The endocrine system -- a brief overview.

I. Introduction

- the endocrine system is an integration system that influences the metabolic activities of cells.

- acts via hormones, chemical messengers produced by endocrine glands -- pineal, hypothalamus, pituitary, thyroid, parathyroid, adrenals, pancreas, gonads.

- endocrine system (ES) vs. nervous system (NS):

    - ES slow acting, long-term effects, metabolic regulation, water and electrolyte balance, nutrient balance, regulation of cell metabolism, energy balance.

II. Hormones

- chemical substances secreted by cells into ECFs that regulate metabolic function of other cells.

A. Chemistry

1. amino aid based hormones: amino acid derivatives, single modified amino acids, peptides, proteins, glycoproteins.

2. steroid based hormones - cholesterol derivatives.

3. eicosanoids -- derivatives of 20-carbon polyunsaturated fatty acid, arachidonic acid

- arachidonic acid is fatty acid found in membrane of all cells
- include prostaglandins, prostacyclins, thromboxanes, leukotrienes
- extremely active biologically
    - smooth muscle contraction (prostaglandins), relaxation (prostacyclins)
    - clot formation:
        - stimulate platelet aggregation (thromboxane)
        - inhibit platelet aggregation (prostacyclin)
    - mediator of allergic and inflammatory response:
        - leukotrienes:
            - bronchoconstriction
            - arteriolar vasodilation

- increased vascular permeability
- chemotaxic: attract WBC

B. Mechanisms of hormone action

- hormones produce effects on target cells by:

- changes in membrane permeability due to opening/closing of channels.
- activation/deactivation of regulatory molecules -- covalent modification.
- synthesis of regulatory molecules -- involves changes in gene expression.

- these effects result in physiological changes:

- induction of secretory activity.
- stimulation of mitosis.
- contraction/relaxation

1. Action of peptide/protein hormones

- hormones non-lipid soluble
- bind a membrane receptor molecule
- activation of G-protein
  - opens channel
  - activates enzyme
    - second messenager produced (cAMP, Ca^{++})
    - second messenger initiates an intracellular cascade of events that bring about changes in cell function

2. Action of steroid hormones

- hormones are lipid soluble, pass through the cell membrane.
- bind a cytosolic/nuclear receptor -- forms HR complex.
- HR complex binds a chromatin site, changes shape of chromatin, exposes binding sites for transcription factors -- transcription of a specific gene stimulated, new proteins synthesized.

C. Hormone target cell specificity: hormones produce effects in target cells that have receptors for hormone

- target cell activation depends on:
  - level of hormone present
  - number of receptors for hormone
    - upregulation/downregulation of receptors
  - affinity of receptor for hormone

D. Duration of hormone activity

- depends on:
  - rate of release vs. rate of degradation/excretion (measured by half life)
    - peptides have short half life, steroids have longer half life.
  - degree of plama protein binding -- in case of lipid hormones
  -
- effects can last seconds to hours/days depending on hormone and mechanism of action.

E. Control of hormone release

- regulation in majority of cases via negative feedback.

- cells stimulated to release hormones by three types of stimuli:

  - humoral stimuli
  - neural stimuli
  - hormonal stimuli.

III. Major endocrine organs

A. The pituitary gland

1. Functional anatomy of pituitary-hypothalamic interactions.
   a. pituitary (anterior/posterior) closely associated with hypothalamus via a stalk, infundibulum.

   b. two two interconnected capillary beds, one in infundibulum a second bed associated with anterior/posterior pituitary.

c. anterior pituitary -- glandular epithelium; manufactures, releases a number of hormones; AP hormones released in response to presence of releasing hormones produced by neurons in the hypothalamus and released into the capillary bed of the infundibulum.

d. posterior pituitary -- neural tissue, neuron endings; stores and releases neurohormones that are synthesized in the cell bodies of its neurons in the hypothalamus; when neurons are activated, hormones released at posterior pituitary.

2. Adenohypophyseal hormones (AP)

- secretion under influence of hypothalamic releasing hormones.
- four of adenohypophyseal hormones are tropic hormones -- regulate secretory activity of other endocrine glands (ACTH, FSH, LH, TSH).
- other two hormones exert their influence on non-endocrine targets - GH, prolactin.

a. growth hormone (GH)

-protein.

- stimulates virtually all cells of body to increase in size and divide, but main targets are bones (stimulation of epiphyseal plate growth) and skeletal muscle (stimulate increase in muscle mass).

- stimulates increased amino acid uptake from blood; mobilizes fats; spares glucose.

b. thyroid-stimulating hormone (TSH)

- glycoprotein.

- stimulates normal development and secretory activity of the thyroid.

c. adrenocorticotropic hormone (ACTH)

- peptide.

- stimulates the adrenal cortex to release glucocorticoids and androgens (corticosteroids).

d. gonadotropins (FSH, LH)

- glycoproteins.

- FSH stimulates gamete production, LH stimulates productions of gonadal hormones.

e. prolactin

- protein.

- stimulates milk production by breast secretory tissue.

3. Neurohypophyseal hormones (PP)

a. antidiuretic hormone (ADH)

- peptide

- firing of hypothalamic neurons that store ADH at their terminal endings stimulated by increased osmolarity of blood.

- regulation of water balance, plasma volume.

b. oxytocin

- peptide

- stimulated by impulses from hypothalamic neurons in response to cervical/uterine stretching and suckling of infant at breast.

- childbirth,; suckling reflex.

B. Thyroid gland

- largest endocrine gland, inferior to larynx.

1. internal anatomy

- thyroid composed of follicles
- follicular cells secrete large glycoprotein, thyroglobulin to follicular space, and pump iodide into follicular space; thus follicular space contains thick proteinaceous material, colloid, the major component of which is thyroglobulin.
- thyroglobulin contains many tyrosines -- iodination and coupling of tyrosine residues involved in formation of thyroid hormones.

2. synthesis of thyroid hormones

a. synthesis/secretion of thyroglobulin to follicle

b. iodide trapping, oxidation to iodine -- to lumen of follicle.

c. iodination of tyrosines of thyroglobulin (MIT, DIT)

d. coupling of iodinated tyrosines (T3/T4)

e. colloid endocytosis -- iodinated thyroglobulin taken into cell.

d. cleavage of thyroglobulin by lysosomal enzymes -- T3 and T4 released (modified amino acids).

3. TSH stimulates all above steps; an enzyme critical for iodide trapping, iodination, and coupling is thyroid peroxidase.

4. T3 and T4 are transported bound to plasma proteins, only a small amount of hormone is free in plasma; this protects hormones from degradation and provides body with a pool of ready to use thyroid hormone.

5. Target tissues convert T4 to T3 -- hormone finally acting on tissues is T3.

6. T3 acts via nuclear receptor model of steroid hormones.

7. Effects of thyroid hormone

a. promotes normal oxygen consumption and BMR -- by stimulating enzymes concerned with glucose oxidation.

b. due to effects above it increases body heat production - calorigenic effect

- modulates normal tissue growth and development.

C. Parathyroid glands and parafollicular cells of thyroid

- parathyroid glands synthesize and release parathyroid hormone; parafollicular cells of thyroid synthesize and release calcitonin.
- calcium metabolism.

D. Adrenal glands

1. Adrenal cortex -- outer layer of adrenal gland, produces corticosteroids

a. zona glomerulosa (outer cortex)

- mineralocorticoids -- aldosterone; role in electrolyte balance.

b. zona fasciculata (middle cortex)

- glucocorticoids -- cortisone, cortisol, hydrocortisone; essential effects on carbohydrate metabolism, maintenance of blood volume, stress response, depress immune system.

c. zona reticularis (inner cortex)

- androgens -- androstenedione, estrogens; onset of puberty, appearance of axillary and pubic hair.

2. Adrenal medulla -- a sympathetic "ganglion"; epinephrine, norepinephrine.

E. Pancreas - insulin and glucagons

F. Gonads -- sex hormones, estrogen, progesterone, testosterone.