GONADOTROPHIN (LUTEINISING)- RELEASING HORMONE AND ANALOGUES (GnRH OR LHRH)

Naturally occurring hormone, produced by the hypothalamus and transferred to the anterior pituitary gland in the hypophyseal portal circulation. It is a peptide and stimulates the release of follicle-stimulating hormone (FSH) and luteinising hormone (LH).

Pharmacological action
Stimulates a short surge of FSH and LH following a single bolus injection.

Indications
Cattle:
- follicular cysts
- delayed ovulation or anovulation
- acyclicity (doubtful if a single bolus is very effective)
- improved pregnancy rates, in cows with poor pregnancy rates, when used as ‘holding injection’ as a single bolus 12 days after insemination
- In oestrus–synchronisation regimens.

Horse:
- induce ovulation (preovulatory gonadotrophin surge lasts several days in mare); single bolus may not be effective, requires frequent repeated doses, or the use of a slow-release implant.

Dose rate
- Buserelin: cow, 10–20 μg; horse 40 μg preferably i.m. but can be given i.v. or s.c.
- Gonadorelin: cow, 0.5 mg i.m., s.c. or i.v.
- Fertirelin: cow, 100 μg i.m.

GONADOTROPHINS

1. **FSH and LH.** Both FSH and LH can be obtained in a semi-purified form, but are expensive. Porcine FSH and recombinant-derived FSH are used to induce superovulation in donor cows for embryo transfer.

2. **Equine chorionic gonadotrophin (eCG).**
Originally called pregnant mare’s serum gonadotrophin (PMSG) but in order to use consistent nomenclature it is now called eCG. A protein hormone produced by the endometrial cups of the mare from about 40–120 days of pregnancy. It mainly has FSH-like activity but with a much longer biological half-life than FSH.

Pharmacological action
Mainly FSH-like in its action but has some LH activity.
Indications
Cattle:
● superovulation of donor cows for embryo transfer; over-stimulation can be a problem
● impaired spermatogenesis in bulls (doubtful value)
● at the time of withdrawal of intravaginal progesterone preparations when used to treat acyclicity.
Sheep and goats:
● in association with intravaginal progestogen sponges to advance the onset of the breeding season.
Pig:
● in association with hCG to stimulate onset of cyclical activity after farrowing.
Dog:
● induce oestrus during physiological anoestrus.

Dose rate
Cattle, 1500–3000 IU s.c. or i.m.
Sheep and goats, 500–800 IU s.c. or i.m. (depending on the breed and time interval to the onset of normal breeding season).
Pig, 1000 IU s.c. or i.m.
Dog, 50–200 IU.

3. Human menopausal gonadotrophin (hMG). Extracted from the urine of menopausal women, this has primarily an FSH-like action. Used to a limited extent in superovulating donor cows for embryo transfer. It has a shorter biological half-life than eCG.

4. Human chorionic gonadotrophin (hCG).
A protein hormone extracted from the urine of pregnant women, this hormone has primarily an LH-like effect and hence is used as a substitute for the more expensive LH; it also has a longer half-life than LH.

Pharmacological action
Stimulates androgen production by the thecal cells of the ovary and Leydig cells of the testis; stimulates follicular maturation and ovulation, corpus luteum formation and maintenance.

Indications
Cattle:
● delayed ovulation or anovulation
● ovarian cysts (especially follicular)
● luteal deficiency
● improve chances of pregnancy in cyclic nonbreeders (repeat breeder cows), rationale is not always apparent
• improve libido in bull (doubtful value and may make temperament more aggressive).

Horse:
• induce or hasten ovulation
• ‘rig test’, stimulate rise in testosterone in peripheral blood of suspected cryptorchid.

Pig:
• with eCG to stimulate onset of cyclical activity after farrowing
• improve libido in boar (doubtful value).

Sheep and goat:
• improve libido in ram and male goat (doubtful value)
• cystic ovaries in female goat.

Dog:
• curtail prolonged or persistent pro-oestrus/oestrus in bitches
• determination of abdominal cryptorchidism as in the ‘rig’ test in horses
• improve libido in male dog (doubtful value).

Cat:
• induce ovulation.

Dose rate
Cattle, 1500–3000 IU i.v. or i.m.
Horse, 1500–3000 IU i.v. or i.m.
Pig, 500–1000 IU i.m. or s.c.
Sheep and goat, 100–500 IU i.v. or i.m.
Dog, 100–500 IU i.m.
Cat, 100–200 IU i.m.

OXYTOCIN AND POSTERIOR PITUITARY EXTRACTS

Oxytocin is a peptide hormone produced by the neurones of the supraoptic nucleus and is transported to, and stored in, the posterior pituitary gland. Synthetic oxytocin is available commercially and is thus highly purified; however, aqueous extracts of mammalian pituitary glands are also available. These latter products will also contain other posterior pituitary hormones such as vasopressin and antidiuretic hormone (ADH).

Pharmacological action
Causes milk letdown, myometrial contractions to facilitate gamete transport, myometrial contractions during parturition and postpartum.
Indications
Cattle:
• induce milk letdown
• hasten uterine involution following dystocia, caesarean operation, after replacement of uterine prolapse, uterine trauma or haemorrhage.
Horse:
• induce foaling
• cause expulsion of retained fetal membranes
• induce milk letdown.
Sheep
• As for cow.
Pig:
• induce milk letdown
• hasten second stage of parturition
• treatment of uterine inertia
• cause expulsion of retained fetal membranes
• hasten uterine involution.
Dog:
• treat uterine inertia
• expulsion of retained fetal membranes
• hasten uterine involution after dystocia or caesarean operation (perhaps treat subinvolution of placental sites)
• induce milk letdown.
Where there is trauma to the uterus, especially with haemorrhage, pituitary extracts should not be used.

Dose rate
Many recommended dose rates are too high. The myometrium is very sensitive to the effects of oxytocin and high dose rates can cause spasm rather than synchronised contractions. The myometrium will also become refractory to its effect, hence increasing incremental dose rates should be used. Most effective when used in an intravenous drip in saline.
Cattle, 10 IU i.m. or i.v.
Horse, 10 IU i.m. or i.v.
Pig, 5 IU i.m. or i.v.
Sheep and goat, 2–5 IU i.m. or i.v.
Dog and cat, 0.5–5 IU i.m. or i.v.

OESTROGENS
Oestrogens, which are steroids, play a wide role in the reproductive process. However, there are relatively few rational indications for oestrogen therapy in the treatment of reproductive disorders in domestic species. In recent years, several of the synthetic oestrogens have been withdrawn from use because of concern about residues in human food products.
Pharmacological action
Oestrogens are primarily responsible for oestrous behaviour in the female; they stimulate changes in the tubular genital tract which control gamete transport and, with progestogens, cause development of the mammary gland and increase the resistance of the genital tract to infection. They potentiate the ecbolic action of oxytocin and prostaglandins on the myometrium. They stimulate the preovulatory surge of gonadotrophins. They also reverse the effects of androgens on androgen-dependent tissue changes.

Indications
Horse:
- ripening of the cervix before oxytocin-induced foaling.
Cattle:
- treatment of endometritis (contraindicated in acute toxic metritis).
Dog:
- prevention of unplanned pregnancy
- urinary incontinence in the spayed bitch
- prostatic hyperplasia and anal adenoma in the male dog
- depress hypersexuality in the male dog.

Dose rate
Horse, 3–6 mg i.m.
Cattle, 3–5 mg i.m. (probably too high)

PROGESTOGENS
These include the naturally occurring steroid progesterone, and a number of synthetic progestogens which are much more potent and have a longer half-life. Progestogens are used widely in all domestic species, mainly to control cyclical activity; this is because, as a group, they exert a powerful negative feedback effect upon the hypothalamus and anterior pituitary gland, thus inhibiting gonadotrophin release. The consequence of this effect is to suppress cyclical activity so that, following cessation of treatment in polyoestrous species, there is ovarian rebound within a few days.