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
Fallopius (1562): discovered and described the ovary
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 cyclicity 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. PGF2α 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).

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 extracellular 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)

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

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<thead>
<tr>
<th>Hypothalamic hormones: (&lt;20 AA)</th>
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<tbody>
<tr>
<td>GnRH, oxytocin, neuropeptides</td>
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<tr>
<td>[STH-RF, STH-IF, CRH, TRF, PRF, PIF]</td>
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<th>Pituitary hormones: gonadotropins +...</th>
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<th>Gonadal hormones: affecting functions of the hypothalamus, pituitary, reproductive tracts (E2, P4), and 2° sex characteristics</th>
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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

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Peptide hormones are not given orally.

**Amino acid sequence of GnRH**

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**Steroids hormones:** (Steroidogenesis)

Cyclopentane-pentahydro-phenanthrene nucleus (A, B, C, and D rings)

(Figs. 5-9, 5-10: P113-114)
Prostaglandins
(fatty acid, arachidonic acid derivatives)

\[ \text{PGF}_{2\alpha} \quad \text{PGE}_2 \]
(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.
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.

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). Functions: to influence the onset of puberty, the identification of estrus by the males, other behavioral and physiological traits.