COURSE CODE: ANP 506

COURSE TITLE: Endocrinology

NUMBER OF UNITS:

COURSE DURATION:

COURSE DETAILS:

Course Coordinator: **Dr. Olusiji. F. Smith**
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COURSE CONTENT:

Definition of endocrine glands and hormones. Hormonal effects, morphogenetic effects, homeostatic effects and integrative effects. Classification and functions of hormones, chemical classification, peptide and protein hormones, steroid hormones, classification based on site of production, hypothalamic hormones, hypophysial hormones, gonadal hormones, adrenal hormones, functional classification, primary hormones of repreoduction, secondary hormones of reproduction. Hormonal fuctions. Chemistry of steroid hormones, structure, trivial and systematic names, biosynthesis. Mechanisms of hormone action, steroid hormones, peptide hormones. Hormonal assays

COURSE REQUIREMENTS:

Student Lecture: Each student will give a lecture on a topic in reproduction drawn by lottery. The lecture will be 40-45 minutes in length. A skeleton outline will be given to Dr. Smith the day before the lecture. A more detailed outline of each lecture will be submitted on disk (IBM-compatable) to Dr. Smith to put on the Webpage for the class.

OR

Journal Paper Review: Each student will lead a 25 minute discussion of a scientific research paper of their choice on any topic in reproduction. Papers discussed must be published during 2002 or 2003. Students must make and give copies to classmates and instructors by the Friday before the presentation if not earlier.

Lecture Exam: An Exam will be given on the material from the Instructor and Student Lectures. Each Student will submit two short answer type questions to the instructors following their lecture. These questions may or may not be used on the exam.

Grading Breakdown:

40%	Lecture
30%	Exam (Lectures)
25%	Paper Review
5%	Class Participation
100%	Total

The instructors reserve the right to lower the curve as appropriate.
The curve will not be raised. Unexcused absences will not be tolerated.
10% will be taken from your grade for each unexcused absence.

READING LIST:

1. **E.S.E. Hafez and B. Hafez. Reproduction in Farm Animals, 2000. 7th Edition. Wiley-Blackwell Publishing, USA. 509pages**
2. **Ian R. Gordon. Reproductive Technologies in Farm Animals. 2004. First Edition CABI Publishing 332pages**
3. **Manju Yadav. Animal Endocrinology. 2008. First Edition Discovery Publishing House 282pages**
4. **Mac E. Hadley. 1988. Endocrinology. 6th Edition Prentice Hall Publishing House 549pages**
5. **M.H. Pineda and Mihael Patrick Dooley 2003. McDonald's Veterinary Endocrinology and Reproduction. Fifth Edition. Wiley-Blackwell Publishing 597pages**

LECTURE NOTES

Endocrinology

This is the study of endocrine glands and their secretory products, the hormones, which provide a chemical, as distinct from a nervous, transmission of information from one cell to another

- It is a science dealing with the endocrine glands
- Science of endocrine system

Endocrine System

- Classic Definition
  - (i) ductless glands
  - (ii) secretes hormones into the blood
  - (iii) acts on distant targets
  - (iv) regulates a pre-existing cellular activity – coordinates the activities of various tissues to maintain "systemic homeostasis"
  - (v) minimal overlap of biological activities (deficiencies cause marked abnormalities)
- Modern Definition

  It is the study of the adjustments of homeostatic and other activities accomplished by chemical messengers

- Neurohumoral interaction

  The nervous and endocrine systems are related in three main areas, structure, chemical, and function. The endocrine and nervous system work parallel with each other and in conjunction function in maintaining homeostasis, development and reproduction. Both systems are the communication links of the body and aid the body's life systems to function correctly and in relation to each other. Structurally many of the endocrine systems glands and tissues are rooted in the nervous system. Such glands as the hypothalamus and posterior pituitary are examples of nerve tissues that influence the function of a gland and its secretion of hormones. Not only does the hypothalamus secrete hormones into the bloodstream, but it regulates the release of hormones in the posterior pituitary gland. Chemically both the endocrine and nervous system function in communication by means of the same transmitters but use them in different ways. Hormones are utilized by both systems in signaling. An example of this can be seen in the use of Norepinephrine. Norepinephrine functions as a neurotransmitter in the nervous system and as an adrenal hormone in the endocrine system. Functionally, the endocrine and nervous system work hand in hand acting in communicating and driving hormonal changes. They work in maintaining homeostasis and respond to changes inside and outside the body. Besides functioning in similar manners they also work in conjunction. An example of this can be seen in a mothers' release of milk. When a baby sucks the nipple of its mother, sensory cells in the nipple sends signals to the hypothalamus, which then responds by releasing oxytocin from the posterior pituitary. The oxytocin is released into the bloodstream where it moves to its' target cell, a mammary gland. The mammary gland then responds to the hormones signal by releasing milk through the nipple. Besides working in conjunction with each other, both systems affect one another. The adrenal medulla is under control of nerve cells, but the nervous systems development is under the control of the endocrine system.

- Hormones

  This is a physiologic, organic, chemical substance produced by certain specialized cells which passes into the circulatory system for transport in order to stimulate or inhibit the functional activity of the target organ or tissue.

Homeostasis

This is the property of either an open system or a closed system, especially a living organism, which regulates its internal environment so as to maintain a stable, constant condition. Multiple dynamic equilibrium adjustments, regulation mechanisms, make homeostasis possible. The concept was created by Claude Bernard, often considered as the father of physiology, and published in 1865. the term was coined in 1932 by Walter Bradford Cannon from the Greek "homoios" (same, like, resembling) and "stasis" (to stand, posture). Homeostasis is divided into several areas. They include: (i) biological homeostasis (ii) ecological homeostasis (iii) reactive homeostasis (iv) risk homeostasis (v) metabolic homeostasis etc but we will discuss only on biological homeostasis.

Biological homeostasis

With regard to any given life system parameter, an organism may be a conformer or a regulator. Regulators try to maintain the parameter at a constant level over possibly wide ambient environmental variations. On the other hand, conformers allow the environment to determine the parameter. For instance, endothermic animals maintain a constant body temperature, while ectothermic animals exhibit wide body temperature variation. Examples of endothermic animals include mammals and birds, examples of ectothermic animals include reptiles and some sea creatures. This is not to say that conformers don't have behavioral adaptations allowing them to exert some control over a given parameter. For instance, reptiles often rest on sun-heated rocks in the morning to raise their body temperature. Likewise, regulators' behaviors may contribute to their internal stability: the same sun-baked rock may host a ground squirrel, also basking in the morning sun.

Most homeostatic regulation is controlled by the release of hormones into the bloodstream. However other regulatory processes rely on simple diffusion to maintain a balance. Homeostatic regulation extends far beyond the control of temperature. Mammals regulate their blood glucose with insulin and glucagon. These hormones are released by the pancreas. If the pancreas is for any reason unable to produce enough of these two hormone diabetes results. The kidneys are used to remove excess water and ions from the blood. These are then expelled as urine. The kidneys perform a vital role in homeostatic regulation in mammals removing excess water, salt and urea from the blood. These are the body's main waste products.

Control Mechanisms

All homeostastic control mechanisms have at least three independent components for the variable being regulated: the receptor is the sensing component that monitors and responds to changes in the environment. When the receptor senses a stimulus, it sends information to a control center, the component that sets the range at which a variable is maintained. The control center determines an appropriate response to the stimulus. The result of that response feeds to the receptor, either enhancing it with positive feedback or depressing it with negative feedback.

Negative Feedback Mechanisms

Negative feedback mechanisms reduce or suppress the original stimulus, given the effector's output. Most homeostatic control mechanisms require a negative feedback loop to keep conditions from exceeding tolerable limits. The purpose is to prevent sudden severe changes within a complex organism. There are hundreds of negative feedback mechanisms in the animal body. Among the most important regulatory functions are: thermoregulation; osmoregulation; and glucoregulation. The kidneys contribute to homeostasis in four important ways: regulation of blood water levels, reabsorption of substances into the blood, maintenance of salt and ion levels in the blood, and excretion of urea and other wastes.

A negative feedback mechanism for example is the typical home heating system. Its thermostat houses a thermometer, the receptor that senses when the temperature is low. The control center, also housed in the thermostat, senses and responds to the thermometer when the temperature drops below a specified set point. Below that target level, the thermostat sends a message to the effector, the furnace. The furnace then produces heat, which warms the house. Once the thermostat senses a target level of heat has been reached, it will signal the furnace to turn off, thus maintaining a comfortable temperature – not too hot nor cold..

Positive Feedback Mechanisms

Positive feedback mechanisms are designed to accelerate or enhance the output created by a stimulus that has already been activated.

Unlike negative feedback mechanisms that initiate to maintain or regulate physiological functions within a set and narrow range, the positive feedback mechanisms are designed to push levels out of normal ranges. To achieve this purpose, a series of events initiates a cascading process that builds to increase the effect of the stimulus. This process can be beneficial but rarely used by the body due to risks of the acceleration becoming uncontrollable.

One bodily positive feedback example event is blood platelet accumulation which in turn causes blood clotting in response to a break or tear in the lining of blood vessels. Another example is the release of oxytocin to intensify the contractions that take place during childbirth.

Positive feedback can also be harmful. An example being when you have a fever it causes a positive feedback within homeostasis that pushes the temperature continually higher. Body temperature can reach extremes of 45^0C (113^0F), at which cellular proteins denature, causing the active site in proteins to change, thus causing metabolism stop and ultimately resulting in death.

Definitions

- Glands
- Endocrine glands
- Exocrine glands
- Hormone
- Endocrinology

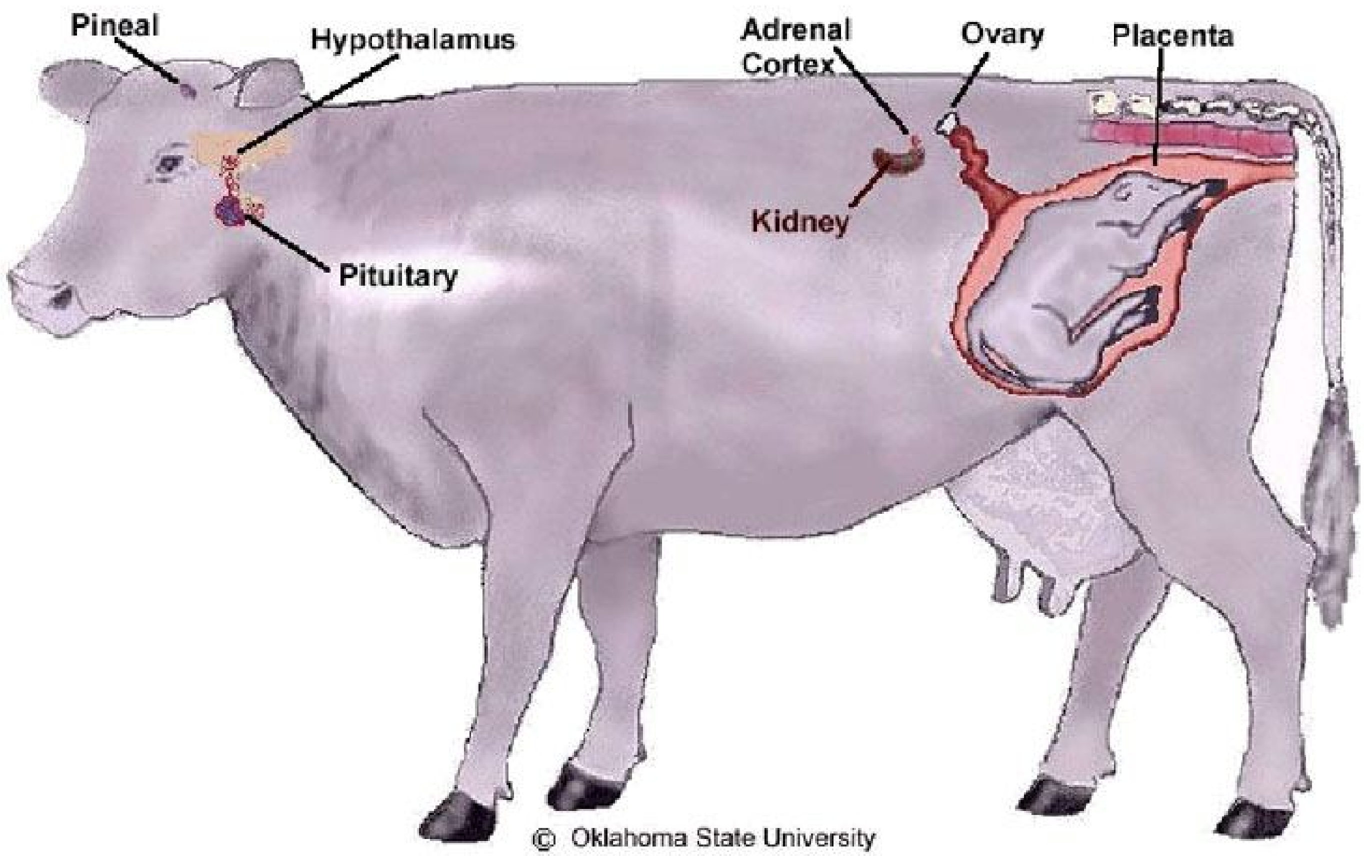
What is a gland

A gland is an organ in an animal's body that synthesizes a substance for release such as hormones or breast milk, often into the bloodstream (endocrine gland) or into cavities inside the body or its outer surface (exocrine gland). Glands can be divided into two groups: **Endocrine glands** are glands that secrete their product directly onto a surface rather than through a duct while **Exocrine glands** secrete their products via a duct and the glands in this group can further be divided into three groups.

Endocrine Glands

- Name, location, hormone produced, function

Body Diagram of Endocrine Glands



Classification of hormones

- Type of action
  1. Primary hormones of reproduction (FSH, LH, estradiol, progesterone)
  2. Metabolic hormones (thyroxin, insulin, STH)

- Chemical Structure
  1. Proteins and polypeptides : these hormones are made up of amino acids which are strung together and they are composed of as few as 3 to as many as 237 amino acids. They are synthesized in the hypothalamus, pituitary, parathyroids and pancreas. Examples are oxytoxin, vasopressin, insulin thyrotropin, follicle stimulating hormone (FSH), luteinizing hormone (LH) and gonadotropin releasing hormone (GnRH)
  2. Steroids : they are made from cholesterol which forms a characteristic four ring structure. Steroid hormone bond to their receptors inside the cell membrane. They play an important role in carbohydrate metabolism and electrolyte balance. Steroids are synthesized in the adrenal glands, ovaries and testes.
  3. Fatty acids (prostaglandins)
  4. Modified amino acid (melatonin)

Polypeptide	**Modified Amino acid**	**Protein**	**Sex steroid**	**Fatty acid**
GnRH	Melatonin	Relaxin	Estradiol	PGF
TRH		Inhibin	Progesterone	
CRH		Prolactin	Testosterone	
GHRH		ACTH		
Somatostatin		TSH		
Oxytocin		GH or STH		
		FSH		
		LH		

- Classification based on site of production

Hormones are produced in endocrine glands. The various endocrine tissues are structurally and chemically diverse. Some contain more than one kind of secretory cell, each elaborating different hormone. Such secretory cells must be proven to elicit endocrine function and releasing their content, the hormones. It has proved difficult in some cases to establish unequivocally whether tissues suspected of having an endocrine function actually have such function. Therefore, the following set of criteria has been used to establish whether a tissue has an endocrine function:

1. Ablation: The surgical removal of the endocrine gland will lead to a deficiency syndrome of the hormone produced by that gland. One of the oldest and most common examples of ablation of an endocrine gland is castration of male domestic animals. This removes androgen from the male animal, which results in a change in physical characteristics.
2. Replacement therapy (i.e. reimplantation): The deficiency syndrome caused by ablation may be overcome by implantation of the organ back into the animal or by injection of crude extracts from the removed gland. In 1949, Bertholt transplanted testes into a previously castrated cockerel and found that it prevented the retrogressive changes in sexual maturation and behavior. As a result of this, he concluded that the effects of the transplanted testes might be due to some substances that was secreted into the blood.
3. Isolation of hormone: Isolation or separation of the hormone from other substances in the crude extract of the endocrine gland has involved intensive chemical separation procedures coupled with sensitive assays to measure the hormone. Once the hormone has been isolated, it is then chemically identified and if possible, synthesized.
4. Regulation of endocrine glands: The changes in synthesis and release rate of the hormone from the endocrine gland are studied under physiologic conditions by assay techniques. The effects of the hormone in controlling reproduction is studied for its application to animal production and human medicine.

Apart from endocrine glands, hormones are also produced in: (ii) isolated secretory cells (iii) extracellular fluids (plasma)

Hormone – producing organs/ tissues

- pituitary gland	- ovaries	- hypothalamus	- heart
- pineal gland	- testes	- kidney	- adipose tissue
- thyroid gland	- pancreas	- liver	- placenta
- parathyroid	- thymus	- intestines	- blood
- adrenals		- lung	- skin

Regulation of Hormone Secretion

Feedback control

There are two types of feedback: the negative and positive feedbacks. Negative feedbacks as the name implies, usually has some inhibitory effect. As the concentration of the hormone rises, it indirectly inhibits any further increase in its own plasma concentration. The negative feedback signal acting to slow the output of an endocrine tissue may be physiological response to the hormone secreted by that tissue e.g. high estrogen levels inhibit production of the gonadotropic hormone that stimulate estrogen production. Thus, the negative feedback signal may be simply the reduction of a stimulus to the endocrine cells or it may be an active inhibition of secretion of the hormone. Although negative feedback is common in physiological processes, positive feedback is rare. Nevertheless, an interesting example of positive feedback is the generation of the secretion of follicle-stimulating hormone (FSH), which in turn stimulate the secretion of estrogen – a positive a positive feedback relationship that increases the levels of both estrogen and FSH in the blood. As the hormone levels rise sufficiently, positive feedback is terminated as negative feedback takes over. This happens because high concentrations of the estrogen inhibit FSH production, causing a change in feedback sign. Secretion
of both FSH and estrogen is thereby largely curtailed until another cycle of positive feedback begins to build up the concentrations of these hormones.

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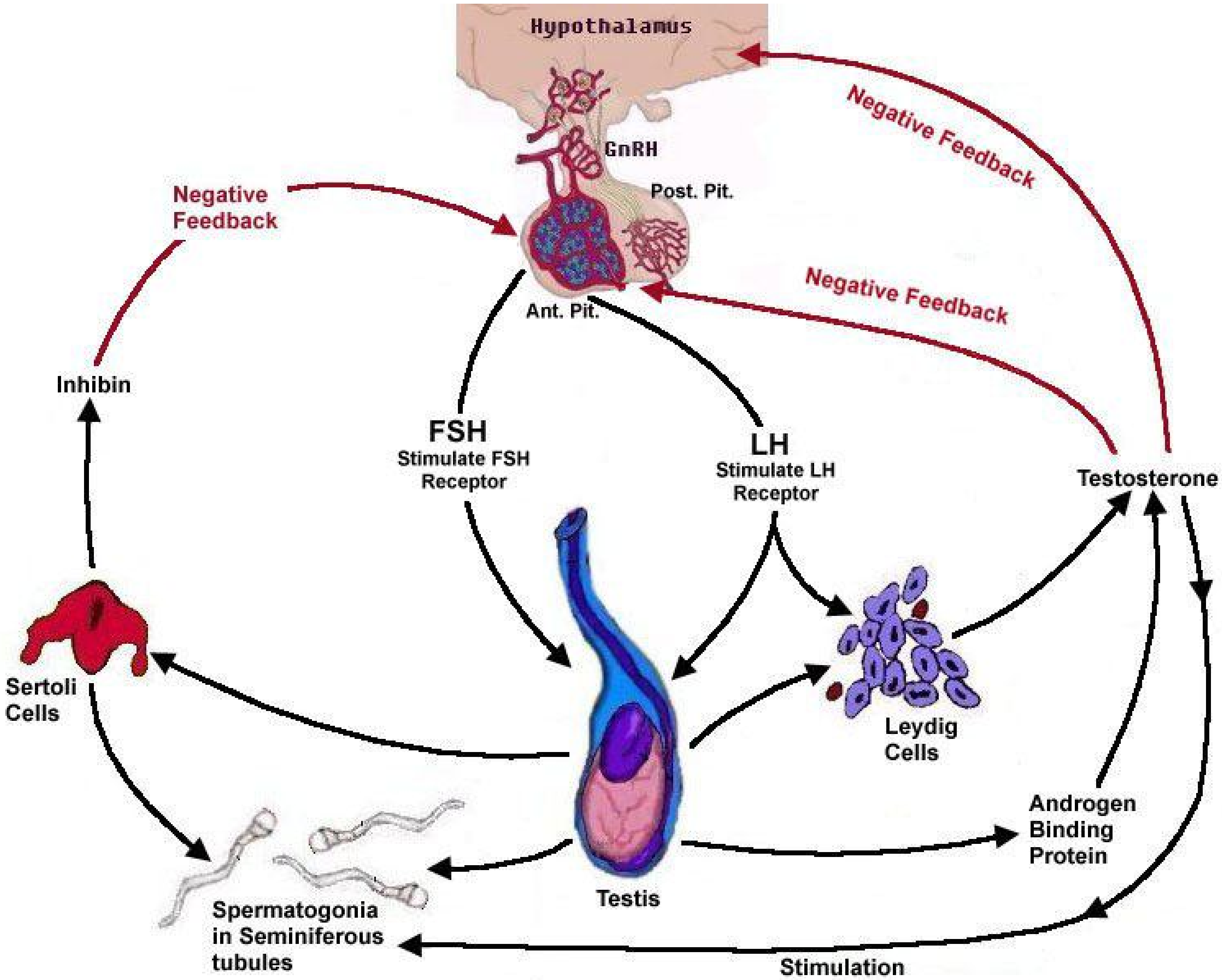
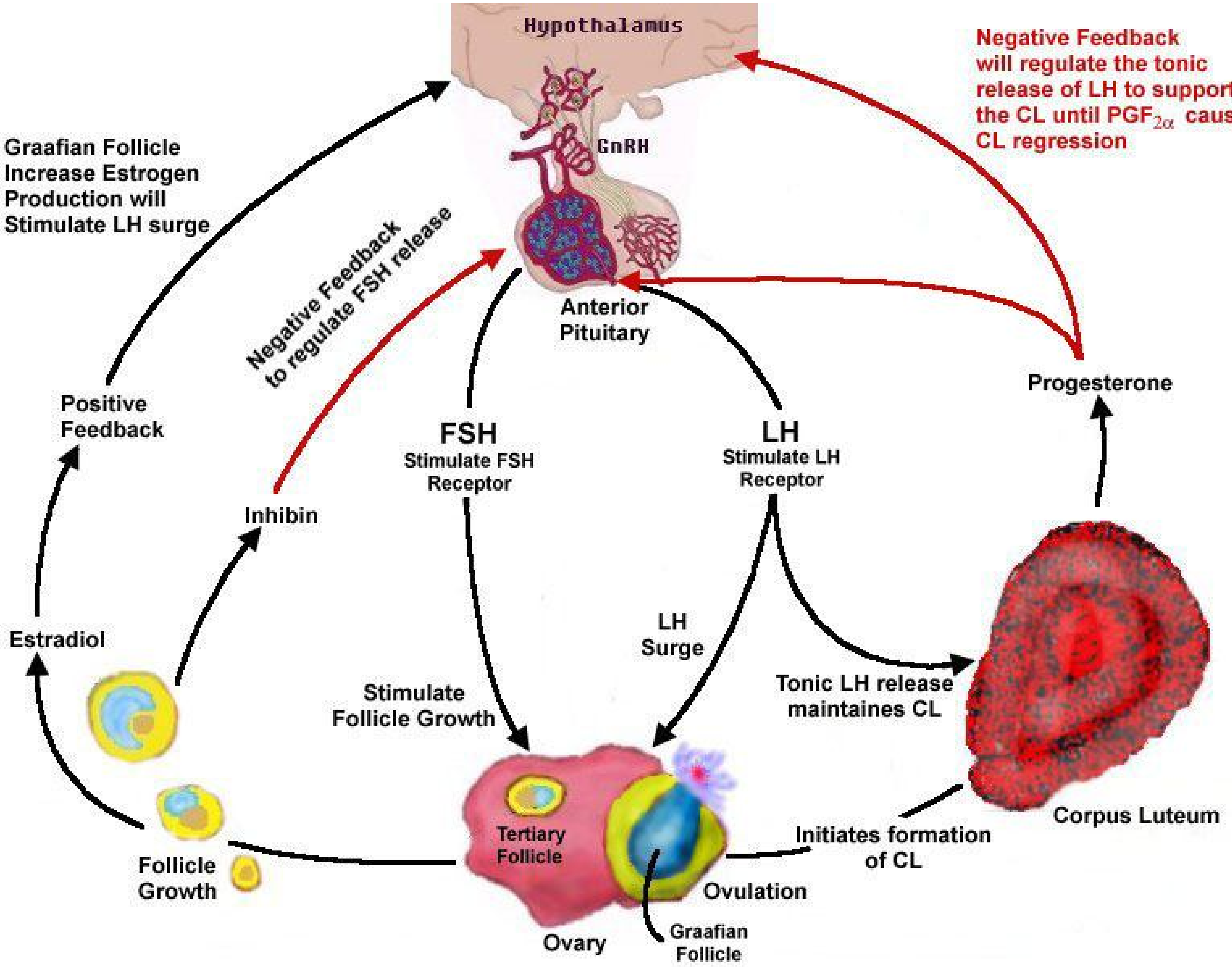
Endocrine Glands & Hormones (Hypothalamus Feedback Diagrams)

Male Feedback Diagram



Female Feedback Diagram



Hypothalamus - Releasing Hormones of the Hypothalamus

- Structure
    1. short chain polypeptides (3 – 44 amino acids)
- General Function
    1. to cause the release of trophic hormones from the anterior pituitary gland
- Hormones
    1. Gonadotrophin releasing hormone (GnRH) – releases of FSH and LH from anterior pituitary
    2. Thyrotrophin releasing hormone (TRH) – releases TSH and prolactin from anterior pituitary
    3. Corticotrophin releasing hormone (CRH) – releases ACTH from anterior pituitary
    4. Growth hormone releasing hormone (GH-RH) – releases growth hormone from anterior pituitary
    5. Somatostatin (growth hormone inhibiting hormone) – inhibits growth hormone release from anterior pituitary

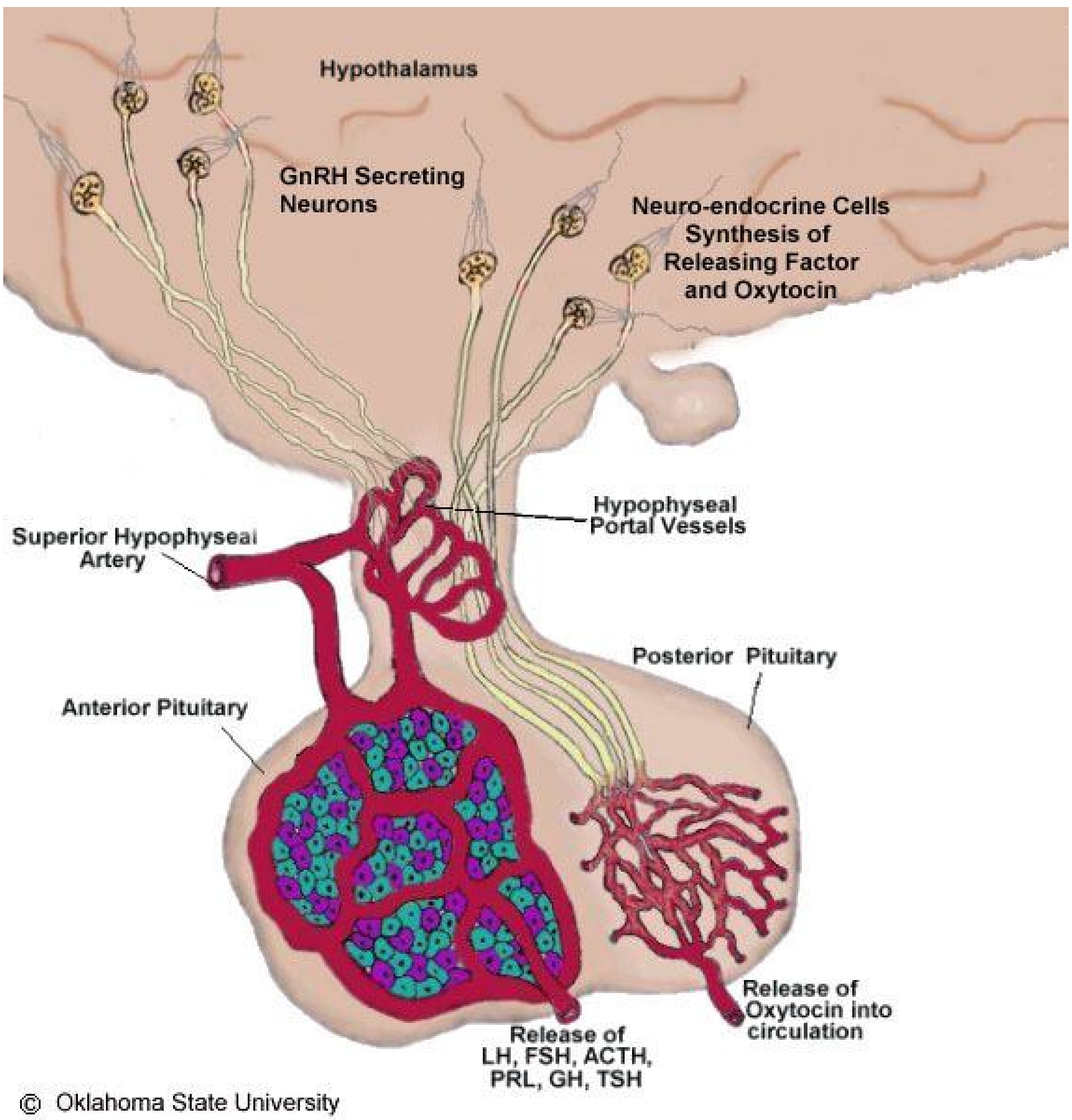
Hormones Released in the Anterior Pituitary Gland (Adenohypophysis)

- Structure
    1. glycoproteins or proteins
- Hormones
    1. Gonadotropins
        - Follicle stimulating hormone (FSH) – stimulates follicle growth and spermatogenesis
        - Luteinizing hormone (LH) – causes ovulation and maturation of oocytes, maintains the corpus luteum, stimulates androgen secretion by Leydig cells
        - Prolactin – in rodents helps to maintain CL, stimulates maternal behavior
    2. Other trophic hormones
        - Corticotrophin (ACTH) – stimulates cortisol release from adrenal gland
        - Thyroid stimulating hormone (TSH) – stimulates thyroxine release from thyroid gland
        - Growth hormone (GH or STH) – growth of long bones

Hormones Released in the Posterior Pituitary Gland (Neurohypophysis)

- Structure
    1. polypeptides (9 amino acids)
- Hormone
    1. Oxytocin – causes contraction of smooth muscle such as in mammary gland, uterus, oviduct
- Other facts of importance

Hypothalamus - Pituitary interrelationships



1. produced in the hypothalamus but secreted in posterior pituitary
2. also produced in the corpus luteum of some species

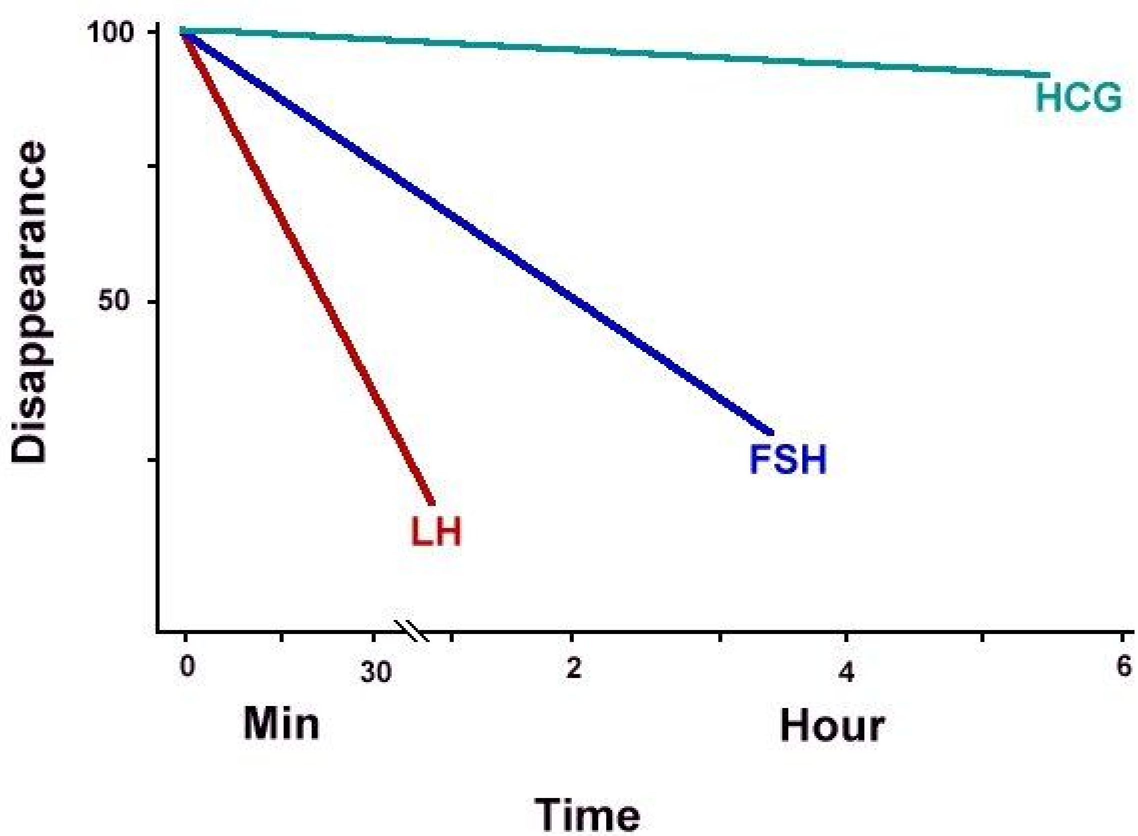
Placental Hormones

- equine Chorionic Gonadotropin (eCG)
  1. Contains mainly FSH-like activity but also some LH-like activity
  2. Has a longer half-life than FSH
  3. Found in the blood and not the urine
  4. Function
     - Stimulates follicular development during pregnancy in the mare
     - LH-like activity stimulates some developing follicles to ovulate and form accessory CLs
  5. Other commercial hormones from the equine placenta
     - Estrogens
       - found in mare urine
       - Premarin is the commercial product
       - treatment of postmenopausal women
         - estrogen replacement therapy
         - prevention of osteoporosis
     - prevention of heart disease
- Human Chorionic Gonadotropin (HCG)
  1. Has LH-like activity
  2. Found in blood and urine
  3. Function
     - Prevents CL regression
- Placental Lactogen
  1. Has both GH – and prolactin – like activity. The primary effect is to prepapre the mother's mammary gland for lactation.

Gonadal Polypeptide Hormones

- Relaxin
  1. Made of 2 polypeptides that are connected with disulfide bonds. It is similar in size and structure to insulin
  2. Secreted by CL during pregnancy
  3. In some species it may be secreted by the uterus and/or placenta
  4. Generally, the tissues affected must first be exposed to estrogens for its effects
  5. Functions
     - Cervical dilation
     - Inhibits uterine contraction

Hormone Disappearance Rate



- Inhibin
  1. **1.** Secreted by sertoli cells in the male and granulosa cells in the female
  2. **2.** Function
     - inhibits FSH secretion without altering LH secretion

Gonadal Steroids

- General
  1. Origin – ovary, testis, adrenal
  2. Basic structure
  3. Type of activity can be predicted by structure
     - Estrogen – 18 carbons
     - Progestin – 21 carbons
     - Androgen – 19 carbons
     - Cholesterol – 27 carbons
- Steroid Synthesis
- Androgens
  1. An example is testosterone
  2. Produced by Leydig cells in the testis, theca interna in the follicle and by the adrenal gland
  3. Transported in the blood by binding to protein, steroid binding globulin
  4. Active form is often dihydrotestosterone
  5. Function in the male
     - Stimulates spermatogenesis
     - Maintain the function of the epididymis
     - Promotes the growth, development, and activity of accessory sex glands and secondary sex organs
     - Development of male secondary sex characteristics
     - Anabolic activity
     - Inhibits GnRH release

- Estrogens
  1. An example is estradiol
  2. Produced by granulose cells of the follicle, sertoli cells in the testis, the placenta, and the adrenal gland
  3. Transported in blood by steroid binding globulin
  4. Functions
     - Effects on the CNS
     - Increases the mass of the uterus
     - Increases the contractility of the uterus
     - Development of female secondary sex characteristics
     - Growth of mammary gland ducts
     - Stimulates or inhibits GnRH release
     - Nonreproductive
       1. calcium uptake and bone ossification
       2. anabolic and growth effects
- Progestins
  1. An example is progesterone
  2. Produced in the CL, the placenta and the adrenal gland
  3. Transported in the blood bound to steroid binding globulin
  4. Functions
     - Prepares the uterus for implantation and pregnancy
     - Acts with estrogen to induce the behavior patterns of estrus
     - Develops alveoli of mammary gland
     - Inhibits the rise of LH that causes ovulation

Prostaglandins

- An example is PGF
- Produced in many tissues and organs but generally acts locally, although it can have effects through the vascular system
- Function
  1. to regress the CL
  2. contraction of the uterus

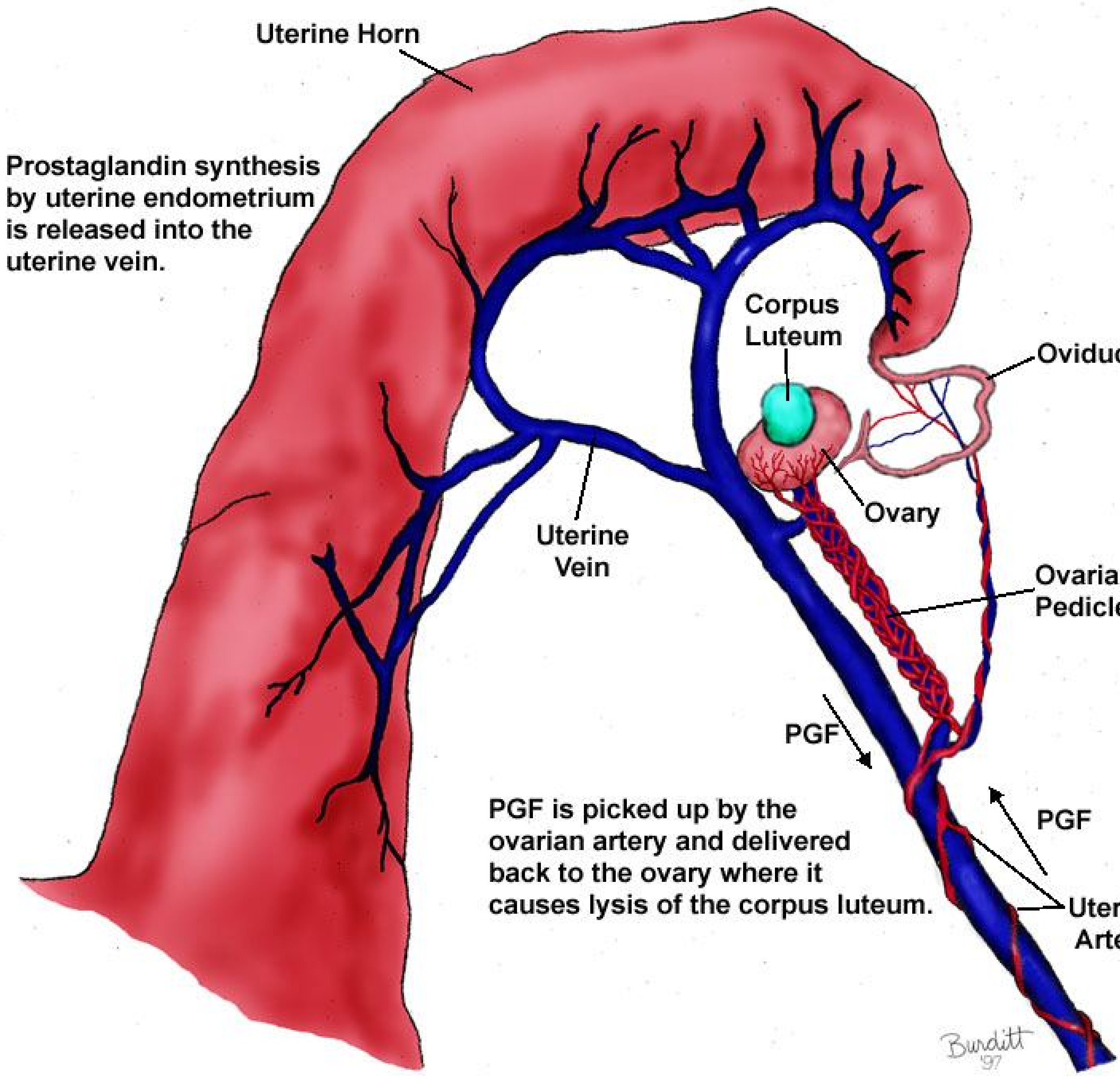
Melatonin

- Secreted from the pineal gland
- Is a modified amino acid
- Functions to integrate effects of light on reproductive processes

Human Menopausal Gonadotropin (hMG)

- Secreted from the anterior pituitary gland during and after menopause
- Has FSH-like activity and is actually a modified FSH molecule with a longer half-life. Results from lack of estradiol feedback
- Can be collected in the urine and sold to stimulate follicular development in women.

Prostaglandin Control in Luteolysis



Primary Hormones of Reproduction

Molecular Size of Hormones that Regulate Reproduction

Hormone	Molecular Weight
FSH	30,000 to 37,000
LH	26,000 to 32,000
Prolactin	23,000 to 25,000
ACTH	4,500
Inhibin	>10,000
Oxytocin	1,007
GnRH	1,200
HCG	37,700
PMSG	28,000
Relaxin	6,500
Estradiol	300
Testosterone	300
Progestrone	300
PGF	300

A. Hypothalamic Hormones

1. Oxytocin

Oxytocin is synthesized in the hypothalamus and stored in the neurohypophysis (posterior pituitary). It is one of the hormonal peptides first to be synthesized and is found in all mammals. It is also produced in the corpus luteum of the ewe, cow and human, therefore, oxytocin has two sites of origin, the ovary and the hypothalamus

Function

(i) Oxytocin in Greek means “rapid birth” which describes its function which is contraction of uterine muscle

(ii) Transport of both female and male gametes in the oviduct

(iii) In lactating female, it is associated with milk ejection reflex or milk let-down. This is an example of neuroendocrine reflex. During suckling or milking, the condition induces the release of oxytocin into the circulation. Oxytocin then acts on the myoepithelial cells (smooth muscle cells) that surround the alveoli in the mammary gland. The contraction of the myoepithelial cells puts pressure on the alveoli, which displaces milk into the duct system of the mammary gland resulting in milk let-down

(iv) Exogenous oxytocin has a luteolytic action in the cow and goat. This suggests that ovarian oxytocin may be involved in luteal function by acting on the endometrium of the uterus to induce prostaglandin $F_2\alpha$ release, which has luteolytic action (regression of the corpus luteum)

Application

(i) Oxytocin is used in the livestock industry to induce female animals to let-down milk after parturition.

(ii) Induce explusion of retained placentas

(iii) Aid delivery in young animals when the female has been in labour for an extended period

2. Gonadotropin Releasing Hormone (GnRH) or Luteinizing Hormone Releasing Hormone (LH-RH)

Substances of the hypothalamus that control the release of pituitary hormones were initially called releasing factors but now known as releasing hormones since their chemical structures are now known. LH-RH is a decapeptide hormone (10 amino acid).

Function

It induces the release of both luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary

Application

LH-RH is effective in overcoming cystic follicles in cows. In this instance, 100µg of LH-RH induces the release of substantial amount of endogenous LH induce luteinization or rupture of the cystic follicles. A cow with a treated cystic ovary will exhibit estrus 19 to 23 days later and can then be bred.

B. Pituitary Gonadotropic Hormones

The anterior pituitary gland secretes three gonadotrpic hormones, follicle stimulating hormone, luteinizing hormone and prolactin.

1. Follicle Stimulating Hormone

FSH has also been termed follicotrophin. It is secreted by the anterior pituitary gland. It can be separated into 2nonidentical subunits by propionic acid. The two subunits are termed c (alpha) and β (beta). The α and β subunits of any of these hormones by themselves have no biologic activity. If the α subunit of one hormone (LH α) is recombined with the βsubunit of another hormone (FSH β), the molecule regains FSH biologic activity or the activity of the β subunit. If 2α subunits or 2 β subunits are combined, no biologic activity is noted.

Function

Female

(i) FSH stimulates the growth and maturation of the Graafian follicle in the ovary. This means, it is the primary factor in inducing growth of the ovary.

(ii) FSH will not cause estrogen secretion from the ovary by itself, but in the presence of LH, it will stimulate estrogen production fron either the ovary or testis

Male

(i) FSH acts on the germinal cells of the seminiferous tubule to enlarge the testis

(ii) FSH is responsible for spermatogenesis up to the secondary spermtocytes after which androgens are responsible for final stages of spermatogenesis.

Menopause

At this stage, the pituitary output of FSH in women increases tremendously due to the lack of steroid output (e.g. estrogen feedback). This increase in FSH output is at such concentrations that it passes through the kidney and goes directly to the urine and is called human menopausal gonadotrophin. The biologic activity of hMG is increased over FSH from women with active ovaries and is sold as a fertility hormone for women under the trade name of Pergonal.

Application

FSH is primarily used in the stimulation of follicular development to induce multiple ovulations for embryo transfer

2. Luteinizing Hormone

LH has also been termed luteotrophin and interstitial cell-stimulating hormone (ICSH). It is a glycoprotein composed of an α and β subunits

Function

(i) Tonic or basal levels of LH act in conjunction with FSH to induce estrogen secretion from the large graafian follicle

(ii) The preovulatory surge of LH is responsible for rupture of the follicle wall and ovulation

(iii) It is the main luteotrophic substance in domestic animals

(iv) The interstitial cells of both the ovary and testis are stimulated by LH. In the male, the interstitial cells (Leydig cells) produce androgens after LH stimulation.

Application

(i) to induce ovulation, primarily in cows with cystic ovaries

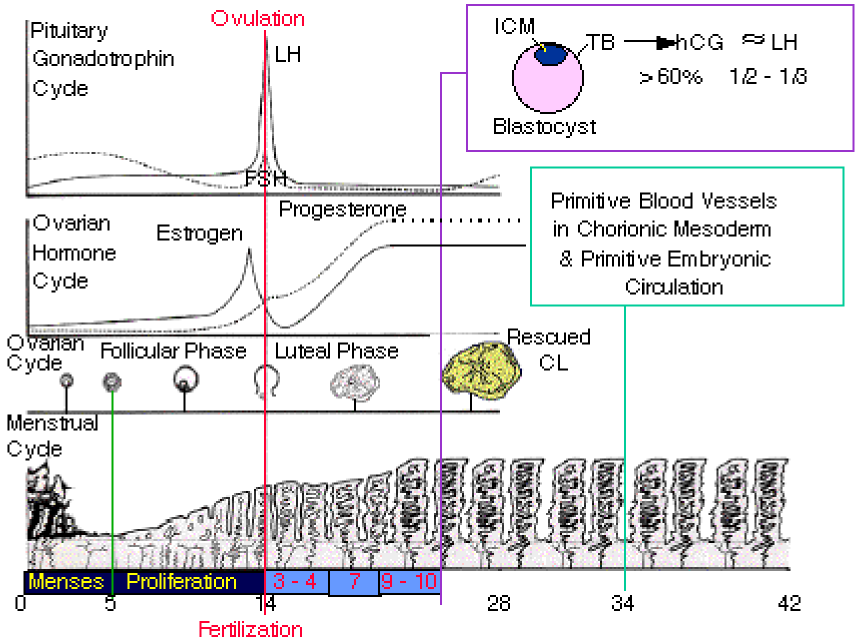
(ii) aid in superovulation of embryo transfer cows

Tonic LH and FSH release

Serum LH and FSH are released in a tonic or basal fashion in both the female and male. Tonic levels of LH and FSH are controlled by negative feedback from the gonads. The tonic level of LH is not stationary, but shows oscillations about every hour. In castrated male and female, tonic serum LH Concentrations are elevated. This is due to the lack of a negative feedback from the Gonadal steroids on the tonic LH control center in the hypothalamus after gonadectomy.

Preovulatory LH and FSH release

A second type of LH and FSH release, called the preovulatory surge of LH and FSH, is evident in the female prior to ovulation. The preovulatory surges of LH and FSH are responsible for ovulation and they last from 6 to 12 hours in most species. The preovulatory surge of LH is initiated by an increase in the circulating estrogen concentration, which has a positive effect on the hypothalamus inducing release of LH-RH that results in the preovulatory surge of LH and FSH.



Hormonal Changes and Female Reproductive Cycles

Regulation and actions of the female sex hormones in mammals

High progesterone levels initiate the release of FSH/LH-RH. The FSH stimulates development of the follicles becoming mature and eventually rupturing to become graafian follicle. Estrogen secreted by the follicle and by the interstitial cells eventually reaches levels that inhibit FSH/LH-RH and induce LH surge associated with ovulation and subsequent development of the corpus luteum. This endocrine tissue secretes primarily progesterone which functions to maintain pregnancy.

C. Placental Hormones

The placenta seems to be able to produce hormones either identical to, or with similar biologic activity, to almost any of the known hormones of the mammalian system. These are pregnant mare serum gonadotrophin (PMSG) and Human chorionic gonadotrophin (hCG)

1. Pregnant Mare Serum Gonadotrophin (PMSG)

PMSG was discovered when blood from pregnant mares produced sexual maturity in immature rats. It is a glycoprotein with α and β subunits similar to LH and FSH but with a higher content of carbohydrates especially sialic acid. The higher sialic acid content appears to account for the long half-life of several days for PMSG. This is why a single injection of PMSG can have biologic effects at the target gland for more than a week.

Function

The secretion of PMSG stimulates development of follicles on the ovary due to the FSH effect. Some of these follicles ovulate, but most follicles simply form a luteinized follicle due to the LH-like action of the PMSG. PMSG is described as having both FSH and LH biologic actions with the FSH actions being dominant.

Application

PMSG was one of the first commercially available gonadotrophins and is used to induce superovulation in domestic animals. It is used in embryo transfer in cattle, sheep and pigs but ineffective in the mare.

2. Human Chorionic Gonadotrophin (hCG)

The chemical structure of hCG has been defined as glycoprotein consisting of α and β subunits. It is synthesized by the syncytiotrophroblastic cells of the placenta of the pregnant primate and is found in both the blood and urine. It has both LH and FSH-like actions, but has predominantly LH-like biologic actions. It converts the corpus luteum of the menstrual cycle in the human to the corpus luteum of pregnancy.

Application

(i) it is used as the basis of immunological human pregnancy tests since it appears early in human pregnancy

(ii) the LH-like action of hCG has made it available for treatment of cysticovaries in dairy cattle.

D. Gonadal Hormones

Steroid hormones are secreted not only by the ovary and testes, but also by the placental and adrenal cortex

1. Androgens

Testosterone belongs to the class of steroids known as androgens. In the male, androgens are produced by the interstitial cells (Leydig cells) of the testes, with a limited amount being produced by the adrenal cortex. It is transported in the blood by an alpha globulin called steroid-binding globulin

Function

(i) Androgens stimulate the latter stages of spermatogenesis and prolong the life span of epididymal sperm

(ii) They promote growth, development and secretory activity of the accessory sex organs of the male such as the prostrate, vesicular glands, bulbourethral gland, vas deferens and the external genitalia (penis and scrotum)

(iii) The maintenance of secondary sex characteristics and sexual behavior or libido of the male

(iv) They induce protein anabolic activity

(v) They have a negative feedback effect on the hypothalamic-pituitaryaxis in control of LH and FSH release

Application

(i) The synthetic androgen, testosterone propionate, is administered to cows or steers used as teaser animals for detection of estrus. The use have become popular in the industry instead of sterilization of bulls for teaser animals (heat detection animals)

(ii) Androgens are also used by some professional athletes to increase muscle mass and to give a feeling of well-being.

2. Estrogens

Substances of estrogenic activity have been found in both the animal and plant kingdom. Like androgens, they are carried by binding proteins in the circulation

Functions

(ii) It acts on the central nervous system to induce behavioural estrus in the female, however , small amounts of progestogen with estrogen are needed in some species such as the ewe and cow to induce estrus

(ii) It stimulates duct growth and causes the development of the mammary gland

(iii)Estrogen have both a negative and positive feedback control through the hypothalamus on LH and FSH release. The negative effect is on the tonic center in the hypothalamus and the positive effect is on the preovulatory center.

Application

(i) Synthetic nonsteroidal estrogens have been used widely in the livestock industry primarily as growth promotants in ruminants e.g. Ralgro, Melengesterol acetate etc.

(ii) Estrogens have luteolytic effects in cows and sheep i.e. regression of CL probably caused by prostaglandin $F_2\alpha$. In sows, estrogen have a luteotrophic action (helps to maintain CL) and have been used in synchronization of estrus followed by a $PGF_2\alpha$ injection, which causes regression of the CL.

3. Progestogens

Progesterone is the most prevalent, naturally occurring progestogen and is secreted by luteal cells of the corpus luteum. This hormone is also secreted by the placenta and adrenal gland. It is transported in the blood by a binding globulin much like androgens and estrogens.

Function

(i) it prepares the uterus for implantation and maintenance of pregnancy by increasing secretory glands in the endometrium and inhibiting the motility of the myometrium

(ii) Progesterone acts synergistically with estrogens to induce behavioral estrus in sheep and possibly in cattle.

(iii) It develops the secretory tissue (alveoli) of the mammary gland

(iv) The high levels of progesterone inhibit estrus and ovulatory surge of LH. This establishes the importance of the hormone in the regulation of estrous cycle.

Application

(i) In humans and domestic animals, progestogens are given to prevent abortion in females prone to abortion or miscarriage due to insufficient endogenous progesterone production

(ii) The most common use is in birth control pills to prevent LH surge and subsequent ovulation

(iii) In cattle, a synthetic progestogen (norgestomet) is on the market to synchronize the estrous cycle of cows. This synthetic steroid is marketed as Synchromate B

(iv) Melengesterol acetate is a synthetic progestogen used in increasing gains in feedlot heifers. MGA is effective only in heifers with intact ovaries. Continuous administration of MGA appears to inhibit a surge of LH release, which prevents ovulation but allows development of ovarian follicles. Estrogen produced by these follicles increases GH release, which promotes nitrogen retention and increased feed efficiency.

E. Uterine Hormones

Prostaglandins

Prostaglandins are not localized in any particular tissue. Most of them act locally at the site of their production on a cell to cell interaction which does not conform to a classic definition of hormones. Prostaglandins exist in the form of at least six parent compounds and numerous metabolites. Arachidonic acid, an essential fatty acid, is the precursor for prostaglandins.

Prostaglandins that are closely associated with reproduction are Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) and Prostaglandin E_2 (PGE_2)

Function

(i) Evidence that prostaglandins are involved in ovulation is found in the ewe and cows

(ii) $PGF_{2\alpha}$ stimulates contraction of the uterus, aids in sperm transport in the male and female, causes constriction of blood vessels and has luteolytic properties in domestic animals.

(iii) PGE_2 stimulates contraction of the uterus, dilates blood vessels and has luteolytic action

Applications

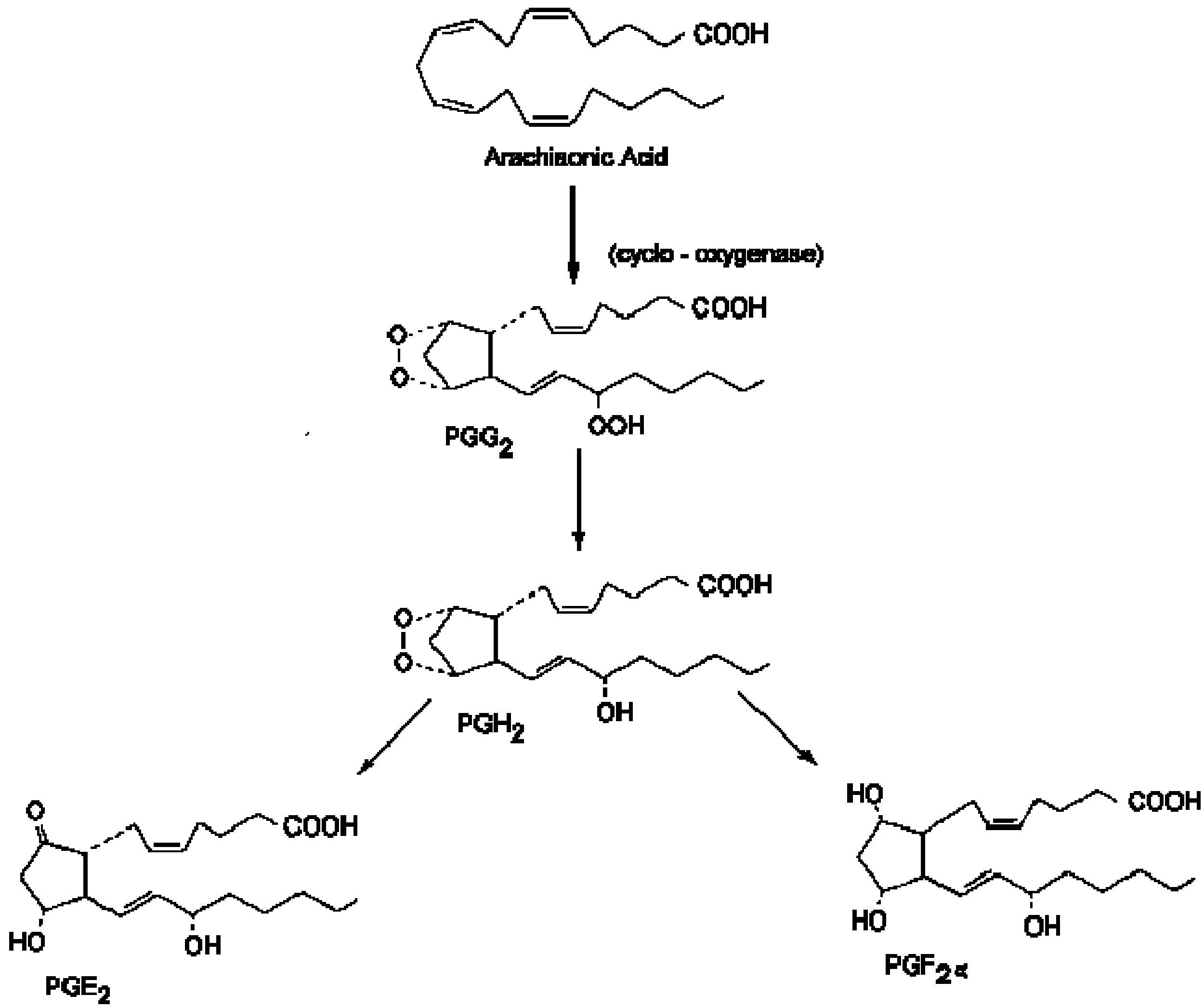
(i) Prostaglandins are used in timed breeding in cows and mares. In cow and ewe, $PGF_2\alpha$ will not cause regression or prevent formation of the CL during its first 5 days of life in sows, it will not cause regression of the estrous cycle until day 12 of the estrous cycle. In all species, the CL is responsive to luteolytic agents only during certain stages of its development. Therefore, administration of a single dose of a luteolytic agent will only synchronize estrus in those animals that are within the responsive stage at the time of treatment. To overcome this constraint, cows and ewes should be treated twice with PGF2α at 10 day intervals after which they will all exhibit estrus 3 days after the second injection

(ii) $PGF_2\alpha$ is used in aborting fetus in cattle with problems during pregnancy

(iii) Prostaglandin $F_2\alpha$ has also been found to aid in treating infected uterus of dairy cows. Its mechanism of action is possibly two-fold: first by regression of the CL, if present, this then induces follicle growth and estrogen production. Second, by contraction of the uterus both from its action and from the action of estrogen.

(iv) Trade names of these compounds in the market are Lutalyse, Estrumate and recently Fenprostalene was added

Fatty Acid



F. Secondary Hormones of Reproduction

1. Prolactin (PRL)

Prolactin molecules are similar in structure to growth hormones and in some species these hormones have similar biologic properties.

Function

(i) Prolactin is termed a gonadotrophic hormones because of its luteotrophic properties (maintenance of corpus luteum) in rats and mice. In domestic animals, LH seems to be the main luteotrophic hormone with prolactin being of less importance.

(ii) In domestic animals, prolactin acts on the central nervous system to induce maternal behavior. This may be noted in some male species, such as the pigeon, in which both the female and male incubate the eggs and feed the young.

(iii) In lower forms of animal, prolactin has been classified more as a metabolic hormone than a reproductive hormone.

(iv) In woman, high levels of prolactin suppress menses (galactorrhea-ammenorrhea syndrome)

Application

There are presently no products available on the market made from the hormone prolactin

2. Placental Lactogen (PL)

Placental lactogen is a protein with chemical properties similar to prolactin and growth hormone. It was isolated from placental tissue, but cannot be detected in the serum of the pregnant animal until the last trimester of pregnancy. The exact function of PL is unknown; however, it may be more important for its growth hormone properties than its prolactin properties. It is important in regulating maternal nutrients to the fetus and possibly important for growth of the fetus. Placental lactogen may play a role in milk production since the level is higher in dairy cows (high milk producers) than in beef cows (low milk producers).

3. Protein B

It was isolated from placental tissue of the bovine and can be detected in the blood of pregnant cows 22 days after conception. Its physiologic action of this substance is still unknown but it may be involved in sending a message from the placenta to the cow or ewe, preventing destruction of the corpus luteum spurium.

4. Relaxin

Relaxin is a polypeptide hormone consisting of α and β subunits connected by 2 disulfide bonds. Relaxin and insulin have similar structure but different biologic actions

Function

(i) Relaxin is secreted primarily by the corpus luteum of the ovary during pregnancy

(ii) Main biologic action is dilation of the uterine cervix and vagina prior to parturition

(iii) If given in conjunction with estradiol, causes increased growth of the mammary gland.

5. Inhibin

Inhibin, also termed folliculostatin, is a protein hormones that has not been chemically identified. It is produced by the sertoli cells in the male and granulose cells in the female. Inhibin can inhibit FSH release and is partially responsible for the differential release of LH and FSH from the pituitary.

Mechanisms of Hormone Action

Hormones regulate bodily functions and are specific in what responses they elicit. As hormones are released into the blood stream they can only initiate responses in target cells, which are specifically equipped to respond. Each hormone due to its chemical structure is recognized by those target cells with receptors compatible with their structure. Once a hormone is released, the first step is the specific binding of the chemical signal to a hormone receptor, a protein within the target cell or built into the plasma membrane. The receptor molecule is essential to a hormone function. The receptor molecule translates the hormone and enables the target cell to respond to the hormones chemical signal. The meeting of the hormone with the receptor cell initiates responses from the target cell. These responses vary according to target cell and lipid solubility.

Hormones are either lipid-soluble, or lipid-insoluble, depending on their biochemical structure. The lipid solubility of the hormone determines the mechanism by which it can affect its target cell. Lipid-soluble hormones are able to penetrate through the cell membrane and bind to receptors located inside the cell. Such hormones diffuse across the plasma membrane and target those receptor cells found within the cytoplasm. Lipid-soluble hormones target the cytoplasmic receptors which readily diffuse into the nucleus and act on the DNA, inhibiting and stimulating certain proteins. DNA function is of great influence over the cellular activities of the body and therefore such hormonal-DNA interaction can have effects as long as hours and in some cases days. Two main types of lipid soluble hormones are steroids and thyroid hormones. Both travel over long courses of time via the bloodstream and both directly affect DNA functions

Those hormones which are lipid-insoluble are unable to penetrate through the plasma membrane and function with their target cells in a much different and complex manner. Lipid-insoluble hormones must bind with cell surface receptors which follow a different path involving a second messenger. The hormone inability to penetrate the membrane requires a second messenger which translates the outer message and functions within the cell. Once a lipid-insoluble hormone binds with a cell surface receptor, its' signal is translated into the cell by specific secondary messengers. There are three known and accepted secondary messengers which vary in structure and function, but all three carry out the external signal internally. The

three known secondary messengers are (1) cyclic nucleotide compounds (cNMPs), cAMP and cGMP; (2) inositol phospholipids and (3) Ca2+ ions. After a hormone binds with a receptor molecule it via a tranducer protein sends the hormones signal through the membrane. The protein receptor initiates the formation of a second messenger, whether it be cAMP or an inositol phospholipid, which then bids to an internal regulator. The internal regulator controls the target cells' response to the hormone's signal.
Each different type of secondary messenger evokes different responses by those cells they affect. cAMP has wide range of tissues it targets and those responses it elicits. cAMP pathways can increase the heart rate and force a contraction in a heart, it can decrease lipid breakdown in fat cells, it can stimulate resorption of water in a kidney. An inositol phospholipid pathway can initiate breakdown of liver glycogen and DNA synthesis in fibroblasts. Ca2+ pathways are linked to initiating responses in striated muscles most notably contraction. These responses, however, are short lived responses, much even shorter than those by lipid-soluble affected cells.

Hormonal Assay

FACTORS IN VALIDATION OF HORMONAL ASSAYS

Criterion	*Definition*
Accuracy	nearness to true
Precision	repeatability
Sensitivity	minimum detectable quantity
Mol > millimol > micromol > nanomol > picomol > femtomol 10^{-3} 10^{-6} 10^{-9} 10^{-12} 10^{-15}	
Specificity	ability to exclusively discriminate a single entity

Hormonal analyses. Most hormone assays performed today are of the competitive-binding variety. For a competitive-binding assay to be of value it must be practical and reliable.

The RIA is the conventional prototype of a competitive-binding assay. There are three fundamental components to the RIA - radioactive ("hot") hormone, unlabeled ("cold") hormone (standard or sample), and antibody. Radioisotopes of tritium (β emitter) and iodine (high specific activity γ emitter) are incorporated into steroid and protein (Tyr or His residues) hormones, respectively; this must be done without significant damage to the immunoreactivity of the hormone. Tracer and standard or unknown sample compete for a limited number of binding sites on the antibody. Amounts of (excess) tracer and antibody for each reaction are held constant, while quantities of standard hormone are increased step-wise. Reactions are allowed to proceed to equilibrium, and free (unbound) hormone is segregated from antibody-hormone complexes. Emission of energy from the bound complex is monitored by radiation detection equipment. As content of standard is increased from 0 (ie., 100% of antibody is bound by tracer), the amount of antibody-bound tracer declines reciprocally - a standard curve is constructed from these data. Reaction tubes containing sample in place of standard are assayed simultaneously. Estimates of mass of hormone within a sample are interpolated from the standard curve.

Antibodies belong mainly to the gamma globulin (IgG) class of immunoglobulins. Each Fab arm of the (bivalent) antibody can bind a molecule of ligand. Binding is mediated by weak noncovalent forces (ionic interactions, hydrogen bonding, hydrophobic attractions, van der Waals attraction); therefore, like that of enzyme-substrate binding, the reaction is reversible.

Antisera can be generated by injecting purified hormone into a species of animal that is capable of mounting an immunological reaction to that hormone (ie., do not produce the hormone in a chemical form that is exactly similar). Some small molecules (haptens) are not antigenic on their own (eg., steroid and peptide hormones, prostaglandins) and must first be coupled (at a nonactive site) to an immunogenic carrier (eg., albumin, keyhole limpet hemocyanin) before injection.

Even under the best of conditions of immunization, antisera can contain antibodies (polyclonal) that cross-react with related substances - the development of technology using monoclonal (homogenous) antibodies has helped in this respect. To obtain monoclonal antibodies an animal (eg., mouse) is injected with purified antigen, spleen cells capable of secreting a single type of antibody (clones) are screened and isolated, and selected cells are fused with myeloma (immortal) cells to produce a hybridoma. Cells maintained in culture provide a continuous source of antibody. A single hybridoma can yield approximately 1000 specific molecules of antibody per second.

A convenient method to separate antibody-hormone complexes from free hormone is to adhere the antibody to a solid phase, such as to the walls of a test tube. The free hormone can then be decanted (a centrifugation step is not required). Because proteins attach nonspecifically to plastic (eg., polyvinyl chloride or polystyrene), tubes can be coated by simply incubating with a solution containing antibody. Remaining unoccupied sites are then filled with an irrelevant protein, such as serum albumin or gelatin. One criticism of antibody-coated tubes is adsorption can mask immunoreactive (Fab) sites: to overcome this problem, protein A, a molecule derived from staphylococcus aureus that binds the Fc tail of IgG, can be coated to the solid phase (this permits extraction of IgG from the fluid-phase reaction mixture). Alternatively, precipitation of hormone-antibody complexes can be achieved using ammonium sulfate, magnetically-activated antibody, or with a second antibody generated against the first antibody (ie., anti-IgG). Adsorption of free (low molecular weight ligand) can be achieved with dextran-coated charcoal.

Other analytical systems that exploit the same basic principle as the RIA include the protein-binding assay, radioreceptor assay (RRA), scintillation proximity assay (SPA), enzyme immunoassay (EIA), fluoroimmunoassay (FIA), and chemiluminescent assay (CIA). Protein-binding and radioreceptor assays are radioligand assays that utilize an endogenous plasma protein (eg., for steroid hormones) or cellular receptor, respectively - instead of an antibody. Protein-binding assays lack the specificity of an immunoassay. The radioreceptor assay has an advantage over the RIA in that it only detects bioactive hormone (ie., antibodies can interact with sites on the hormone molecule not involved in receptor binding). Notwithstanding, it is difficult to isolate abundant quantities of stable receptor for routine analyses. Fortunately, data obtained from RIAs and RRAs are usually comparable.

A newly-developed methodology, SPA, does not require separation of bound from free ligand. Competitive binding of labeled ligand in proximity to antibody- or receptor-coated fluoromicrospheres allows the energy emitted to excite the fluor and produce detectable light that can be measured in a scintillation counter without liquid cocktail. Unbound tracer is too far from the microsphere to enable energy transfer before it is absorbed by the aqueous solution.

In the EIA, FIA ,and CIA, radioactive hormone is replaced by an enzyme-, fluorescein- or luminol-tagged ligand, respectively. Quantification is accomplished with a fluorometer in FIA and a luminometer in CIA. In EIA an extra step is required first - addition of substrate. An example of an enzyme commonly used in enzyme immunoassays is horseradish peroxidase: hydrogen peroxide (substrate) is reduced by this enzyme, and in the process an appropriate hydrogen donor (eg., o-phenylenediamine) is oxidized, causing a change in color of solution - appearance of product is measured by spectrophometric analysis of color reactions (ie., absorbance) to graded concentrations of hormone.

Antibody-excess immunoassays include the immunoradiometric assay (IRMA) and enzyme-linked immunosorbent assay (ELISA). In the IRMA cold ligand is "sandwiched" between an antibody coated to a solid phase and a second radiolabeled antibody raised against a different hormonal epitope (this works best with macromolecular hormones); sensitivity is not mandated by competition, and therefore, reactions can be carried out expeditiously over a wide range of detection. In a sandwich ELISA, hormone is bound to an antibody attached to a solid phase, and then an antibody-enzyme conjugate and substrate are added. These methods engender a direct relationship between radioactivity measured in the final complex and concentration of standard or analyte (in contrast to the inverse correlation between bound radioactivity and standard or sample concentrations in an RIA).

Nonradioisotopic procedures, such as ELISAs, are becoming popular because of lowered equipment costs, reduced hazard to users and the environment (ie., associated with handling and disposal of radionuclides), and can be adapted (subjective appraisal of color-change) for in-the-home or on-the-farm/ranch diagnostics. However, ELISAs tend to be less sensitive than the RIA.

A reverse hemolytic plaque assay is used to detect secretion of hormone from individual cells (eg., gonadotropes) contained within a heterogeneous population. The concept is that a secretory product of a cell can be measured by specific antibodies in the presence of erythrocytes coated with protein A and added complement. Interaction of hormone with binding sites on the antibody causes stearic alterations in the antibody allowing for fixation of complement by juxtaposed Fc. Complement-induced hemolysis leads to the formation of a clear zone of erythrocyte membrane "ghosts" (ie., a plaque) surrounding the secretory cell. The plaque technique is sensitive and areas of lysis can be quantitated.

1. Immunologic Methods
   This methods consists Radioimmunoassay (RIA), Enzyme-Linked Immunosorbant Assay (ELISA) and Immunohistochemistry.
2. Bioassays
3. Radioisotope Techniques
4. Molecular Biology Techniques

COMPARISON OF HORMONAL ASSAY SYSTEMS (versus RIA)

Assay	B*inding Component*	*Advantage*	*Disadvantage(s)*
1. Bioassay	innate receptor	biological	lacks practicality, precision, and sensitivity
2. Protein-binding	nonimmune carrier	no immunization	lacks specificity
3. RRA	isolated receptor	biological	lacks practicality
4. EIA	antibody	no radioactivity	lacks sensitivity, must add substrate
5. SPA	antibody, receptor	no separation step	patented technology
6. IRMA	antibody	short incubation	requires two antibodies
7. ELISA	antibody	no radioactivity	same as EIA and IMRA (sandwich)

TUTORIAL QUESTIONS ON ANP 506

1. Hormone Released by the area of the brain known as the hypothalamus beginning at the onset of sexual maturity in both males and females is A. Follicle stimulating hormone (FSH) B. Luteinizing hormone (LH) C. Progesterone D. Gonadotropin releasing hormone

   Answer **D – Gonadotropin releasing hormone**

   - GnRH is needed for sexual maturity and normal reproduction. GnRH acts by stimulating the release of luteinizing hormone and follicle stimulating hormone from the anterior pituitary. These two gonadotropins (FSH and LH) act by stimulating the production of sex hormones in the gonads (testes and ovary).

2. What pituitary hormone(s) control ovulation and production of female hormones by the ovary? A Estrogen B Gonadotropin releasing hormone C. Human chorionic gonadotropin D. Follicle stimulating hormone (FSH) and Luteinizing hormone (LH) E. Progesterone

   Answer **D – FSH and LH**

   - The pituitary gland has two sections: the posterior and the anterior pituitary. These sections have different origins and produce different hormones. With the onset of puberty, the hypothalamus increases the release of gonadotropin releasing hormone. This causes the anterior pituitary gland to start producing follicle stimulating hormone (FSH) and luteinizing hormone (LH)

3. Which of the following could be found in the ovary? A. Oviduct B. Corpus luteum C. Endometrium D. Cervix E. Sperm

   Answer **B – Corpus luteum**

   - The ovaries contain eggs stored in small pockets called follicles. A follicle is an egg cell surrounded by a layer of cells involved in egg maturation. These ovarian follicles are formed in the animal's body. After ovulation, changes continue to take place in the ovaries. The remaining follicular cells undergo structural and biochemical changes. They develop into the corpus luteum. While the ovarian follicles produced estrogen, the corpus luteum produce both estrogen and progesterone

4. What hormone normally produced in the corpus luteum that inhibits development of ovarian follicles is a common component of oral contraceptives? A. Testosterone B. Follicle stimulating hormone C. Luteinizing hormone D. Prolactin E. Progesterone

Answer **E – Progesterone**

- After ovulation, the ruptured ovarian follicle becomes the corpus luteum. The CL produces both estrogen and progesterone. Progesterone is required for maintenance of the endometrial lining of the uterus where the blastocyst is implanted. If the released egg is not fertilized, the corpus luteum regress, and the production of progesterone drops. The uterine lining id sloughed off, completing the monthly uterine cycle. Oral contraceptives normally contain progesterone, or in combination with other estrogens. By maintaining a slightly elevated level of progesterone via oral contraceptives (or injectible contraceptives), the signals from the brain to the ovaries to initiate the ovarian cycle that lead to follicle maturation are repressed and ovulation does not occur

Fill the gap with one of the correct answer listed below

-------1----------- occurs in the ovaries so that a normal female infant has about 2million primary oocytes, with the division process halted in the meiosis 1 stage. By age seven, only about ---------2------------- remain. A primary oocyte surrounded by a nourishing layer of granulosa cells is a(n) --------3-----------. When a female enters puberty, at the start of a menstrual cycle, the -------4-------- secretes a hormone (GnRH) in amounts that cause the ----------5------- pituitary to step up its secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH). The blood concentration of these hormones increases and is carried by the blood to all parts of the body. That increase causes the -------6---------- to grow. The ------------7--------- begins to increase in size, and more layers of cells form around it. ---------8----------- deposits accumulate between the oocyte and the layers. In time, all the deposits form the ------------9----------, a noncellular coating around the oocyte.

A. oocyte B vagina C follicle D ovary E cervix F zona pellucida G clitoris H 300,000 I anterior J oviduct K labia majora L endometrium M glycoprotein N myometrium O labia minora P urethra Q hypothalamus R meiosis S uterus

Matching: Match the hormone to its corresponding action

1. --------------- ACTH A. stimulates egg and sperm formation in ovaries and testes
2. --------------- ADH B. targets pigmented cells in skin and other surface covering, induces color changes in response to external stimuli and affects some behaviors.
3. --------------- FSH C. stimulates and sustains milk production in mammary glands
4. --------------- STH D. stimulates progesterone secretion, ovulation and corpus luteum
5. --------------- LH E. induces uterine contractions and milk movement into secretory ducts of the mammary gland
6. --------------- MSH F. stimulates release of thyroid hormones from the thyroid gland
7. --------------- OXY G. acts on kidneys to conserve water required in control of extracellular fluid volume
8. --------------- PRL H. stimulates release of adrenal steroid hormones from the adrenal cortex
9.---------------- TSH I. promotes growth in young, induces protein synthesis and cell division; has roles in adult glucose and protein metabolism

Theory Aspect

1. What hormones are produced by the hypothalamus, and what do they do?
2. What is the intricate and coordinated interplay of the hypothalamus, pituitary, ovary, and uterus
3. Describe the way that releasing factors and peptide hormones control testosterone release from the testis. How does negative feedback operates in this system?