REPRODUCTION IN ANIMALS

The organization of the gonads is under genetic control. The initial development of the embryonic ovary involves the migration of germ cells into the genital ridge from the yolk sac. These primordial (primitive) germ cells populate sex cord that have formed in the cortical region of the embryonic gonad from the proliferation of cells from the coelomic epithelium (so called germinal epithelium) of the genital ridge. The sex cords contribute cells, known initially as **follicle cells** and subsequently as **granulosa cells**, which immediately surrounds the oocyte. The mesenchyme of the genital ridge contributes cells that will become the theca. The entire structure is called a **follicle**, which includes **oocytes**, **granulosa**, and the **theca cells**. No direct connections are formed between the oocytes and the tubes destined to become the oviducts, which are derived from Mullerian ducts. The final result is that oocytes are released through the surface of the ovary by rupture of tissue elements that surround the ovary, this process is termed **ovulation**. A specialized end of the oviduct, the fimbria, develops to enable the oocyte to be removed efficiently from the surface of the ovary. In some animals, oocytes are funneled to the fimbria through the use of a bursa, which tends to encompass the ovary; oocytes are then directed to a relatively small opening in the bursa.

In the male, development of the embryonic testis is similar to that of the ovary; germ cells migrate into the genital ridge and populate sex cords that have formed from the invaginations of the (coelomic) epithelium. Sertoli cells (male counterpart of granulosa cells) develop from the sex cords, and Leydig cells (male counterpart of thecal cells) develop from the mesenchyme of the genital ridge. One fundamental difference from the ovarian developments is that the invagination of the sex cords in the male continues into the medulla of the embryonic gonad, where connections are made with medullary cords from the mesonephros (primitive kidney). The duct of the mesonephros (the Wollfian duct) becomes the epididymis, vas deferens and urethra, which has a direct connection to the seminiferous tubules. Thus, male germ cells pass to the exterior of the animal through a closed tubular system.

IMPORTANCE OF TESTOSTERONE IN THE DEVELOPMENT OF THE REPRODUCTIVE SYSTEM

Sexual organization of the genitalia depends on the presence or absence of testosterone. The development of the genital tubular system and the genitalia is under the control of the developing gonad. If the individual is female i.e. developing gonad is an ovary, the **Mullerian duct develops into oviduct, uterus, cervix and vagina** whereas the Wolffian duct regresses. The absence of testosterone is important for both changes. If the individual is male, the rete testis (embryonic) produces Mullerian inhibiting factor which causes regression of the Mullerian duct. ***The Wolffian duct is maintained in the male because of the influence of antigens produced by the testis.***

In summary, the Mullerian ducts are "permanent" structures and the Wolffian ducts are "temporary" structures unless acted upon by the presence of male hormones.

Note: The presence of an enzyme: 5 α-reductase is important for the effect of the androgens because testosterone must be converted intracellularly into dihydrotestosterone for masculinization of the tissues to occur.

Development of the external genitalia follows the development and direction of the gonads. If the individual's genotype is female, folds of tissue called labia form the vulva and a clitoris develops. If the individual is male, androgens from the testis direct formation of the penis (male counterpart of the clitoris) and the scrotum (male counterpart of the labia). Again, the absence or presence of androgens is an important factor influencing the formation of external genitalia.

The final organization of the individual animal with regards to gender comes with sexual differentiation of the hypothalamus. Exposure of the hypothalamus to androgens at about the time of birth causes the hypothalamus to be organized as male. In the absence of androgens, the hypothalamus is organized as female. The fundamental concept of organization of the reproductive system with regards to genotype is that the female system is organized in the absence of testes. If the individual is to be male there must be active intervention by the testes through the production of androgens and appropriate tissue enzymes in two circumstances:

(i) Within the internal genitalia for conversion to more potent androgens.

(ii) Within the hypothalamus for conversion to oestrogen.

HYPOTHALAMO-PITUITARY CONTROL OF REPRODUCTION

The hypothalamus and anterior pituitary (adenohypophysis) secrete protein and peptide hormones which control gonadal activity. The hypothalamus is a relatively small structure that lies mid-central in the base of the brain. It is divided into halves by the third ventricle and actually forms the ventral and lateral walls of the third ventricle. The hypothalamus has clusters of neurons collectively called nuclei which secrete peptide hormones important for controlling pituitary activity. These peptides move to the pituitary either directly by passage, through the axons of neurons or by a vascular portal system. The pituitary responds to hypothalamic peptides to produce hormones that are important for the control of the gonads.

The anterior pituitary produces FSH (follicle stimulating hormones), LH (Luteinizing hormones) and prolactin all of which control reproductive process. Other pituitary hormones include growth hormone, ACTH (adrenocorticotrphic hormone or corticotropin) and TSH (thyroid stimulating hormone). FSH and LH are synergestic in folliculogenesis and ovulation in the ovary. FSH plays a more dominant role during the final stages of follicle maturation through ovulation.

Gonadotropins, as well as TSH are called glycoproteins because their molecules contain carbohydrate moieties that contribute to their functions. Oxytocin, which is released by the posterior pituitary, is a hormone of reproductive importance.

There are 2 sets of neurons within the hypothalamus: - the supraoptic and paraventricular nuclei are responsible for the synthesis of vasopressin and oxytocin respectively. These small peptide hormones are coupled to larger particle molecules called **neurophysins** and are transported from the site of synthesis in the hypothalamus (neural cell bodies), through axons to the site of storage and eventual release (the neurohypophysis).

N.B: Oxytocin and vasopressin are the only hormones produced by the hypothalamus but are stored in the neurohypophysis (posterior pituitary)

There is also a venous portal system which connects the median eminence within the hypothalamus to the adenohypophysis.

Hypothalamic substances that control the anterior pituitary are carried from the median eminence of the hypothalamus to the pituitary by a venous portal system e.g GnRH (gonadotropin releasing hormone), a peptide is produced in the medial preoptic nucleus, and dopamine, an amino acid, is produced in the arcuate nucleus. Axons transport both substances from the hypothalamus to the median eminence where they are released into the venous portal system.

GAMETOGENESIS

Gametogenesis is the production of gametes. Production of eggs is termed oogenesis, while production of sperm cells is termed spermatogenesis. Both processes take place in the gonads namely testes in male and ovaries in the female. These two processes involve meiosis, the type of nuclei division which halves the number of chromosomes from 2 sets (diploid condition) to 1 set (haploid condition). The cells undergoing meiosis are called mother cells. Sperm mother cells are spermatocytes while that of eggs are called oocytes.

Gametogenesis in the male animals and female animals starts with cells in the outer layer of the gonads known as the germinal epithelium. This process involves 3 stages in both sexes: -

- ***Multiplication stage***
- ***Growth stage***
- ***Maturation stage***

Multiplication involves repeated mitotic divisions producing many spermatogonia and oogonia. Each then undergoes a period of growth in preparation for the first mitotic division and cell division. This marks the beginning of the maturation stage during which the 1^{st} and 2^{nd} mitotic division occur followed by the formation of matured haploid gametes.The gametes produced by a given individual will show variation as a result of independent assortment of chromosomes and crossing over during meiosis.

MALE REPRODUCTIVE PROCESSES

The major functional part of the male genital system of domestic animals includes the scrotum, testes, rete tubules, efferent tubules, epididymis, penis and several accessory glands including the prostate, seminal vesicles and bulbourethral glands. The spermatozoa are produced within the seminiferous tubules in the testes by the process of spermatogenesis and spermiogenesis. The spermatozoa pass into the epididymis where they are stored and undergo maturation until the time of ejaculation. Many of them (spermatozoa) degenerate and are reabsorbed by the epididymal epithelium and ductus deferens. Many are also lost in the urine.

The secretions of the accessory glands are added to the spermatozoa at the time of ejaculation.

The reproductive organs of the ram have several unique features. These include:

- the prostate gland is disseminate (spreads widely)
- the penis is characterized by a filiform appendage containing the urethra.

The reproductive organs of the boar are characterized by relatively large seminal vesicles and bulbourethral glands which contribute in a major way to the large volume of semen produced.

The penis of the stallion is extremely vascular and does not have the sigmoid flexure as the ram and boar. The urethra produces several centimeters of the glans penis.

The most remarkable features of the male dog's reproductive tract are the os penis and the absence of all accessory glands except the prostate.

Under the influence of the pituitary gonadotropins, the testis produces male or androgenic hormones. The interstitial cells sometimes called the Leydig cells intersparsed among the seminiferous tubules are the major source of the androgenic hormones.

SPERMATOGENESIS

This represents the total of all changes that results in the transformation of the stem cells or spermatogonia lining the seminiferous tubules into free spermatozoa within the lumen. This changes in the seminiferous epithelium all occurs in proximity to a second cell type the, Sertoli cell. These large cells are attached to the basement membrane and have numerous long processes which may contact other cells within the tubules. They are believed to serve as nurse cells for the developing spermatids.

The process of spermatogenesis consists of a complex series of events in all of the domestic animals. The primordial germ cells or gonocytes are contained in the seminiferous tubules during the foetal period and at birth. These multiply and give rise to spermatogonia which undergo a series of mitotic divisions resulting in primary spermatocytes.

There are 3 types of spermatogonia that are present in most animals. The type A spermatogonia divides to yield intermediate spermatogonia and dormant Type A cells. Intermediate cells further divide to yield type B spermatogonia which further divide to yield 16 primary spermatocytes. Thus 4 division yields 16 primary spermatocytes from type A spermatogonium. The dormant type A cells later behaves as its parents, thus ensuring the continuity of spermatogenesis.

The primary spematocytes later undergo a long evolution known as meiotic prolapsed, via leptotene, zygotene, pachytene and diakinesis resulting in secondary spermatocytes. The secondary spermatocytes then divide, forming the spermatids each containing half of the chromosomes. Thus before spermatids are theoretically produced from each sperm cell, some of these cells degenerate during normal spermatogenesis. The remaining then undergoes a long series of developmental changes resulting in the formation of spermatozoa. The exact number of spermatogonial divisions is specie specific and stable.

Gonocytes

↓

Type A spermatogonia

↓

Intermediate spermatogonium &

Dormant Type A

↓

Type B spermatogonium

↓

1^o spermatocytes

↓

2^o Spermatocytes

↓

Spermatids

EFFECT OF CASTRATION

If an animal is castrated, it becomes sterile. In some species, involution of the secondary sexual characters occurs. Castration of the cockerel is followed by atrophy of the comb and wattles with a loss of the red colour and loss of courtship behaviour and loss of pugnacity.

In mammals, the accessory ducts and glands involute following castration. If castration is performed pre-puberally, the secondary characteristics do not develop.

In man, the larynx remains small and the voice high pitched. Hair growth on the face and body is suppressed and there is lack of libido. After castration, the body conformation typical of the male of various animal species does not develop.

Castration retards closure of the epiphyses of long bones. If castration is performed after the age of puberty has been attained, the male secondary sex characters persist to a variable degree depending on age, species and other factors.

SPERMATOZOON

The bovine sperm head can be described as consisting of homogenous, flattened nucleus, covered anteriorly by a loose, thin dense, post nuclear cap. The head or cap covers the anterior 55-60% of the anterior portion of the nucleus.

It also has a thick, middle piece with inner and outer membrane. The tail of the spermatozoon consists of a thick, middle piece, a long thin principal piece and a short terminal piece.

COMPOSITION OF SEMEN (using the bull as an example)

Semen is composed of the spermatozoon and fluid from the testes and the secretions of the accessory glands and ducts particularly the prostate and seminal vesicles. The bulbourethal glands also contribute to the fluid portion of the ejaculate.

The fluid portion of semen is referred to as seminal plasma. The volume of the ejaculate in domestic animals ranges from about 1ml in the ram to about 20ml or more in the boar. There is remarkable difference in chemical composition of semen from the several species of domestic animals. The differencess are both quantitative and qualitative but unfortunately, the physiologic significance of many of these differences is unknown.

FEMALE REPRODUCTIVE PROCESSES

Reproductive hormones are divided into gonadal (sterioid) hormones and anterior pituitary hormones. Steroid hormones are the major type of hormone involved in the female reproductive system and they are divided into pregnanes and estranes. The most important pregnane is progesterone produced by the corpus (CL), placenta and the adrenal cortex. Control of progesterone synthesis is handled by corpus luteum and is via the luteinizing hormone (LH) in the non-pregnant animal.

Prolactin also has a luteotropic role in some species particularly in the rat, mouse and ewe.

The most important estranes are estradiol-17β and estrone and predominate in the domestic non-pregnant and pregnant animals respectively. Estriol, another important estrane is found only in primates during pregnancy.

The sites of estrogen production are the ovary, the foetoplacental unit and the adrenal cortex. The control of ovarian estrogen synthesis is by FSH.

Functions of Oestrogen

1. Stimulates growth of endometrial glands (the glands lining the internal wall of the uterus) which is necessary for maintenance of the zygote prior to implantation.
2. Stimulates ductal growth in the mammary gland.
3. Causes secretory activity in the oviduct which enhances survival of oocytes and spermatozoon.
4. Initiates sexual receptivity (during the heat period).
5. Regulates gonadotropin secretion including the ovulatory release of LH from the anterior pituitary.
6. May be responsible for the release of PGF-$_{2\alpha}$ (prostaglandin $F_{2\alpha}$) from both the non-gravid and gravid uterus in both cases to cause the regression of the corpus luteum.
7. Stops growth of long bones by initiating closure of the epiphyseal growth plate.
8. Promotes protein anabolism.
9. Estrogen is epithelotropic i.e. promotes the growth of epithelium.

Functions of progesterone

1. Promotes endometrial gland growth.
2. Promotes lobulo-alveolar growth in the mammary gland.
3. Promotes secretory activity of the oviduct and endometrial glands to provide nutrients for the developing zygote prior to its implantation.
4. Promotes cyclic estrus in some species (ewe and bitch) in conjunction with estrogen.
5. Prevents contractility of the uterus during pregnancy and promotes pregnancy by preventing uterine contractions.
6. Regulates secretions of Gonadotropins.

N.B: It is important to recognize that the action of progesterone often occurs in synergism with estrogen and often requires estrogen priming..

ANTERIOR PITUTARY HORMONES

FSH, LH and Prolactin are the three hormones produced by the anterior pituitary that are important for the reproductive processes in the female. FSH and LH are carbohydrate moieties and together with thyrotropic hormone (TSH) form a group of pituitary hormones classified as glycoproteins.

The main function FSH is to promote follicle growth. LH is important for ovulatory processes and luteinization of the granulosa which is essential for the formation of the corpus luteum (luteal body). The actions of FSH and LH are synergistic.

In mammals, the most important function of prolactin is concerned with the development of secretory tissue in the mammary gland and the maintenance of lactation. Prolactin is luteotropic in some species (rat, mouse and probably sheep).

OVARIAN FUNCTION

Folliculogenesis

The establishment of cyclic ovarian activity at puberty is important both for the production and release of gametes as well as for the establishment of full sexual development.

In the female the hypothalamo-pituitary system develops in the absence of hormonal stimuli while in the male, neuro-endocrine system develops in late foetal and early neonatal life. The female system reaches maturity much later.

Gamete production proceeds by means of mitotic divisions of the primordial germ cells that populate the embryonic ovary. Mitosis ceases at around birth in the female at which time gametes are induced to begin meiosis by a factor originating from the rete ovarii. At this point all oocytes a female will ever have are present and if destruction of the gametes should occur, the animal will be rendered infertile.

During the initiation of meiosis, the oocytes are surrounded by a single layer of cells that form the primordial follicle.This unit is complete with the formation of a surrounding basement membrane produced by the follicular cells.

Meiosis is soon arrested by an unknown factor at dictyotene (the resting stage) with resumption not occurring until puberty and then gradually for only a few follicles each day as follicles begin actively growing during the reproductive life of the animal.

The control of the re-establishment of growth and development of the **primordial follicles** is not fully understood except that it is independent of gonadotropic hormone influence. During the initial (hormone independent) phase of follicle development, the oocytes increase in size and activity which includes the production of RNA and ribosomes. The follicles cells that begin to grow and divide during this period are called **granulosa cells**. These cells produce a glycoproeteinaceous substance that form a layer immediately around the oocytes called the **zona pellucida**. Granulosa cell are more important for communication among these cells which lack a direct blood supply. Granulosa cells maintain contact with oocytes by cytoplasmic processes that form gap junctions with the oocytes. Gap junctions also form between the granulosa cells and are important for communication among these cells. Spindle shaped cells that organize around the exterior of the basement membrane become the theca. Nutrient supply to the granulosa cells and oocytes come from the vascularized theca.

The follicle at the end of the hormone-independent stage is still pre-antral. The synthesis of the receptors for FSH and estrogen in the granulosa and of the LH receptors in the theca is important for follicles to enter the hormone-dependent stage.

Selection of the ovulatory follicles

A few follicles leave the primordial state each day and begin to develop. Follicular development results in either regression (atresia) and destruction or ovulation. What determines which will undergo atresia and which undergoes ovulation is not known for certain.

Follicles continue to grow and develop during all phases of the estrus cycle though the process is reduced during the luteal phase. The follicles to be ovulated will usually be the largest, actively growing follicles that are present at the time of regression of the corpus luteum

Spontaneity of Ovulation

In many species, ovulation takes place continuously following normal follicle growth at the proper stage of the estrus or menstrual cycle. This means that a proper secretory pattern of estrogen is almost always able to elicit a surge release of LH that results in ovulation **(i.e. pre-ovulatory LH surge)**. Examples of spontaneous ovulators include the bitch, cow, doe, mare, sow, primates and some laboratory species including the mouse, rat and guinea pig.

Animals that are called induced ovulators are those that ovulate spontaneously even if follicle growth and development are normal. These animals require coital contact for ovulation to be induced. Examples are cats, rabbits