Academic year 2023-24

HORMONES OF REPRODUCTION

Dr. Krishan Yadav
Assistant professor
Department of Veterinary Gynaecology and Obstetrics
MJFCVAS, Chomu

HORMONES OF REPRODUCTION

Hormone is a chemical substance synthesized and secreted by specialized cells or glands and is transported through the blood at the target site where it exerts the action. These are secreted by ductless endocrine glands. Hormone binds at receptor which is specific. Hormone can be:

a) Primary hormones: These directly regulate various reproductive processes like oogenesis, ovulation, fertilization, implantation, gestation and parturition.

b) Secondary hormones: These control the physiological function of other system which may directly or indirectly influence the reproductive process /system. These hormones are also called as metabolic hormones

3. Fatty acids: These are derived from Arachidonic acid and have a molecular weight of about 400 Daltons.

4. Amines: These compounds are derived from tyrosine or tryptophane.g. melatonin.

Hypothalamus occupies a very small portion of the brain. It consists of the region of the third ventricle, Pituitary is present below the hypothalamus in the depression of sphenoid bong known as sella turcica. There are neural connections between the hypothalamus and the posterior lobe through the hypothalamic-hypophyseal tract and vascular connections between the hypothalamus and the anterior pituitary lobe. This system transports the hormones from the hypothalamus to pituitary.

The pituitary has two lobes: Anterior lobe or adenohypophysis and posterior lobe or neurohypophysis

The adenohypophysis has two types of cells:

a) Chromophores: These are round and clear cells and they don't take any stain.

b) Chromophils: These can be stained and these can be basophiles and acidophiles. These are stained by acidic stain(eosin).

Acidophiles can be orangeophiles- from these cells growth hormone is synthesized. Carminophiles- from these cells prolactin (also known as luteotropic hormone or luteotropin or LTH) is synthesized.

Basophiles- These are stained by basic dye (Haematoxylin). These can be-

a) Gonadotrophs- These produce FSH and LH.

b) Thyrotropins- These produce TSH.

c) Corticotrophs- From these cells ACTH is produced.

In the blood the pattern of hormones may be:

Pulsatile- Concentration of hormones changes several times within an hour. e.g. LH & glucocorticoids.

Circadian- The concentration of hormones remain constant for atleast 24 hrs e.g. cortisol hormones in mare.

Based upon the concentration and time interval the level of hormones may be -

Basal level- In this low concentration of hormone remains constant for a longer period.

Pulse- A slight high concentration remains constant for less than one hour.

Surge- In this a very high concentration remain constant for more than one hour. e.g. preovulatory surge of LH during astrus period. It remains high for 6-7 hours.

For protein hormones the receptors are present at surface of cells and for steroid hormones receptors are present at nucleus

There are four modes of intercellular communications:

1. Neural communication: In this neurotransmitters are released at synaptic junctions from nerve cells and act across narrow synaptic clefts between as neurotransmitters.

2. Endocrine: In this, hormones are transmitted through blood circulation, typical of most hormones.

3. Paracrine communication: In this, the products of cell diffuse through extracellular fluid to affect the neighbouring cells that are at a distance. e.g. prostaglandins.

4. Autocrine communication: Cells secrete chemical messengers that bind to receptors on the same cell that secreted the messenger.

Neuro-endocrine reflex: Nervous system also controls release of certain hormones through neural pathways. e.g. Oxytocin in milk let down and LH release following copulation in induced ovulators.

Principles of hormone therapy: Hormones are used for therapeutic as well as growth promoters. The action of hormone depends upon its half-life and it varies with species and individual. The major problem of hormonal therapy is residual effect. The residual effect depends upon the metabolic rate. The maximum concentration of hormone is always present in liver and kidney/The steroid hormone remains for a longer period in liver & kidney as compared to protein hormones.

The action of hormone is different in different species. For example, hCG & natural LH are effective in all species whereas PMSG (eCG) is effective in all species except mare so, not used in mare.

The concentration of hormone in the blood also depends upon the structure of hormone; if oily preparation of progesterone is given intramuscular its level in the blood remains high for about 5-6 days.

The action also depends upon the dose of hormone for e.g. if you give low doses of estrogen then it causes contraction of uterus and helps in elimination of infection but if given in high doses it causes regression of CL so, can be used for the treatment of uterine pathology like pyometra and mummification of foetus.

HORMONES SECRETED BY HYPOTHALAMUS

- Gonadotropin releasing hormone (GnRH)

Dopamine

Corticotropic releasing hormone (CRH)

Growth hormone- releasing hormone

Oxytocin

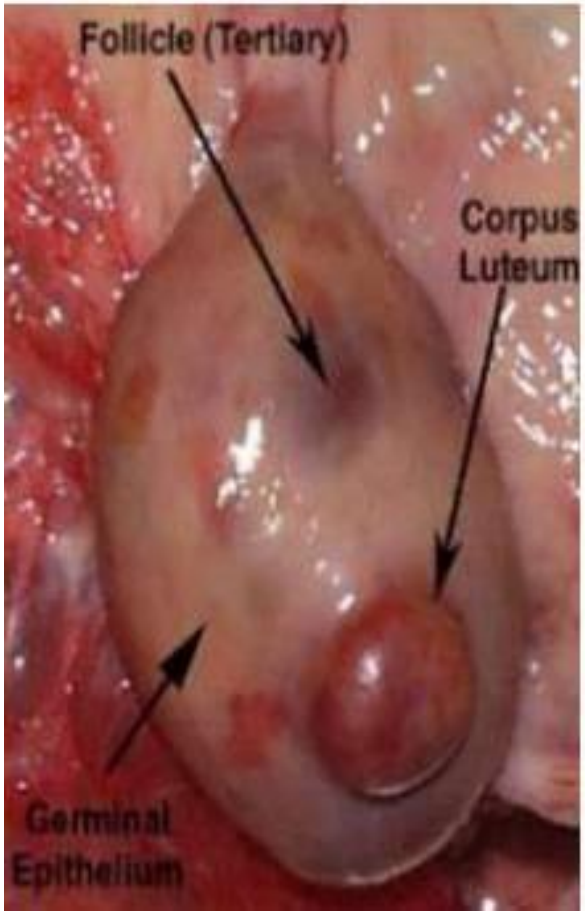
Hormones secreted by pituitary gland

- **Anterior Pituitary**

- **Follicle stimulating hormone**
- **Luteinizing hormone**
- **Prolactin**
- **Adrenalocorticotropic hormone**

- **Posterior pituitary** ⟶ **Oxytocin**

HORMONES SECRETED BY OVARY



Graaflan Follicle

Estrogen **Inhibin**

Corpus Luteum

Progestins **Relaxin**

HORMONES SECRETED BY TESTIS

- **Leydig cells** → **Androgens**

Sertoli cells → **Inhibin**

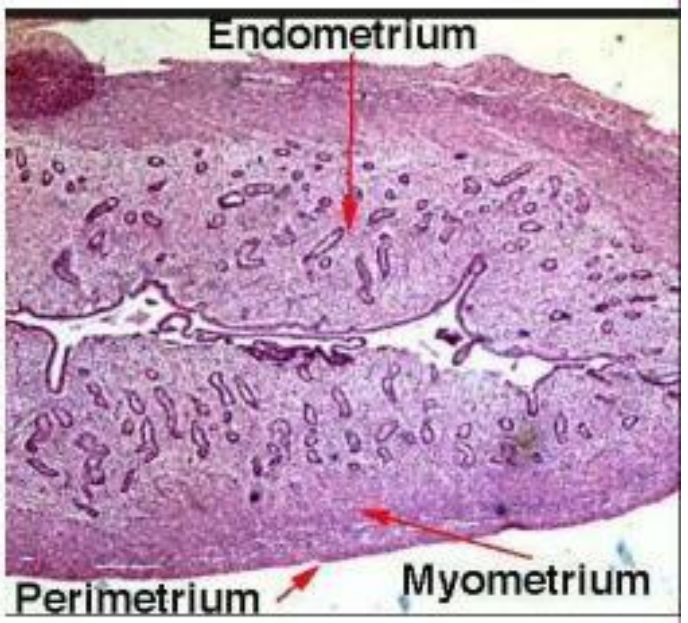
HORMONES SECRETED BY PLACENTA

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

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

↓

Prostaglandin F2α (PGF2α)



Histology of Bovine Uterus

HYPOTHALAMIC HORMONES

1. **GnRH/ FSH-RH/ LH-RH**: Schally and Guillemin (1977), two American scientists shared the Noble Prize for their independent research on determining the chemical structure of GnRH. It is a decapeptide (10 amino acids) having a molecular weight of 1183 dalton. It is synthesized and stored in the medial basal hypothalamus. The half-life is 7 minutes) It controls the function of anterior pituitary.

Main function: It causes release of FSH and LH.

Clinical applications/Therapeutic Uses:

i. It can be used to induce estrus.

ii. For treatment of delayed ovulation or anovulation

iii. For treatment of follicular cyst

iv. Treatment of low libido in male animals.

v. Used for treatment of impaired spermatogenesis

Preparations- Receptal, Fertagyl, Ovulanta, Gynarich.

Dose:10-20 ug.

Buserelin most potent analog
Fertirelin
Gonadorelin
Analogs ------Leuprolide and deslorelin

2. Oxytocin- it is nonapeptide (9 amino acids). Half life of 3-5 minutes, it is synthesized and produced in hypothalamus by SON (supraoptic nucleus) & PVN (paraventricular nucleus) but it is stored and released by posterior pituitary i.e. it is also called as posterior pituitary hormone. It is also secreted by corpus luteum. Thus, oxytocin has two sites of origin, the ovary and the hypothalamus.

Main Functions:

i. Causes contraction of smooth muscles of uterus

ii. Contraction of oviduct thus helps in gamete transport.

iii. Contraction of myoepithelial layer of the alveoli thus displaces the milk from alveoli into the duct & result in milk letdown.

iv. The stretching of the cervix at parturition caused by the passage of fetus stimulates a reflex release of oxytocin Ferguson's reflex)

v. Ovarian oxytocin is involved in luteolysis process

Clinical applications:

i. Used for milk let down

ii. For treatment of uterine inertia.

iii. For treatment of retention of placenta.

iv. In mare used to induce parturition.

Preparations: Gynotocin, Pitocin, Biotocin, Syntocin

5 IU / ml oxytocin

Dose: 10-15 IU, i/m. High dose will cause spasm of uterus. Repeat it after every 3-4 hrs because half- life is very short. It should be used very slow i/v but dose is 40-60 I.U in 500 ml NSS for a period of 3-4 hrs.

GONADOTROPHIC HORMONE

From anterior pituitary 3 main gonadotrophic hormones i.e.. FSH, LH &Prolactin are released. Their release is controlled by steroid and inhibin hormones.

1. FSH- It is a glycoprotein hormone. It has two polypeptides chain known as alpha & beta subunits. Presence of both the chains is essential for the action of FSH. The half life 2-4 hours

Main Functions:

i. Causes growth of follicles.

ii. Growth of seminiferous tubules.

iii. Required for spermatogenesis up to secondary spermatocyte stage.

iv. In human being after menopause FSH is excreted in the urine called (hMG (Human menopausal gonadotropin), also used as fertility hormone in domestic animals.

Clinical applications:

i. Used to induce estrus.

ii. For superovulation.

iii. Treatment of impaired spermatogenesis.

700IU FSH as freeze-dried powder.

Preparations: FSH-ovine (P), FSH- porcine (P), FSH-equine (E).

Dose: 30-40 mg (Total Dose) and given in divided dose for a period of 4-5 days.

2. LH: Also called as ICSH (Interstitial cell stimulating hormone) in case of male. It is a glycoprotein hormon & has two subunits alpha and beta. Half-life is 30 minutes & the molecular weight is 30 k Dalton

Main Functions:

i. Causes maturation & ovulation of the follicle.

ii. Luteotrophic hormone (helps in formation and maintenance of CL).

iii. Stimulate Leydig's cells which produce androgens and maintain libido.

Clinical application:

i. Used for treatment of follicular cyst..

ii. For treatment of delayed ovulation.

iii. For treatment of low libido in male animal.

Preparation: LH-O, LH-P, LH-E.

3. **Prolactin:** Similar to Growth hormones and Placental lactogen. It is a polypeptide hormone. It helps in lactogenesis.

It acts on the CNS of female and induces maternal behaviour. Half-life is 15 minutes. Prolactin initiates and maintains lactation. It is regarded as a gonadotropic hormone because of its luteotropic properties (maintenance of corpus luteum) in rodents. However, in domestic animals, LH is the main luteotropic hormone, with prolactin being of less importance in the luteotropic complex.

PLACENTAL HORMONES

From the placenta many gonadotrophic hormones are produced. The structure and function are similar to gonadotrophins which are produced by anterior pituitary.

1. **hCG (Human chorionic gonadotropin):** Human chorionic gonadotropin is a placental hormone initially secreted by cells yncitiotrophoblasts from the implanting conceptus during week 2, supporting the ovarian corpus luteum, which in turn supports the endometrial lining and therefore maintains pregnancy.

It is excreted in urine of pregnant women and can be detected in urine as early as 8 days after conception & in women, as a hormone for pregnancy diagnosis. It is found in both blood and urine.

It is a glycoprotein & has two subunits alpha & beta. The main functions are similar to LH But also have some FSH activity.

i. It causes maturation of follicle, ovulation & CL formation.

ii. In male, cause secretion of testosterone.

Clinical applications:

i. Used as reliable assay for Pregnancy diagnosis in women.

ii. For treatment of follicular cyst.

iii. Treatment of delayed ovulation.

iv. Treatment of low libido in male animals.

v. Detection of remnant of testicular tissues in castrated dog & cat.

Preparations:Chorulon-1500 I.U. in delay/anovulation and 3000 I.U. in follicular cyst

2 PMSG: Also called as eCG (equine chorionic gonadotropin). It is present in blood of pregnant mare broadly between days 40-140 of gestation.

It is produced by endometrial cups. Usually, there are about 12 cups Bresent at the junction of gravid horn and body as a circumferential band.

These are formed by attachment of trophoblast of chorion with endometrium of uterus.
PMSG is first detected first in the blood on day 38-42 after ovulation, reaches maximum at 60-65 days declines thereafter and disappear by 150 days of gestation.
It circulates in the blood of the pregnant mares and not excreted in the urine.
It has both FSH and LH biologic actions with FSH actions being dominant.

The PMSG is a glycoprotein & it has alpha & beta subunits. The half life is about 7 days. It is a glycoprotein with alpha, beta sub-units similar to FSH and LH but with a higher carbohydrate (especially, sialic acid) content.

The higher sialic acid is responsible for long half-life of eCG. In pregnant mare it causes growth of follicles which either ovulate or become luteinized (without ovulation CL is formed) & thus it forms secondary CL or accessory CL.

These accessory CL produce progesterone which helps in maintenance of pregnancy in mare. The functions are similar to that of FSH. eCG was one of the commercially available gonadotropins used to induce superovulation in farm animals.

Preparation: Folligon 1000 I.U.

In mare, the main source of progesterone, in early pregnancy is the true CL/CL verum (formed from the follicle that ovulated and generated the oocyte that was fertilized) and the accessory CL. The true CI. ís active for first three months of gestation and regress at the same time as accessory CL. The placenta takes over the production of progesterone after regression of accessory CL.

The conceptual bulging in first month of gestation in mare is ventral whereas dorsal in case-of cattle and buffalo.

Bilateral ovariectomy in (55 days pregnant ewes will not result in abortion because by this stage of gestation, the placenta takes over the major role of progesterone production.

In mare around day 100 of pregnancy, at the site of contact between allantochorion and endometrium, there is formation of multibranched interdigitations which are known as microcotyledonary placenta

3. Placental Lactogen: Similar to growth hormone and prolactin. It has lactogenic activity & prolactin like action. It is glycoprotein & has alpha and beta-subunits.

It regulates the nutrition of foetus from the dam. It also regulates the growth of mammary gland.

It stimulates progesterone synthesis.PL is detected in the serum of pregnant animal in the last trimester of pregnancy.

It is more important for its growth hormone properties than its prolactin properties.

It is important in regulating maternal nutrients to the fetus and possibly it is important for fetal growth.

4. PSP (Pregnancy specific protein) also known as PSP-bovine (PSP-B) or PSP ovine. It can be extracted from placenta during early gestation.

In bovine it appears from day 24 of gestation & the level remains constant throughout the pregnancy.

It is used as an assay for early pregnancy diagnosis. This placental hormone has the potential to be the first reliable hormonal pregnancy test for cattle.

GONADAL HORMONES

1. Relaxin: it is polypeptide & also has alpha and beta subunits connected by two disulphide bond It is (similar to insulin but the biological properties are entirely different. It is mainly produced by CL of pregnancy. In smaller amounts it may be produced by the uterus & placenta.

Main functions:

a. Causes relaxation of uterus, cervix & vagina during parturition.

b. Cause relaxation of pubic symphysis and dilatation of cervix.

c. Causes growth of mammary gland if given in conjunction with estradiol.

d. Inhibit uterine contraction.

2. Inhibin: also called as folliculostatin.) It is a polypeptide with alpha & beta subunits. It is produced by granulosa cells of follicle & Sertoli cells of testis Due to negative feedback on the hypothalamus & pituitary it controls the release of FSH. In male, inhibin is released via the lymph and not by venous blood as in the female.

3. Steroids: These are mainly produced by ovaries &testis. And, may also be produced by adrenal cortex & placenta. The precursor for steroid is cholesterol. All the steroids have a common structure called as cyclo-pentano-perhydro-phenanthrene ring.

a) **Androgens:** are 19 carbon steroids Most common is testosterone. It is produced by Leydig's cells of testis & also produced by adrenal cortex.

In equine it is produced in large amount by epididymis so, if during castration a small tissue of epididymis is left the castrated stallion will behave like a normal stallion, because androgens are produced by the remaining epididymis. Allowing part of the epididymis to remain is termed "cutting a horse proud".

In blood the testosterone is bound with globulin & it is also called as SBG (steroid binding globulin). About 97-99% of the testosterone is bound with globulin and only 1-3 % is free & this free testosterone is responsible for biological action.

It enters the cells and is converted into DHT (Dihydrotestosterone). The enzyme involved in this conversion is 5a-reductase.) DHT is responsible for the action of testosterone.

Main functions:

i. Causes growth of male genitalia.

ii. Maintain the secondary sexual characters.

iii. Acts as a growth promoter (Anabolic hormone).

iv. Maintain the libido.

v. Required for spermatogenesis after the secondary spermatocyte stage.

vi. Prolongs the life of spermatozoa in epididymis.

vii. Cause growth of accessory sex glands.

Clinical applications:

i. Used for treatment of impaired spermatogenesis.

ii. Treatment of low libido in male animals.

iii. To produce cow steer (castrated male) which are used for heat detection.

Preparations: Testobion

b). Estrogens: It is an 18 carbon steroid hormone. These are mainly produced by the ovary & in small amount may also be produced by placenta & adrenal cortex. For the synthesis of estrogen there are two cells two gonadotrophin hypothesis or theory-

Aromatization: Conversion of testosterone into estrogen.

Main functions:

1. Causes growth of uterus.
2. Helps in maintaining secondary sexual characteristics.
3. Used as growth promoter (anabolic hormone).
4. Causes the growth of ducts of mammary gland.
5. Act on CNS to induce behavioural estrus in the female, however, small amount of progesterone along with estrogen is also needed.
6. Act on uterus to increase both amplitude and frequency of contractions by potentiating the effects of oxytocin and PGF2alpha.
7. Luteolytic in cattle, buffalo and sheep but luteotrophic in sow
8. It helps in calcium uptake.
9. It causes maturation of epiphyseal cartilage of long bones due to which after attaining puberty there is no increase in height of female.

Also produced by some plants mainly the legumes (berseem) & these are known as phytoestrogens. If the berseem is fed in excess it may cause infertility. Diethylstilbestrol (DES),) a synthetic non-steroidal estrogen formerly used as growth promoter in cattle and sheep binds with estrogen receptor and acts with same potency as 17-beta estradiol. Because of its carcinogenic effect, it has been replaced with other estrogenic implants.

Clinical applications:

1. Used to induce estrus.

2. Used to induce abortion.

3. Used for treatment of endometritis & ROP

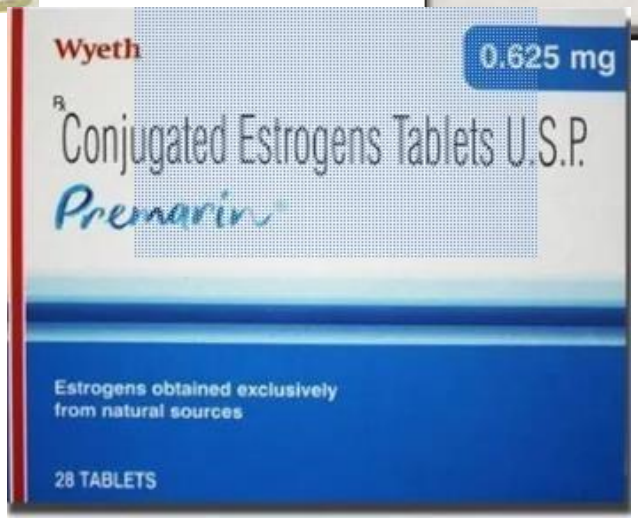
4. High dose use for treatment of pyometra & mummification of foetus.

5. In bitch-treatment of mis-mating

6. Used as oral contraceptive.

Preparations: Progynon depot - 10mg/ml have estradiol valerate.

Mixogen- contain estradiol benzoate, preparation are 4, 20 & 40 mg.



Anti estrogens –Tamoxifen, Clomiphene citrate

c) Progesterone: It is a 21 carbon steroid hormone secreted by CL & also by placenta & adrenal cortex. It is the most prevalent, naturally occurring Progestogen.

Functions:

i. Growth of alveoli of mammary gland.

ii. Regulate estrus cycle.

iii. Prevent contraction of uterus.

iv. Prepare the uterus for implantation and maintenance of pregnancy.

v. Acts synergistically with estrogens to induce estrus behaviour.

vi. Inhibits estrus and ovulatory surge of LH at high levels.

vii. Main hormone for regulation of the estrous cycle.

Clinical applications:

i. Used to induce & synchronize estrus.

ii. Used to prevent abortion.

iii. Used as contraceptive pill which prevent the ovulation.

Preparations: Proluton depot, Duraprogen, P-depot, Hyprogen. Preparations are in the 2 and 3 ml containing 500 mg and 750 mg, respectively.

Progesterone agonist:-

Medroxyprogesterone acetate (MPA)

Megestrol acetate

Melengestrol acetate MGA

Proligestone

Norgestomet

Progesterone vaginal implants

Altrenogest (Nor-testosterone derivative with progesterone like activity)

Hydroxyprogesterone caproate


EAZI-BREED
CIDR


Apollo
PHARMACY
5 Dispo-packs of 2 ml
℞
Hydroxyprogesterone Caproate Injection IP
Proluton® Depot 500 mg/2ml
प्रोल्यूटन डेपो ५००
For Intramuscular Injection
To report adverse events, call toll free on
1800 419 1141 or visit www.zydusadila.com

UTERINE HORMONES

Prostaglandins, first isolated from accessory sex gland fluids, were termed prostaglandins because of their association with the prostate gland.

PGs are 20-carbon unsaturated hydroxyl fatty acids. Arachidonic acid & linolenic acid are the precursor of PG.

PGF2a is natural luteolysin that causes regression of CL. Endomethacin is PGF2a antagonist it prevent synthesis of PGF2a, and prolongs the life span of CL.

Most of PG they act locally at the site of production but sometimes they may be transported to the target organs away from the site of production.

Functions-

1. Causes regression of CL.

2. Helps in ovulation.

3. Contraction of myometrium.

4. Help in gamete transport to site of fertilization.

Clinical applications:

1. Induce abortion.

2. Induce parturition.

3. Treatment of pathological conditions like pyometra in cattle and buffaloes.

4. Treatment of fetal mummification

5. Used in estrus synchronization protocols.

Preparations:

Natural (Dianaprost tromethamine) e.g. Lutalyse :5 ml (25 mg) i.m

Synthetic (Cloprostenol) e.g. Vetmate, Metrum, Pragma, Repragna - 2ml vial (500ug)

Pheromones: These are also called as sex attractants. These are chemical substances produced by exocrine glands.

These are low molecular weight fatty acid derivatives. These are released in environment where they are ingested or absorbed or perceived by olfaction and then evoke a specific response in that animal.

These are intra-species (act between same species). These are not hormones because hormones are produced by endocrine glands and act within the individual. Pheromones can be:

1. **Signalling Pheromones:** Their action is rapid and acts through the CNS and their effect is reversible.

For example if two groups of unfamiliar mice ate kept together, they become aggressive and bite each other. This is because of secretion of pheromone from urine and foot pad of the mouse. If their nasal epithelium is destroyed, then aggressive behaviour is lost.

Australian rabbit produces a pheromone from chin gland which is repellent means prevent the entry of other male in his territory.

2. Priming pheromones: They require a prolonged stimulation for action and their response is irreversible or permanent. For example –

a. In honey bees, the queen bee produce a pheromone called 9-ketodecanoic acid which is ingested by other females and prevent the development of the ovaries. So all the females become sterile and act as workers.

b. Lee-Boot effect: If a group of female mice are kept together, then their estrous cycle is disturbed and estrus is followed by prolonged anestrous.

C. Whitten effect: If a male is introduced in a group of female mice, their estrous cycle is shortened and it is called as whitten effect.

d. Bruce effect: If a strange male is introduced in a group of pregnant female mice, then abortion occurs.

Thank you