HORMONES: GENERAL PRINCIPLES

Hormone:
- Chemical substance which is secreted into body fluids
- Has a physiological control effect on other cells

TYPES OF HORMONES

Local hormones: have specific local effects (examples)
- Acetylcholine (parasympathetic and skeletal nerve endings)
- Secretin: released by duodenal wall causing watery pancreatic secretion
- Cholecystokinin:released by small intestine causing GB to contract and pancreas to secrete enzymes

General hormones: secreted by specific endocrine glands (example)
- Epinephrine and norepinephrine - both from adrenal medulla
  - Secreted in response to sympathetic stimulation
  - Constrict blood vessels; elevate arterial pressure
- Growth hormone (GH) - from anterior pituitary - effects all or most body cells
- Thyroid hormone
  - From thyroid gland
  - Increases rate of chemical reactions eg metabolism

BIOCHEMISTRY OF HORMONES: 3 basic types

1. Steroid hormones:
   - Chemical structure similar to cholesterol
   - Most instances derived from cholesterol
   - Secreted by endocrine glands
     - Adrenal cortex: cortisol and aldosterone
     - Ovaries: estrogen and progesterone
     - Testes: testosterone
     - Placenta: estrogen and progesterone

2. Derivatives of the amino acid tyrosine
   - Thyroid hormones: iodinated forms of tyrosine derivatives
     - Thyroxine (T4)
     - Triiodothyronine (T3)
   - Adrenal medulla hormones: catecholamines derived from tyrosine
     - Epinephrine
     - Norepinephrine
3. Proteins or peptides (all remaining hormones are either proteins, peptides or derivatives)
   - Anterior pituitary: proteins or large polypeptides
   - Post pituitary: peptides
   - Insulin, glucagon, parathormone: large polypeptides

ONSET OF HORMONE SECRETION AND DURATION OF ACTION

- Widely variable: minutes to months
  - Epinephrine, norepinephrine: adrenal medulla
    - Onset within first second
    - Reaches maximum concentration within a minute after onset of stimulation ion.
    - Rapidly destroyed: action 1-3 min past when stimulation is over.
  - Thyroid hormones: thyroid gland
    - Stored in thyroglobulin in follicles for months.
    - Hours to days required for initial action after secretion begins
    - Effect on tissue metabolism can last 6 weeks

CONCENTRATION AND SECRETION RATE OF HORMONES

- Quantitative amounts are very small
  Blood concentration range from 1 picogram (1 millionth or a millionth of a gram) to a few micrograms (1 millionth of a gram)
- Rates of secretion extremely small: micrograms or milligrams per day

**Negative feedback:** mechanism of control for hormone secretion rate

- Endocrine gland secretes hormone which exerts increasing effect on end organ.
- When a certain too much function occurs, some factor about that function feeds back to the endocrine organ and causes a negative effect which results in decrease its secretory rate.

  Example: FSH (anterior pituitary) stimulates ovaries to secrete estrogen. Estrogen levels gradually rise over the cycle and feed back on the pituitary to shut off production of FSH

- If target organ responds poorly to hormone, endo gland will secrete more and more until garget organ eventually responds
  - Results in excessive secretion of stimulating hormone
  - Example: TSH/thyroid function - lack of thyroid hormone causes continued secretion of TSH (no negative feedback) which results in a goiter
Measurement of Hormone Concentration:

- Extremely small concentration - impossible to measure via usual chemical assays
- Radioimmunoassay used to measure hormones
  - Antibody is made in large quantities in some lower animal which is highly specific for hormone in question
  - Small quantity of antibody mixed with

1. Fluid containing hormone (i.e. blood) to be measured for presence of hormone.
2. Appropriate amount of purified standard hormone that has been tagged with radioactive isotope.

   - Assay structured such that there is too little antibody to bind with both tagged hormone and hormone in fluid to be assayed thus competition for binding sites
   - In process of competition, radioactive and natural hormone bind in proportion to their respective concentrations.

3. Antibody-hormone complex is separated from remainder of solution; quantity of radioactive hormone bound with antibody measured via radioactive counting techniques

   - If large amt radioactive hormone can conclude there was only a small amount of natural hormone to compete
   - If small amt of radioactive hormone then there was large amt of natural hormone to compete for binding sites

4. Radioimmunoassay procedure is performed for "standard" solutions of untagged hormone at several different concentration levels thus a "standard curve" is plotted.

   - Other competitive binding assay procedures

     - Use of specific carrier globulin of plasma (instead of antibody) that is a natural binding agent for some specific hormone.
     - e.g. Plasma-binding globulin for adrenocortical hormone cortisol (highly specific) assay then carried out same as radioimmunoassay

Metabolic Clearance of Hormones

- Metabolic destruction by the tissues
- Binding with the tissues
- Excretion by liver into bile
- Excretion by kidneys into urine

Decrease in metabolic clearance rate can cause excessively high concentration of circulating hormone

   e.g. liver disease: steroid hormones are elevated because they are mainly conjugated in liver and cleared in bile. (gynecomastia in liver disease)
PITUITARY AND HYPOTHALAMUS

HYPOTHALAMUS:
- Area located in the middle of the limbic system of the brain
- Considered by some to be a structure separate from the limbic system
- Physiologically, it is one of the central elements of the limbic system

PITUITARY GLAND (a.k.a. hypophysis)
- Connected to hypothalamus via pituitary stalk
- Two distinct portions
  - Anterior pituitary a.k.a. adenohypophysis
  - Posterior pituitary a.k.a. neurohypophysis

Almost all secretion by pituitary is controlled via hormonal or nervous signals from hypothalamus
POSTERIOR PITUITARY: HYPOTHALAMIC NEURO-REGULATION

- Hormonal secretion controlled via nerve signals originating in hypothalamus and terminating in pituitary
  - Nerve fibers from the supraoptic nucleus project downward thru infundibulum into posterior pituitary where they secrete a hormone called ADH (vasopressin)
  - Simulation of paraventricular nucleus of causes neuronal cells to secrete oxytocin (expelling milk thru nipples plus uterine contractions)

ANTERIOR PITUITARY: HYPOTHALAMIC NEURO-REGULATION

- Blood courses thru hypothalamus
- Hormones are released before blood reaches anterior pituitary
  - Releasing and inhibitory hormones secreted into blood by various hypothalamic nuclei
  - Hormones transported via blood to anterior pituitary
  - Hormones act on glandular cells to control release of anterior pituitary hormones.

- Hormonal secretions
  - Controlled by hormones called releasing and inhibitory hormones (factors)
  - Secreted within hypothalamus and conducted via minute blood vessels called hypothalamic-hypophysial portal vessels.

- Releasing and inhibiting factors act on glandular cells in anterior pituitary to control secretion.
  - Releasing hormones is most important for most of anterior pituitary function
  - Inhibiting factors exerts most of the control for prolactin
  - TRH: thyroid-stimulating hormone releasing hormone - causes release of TSH
  - GHRH: growth hormone releasing hormone - causes release of growth hormone (GH)
  - GHIH: growth hormone inhibitory hormone a.k.a somatostatin: inhibits release of GH
  - GnRH: gonadotropin-releasing hormone - causes release of LH and FSH
  - PIF: prolactin inhibitory factor - causes inhibition of prolactin.

- Hypothalamus receives signals from all possible sources in nervous system:
  - Sources
    - Pain, depressing/exciting thought, olfactory stimulation, conc of nutrients, electrolytes, water and various hormones.
  - Collecting center for information
  - Controls secretions of globally important pituitary hormones
  - Difference between a factor and a hormone
    - A substance that has the actions of a hormone but that has not been purified and identified as a distinct chemical is called a factor. Once it is so identified, it is known as a hormone.
ANTERIOR PITUITARY HORMONES

Growth Hormone (GH): a.k.a. somatotropic hormone (SH) or somatotropin

- Causes growth of almost all cells and tissues of body
- Protein formation, cell multiplication, cell differentiation.
- Enhances body protein, uses up fat stores, conserves CHO

- Pygmies in Africa and certain other dwarfs (Levi-Lorain dwarf) have congenital inability to synthesis significant amounts of somatomedin-C (proteins synthesized by liver under influence of GH which increase all aspects of bone growth)

- Previously through GH ceased after adolescence but not so: post-adolescent secretion decreases slowly with aging to 25% of adolescent level in very old age.

- Increases during first 2 h of deep sleep; also in response to strenuous exercise, excitement/trauma, hypoglycemia, low blood conc fatty acid

- Panhypopituitarism: decrease secretion of all ant pit hormones (congenital, sudden onset or insidious onset during any period of lifetime).

- Dwarfism: most panhypopituitary during childhood:
  - Habitus is proportionate but rate of development decreased.
  - 2/3 do not pass through puberty; 1/3 lack only GH and do sexually mature
  - Majority do not secrete enough hormones for adult sexual development

- Treatment with human GH (hGH): species specific.
  - Lower animals not effective
  - Primates limited effectiveness for humans.

- Recombinant DNA technology has improved availability of GH
  Previously very difficult to get hGH due to need to obtain from pituitary glands.
  Now synthesis with recombinant DNA techniques from E. Coli therefore now more available and dwarfs with pure GH deficiency can be cured.

- Acromegaly excessive GH after adolescence
  - GH stimulates membranous bones
    Jaw causing forward protrusion of chin and lower teeth and skull bone thickening cause bony protrusions over eyes).
  - Hands and feet enlarge, nose enlarges, kyphosis, frontal bossing.

- Gigantism: excessive GH pre-puberty results in excessive height (8-9 feet)
  - Usually with hyperglycemia; 10% full blown DM.
  - Most will develop panhypopituitarism (death in early adulthood if untreated)
  - Treatment: surgery, radiation, adrenocortical and thyroid hormones.

- Panhypopituitarism in adult: (tumors or thrombosis of pit blood vessels)
  - Hypothyroidism, depressed adrenal corticoid production
  - Suppression of gonadotropins.
  - Treatment with thyroid hormones and adrenocorticoesteroid.
- Decreasing GH thought to be associated with the normal aging
  - Normal age related changes
    - Wrinkling, diminished rates of organ function, decreased muscle mass and strength
  - Normal levels
    - 05-20 years: 6 mg/ml plasma conc of GH
    - 20-40 years: 3 mg/ml plasma conc of GH
    - 40-70 years: 1.6 mg/ml plasma conc of GH

**Adrenocorticotropic Hormone:** causes adrenal cortex to secrete adrenocortical hormones

  - Secretion of some of the adrenocortical hormones which in turn affect metabolism of glucose, proteins and fats.

**Thyroid-Stimulating Hormone**
- Causes thyroid gland to secrete **thyroxine** and **triiodothyronine**
- Controls rate and secretion of thyroxine
- Thyroxine, in turn, controls rate of most chemical reactions of entire body

**Follicle stimulating hormone:**
- Growth of follicles in ovaries prior to ovulation
- Promotes formation of spermin testes

**Luteinizing Hormone:**
- Promotes ovulation
- Causes secretion of female sex hormones by ovaries and testosterone by testes.

**Prolactin:** promotes development of breasts and secretion of milk.

**POSTERIOR PITUITARY HORMONES**

**Antidiuretic Hormone (Vasopressin):**
- Causes kidneys to retain water thus increasing water content of body.
- High concentration: constricts blood vessels; elevates BP

**Oxytocin:**
- Contracts uterus during birth process
- Contracts myoepithelial cells in breasts: lactation

**ADRENAL CORTEX**

**Cortisol:** multiple metabolic functions for control of metabolism of proteins, CHO, fats

**Aldosterone:**
- Reduces Na excretion and increases K excretion by kidneys
- Results in increasing Na+ and decreasing K+ in body.
THYROID GLAND

Thyroxine (T4) and Triiodothyronine (T3):
- Increase rates of chemical reaction in virtually all cells
- Increases body metabolism

Calcitonin:
- Promotes deposition of calcium in bones
- Decreases calcium concentration in extracellular fluid.

PANCREAS: Islets of Langerhans

Insulin: facilitates glucose uptake by cells thus controls CHO metabolism

Glucagon: increases release of glucose from liver into circ body fluids

OVARIES

Estrogens:
- Stimulates development of female sex organs, breasts, secondary sexual characteristics

Progesterone:
- Stimulates secretion of "uterine milk" by uterine endometrial glands
- Promotes development of secretory apparatus of breasts

TESTES

Testosterone
- Stimulates the growth of male sex organs
- Promotes development of male secondary sex characteristics

PARATHYROID GLAND

Parathormone: controls calcium concentration in extracellular fluid via controlling
- Absorption of ca++ from gut
- Excretion of ca++ by kidneys
- Release of ca++ from bone

PLACENTA

Human Chorionic Gonadotropin (HCG):
- Promotes growth of corpus luteum
- Promotes secretion of estrogens and progesterone by corpus luteum

Estrogens:
- Growth of mothers sex organs
- Growth of some fetal tissues

Progesterone
- promotes develop of uterine endometrium in advance of implantation
- probably promotes growth and development of some fetal tissues and organs
- helps promote development of secretory apparatus of mother's breasts

Human Somatomammotropin:
- Probably promotes growth of some fetal tissue
- Aids in development of mothers breasts