY ACID DERIVATIVES

Prostaglandin (PGF₂α)

- **Found in almost every tissue**
- **Has 20 carbon atoms & 5 carbon ring**
- **Produced within uterine endometrium & vesicular gland**
- **Precursor is arachidonic acid**
- **Target tissue in females**
corpus luteum, uterine myometrium, ovulatory follicles
- **Prostaglandin (PG) has 2 derivatives**
Prostacyclines & thromboxanes

○ **Natural PG analogs**

Dinoprost, tiaprost, carboprost

Synthetic PG analogs

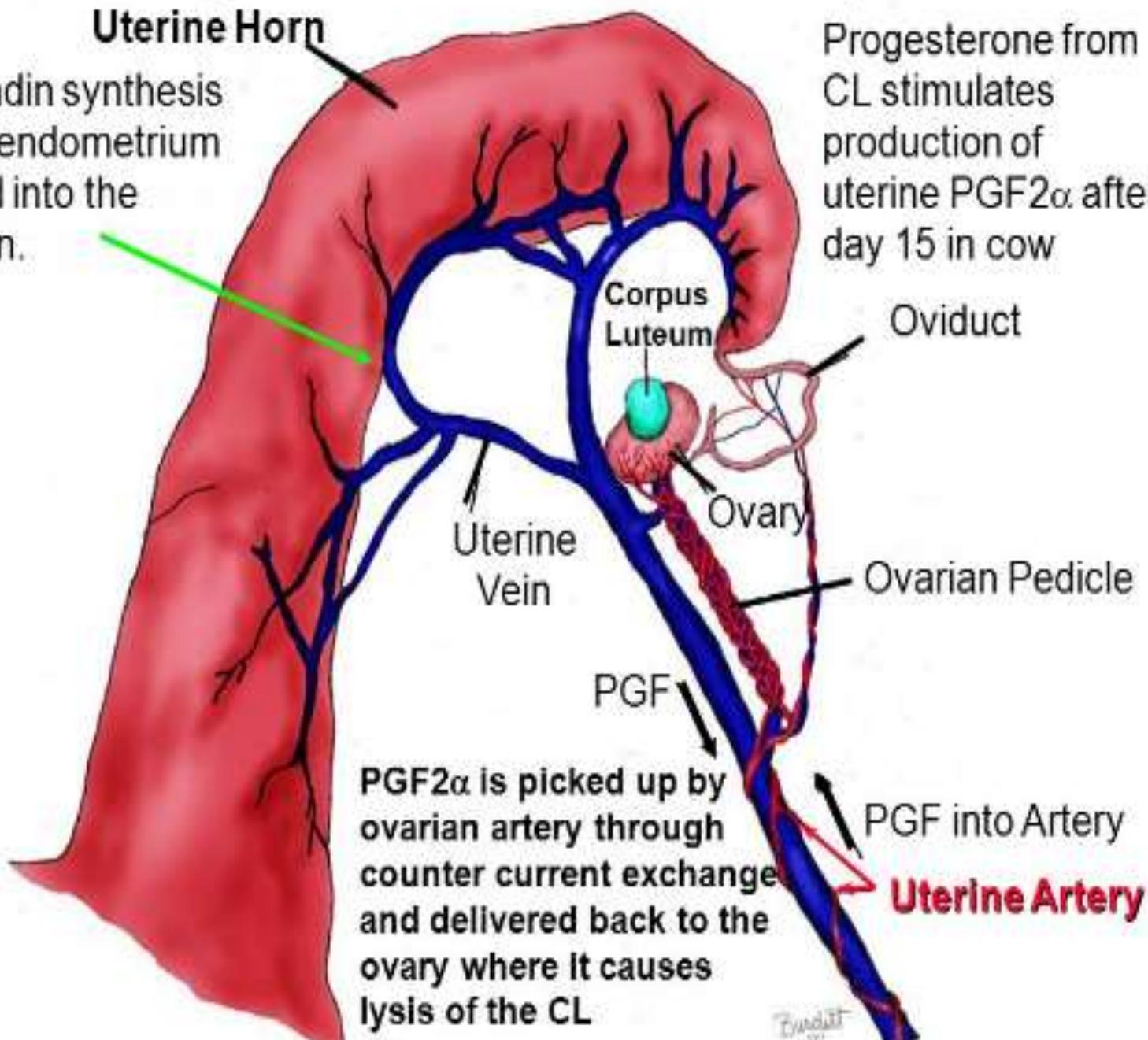
**Cloprostenol, fluprostenol,
prostaglandin, fenprostalene**

Prostaglandin F_{2α} Control of Luteolysis

Uterine Horn

Prostaglandin synthesis by uterine endometrium is released into the uterine vein.

Progesterone from CL stimulates production of uterine PGF_{2α} after day 15 in cow



Oviduct

Corpus Luteum

Ovary

Uterine Vein

Ovarian Pedicle

PGF

PGF_{2α} is picked up by ovarian artery through counter current exchange and delivered back to the ovary where it causes lysis of the CL

PGF into Artery

Uterine Artery

credit

CLINICAL USES

- ◉ **Metritis**
- ◉ **Pyometra**
- ◉ **Mucometra**
- ◉ **Endometritis**
- ◉ **Retention of placenta**
- ◉ **Fetal mummification**
- ◉ **Fetal maceration**
- ◉ **Hydrometra**
- ◉ **Estrus induction**
- ◉ **Estrus synchronization**
- ◉ **Induction of parturition**
- ◉ **Vetromedical termination of pregnancy**

COMMERCIALLY AVAILABLE PG



Carboprost Tromethamine Injection IP **Prostodin[®] 250 mcg**

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PLACENTAL LACTOGEN

- ◉ **Polypeptide placental hormone**
- ◉ **Also called as chorionic somatotropin**
- ◉ **Similar to growth hormone**
- ◉ **Stimulate the growth of alveoli during pregnancy (mammotropic)**
- ◉ **Luteotropic**

RELAXIN

- **Produced by: corpus luteum, placenta, ovaries throughout pregnancy**
- **Target organs: cervix, vagina, pubic symphysis and related structures**
- **Used for pregnancy diagnosis in bitch & cat**

- ◉ The above lectures are also explained in video lectures at my YouTube Channel Govind Narayan Purohit
- ◉ Kindly share the videos and subscribe to my channel if you like them
- ◉ Thanks