

Lecture 4

Reproductive Endocrinology

Oct 9, 2012

Reproductive endocrinology is a branch of medicine that identifies and treats infertility in both humans and animals.

What we have learned from previous Lecture (3)

Why is Reproduction an old and modern science ?

Major historical events of reproductive biology

Aristotle (384-322BC): proposed the fetus originates from menstrual blood

Fallopian (1562): discovered and described the oviduct

Coiter (1573): discovered and described the CL

de Graaf (1672): discovered and described the antral follicle using rabbit model

van Leeuwenhoek (1678): discovered and described spermatozoa in semen

Spallanzani (1780): hypothesized spermatozoa were the fertilizing agents and successfully AI a dog

Dumas (1825): proved that spermatozoa were the fertilizing agents

Modern reproductive biology (1855-): The explosion of knowledge

Major achievements that speed up the development:

1. The **anterior pituitary** controls the function of the gonads.
2. **Gonads produce steroid** hormones that alter the function of the reproductive tissues.
3. Females experience **reproductive cyclicality** and that **ovulation** is predictable.

4. Worldwide success of AI was due to the **understanding of sperm physiology** during 1940s to 1950s.
5. Development of the techniques for **XY-sperm separation**, ET, cryopreservation, and electronic estrous detection, etc.
6. **PGF_{2α}** regulated the length of the estrous cycle in females (1960s).
7. Development of **RIA** for hormone analysis (1950s-60s).

RIA: Radioimmunoassay

RIA

is a sensitive technique, developed by Drs. **Rosalyn Yalow (1921-2011)** and Solomon Berson, to measure hormone (antigen) levels in the blood.

Dr. Yalow received the Nobel prize in medicine in 1977 for the development of the RIA for insulin detection. (a **breakthrough in Endocrinology**)

By allowing the precise measurement of hormone levels in the blood, the mechanism of **hormone deficiency diseases** could be better **identified, studied and treated.**

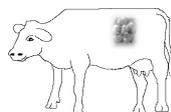
The **RIA technique** is extremely sensitive and specific, requires special equipments, but remains **the least expensive** method to perform.

It requires special precautions and licensing.

Today it has been largely supplanted by the **ELISA method**, where the antigen-antibody reaction is measured using colorimetric signals instead of a radioactive signal.

Reproductive Endocrinology

Animal production, management and basic physiological study



- Classical & reproductive endocrinology
- Clinical & applied endocrinology
- Regulation of hormone secretion
- Hormone action & molecular biology
- Cytokines & growth factors
- Disease or infertility treatment



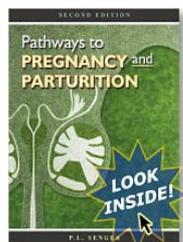
Reproductive endocrinology is also a branch of medicine that identifies and treats infertility in both men and women.

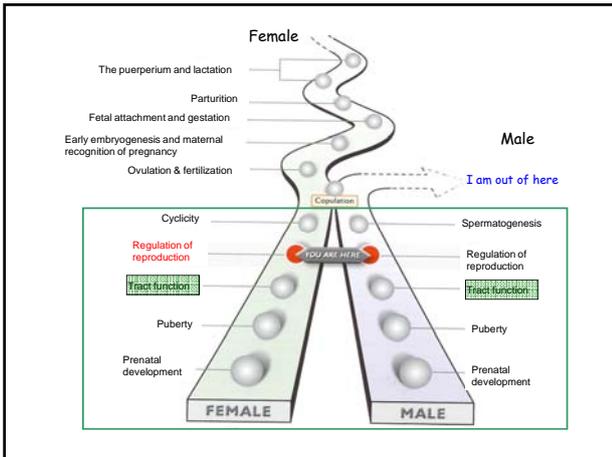
Please read:

Chapter 5

Regulation of Reproduction:

Nerves, hormones & target tissues





Endocrine & Hormone

Endocrine

Endo: from the Greek "endon"; within

Crine: "Krinein"; to release

Hormones

- **Greek verb:** to excite, and encompass (to surround or enclose)
- Signaling molecules produced by the endocrine gland (glandular cells)
- Secreted into the **internal milieu**
- Acts as a catalyst (needs receptors)
- Acts on target cells, tissues or organs at a place other than where it is produced.

Hormones

are **chemical substances** produced in one part of the body that diffuse or is transported in another area where it influences activity and tends to **integrate** component parts of the organism.

Bayliss and Starling (1902)

Two major categories of glands that **secret** in animal body:

1. Exocrine

- a. Having ducts
- b. Non-hormonal products are directed to the surfaces of cell membranes

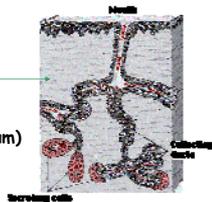
2. Endocrine: hormonal secretions

Exocrine Glands

A gland **with ducts** that are used for secretion.

The secretions pass into a ductal system that lead to the **exterior** of the body.

- EX: Salivary glands
Bile-producing glands (liver)
Prostate gland
Pancreas: pancreas fluid (duodenum)
Sweat glands



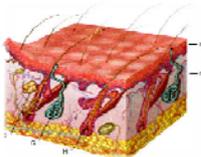
1. Eccrine (merocrine) glands--
Major sweat glands of the human body

Any of the numerous small sweat glands distributed over the body surface that produce a clear aqueous secretion devoid of cytoplasmic constituents -

(to regulate body temperature)

2. Apocrine (gland):

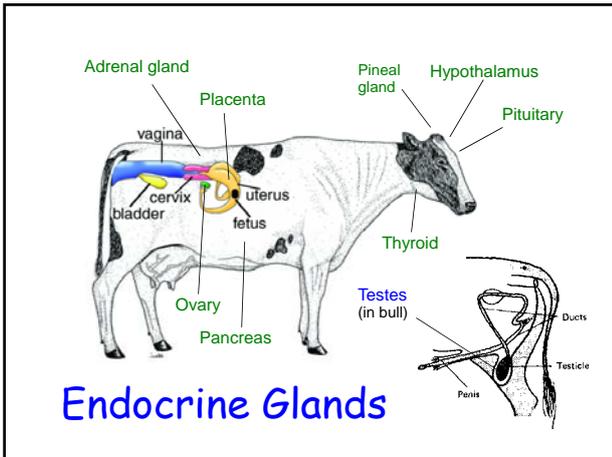
The glandular secretion in which the free end of the secreting cell is cast off along with the secretory products accumulated therein (e.g. large sweat glands in hairy regions).



A coiled, tubular gland whose secretory cells accumulate products on their apical surfaces that are then pinched off to become the secretion. (as in the mammary glands)

Endocrine Glands

- Ductless glands
- Secretes substances into surrounding tissue fluids (in vascular or lymphatic drainage) that affect cells elsewhere in the body.
- The secretion does not involve loss of tissue or provide energy to the target cells.



Different cells may respond to the same hormone differently:

e.g.
Insulin stimulates muscle and adipose cells to uptake glucose, and the liver to store glucose in the form of glycogen.

Endocrinology

The study of chemical communication systems that provide the means to control many physiologic processes (**integration**):

i.e., it is a science that involves **chemical integration** to maintain **homeostasis** of the body.

Other forms of hormone regulation

Paracrine: a cell secretes a compound acts on neighboring cells (a small distance)

The target cells are close to or next to the signal releasing cell.

(The hormone merely diffuses away from the source cell, and the adjacent target cells respond to the signal.)

Autocrine

a cell utilizes the compound it produces by itself, i.e., the target cell is also the cell that released the signal.

e.g., when cytokine interleukin-1 (IL-1) is released from monocytes in response to an external stimuli, the IL-1 can actually bind the cell-surface receptors on the monocyte that produces it (self-stimulation)

Other forms of hormonal regulations

Paracrine: a cell secretes a compound acts on neighboring cells (a small distance)

Autocrine: a cell utilizes the compound it produces by itself

Epicrine: hormones pass through gap junction of adjacent cells without entering extra-cellular fluid.

Intracrine: the regulatory molecules remain and effective within the cell

Neurocrine: hormones diffuse through synaptic clefts between neurons (neurotransmitters)

Classification & properties of hormones base on:

- A. Source of origins**
- B. Type of functions**
- C. Biochemical classifications (mode of action)**

A. Source of origin: site of production; glandular origins

Hypothalamic hormones: (<20 AA)

GnRH, oxytocin, neuropeptides

[STH-RF, STH-IF, CRH, TRF, PRF, PIF]

Pituitary hormones: gonadotropins +.....

Gonadal hormones: affecting functions of the hypothalamus, pituitary, reproductive tracts (E2, P4), and 2° sex characteristics

B. Type of functions/action

1. **Primary** reproductive hormones (FSH, LH, E2, P4, ...)

2. **General** metabolic hormones (thyroxin, insulin, STH,...):
Secondary hormones of reproduction

C. Chemical structures

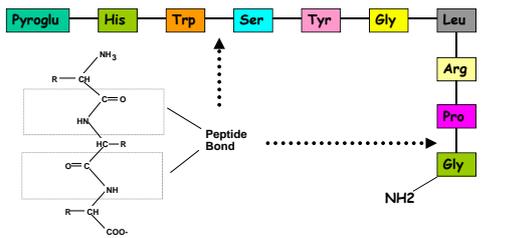
Polypeptides: hypothalamic, GnRH

Proteins/glycoproteins: pituitary, gonads

Steroids: gonadal, adrenal hormones

Fatty acids: many sources, prostaglandins

Modified amino acids: thyroid hormones,
melatonin

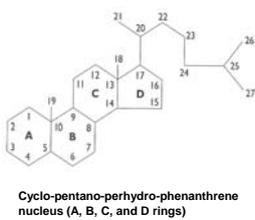


Peptide hormones are not given orally.

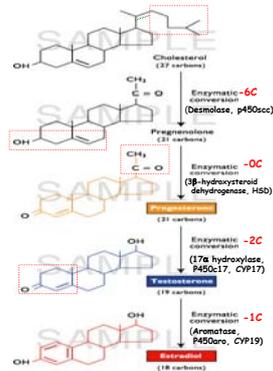
Amino acid sequence of GnRH

[Chemical Structure of Hormones] Cont.

Steroids hormones:
(Steroidogenesis)

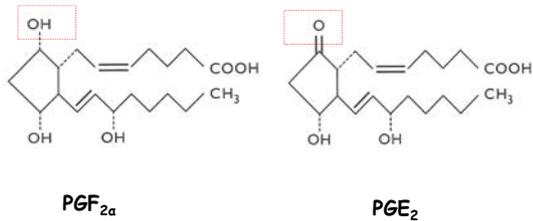


(Figs. 5-9, 5-10; P113-114)



Prostaglandins

(fatty acid, arachidonic acid derivatives)



(Figs. 5-11; P114)

Characteristics of Hormones

- (1) Act in minute quantities (10^{-9} - 10^{-12})
- (2) Have short half-lives in general
(differs between water soluble and insoluble)
- (3) Bind to specific receptors
- (4) Regulate intracellular biochemical reactions

Pheromones

Another class of substances directly influences reproductive processes.

Substances are secreted to the **outside** of the body.

Pheromones

The term "pheromone" was introduced by Peter Karlson and Martin Lüscher in 1959, based on the Greek word *pherein* (to transport) and *hormone* (to stimulate).

They are also sometimes classified as **ecto-hormones**, and also called "**alarm substances**".

These chemical messengers are transported outside of the body and result in a direct effect on hormone levels or behavioral changes.

Pheromones

Another class of substances directly influences reproductive processes.

Substances are secreted to the **outside** of the body.

Volatile and/or non-volatile signals detected by olfactory system (vomeronasal organ)

(Textbook P247-249)

Functions:

to influence the onset of puberty
the identification of estrus by the males
other behavioral and physiological traits