

## Ovulation

Ovulatory follicles are selected at the onset of luteolysis in large domestic animals. Follicular cycles are distinct to the extent that follicle regression usually begins (as indicated by follicle size) before the onset of growth of the next follicle. The first dominant follicle regresses at about mid luteal phase with a second dominant follicle beginning growth immediately. The stage of the follicles at the time of regression of the corpus luteum determines the ovulatory follicle i.e. whether it is the 2<sup>nd</sup> dominant follicle or if a third will develop. If the 2<sup>nd</sup> dominant follicle has begun to regress at the time of regression of the corpus luteum, a 3<sup>rd</sup> dominant follicle develops. Therefore, the 2<sup>nd</sup> selected ovulatory follicle is by chance the dominant follicle in a developmental stage at the time that the regression of the corpus luteum is initiated. The duration for the development of the antral follicle to the point of ovulation has been estimated to be about 10 days in some domestic animals but sometimes longer in some primates.

Antral follicle development apparently occurs in 2 phases in large domestic animals viz,

1. A relatively slow phase that last 4-5 days
2. A second phase of accelerated growth lasting 4-5 days which terminates in ovulation

One of the ways the dominant follicle maintains its status is to produce substances that inhibit the development of some antral follicles. One of such substances, **Inhibin**, is a peptide hormone produced by the granulosa which inhibits the secretion of FSH.

The dominant follicle is able to compensate for the lower FSH concentrations and continues to grow because of the numbers of FSH receptors it has compared with competitor follicles.

Development of the follicle is a dynamic-process once the rapid growth phase is achieved.

The follicle must be acted on thru proper gonadotropin stimulation within a few days or death of the follicles occurs. Atresia of the growing antral follicles begins almost immediately if it is not

exposed to the proper gonadotropin environment. Regressed follicles are invaded by inflammatory cells and areas previously occupied are filled by connective tissue leaving an ovarian scar.

### **Ovulation and Gonadotropins**

Ovulation, which is the discharge of the dominant antral follicle, is caused by an oestrogen induced pre-ovulatory surge of gonadotropin. The pre-ovulatory surge of LH which begins about 24 hours before ovulation in most domestic species including the cow, dog, goat, pig and sheep initiates the critical changes in the follicles that affects it's endocrine organ status and results in the release of the oocyte.

**Before this release, an oocyte inhibiting factor prevents the oocyte from resuming meiosis and a luteinizing inhibiting factor prevents the granulosa from prematurely been changed into luteal tissue. This pre-ovulatory LH surge blocks the production of both these factors.**

The LH surge allows the initiation of the process of luteinization on the granulosa which transforms the cells from estrogen to progesterone secretion. The process begins before ovulation occurs. With the advent of the LH surge, estrogen secretion declines concomitantly with the onset of progesterone secretion.

Also, the pre-ovulatory surge (LH) causes the granulosa to produce substances such as **relaxin and PGF<sub>2</sub> $\alpha$**  which affects the continuity of the connective tissue of the thecal layers of the follicle. The rupture of the follicle is caused by the disintegration of the connective tissue.

In summary, estrogen is used by the follicle(s):

1. To stimulate the growth and development of the granulosa.
2. To signal the hypothalamus and anterior pituitary as to the readiness of the follicle(s) for ovulation.

## **Sexual Receptivity**

The concept of synergism is important in that often several hormones combine to produce sexual receptivity. The sequence in which the hormones appear is important for their synergistic action. There are differences as to hormonal requirements for sexual receptivity among species.

**Estrus is a time of sexual receptivity with ovulation usually occurring at the end of estrus.**

The word 'heat' is a term that is often substituted for estrus.

## **Corpus Luteum (CL)**

The major function of the corpus luteum is the secretion of progesterone which prepares the uterus for the **initiation** and **maintenance of pregnancy**. CL is formed from the wall of the follicle which is collapsed and folded after ovulation with follicle rupture.

There is a breakdown of the tissues that surround the granulosa particularly the membrane propria and haemorrhage into the cavity can occur from vessels in the theca. The folds of tissue that protrude inward into the cavity contain granulosa and theca cells and importantly the vascular system that will support cell growth and differentiation.

Granulosa cell is the dominant cell of the CL but theca cells also contribute significantly to the composition of the structure. The process that granulosa cells undergo during the change from estrogen to progesterone secretion (luteinization) begins with the onset of the pre-ovulatory LH surge and accelerates with ovulation. Significant secretion of progesterone by the CL begins within 24 hours of ovulation in most domestic species.

In some species including the dog and primates, small amounts of progesterone are produced during the pre-ovulatory LH receptivity which occurs as estrogen levels decline while progesterone levels increase.

LH is important for the maintenance of the corpus luteum and it is also the important luteotropin for most domestic animals. The CL is maintained in either pregnant or non-pregnant animals by a relatively slow pulsatile pattern of LH release (1 pulse/2-3 minutes).

Prolactin is the most important luteotropin in rodents. Daily biphasic release of prolactin is initiated by copulation which is essential for the maintenance of the CL. In sheep and dogs prolactin is also the luteotropin.

PGF<sub>2α</sub>, a 20-carbon unsaturated fatty acid is the uterine substance that causes corpus luteum regression in large domestic animals (cattle, goats, horses, pigs and sheep). PGF<sub>2α</sub> has no known natural role in CL regression in cats, dogs and primates.

Regression of the CL is important in large domestic non-pregnant animals so that such animals will enter a potentially fertile state as soon as possible. The corpus luteum's life span after ovulation must be of sufficient duration to allow a newly developing conceptus to synthesize and release factors that allow the corpus luteum to be maintained but it must be relatively short so that a non-pregnant animal can return to a relatively fertile state.

In large domestic animals, luteal phase duration is about 14 days which allows them to recycle at relatively frequent interval approximately every 3 weeks.

### **Ovarian cycle**

The ovarian cycles in non-pregnant animals is defined as the interval between successive ovulations and is composed of 2 phases.

1. Follicular phase
2. Luteal phase

Ovulation separates these 2 phases. Spontaneous ovulators (most domestic animals and primate) go thru an ovulatory process governed by an internal mechanism. Estrogen from the antral

follicles initiates the ovulatory release of gonadotropins. Induced ovulators (cats, rabbits, ferrets, minks, camels, llamas) are animals that require copulation for ovulation. Copulation replaces estrogen as the stimulus that induces the ovulatory release of gonadotropins. However these animals require exposure to elevated concentrations of estrogen before they can respond to copulation by the release of gonadotropins.

Spontaneous ovulators have 2 phases in their ovarian cycles (follicular and luteal) while induced ovulators have only the follicular phase. The period of pregnancy (gestation period) starts with fertilization and ends with parturition. The average length of gestation differs among species and in addition, both breed and specie differences occur.

For example, the average gestation period for brown Swiss cows is 292 days and 278 days for Ayshire and Holstein Fresian cows. Gestation periods are slightly longer when cows or mares have a male as compared to a female foetus.

Specie	Oestrous length	Oestrus Length	Time of Ovulation	Gestation Period
Cow	21 days	18 hours	18 hours after end of estrus	280 days
Ewe	17 days	36 hours	30 hours after beginning of estrus	147 days
Sow	21 days	45 hours	36 - 40 hours after beginning of estrus	113 days
Mare	21 days	5-6 days	Last day of estrus	345 days
Doe	20 days	40 hours	30 – 36 hours after beginning of estrus	147 days
Bitch	In estrus @ 7-8	Proestrus – 9 days	1st or 2nd day of estrus	64 days

	months interval depending on breed	Estrus – 7-9 days		
Queen	16 days	5-6 days	Induced 24 – 36 hours after coitus	65 days

### **Average lengths of various parts of the reproductive cycles of domestic animals.**

#### **Ovum Transport**

At the time of ovulation, the fimbriae of the products are engulfed with blood and are in close contact with the surface of the ovary. The contractile activity of the fimbriae contributes to the transfer of the ova to the funnel shaped opening of the oviduct, the infundibulum.

The ovum is then transported to the ampullary part of the muscular oviduct (where fertilization takes place) via contraction of the oviductal musculature and via movement of mucosal cilia that beat towards the uterus. This allows ova to move against the flow of oviductal fluid.

#### **Fertilization**

In most domestic animals, the ovum remains viable for about 12 - 18 hours after ovulation. The process of fertilization can be defined as the fusion of the male and female gametes to form one single cell, the zygote.

The first important stage of fertilization involves the passage of spermatozoon via the zona pellucida (it is believed that the spermatozoon penetrates the zona pellucida with the aid of the enzymes- **hyaluronidase and acrosin**). The motility of the sperm is also considered important for the penetration of the zona. Once contact with the zona occurs motility ceases.

At the time of fertilization, the ovum consists of a nucleus surrounded by plasma or vitelline membrane. The ovum is invested with a mucoprotein coat. The special granulosa cells called the cumulus oophorus are usually lost rapidly after ovulation.

When the spermatozoon penetrates the zona pellucida, a zona reaction occurs. This reaction is a protective mechanism preventing penetration of the vitelline membrane by other spermatozoa. This is important since polyspermy is deleterious to the development of a normal zygote.

### **Parturition**

For the delivery of the foetus (es) it is important that the uterine myometrium is converted from a quiescent organ (which is essential for pregnancy maintenance) to an actively contracting one.

### **Sequence of Endocrine events in the dam**

Pre-partum rise of oestrogen production occurs approximately 3-4 weeks in the cow. Estrogens are important for the production of uterine contractile proteins during the last stage of pregnancy. It is possible that oestrogen serves as the signal for the release of  $\text{PGF}_{2\alpha}$  in the immediate pre-partum period.  $\text{PGF}_{2\alpha}$  synthesis and release occurs 26-30 hours prior to term in the cow.  $\text{PGF}_{2\alpha}$  initiates regression of the CL and thus cause progesterone withdrawal much in the same manner as occurs during the termination of the luteal phase of the ovarian cycle.

Pre-partum luteolysis passively allows the myometrium to become more contractile.  $\text{PGF}_{2\alpha}$  also has an effect on uterine musculature by increasing its contractile state. This initial increase in contractility of uterine musculature may be important for the start of the first stage of labour i.e. the presentation of the foetus at the internal os of the cervix in the so called diver's position.

The pressure of the foetus on the cervix may also facilitate the opening of the cervix.  $\text{PGF}_{2\alpha}$  also has an indirect effect on uterine contractility by making the uterine musculature more sensitive to oxytocin.

Finally, there is some evidence that  $\text{PGF}_{2\alpha}$  is involved in the relaxation of the substance possibly via the dissolution of the ground substance that binds fibrocytes and fibroblasts together and in a manner similar to the rupture of the follicle (during ovulation).

In the pig, relaxin may also play a role in the softening of the cervix. The positioning of foetus and dilation of the cervix constitute stage 1 of delivery. The stage of expulsion of the foetus is referred to as stage 2 of delivery.