COURSE CODE: VBP202

COURSE TITLE: DIGESTIVE, REPRODUCTIVE AND ENDOCRINE PHYSIOLOGY

NUMBER OF UNITS: 3 Units

COURSE DURATION: Three hours per week

COURSE DETAILS:

Course Coordinator: **Dr. Eyitayo Solomon Ajibola,** D.V.M, M.Sc.
Email: esajibola@ unaab.edu.ng
Office Location: Dept of Veterinary Physiology/ Pharmacology, COLVET, UNAAB
Other Lecturers: **Dr. O.E Adeleye**

COURSE CONTENT:

Digestion and absorption of nutrients in monogastric and ruminanat animals. Endocrine functions of the gastrointestinal tract. Digestion in chickens. Male; Female reproduictive process; Fertilization, Pregnancy, Parturition and Lactation. Comparative reproduction physiology; mechanism of secretion, regulation and functions of hormones from Gonads, Pituitary, Thyroid, Adrenal, Parathyroid, Pancreas. Effects of hyper secretion of hormonal glands

COURSE REQUIREMENTS:

This is a compulsory course for all pre-clinical Veterinary Medical Students. In view of this, students are expected to participate in all the course activities and have a minimum of 75% attendance to be able to write the final examination.

READING LIST:

1. James G. Cunningham and Bradley G. Klein. Textbook of Veterinary physiology, 4thedition. Saunders Elsevier, Missouri, 2007.

2. Duke' Physiology of domestic Animals 10TH ed. Cornell University Press, London. 1984

LECTURE NOTES

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 1st and 2nd 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 interspersed 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, ferrets, minks, camels and llamas.

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 grown 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^{nd} dominant follicle or if a third will develop. If the 2^{nd} dominant follicle has begun to regress at the time of regression of the corpus luteum, a 3^{rd} dominant follicle develops. Therefore, the 2^{nd} 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 $PGF_2\alpha$** 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 propia 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.

$PGF_{2\alpha}$, 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). $PGF_{2\alpha}$ 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 months interval depending on breed	Proestrus – 9 days Estrus – 7-9 days	1st or 2nd day of estrus	64 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 $PDF_{2\alpha}$ in the immediate pre-partum period. $PGF_{2\alpha}$ synthesis and release occurs 26-30 hours prior to term in the cow. $PGF_{2\alpha}$ 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. $PGF_{2\alpha}$ 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. $PGF_{2\alpha}$ also has an indirect effect on uterine contractility by making the uterine musculature more sensitive to oxytocin.

Finally, there is some evidence that $PGF_{2\alpha}$ 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.

REPRODUCTIVE CYCLES

1. Estrous cycle 2. Menstrual cycle

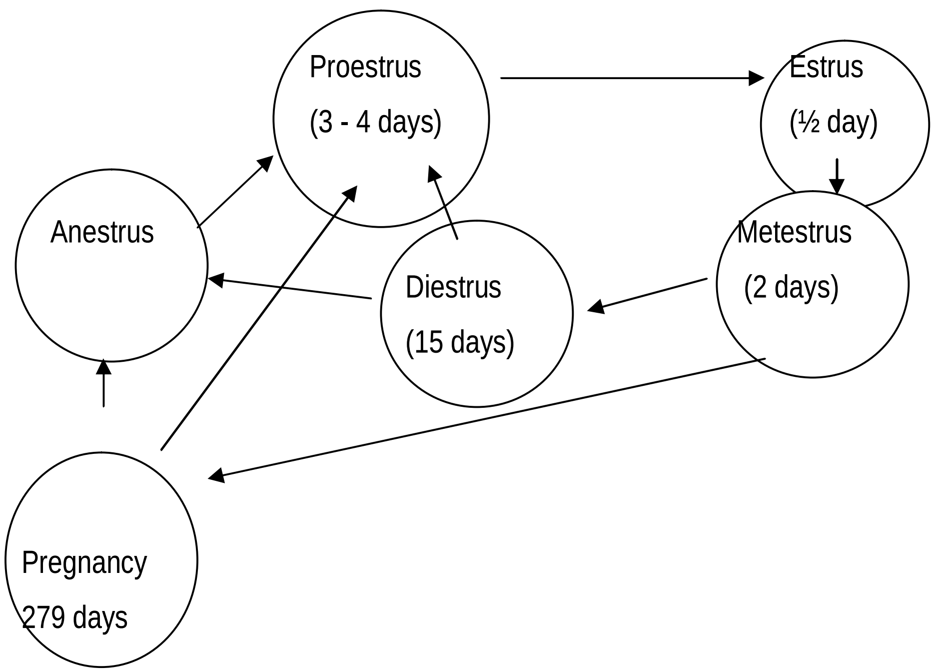
In domestic animals, we have limited period of estrus (sexual receptivity) and the term estrous cycle is used. The onset of proestrus defines the start of the cycle. In primates who are sexually receptive during most of the reproductive cycle, we use the term menstrual cycle. The onset of menstruation (vaginal discharge of blood tinged fluids and tissue) is designated as the start of the cycle. The first day of the cycle for estrus and menstrual cycles in many species begins shortly after the end of the luteal phase.

In the dog, a normal anestrus period lasting approximately 3 months separates diestrus and proestrus. In domestic animals, proestrus usually begins 48 hours after the end of the luteal phase. The dog and pig are exceptions, with proestrus in the pig not occurring for 5-6 days. In primates, menstruation usually begins within 24 hours of the end of the luteal phase. The time of ovulation differs even though both cycles begin at the same time in relation to the luteal phase. This is due to the fact that luteal and follicular phases are separated in primates by ovulation occurring at a minimum of 12-13 days after the onset of menses.

In most domestic animals, the follicular phase overlaps the luteal phase and therefore occurs relatively early in the estrous cycle. The estrous cycle has been divided into stages that represent either behavioural or gonadal events.

1. **Proestrus**: This is a period of follicular development occurring subsequent to luteal regression and ending at estrus.
2. **Estrus**: time of sexual receptivity with ovulation usually occuring at the end of estrus
3. **Metestrus** : This is a period of initial development of the corpus luteum
4. **Diestrus**: This is the period of the mature phase of the CL. This term was originally developed for the guinea pig, rats and mouse.

The common terms used for domestic animals involved behavioural or gonadal activities.



Various stages of the ovarian cycle of the cow.

The cycle can be described in a behavioural manner by indicating whether animals are in oestrus or not, including the stage of proestrus, metestrus and diestrus. The cycles can also be described with reference to gonadal activities if differentiation of follicles and CL is possible.

Animals can be in the folliculars phase (proestrus and estrus) or the luteal phase (metestrus and diestrus). Because the equine corpus luteum is relatively difficult to identify by rectal palpation, horses are usually classified by sexual behaviour into estrus or non-estrus (on heat/not on heat). Also, because of the difficulty in determining ovarian status in domestic species like goat, pig and sheep, behavourial classification is used. In the cow, ovarian status can be determined accurately by rectal palpation and are classified as follicular of luteal. In dogs and cats measurement of serum progresterone levels is used to determine their ovarian status.

N.B: If a corpus luteum can be identified, judgment can be made that ovarian activity is normal in the particular animal because it represents the culmination of follicular growth and ovulation.

Read up – External factors controlling reproductive cycle

Check up – puberty

- Senescence

AVIAN REPRODUCTION

ANATOMY OF THE FEMALE REPRODUCTIVE SYSTEM

The reproductive organ of the adult hen includes the left ovary and the left oviduct. The right ovary and oviduct formed in embryonic life do not persist in adult life.

A persistent right ovary and oviduct have been reported but they are rare. The ovary of an immature bird is made up of a mass of small ova. This enlarges rapidly during sexual development and attains a diameter of about 40 mm before they are ovulated.

The oviduct is quite long and convoluted and is made up of 5 distinct areas viz,

- the in fundibulum or funnel
- the magnum (largest part of the oviduct)
- the isthmus
- the shell gland (uterus) and
- the vagina which is the part leading from the uterus to the cloaca

Located at the uterovaginal junction are tubular glands in which are stored spermatozoa from the male. The functional lifespan of the spermatozoa is greatly prolonged by the storage.

LAYING HABIT

Laying behaviour of birds is influenced by:

1. the sequence in which the eggs are laid
2. lengths of time or interval between breaks/ interruptions in the sequence
3. by whether or not the birds incubate their eggs after laying

*Find out the interval between the laying of an egg and another in commercial birds.

A sequence represents a number of eggs laid on successive days before there is an interruption or a skip. Wild birds usually lay a number of eggs in sequence and then stop laying and sit on their eggs, these are often named clutches. Most hens lay during the daylight hours and the better laying ones lay in the early hours.

Rate of laying or frequency represents the number of eggs laid over a given period of time and is expressed as a percentage. The rate of egg laying in highly bred flocks of chicken averages about 25 eggs per bird per year and may be higher in laying breeds of ducks.

Hormonal Control of Oviposition

The uterus must contract to expel the egg via the vagina and the cloaca. There is evidence that the hormone from the posterior pituitary called vasotocin may initiate the contraction of the uterus which leads to oviposition (dropping of the egg).

The posterior lobe of the chicken contains arginine, vasotocin and the chicken uterus is very sensitive to this hormone.

Other factors that influence oviposition:-

- Acehylcholine increases uterine contractions and causes oviposition or explusion
- Sodium pentobarbital and foreign bodies in the uterus also cause premature expulsion of the egg from the uterus

FORMATION AND GROWTH OF OVA

As sexual maturity is approached the ova begin to grow at a rapid rate and in the chicken may be fully matured between 9-10 days. The matured ovulated ovum weights 16-18 grams.

FSH of the anterior pituitary is responsible for the growth and maturation of the ovarian follicle. The size of the egg yoke is influenced in part by the laying sequence because the first egg of the sequence has a larger yolk than the succeeding one.The yellow pigment **xanthophyll** is responsible for the colour of the yolk.

OVULATION

The release of the ovum from the ovarian follicle (ovulation) is caused by the rupture of the follicular membrane at the **stigma** (a relatively avascular area of the follicle). Ovulation occurs in the chickens usually within 15 to 45 minutes after oviposition.

Daylight or artificial light affects ovulation and laying rates by stimulating the pituitary to release ovulatory hormones. Maximum stimulation is produced in chickens by continuous lighting for 12 to 14 hours.

Light is not the only factor which may affect the release of ovulating hormones.

ANATOMY

The reproductive organs of the male includes the testes, penis, vasa differentia and the epididymis. The paired testes are located in the abdominal cavity and just cephalic to the kidneys and below the kidneys. Birds have no seminal vesicles and bulbourethral glands as in mammals.

The testes are without septa and lobules but consist of seminiferous tubules, rete tubules and vasa efferentia. The penis of roosters is quite small and when erected is engorged with lymph from the lymph nodes. This lymph fluid is added to the semen in the vas deferens and both are ejected simultaneously along the longitudinal groove of the phallus.

Reproductive organs of the turkey are similar to the chicken. Duck and goose have well developed phallus which are spiral and which act as intromitant organs. The sperm passes from the seminiferous tubules via the rete tubules by way of the vasa efferntia and finally via the vasa differentia. Sperm are not usually stored in the epididymis or other accessory organs in the chicken.

The stages of spermatogenesis vary according to the age and growth rate of the bird, but in the chicken, the first stage appears at about 5 weeks of age.

At this stage, there are numerous spermatogonal cells which have undergone organization and multiplication. At about the 6^{th} week and the next week or two thereafter, the primary spermatocytes begin to appear.

By 10 weeks of age, the secondary spermatocytes begin to appear and immature spermatozoa (spermatids) first appear at about 14 weeks of age in the seminiferous tubules. They are present in all tubules at the 20th week.

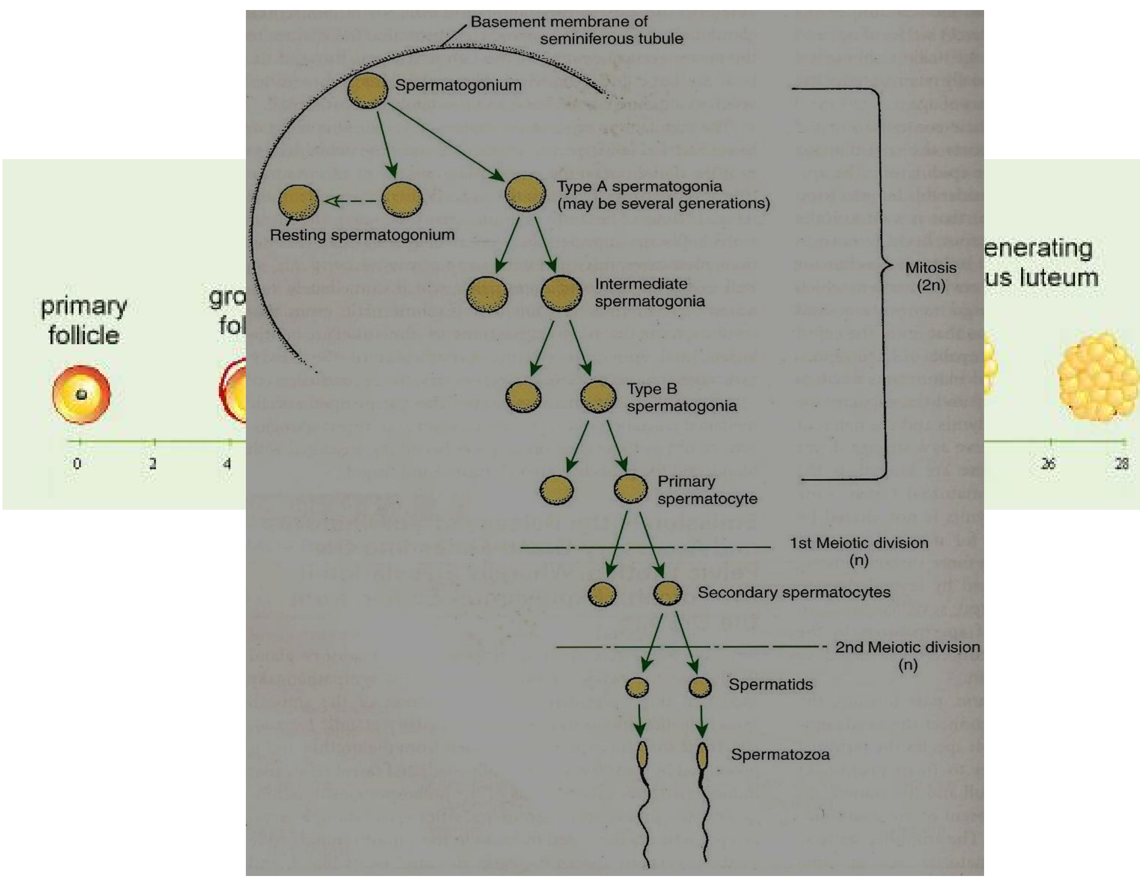
Testis weight may approach 30 to 40 grams in old males. There is a great deal of variation in size and shape of spermatozoa of different birds. The spermatozoon of the chicken has a long head piece with a pointed acrosome and a short mid-piece to which is attached a long tail.

*	Note: Search for the different variations in the size an shape of spermatozoa of different birds – Guinea fowl, pigeon, ostrich, penguin

Growth and development of the testis and spermatogenesis are stimulated by FSH of the anterior pituitary. The interstitial cell of the mature testis secretes androgens (testosterone) which is the male hormone. Chicken semen is usually white and opaque but it may be clear and watery depending on the concentration of the sperm.

The number of spermatozoa in a given ejaculate ranges from about 1.7 to 3.5 billion. Mating frequency of a normal male may range from 25 to 41 times per day or higher.

Among the many factors affecting fertility in chicken is nutrition, state of health, light, season and age of the males and females.



A) Reproductive hormones

a. **Follicle-stimulating hormone** regulates gamete formation.

b. **Luteinizing hormone** plays a key role in controlling breeding because it regulates the secretion of reproductive hormones in the testes and the development of mature ova in the ovaries.

c. **Testosterone** and **estrogen** are produced by the gonads of both males and females, but the relative concentrations of these two hormones differ between the sexes and determine their effects. In many birds, increased testosterone levels in the blood cause the development of secondary sexual characteristics, such as breeding plumage, bright bill and foot colors, growth of skin ornaments, etc.

B) Male reproductive system

a. Male birds have paired testes, which become greatly enlarged during the breeding season.

b. Sperm are produced at night, when body temperatures are slightly lower, and then stored in seminal vesicles which cause a distinct **cloacal protuberance** in breeding males.

C) Female reproductive system

a. Most female birds have only one ovary.

b. In birds, females are the **heterogametic** sex. This means that their sex chromosomes differ as do those of male (but not female) mammals. In birds, females are said to have ZW sex chromosomes, while males are **homogametic** (ZZ).

c. Female birds can store sperm for later use in special tubules in their reproductive tracts.

D) Benefits of oviparity

a. Can produce a larger number of large offspring.

b. Viviparity may be impossible due to the high body temperature of birds.

Endocrine System

Endocrine System: Overview

- Endocrine system – the body's second great controlling system which influences metabolic activities of cells by means of hormones
- Endocrine glands – pituitary, thyroid, parathyroid, adrenal, pineal, and thymus glands
- The pancreas and gonads produce both hormones and exocrine products
- The hypothalamus has both neural functions and releases hormones
- Other tissues and organs that produce hormones – adipose cells, pockets of cells in the walls of the small intestine, stomach, kidneys, and heart

Hormones

- Hormones – chemical substances secreted by cells into the extracellular fluids
- Regulate the metabolic function of other cells
- Have lag times ranging from seconds to hours
- Tend to have prolonged effects
- Are classified as amino acid-based hormones, or steroids
- Eicosanoids – biologically active lipids with local hormone–like activity

Types of Hormones

- Amino acid–based – most hormones belong to this class, including:
- Amines, thyroxine, peptide, and protein hormones

- Steroids – gonadal and adrenocoritcal hormones
- Eicosanoids – leukotrienes and prostaglandins

Hormone Action

- Hormones alter cell activity by one of two mechanisms
- Second messengers involving:
- Regulatory G proteins
- Amino acid–based hormones
- Direct gene activation involving steroid hormones
- The precise response depends on the type of the target cell

Mechanism of Hormone Action

- Hormones produce one or more of the following cellular changes:
- Alter plasma membrane permeability
- Stimulate protein synthesis
- Activate or deactivate enzyme systems
- Induce secretory activity
- Stimulate mitosis

Amino Acid–Based Hormone Action: cAMP Second Messenger

- Hormone (first messenger) binds to its receptor, which then binds to a G protein
- The G protein is then activated as it binds GTP, displacing GDP

- Activated G protein activates the effector enzyme *adenylate cyclase*
- Adenylate cyclase generates cAMP (second messenger) from ATP
- cAMP activates protein kinases, which then cause cellular effects

Amino Acid–Based Hormone Action:
PIP-Calcium

- Hormone binds to the receptor and activates G protein
- G protein binds and activates a phospholipase enzyme
- Phospholipase splits the phospholipid PIP_2 into diacylglycerol (DAG) and IP_3 (both act as second messengers)
- DAG activates protein kinases; IP_3 triggers release of Ca^{2+} stores
- Ca^{2+} (third messenger) alters cellular responses

Amino Acid–Based Hormone Action:
PIP-Calcium

Steroid Hormones

- Steroid hormones and thyroid hormone diffuse easily into their target cells
- Once inside, they bind and activate a specific intracellular receptor
- The hormone-receptor complex travels to the nucleus and binds a DNA-associated receptor protein
- This interaction prompts DNA transcription, to producing mRNA
- The mRNA is translated into proteins, which bring about a cellular effect

Steroid Hormones

Hormone–Target Cell Specificity

- Hormones circulate to all tissues but only activate cells referred to as *target cells*
- Target cells must have specific receptors to which the hormone binds
- These receptors may be intracellular or located on the plasma membrane
- Examples of hormone activity
- ACTH receptors are only found on certain cells of the adrenal cortex
- Thyroxin receptors are found on nearly all cells of the body

Target Cell Activation

- Target cell activation depends upon three factors
- Blood levels of the hormone
- Relative number of receptors on the target cell
- The affinity of those receptors for the hormone
- Up-regulation – target cells form more receptors in response to the hormone
- Down-regulation – target cells lose receptors in response to the hormone

Hormone Concentrations in the Blood

- Concentrations of circulating hormone reflect:
- Rate of release
- Speed of inactivation and removal from the body

- Hormones are removed from the blood by:
- Degrading enzymes
- The kidneys
- Liver enzyme systems

Control of Hormone Synthesis and Release

- Blood levels of hormones:
- Are controlled by negative feedback systems
- Vary only within a narrow desirable range
- Hormones are synthesized and released in response to:
- Humoral stimuli
- Neural stimuli
- Hormonal stimuli

Humoral Stimuli

- Humoral stimuli – secretion of hormones in direct response to changing blood levels of ions and nutrients
- Example: concentration of calcium ions in the blood
- Declining blood Ca^{2+} concentration stimulates the parathyroid glands to secrete PTH (parathyroid hormone)

- PTH causes Ca^{2+} concentrations to rise and the stimulus is removed

Neural Stimuli

- Neural stimuli – nerve fibers stimulate hormone release
- Preganglionic sympathetic nervous system (SNS) fibers stimulate the adrenal medulla to secrete catecholamines

Hormonal Stimuli

- Hormonal stimuli – release of hormones in response to hormones produced by other endocrine organs
- The hypothalamic hormones stimulate the anterior pituitary
- In turn, pituitary hormones stimulate targets to secrete still more hormones

Nervous System Modulation

- The nervous system modifies the stimulation of endocrine glands and their negative feedback mechanisms
- The nervous system can override normal endocrine controls
- For example, control of blood glucose levels
- Normally the endocrine system maintains blood glucose
- Under stress, the body needs more glucose
- The hypothalamus and the sympathetic nervous system are activated to supply ample glucose

Location of the Major Endocrine Glands

- The major endocrine glands include:
- Pineal gland, hypothalamus, and pituitary
- Thyroid, parathyroid, and thymus
- Adrenal glands and pancreas
- Gonads – male testes and female ovaries

Major Endocrine Organs: Pituitary (Hypophysis)

- Pituitary gland – two-lobed organ that secretes nine major hormones
- Neurohypophysis – posterior lobe (neural tissue) and the infundibulum
- Receives, stores, and releases hormones from the hypothalamus
- Adenohypophysis – anterior lobe, made up of glandular tissue
- Synthesizes and secretes a number of hormones

Pituitary-Hypothalamic Relationships: Posterior Lobe

- Posterior lobe – a downgrowth of hypothalamic neural tissue
- Has a neural connection with the hypothalamus (hypothalamic-hypophyseal tract)
- Nuclei of the hypothalamus synthesize oxytocin and antidiuretic hormone (ADH)
- These hormones are transported to the posterior pituitary

Pituitary-Hypothalamic Relationships: Anterior Lobe

- The anterior lobe of the pituitary is an outpocketing of the oral mucosa
- There is no direct neural contact with the hypothalamus

- There is a vascular connection, the hypophyseal portal system, consisting of:
- The primary capillary plexus
- The hypophyseal portal veins

Adenohypophyseal Hormones

- The six hormones of the adenohypophysis:
- Are abbreviated as GH, TSH, ACTH, FSH, LH, and PRL
- Regulate the activity of other endocrine glands
- In addition, pro-opiomelanocortin (POMC):
- Has been isolated from the pituitary
- Is enzymatically split into ACTH, opiates, and MSH

Activity of the Adenohypophysis

- The hypothalamus sends chemical stimulus to the anterior pituitary
- Releasing hormones stimulate the synthesis and release of hormones
- Inhibiting hormones shut off the synthesis and release of hormones
- The tropic hormones that are released are:
- Thyroid-stimulating hormone (TSH)
- Adrenocorticotropic hormone (ACTH)
- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)

Growth Hormone (GH)

- Produced by somatotropic cells of the anterior lobe that:
- Stimulate most cells, but target bone and skeletal muscle
- Promote protein synthesis and encourage the use of fats for fuel
- Most effects are mediated indirectly by somatomedins
- Antagonistic hypothalamic hormones regulate GH
- Growth hormone–releasing hormone (GHRH) stimulates GH release
- Growth hormone–inhibiting hormone (GHIH) inhibits GH release

Metabolic Action of Growth Hormone

- GH stimulates liver, skeletal muscle, bone, and cartilage to produce insulin-like growth factors
- Direct action promotes lipolysis and inhibits glucose uptake

Thyroid Stimulating Hormone (Thyrotropin)

- Tropic hormone that stimulates the normal development and secretory activity of the thyroid gland
- Triggered by hypothalamic peptide thyrotropin-releasing hormone (TRH)
- Rising blood levels of thyroid hormones act on the pituitary and hypothalamus to block the release of TSH

Adrenocorticotropic Hormone (Corticotropin)

- Stimulates the adrenal cortex to release corticosteroids
- Triggered by hypothalamic corticotropin-releasing hormone (CRH) in a daily rhythm
- Internal and external factors such as fever, hypoglycemia, and stressors can trigger the release of CRH

Gonadotropins

- Gonadotropins – follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
- Regulate the function of the ovaries and testes
- FSH stimulates gamete (eggs or sperm) production
- Absent from the blood in prepubertal boys and girls
- Triggered by the hypothalamic gonadotropin-releasing hormone (GnRH) during and after puberty

Functions of Gonadotropins

- In females
- LH works with FSH to cause maturation of the ovarian follicle
- LH works alone to trigger ovulation (expulsion of the egg from the follicle)
- LH promotes synthesis and release of estrogens and progesterone
- In males
- LH stimulates interstitial cells of the testes to produce testosterone
- LH is also referred to as interstitial cell-stimulating hormone (ICSH)

Prolactin (PRL)

- In females, stimulates milk production by the breasts
- Triggered by the hypothalamic prolactin-releasing hormone (PRH)
- Inhibited by prolactin-inhibiting hormone (PIH)
- Blood levels rise toward the end of pregnancy
- Suckling stimulates PRH release and encourages continued milk production

The Posterior Pituitary and Hypothalamic Hormones

- Posterior pituitary – made of axons of hypothalamic neurons, stores antidiuretic hormone (ADH) and oxytocin
- ADH and oxytocin are synthesized in the hypothalamus
- ADH influences water balance
- Oxytocin stimulates smooth muscle contraction in breasts and uterus
- Both use PIP second-messenger mechanisms

Oxytocin

- Oxytocin is a strong stimulant of uterine contraction
- Regulated by a positive feedback mechanism to oxytocin in the blood
- This leads to increased intensity of uterine contractions, ending in birth
- Oxytocin triggers milk ejection (“letdown” reflex) in women producing milk
- Synthetic and natural oxytocic drugs are used to induce or hasten labor

- Plays a role in sexual arousal and satisfaction in males and nonlactating females

Antidiuretic Hormone (ADH)

- ADH helps to avoid dehydration or water overload
- Prevents urine formation
- Osmoreceptors monitor the solute concentration of the blood
- With high solutes, ADH is synthesized and released, thus preserving water
- With low solutes, ADH is not released, thus causing water loss from the body
- Alcohol inhibits ADH release and causes copious urine output

Thyroid Gland

- The largest endocrine gland, located in the anterior neck, consists of two lateral lobes connected by a median tissue mass called the *isthmus*
- Composed of follicles that produce the glycoprotein *thyroglobulin*

Thyroid Gland

- Colloid (thyroglobulin + iodine) fills the lumen of the follicles and is the precursor of thyroid hormone
- Other endocrine cells, the parafollicular cells, produce the hormone *calcitonin*

Thyroid Hormone (TH)

- Thyroid hormone – the body's major metabolic hormone
- Consists of two closely-related iodine-containing compounds

- T_4 – thyroxine; has two tyrosine molecules plus four bound iodine atoms
- T_3 – triiodothyronine; has two tyrosines with three bound iodine atoms

Effects of Thyroid Hormone

- TH is concerned with:
- Glucose oxidation
- Increasing metabolic rate
- Heat production
- TH plays a role in:
- Maintaining blood pressure
- Regulating tissue growth
- Developing skeletal and nervous systems
- Maturation and reproductive capabilities

Transport and Regulation of TH

- T_4 and T_3 bind to thyroxine-binding globulins (TBGs) produced by the liver
- Both bind to target receptors, but T_3 is ten times more active than T_4
- Peripheral tissues convert T_4 to T_3
- Mechanisms of activity are similar to steroids
- Regulation is by negative feedback
- Hypothalamic thyrotropin-releasing hormone (TRH) can overcome the negative feedback

Synthesis of Thyroid Hormone

- Thyroglobulin is synthesized and discharged into the lumen
- Iodides (I^-) are actively taken into the cell, oxidized to iodine (I_2), and released into the lumen
- Iodine attaches to tyrosine, mediated by peroxidase enzymes, forming T_1 (monoiodotyrosine, or MIT), and T_2 (diiodotyrosine, or DIT)
- Iodinated tyrosines link together to form T_3 and T_4
- Colloid is then endocytosed and combined with a lysosome, where T_3 and T_4 are cleaved and diffuse into the bloodstream

Calcitonin

- A peptide hormone produced by the parafollicular, or C, cells
- Lowers blood calcium levels in children
- Antagonist to parathyroid hormone (PTH)
- Calcitonin targets the skeleton, where it:
- Inhibits osteoclast activity and thus bone resorption and release of calcium from the bone matrix
- Stimulates calcium uptake and incorporation into the bone matrix
- Regulated by a humoral (calcium ion concentration in the blood) negative feedback mechanism

Parathyroid Glands

- Tiny glands embedded in the posterior aspect of the thyroid
- Cells are arranged in cords containing oxyphil and chief cells
- Chief (principal) cells secrete PTH
- PTH (parathormone) regulates calcium balance in the blood

Effects of Parathyroid Hormone

- PTH release increases Ca^{2+} in the blood as it:
- Stimulates osteoclasts to digest bone matrix
- Enhances the reabsorption of Ca^{2+} and the secretion of phosphate by the kidneys
- Increases absorption of Ca^{2+} by intestinal mucosal cells
- Rising Ca^{2+} in the blood inhibits PTH release

Adrenal (Suprarenal) Glands

- Adrenal glands – paired, pyramid-shaped organs atop the kidneys
- Structurally and functionally, they are two glands in one
- Adrenal medulla – nervous tissue that acts as part of the SNS
- Adrenal cortex – glandular tissue derived from embryonic mesoderm

Adrenal Cortex

- Synthesizes and releases steroid hormones called *corticosteroids*
- Different corticosteriods are produced in each of the three layers

- Zona glomerulosa – mineralocorticoids (chiefly aldosterone)
- Zona fasciculata – glucocorticoids (chiefly cortisol)

Zona reticularis – gonadocorticoids (chiefly androgens)

Mineralocorticoids

- Regulate the electrolyte concentrations of extracellular fluids
- Aldosterone – most important mineralocorticoid
- Maintains Na^+ balance by reducing excretion of sodium from the body
- Stimulates reabsorption of Na^+ by the kidneys
- Aldosterone secretion is stimulated by:
- Rising blood levels of K^+
- Low blood Na^+
- Decreasing blood volume or pressure

The Four Mechanisms of Aldosterone Secretion

- Renin-angiotensin mechanism – kidneys release renin, which is converted into angiotensin II that in turn stimulates aldosterone release
- Plasma concentration of sodium and potassium – directly influences the zona glomerulosa cells
- ACTH – causes small increases of aldosterone during stress
- Atrial natriuretic peptide (ANP) – inhibits activity of the zona glomerulosa

Glucocorticoids (Cortisol)

- Help the body resist stress by:
- Keeping blood sugar levels relatively constant
- Maintaining blood volume and preventing water shift into tissue
- Cortisol provokes:
- Gluconeogenesis (formation of glucose from noncarbohydrates)
- Rises in blood glucose, fatty acids, and amino acids

Excessive Levels of Glucocorticoids

- Excessive levels of glucocorticoids:
- Depress cartilage and bone formation
- Inhibit inflammation
- Depress the immune system
- Promote changes in cardiovascular, neural, and gastrointestinal function

Gonadocorticoids (Sex Hormones)

- Most gonadocorticoids secreted are androgens (male sex hormones), and the most important one is testosterone
- Androgens contribute to:
- The onset of puberty
- The appearance of secondary sex characteristics

- Sex drive in females
- Androgens can be converted into estrogens after menopause

Adrenal Medulla

- Made up of chromaffin cells that secrete epinephrine and norepinephrine
- Secretion of these hormones causes:
- Blood glucose levels to rise
- Blood vessels to constrict
- The heart to beat faster
- Blood to be diverted to the brain, heart, and skeletal muscle
- Epinephrine is the more potent stimulator of the heart and metabolic activities
- Norepinephrine is more influential on peripheral vasoconstriction and blood pressure

Pancreas

- A triangular gland, which has both exocrine and endocrine cells, located behind the stomach
- Acinar cells produce an enzyme-rich juice used for digestion (exocrine product)
- Pancreatic islets (islets of Langerhans) produce hormones (endocrine products)
- The islets contain two major cell types:
- Alpha (α) cells that produce glucagon
- Beta (β) cells that produce insulin

Glucagon

- A 29-amino-acid polypeptide hormone that is a potent hyperglycemic agent
- Its major target is the liver, where it promotes:
- Glycogenolysis – the breakdown of glycogen to glucose
- Gluconeogenesis – synthesis of glucose from lactic acid and noncarbohydrates
- Releases glucose to the blood from liver cells

Insulin

- A 51-amino-acid protein consisting of two amino acid chains linked by disulfide bonds
- Synthesized as part of proinsulin and then excised by enzymes, releasing functional insulin
- Insulin:
- Lowers blood glucose levels
- Enhances transport of glucose into body cells
- Counters metabolic activity that would enhance blood glucose levels

Effects of Insulin Binding

- The insulin receptor is a tyrosine kinase enzyme
- After glucose enters a cell, insulin binding triggers enzymatic activity that:
- Catalyzes the oxidation of glucose for ATP production
- Polymerizes glucose to form glycogen
- Converts glucose to fat (particularly in adipose tissue)

Regulation of Blood Glucose Levels

- The hyperglycemic effects of glucagon and the hypoglycemic effects of insulin

Diabetes Mellitus (DM)

- Results from hyposecretion or hypoactivity of insulin
- The three cardinal signs of DM are:
- Polyuria – huge urine output
- Polydipsia – excessive thirst
- Polyphagia – excessive hunger and food consumption
- Hyperinsulinism – excessive insulin secretion, resulting in hypoglycemia

Gonads: Female

- Paired ovaries in the abdominopelvic cavity produce estrogens and progesterone
- They are responsible for:
- Maturation of the reproductive organs
- Appearance of secondary sexual characteristics
- Breast development and cyclic changes in the uterine mucosa

Gonads: Male

- Located in an extra-abdominal sac (scrotum), they produce testosterone
- Testosterone :
- Initiates maturation of male reproductive organs

- Causes appearance of secondary sexual characteristics and sex drive
- Is necessary for sperm production
- Maintains sex organs in their functional state

Pineal Gland

- Small gland hanging from the roof of the third ventricle of the brain
- Secretory product is melatonin
- Melatonin is involved with:
- Day/night cycles
- Physiological processes that show rhythmic variations

Thymus

- Lobulated gland located deep to the sternum in the thorax
- Major hormonal products are thymopoietins and thymosins
- These hormones are essential for the development of the T lymphocytes (T cells) of the immune system

Other Hormone-Producing Structures

- Heart – produces atrial natriuretic peptide (ANP), which reduces blood pressure, blood volume, and blood sodium concentration
- Gastrointestinal tract – enteroendocrine cells release local-acting digestive hormones
- Placenta – releases hormones that influence the course of pregnancy

- Kidney – secrete erythropoietin, which signals the production of red blood cells
- Skin – produces cholecalciferol, the precursor of vitamin D
- Adipose tissue – releases leptin, which is involved in the sensation of satiety

Developmental Aspects

- Hormone-producing glands arise from all three germ layers
- Endocrine glands derived from mesoderm produce steroid hormones
- Endocrine organs operate smoothly throughout life
- Most endocrine glands show structural changes with age, but hormone production may or may not be effected
- GH levels decline with age and this accounts for muscle atrophy with age
- Supplemental GH may spur muscle growth, reduce body fat, and help physique
- TH declines with age, causing lower basal metabolic rates
- PTH levels remain fairly constant with age, and lack of estrogen in women make them more vulnerable to bone-demineralizing effects of PTH

Developmental Aspects: Gonads

- Ovaries undergo significant changes with age and become unresponsive to gonadotropins
- Female hormone production declines, the ability to bear children ends, and problems associated with estrogen deficiency (e.g., osteoporosis) begin to occur
- Testosterone also diminishes with age, but effect is not usually seen until very old age