

## Reproductive hormones

Hormones may be classified according to either their biochemical structure or mode of action . The biochemical structure of hormones includes glycoproteins , polypeptides , steroids , fatty acids , and amines .

### Structure of reproductive Hormones

According to their chemical structure , the hormones of reproduction are divided into four groups :

**Proteins :** These are polypeptide hormones ranging from a molecular weight of 300 up to 70,000 daltons , e.g., **oxytocin** , **FSH** , and **LH** .

**Steroids :** These are derived from cholesterol and have a molecular weight of 300 to 400 daltons , e.g., **estrogens**, **progesterone**.

**Fatty acids :** These are derived from arachidonic acid and have a molecular weight of about 400 daltons , e.g. , **prostaglandin F2 $\alpha$**  .

**Amines :** These compounds are derived from tyrosine or tryptophane , e.g. , **melatonin** .

### Reproductive hormones

Reproductive hormones are derived primarily from four major systems or organs :

- Various areas of hypothalamus .
- Anterior and posterior lobes of pituitary gland.
- Gonads ( testis and ovary and corpus luteum ) .
- The uterus and placenta .

### Hypothalamic Releasing / Inhibiting Hormones

The hormones of the hypothalamus that regulate reproduction are **gonadotropin- releasing hormone (GnRH or LH-RH )** , **prolactin- inhibiting factor (PIF)** and **prolactin releasing factor (PRF)**. The hypothalamus also is the source of **oxytocin** and **vasopressin** .

**GnRH:** is a decapeptide ( 10 aminoacids ) with a molecular weight 1183 daltons.

It is synthesized and then stored in the medial basal part of hypothalamus . GnRH provides a humoral link between the neural and endocrine system. In response to neural signals , pulses of GnRH are released into the portal system for the release of LH.,and FSH from the anterior pituitary .

### Adenohypophyseal (anterior lobe of pituitary gland) Hormones

The anterior pituitary gland secretes three gonadotropic hormones; FSH, LH. , and prolactin

LH. and FSH are glycoprotein hormones with a molecular weight of about 30,000 - 32,000 daltons .

Gonadotropes in the anterior pituitary secrete both hormones . Each hormone consists of two dissimilar subunits termed the alpha and beta subunits . The alpha subunit is common to both FSH and LH. Within species , whereas the beta subunit is distinct and confers specificity of each hormone .both FSH and LH are called **gonadotropins**.

**Follicle Stimulating Hormone ( FSH )** . This hormone stimulates the growth and maturation of ovarian follicle . FSH does not cause secretion of estrogen by itself; instead, it needs the presence of LH., to stimulate estrogen production from large ovarian follicle.

**Luteinizing Hormone (LH.)** . The molecular weight of this hormone is 30.000 daltons and the biologic half life of this hormone is 30 minutes .It acts in conjunction with FSH to induce estrogen secretion from the large ovarian follicle. The preovulatory surge of LH., is responsible for the rupture of mature follicle wall and ovulation. After ovulation LH., Stimulates luteinization of ruptured follicle to form corpus luteum .

**Prolactin** . Is a polypeptide hormone secreted by the adenohypophysis , ovine prolactin is a 198 amino acids protein with a molecular weight of 24,000 daltons. An inhibiting hormone termed prolactin inhibiting factor ( PIF ) regulates secretion of prolactin . It is regarded as a gonadotropic hormone because of its luteotropic properties ( maintenance of corpus luteum ) In rodents.

### **Neurohypophyseal (Posterior lobe of pituitary gland) Hormones .**

The hormones of the posterior pituitary ( neurohypophysis ) differ from the other pituitary hormones in that they do not originate from the pituitary, but are only stored there until needed . The two hormones, **oxytocin** ( milk let down hormone ) and **vasopressin** (antidiuretic hormone or ADH ) are actually produced in the hypothalamus . These hormones are transferred from the hypothalamus to the posterior pituitary not through the vascular system , but along the axons of the nerve cells.

**Oxytocin**. Is synthesized in the supraoptic nucleus of the hypothalamus and transported in small vesicles enclosed by a membrane down the hypothalamic –hypophyseal nerve axons . They are stored at the nerve endings next to the capillary beds in the neurohypophysis until their release into circulation .this hormone consists of nine amino acids.

As stated earlier , oxytocin is also produced in the corpus luteum. Thus , oxytocin has two sites of origin , the hypothalamus and the ovary.

### **Functions of oxytocin .**

During follicular phase of estrous cycle , oxytocin stimulates uterine contractions , which facilitates sperm transport to the oviduct at estrus.

The stretching of the cervix at parturition caused by the passage of fetus stimulates a reflex release of oxytocin leads to facilitate the fetus liberation to the birth canal.

In the lactating and milking females, visual and tactile stimuli associated with suckling or milking induce the release of oxytocin into the circulation. Oxytocin causes contraction of myoepithelial cells (smooth muscle cells) that surround the alveoli in the mammary gland, resulting in milk letdown.

**Ovarian oxytocin is involved in luteal function. It acts on endometrium to induce prostaglandin (PGF<sub>2</sub>α) release, which has a luteolytic action (regression of the corpus luteum).**

**Melatonin.** Melatonin is synthesized in the pineal gland. Synthesis and secretion of melatonin is greatly elevated during darkness. Long daily periods of elevated secretion of melatonin are probably responsible for the induction of ovarian cycles in ewes and the decreased secretion of melatonin lead to the inhibition of ovarian cyclicity in mares.

### **Gonadal steroid hormones**

The ovaries produce two steroid hormones, estradiol and progesterone, and a protein hormone, relaxin; the testis secretes a single hormone which is testosterone. The secretory activity of steroid hormones by the gonads is under endocrine control of anterior pituitary.

### **Estrogens**

Estradiol<sub>17</sub>Beta, is the primary estrogen. It is biologically active estrogen produced by ovary (secreted by granulosa cells of the ovarian follicle) consists of 18 carbon atoms. With smaller quantities of estrone, and estriol (produced by ovary in the luteal phase of estrus cycle).

Plant estrogens (isoflavons) are found primarily in the legumes such as clover and alfalfa. Two of these compounds, genistein and coumestrol cause infertility in females, and, less frequently in males. Zeronal (Ralgro) is a compound with estrogenic activity, produced as an ear implant, it promotes growth of feedlot animals.

**Estrogens have the widest range of physiologic functions. Some of these functions are:**

1. Act on CNS to induce behavioral estrus in the females; however, small amounts of Progesterone with estrogen are needed to induce estrus in some species such as cow and ewe.
2. Act on the uterus to increase both amplitude and frequency of uterine contractions by potentiating the effects of oxytocin and PGF<sub>2</sub>α.
3. Physical development of female sexual characteristics.
4. Stimulate duct growth and cause the development of the mammary gland.
5. In ruminants, estrogens also have a protein anabolic effect to increase body weight gain and growth. The possible mechanisms for increased growth may be due to the ability of estrogens to stimulate the pituitary to release more growth hormone.

Diethylstilbestrol (DES), a synthetic nonsteroidal estrogen, was formerly used for growth promotion in cattle and sheep. Because of carcinogenic effect, it has been replaced by other Estrogenic implants.

**Progestogens .** Progesterone is the most prevalent , is secreted by luteal cells of the corpus luteum . It is a 21-carbon steroid . it is also secreted by placenta , and adrenal gland . Progesterone is transported in blood by a binding globulin as for estrogens . LH. Primarily Stimulates progesterone secretion .

Progesterone performs the following functions :

- Prepares the endometrium for implantation and maintenance of pregnancy by increasing activity of secretory glands in the endometrium and by inhibiting the motility of the myometrium.
- Acts synergistically with estrogen to induce behavioral estrus .
- Develops the secretory tissue ( alveoli ) of the mammary glands .
- Synthetic progesterone is available to synchronize the estrus cycles in ruminants.

### **Relaxin .**

Relaxin is a polypeptide hormone consisting of alpha and beta subunits that are connected by two sulfide bounds . It has a molecular weight of 5700 daltons . Relaxin is secreted primarily by the corpus luteum during pregnancy . In some species, the placenta and uterus also secrete relaxin .

The main biologic function of relaxin is dilation of cervix and vagina before parturition .

In guinea pig , relaxin causes separation of the pubic symphysis bone within 6 hours after injection . This separation normally occurs during parturition in this species .

**Inhibins and activins .** Inhibins and activins were isolated from gonadal fluids .their effects are on the production of FSH .

**Inhibins .** The granulose cells in the ovary produce inhibins , Inhibins are not steroids but proteins comprising two sulfide bridged subunits called alpha and beta .

Inhibins play an important role in the hormonal regulation of folliculogenesis during estrus cycle . Inhibins reduce the secretion of FSH to a level , which maintains the species-specific number of ovulations in both single and litter bearing species .

**Activins .** Follicular fluids contains proteins that stimulate the secretion of FSH , these proteins were characterized as activins . activin is a fully functional member of the growth factors.

**Follistatin .** Follistatin is another protein isolated from follicular fluid . Follistatin not only inhibits the secretion of FSH likes inhibins but also binds activin and neutralizes its biological activity. Thus , it modulates the secretion of FSH.

### **Placental Hormones .**

The placenta secretes several hormones with biologic activity similar to hormones of mammalian reproduction . these hormones are :

Equine chorionic gonadotropin (eCG ) , human chorionic gonadotropin ( hCG ) , placental lactogen ( PL ) , and protein B .

**Equine Chorionic Gonadotropin .** The hormone eCG (PMSG ) was discovered when blood from pregnant mares produced sexual maturity in immature rat . eCG is a glycoprotein with alpha and beta subunits similar to LH. and FSH but with higher carbohydrate content , especially sialic acid .This higher sialic content appears to account for the long half-life of several days for eCG.

The uterus of pregnant mare secretes this placental gonadotropin . The endometrial cups are the source for the eCG. The cups that are formed at about day 40 of pregnancy persist until day 85 of pregnancy. eCG has both FSH and LH. Biologic actions, with the FSH action being dominant. eCG circulates in the blood of pregnant mares and not excreted in urine .

The secretion of eCG stimulates development of ovarian follicles in mare . Some follicles ovulate , but most become luteinized follicles, due to the LH like action of the eCG. These accessory corpora lutea produce progestogens, which maintain pregnancy in the mare .

**Human Chorionic Gonadotropin .** hCG is a glycoprotein consists also of alpha and beta subunits with molecular weight of 40,000daltons .The trophoblastic cells in the primate placenta synthesize hCG; hCG is found in both blood and urine. hCG is primarily luteinizing and luteotropic and has little activity of FSH. Its presence in the urine in early pregnancy is the basis of the various laboratory tests for detection of human pregnancy. It is detected in the urine 8 days after conception by sensitive immunoassay.

**Placental Lactogen.** is a protein with chemical properties similar to prolactin and growth hormone . Its molecular weight is 22,000 to 23,000 daltons in ovine with 192 aminoacids . It is isolated from placental tissue but can not be detected in the serum of the pregnant animal until the last trimester of pregnancy . It is important in regulating maternal nutrients to the fetus and possibly is important for fetal growth . Placental lactogen may play a role in milk production because its level is higher in dairy cows than in beef cows.

**Protein B.** The bovine conceptus produces numerous signals during early pregnancy. Currently only one protein from placental tissue has been partially purified **pregnancy-specific protein B ( bPSPB )** . The physiologic action of protein B may be involved in preventing destruction of the corpus luteum in early pregnancy of the cow or ewe . This Placental hormone has the potential to the first reliable hormonal pregnancy test for cattle .

### **Uterine Hormones**

**Prostaglandins .** Prostaglandins , first isolated from accessory sex gland fluids , and were termed prostaglandins because of their association with prostate gland . Almost all body tissues secrete them. All prostaglandins are 20-carbon unsaturated fatty acids with a cyclopentane ring . Arachidonic acid , an essential unsaturated fatty acid , is the precursor for prostaglandins. Most prostaglandins act locally at the site of their production and therefore do not conform exactly to the classic definition of a hormone. The most closely associated with the reproduction , are **PGF2 $\alpha$**  and Less extent**PGE2**.

PGF2 $\alpha$  is the natural luteolytic agent( produced by endometrium ) that ends the luteal phase (corpus luteum) of the estrus cycle and allows for the initiation of a new estrus cycle in the

absence of fertilization. Prostaglandins also regulate several physiologic phenomena, such as contraction of smooth muscles in the reproductive tract, ovulation, parturition and milk ejection.

In pregnant animals, the developing embryo sends a signal to uterus, preventing luteolytic effect of PGF<sub>2</sub>α ( **maternal recognition of pregnancy** ).