The Endocrine System - General

no clear distinction between nervous and endocrine systems
=neuroendocrine system

they are intimately interrelated
→ complement each other
→ two ends of a single spectrum

Similarities

a. both coordinate and control
b. both produce biologically active chemicals
Neurotransmitters vs hormones
→in some cases use same chemical
c. hormones affect nervous system/
nervous sytem affects hormone releases
d. some major parts of brain are glands:
pineal
anterior pituitary
posterior pituitary
e. some endocrine glands are effector organs for brain
adrenal medulla
posterior pituitary
f. some responses begin as nervous reflexes and end as hormonal responses:
eg. emergency and adrenal medulla
eg. digestive physiology
g. one may override normal effects of the other:
eg Bld sugar: normal = 80-120 mg/100ml →
regulated by hormones
stress → sympathetic stimulation
→ increases blood sugar levels

Differences:

Nervous

localized effects: cell to cell
targets: →other neurons,
→muscle cells,
→glands,
transmits long range information by nerve impulses
uses chemical signals (=neurotransmitters)
only cell to cell
neurotransmitter only produced by neurons
immediate response

short lived (ms – minutes)

Endocrine

widespread effects
targets: all organs and tissues
transmits long range information as chemical signals only = hormones, through circulatory system
gradual response (seconds – hours)
longer – lived effects (minutes – days)

Endocrine Physiology - General

hormones affect virtually every aspect of physiology

some **general effects of hormones** on body:

a. enhance or moderate neural control of effectors
b. affects overall metabolic rate
c. helps to maintain homeostasis of body's internal environment by regulating concentrations of salts, nutrients, hormones, and fluids
d. helps body cope with and respond to environmental changes that can cause infection, trauma, thirst, hunger
e. contributes to all aspects of the reproductive process
f. provides smooth, sequential integration of all factors involved in growth and development
g. affect moods and behavior

Characteristics of Hormone Function

1. most if not all organs produce hormones

"officially" the endocrine system consists of several major glands and many minor glands

2. Structurally, the major hormones are of two basic types:

a. amino acid derived hormones

i. amines
(acetylcholine, thyroid hormone, epinephrine, norepinephrine

ii. polypeptides and glycoproteins
(ADH, Insulin, TSH)

b. steroid hormones
(cortisol, testosterone, estrogen)

hormones are often derived from less active precursor in gland cells
eg. long chain "prohormone"
→ cut and spliced to form active hormone

3. Hormones are secreted in response to specific stimuli

3 mechanisms: **neural, humoral, hormonal**

Many endocrine glands secrete more than one hormone

hormones can be secreted independently of one another

hormones may be secreted for long periods of time

→at any one time there may be up to 40 major hormones and other minor hormones circulating in body

4. Hormones are transported to target organs in the blood and body fluids

the major hormones are secreted from ductless glands directly into blood

(exocrine vs endocrine glands)

all major endocrine glands are richly supplied with blood capillaries
→most are fenestrated capillary beds

hormones often circulate in blood attached to transport protein

(inactive form)

eg testosterone circulates in inactive form
→ must be activated by target cell

5. hormone effects are highly specific to "target organ"
→ requires specific binding site (receptor proteins)

even though every hormone comes in contact with every cell

target cells respond only to specific hormones

they are generally effective in minute quantities

6. At the cellular level each hormone can affect a target cell in only a few ways:

a. can change in cell membrane permeability
eg. change in secretory activity of a cell
b. can alter metabolic pathway(s)
eg. enzymes activated or inactivated
→ make new products
→ cease making product
c. can change rate of cell division
eg. speed up or slow down

Each hormone can affect each target cell in >1 of these ways

Maybe different effects in different target cells for same hormone

7. Most cells have receptors for more than one type of hormone

hormones can interact with each other

→ **synergistic effects**
= presence of 1 enhances effects of other
→ **antagonistic effects**
= 1 counteracts effects of other
→ **permissive effects**
= one hormone "primes" target organ for another hormone;

eg estrogen then progesterone on uterus

8. the extend of target cell activation can depend on:

a. blood levels of hormones

Hormones effects are **concentration dependent**

hyper and hypo secretion
→ much of our knowledge of hormones effects comes from study of abnormal production

b. relative # of receptor proteins on target cells

similar problems if too little or too many receptor proteins or target cells

c. affinity of binding

overstimulation can cause desensitization

9. the time required for the onset of hormone effects varies greatly
→ some hormones provoke **immediate response**
→ others (eg steroid) may require **hours to days** before their effects are seen

10. Hormones don't accumulate in blood

typical duration of hormones effects = 20 min to several hours

those that bind to target cells are destroyed
→ half-life ~ seconds – 30 minutes

excess are continually cleared by **liver** and **kidney**

→effects may disappear rapidly as blood levels drop or may persist even though blood levels are low

therefore for prolonged effect
→ hormones must be continuously secreted

Control of Hormone Release

The synthesis and release of most hormones are regulated by some type of negative feedback system

three major mechanisms:

1. **Humoral**
2. **Neural**
3. **Hormonal**

some endocrine glands respond to multiple stimuli

1. Humoral

hormones secreted in direct response to changing blood levels of certain chemicals in blood

affect endocrine gland directly

eg. parathyroid gland

cells directly monitor conc of Ca++ions
when Ca++ decline they respond by secreting PTH

eg. pancreas

insulin and glucagon secreted in response to blood sugar concentrations

eg. adrenal cortex aldosterone

2. Neural

hormones secreted due to direct nervous stimulation

eg. adrenal gland

directly stimulated by sympathetic fibers of ANS
produces same effects as Sympathetic NS but lasts
10 times longer:
Δ cardiac output
Δ heart rate
Δ alertness
Δ respiratory rate

eg. Posterior Pituitary

secretes oxytocin in direct response to nerve impulses from hypothalamus

3. Hormonal

Anterior Pituitary = master gland

secretes several hormones that control the secretion of other endocrine glands

→ **Tropic Hormones**

each tropic hormone has a **target gland** which it stimulates to produce its characteristic hormones

eg. TSH, ACTH, FSH LH

The release of trophic hormones is controlled by hypothalamus:

hypothalamus receives nerve impulses from all areas of brain

no direct neural connection between anterior pituitary and hypothalamus

they are connected by dense capillary bed

no blood brain barrier between them

hypothalamus contains neurosecretory cells

these cells serve as link between nervous and endocrine systems

neurosecretory cells are activated by nerve impulses and react by secreting neurohormones = **releasing hormones**

produces specific **Releasing Hormones** for each tropic hormone
eg. TSH-RH

releasing hormones travel in capillary bed to anterior pituitary

trigger release of appropriate tropic hormone

→ translates nerve impulses into hormone secretions

sensory information in form of nerve impulses can be interpreted and acted on by the release of hormones =**Neuroendocrine Reflex**

eg. rapid response to stress
eg. thoughts and emotions affect body's hormone levels

Off

Hormones are switched off by **negative feedback** mechanisms
require receptor – CNS – effector

eg. Negative Feedback for Hormonal Regulation

hypothalamus contains chemoreceptors for hormones switched on by tropic hormones

↓

when levels get too high this inhibits the production of releasing hormones

↓

stops production of tropic hormones

↓

stops production of specific hormone

Mechanism of Hormone Action on Target Cell

depends on hormone structure and location of receptors on target cell

A. Steroid Hormones

are nonpolar and fat soluble

and thyroid hormone which is also nonpolar)

receptors are located inside cytoplasm and nucleus
→ intracellular receptors

hormone enters cell and binds to receptor and activates it

hormone/receptor complex inters nucleus
→ binds to a protein on chromosome
→ triggers transcription

therefore: steroid hormones have a direct effect on DNA activity

B. Amino Acid Derived Hormones

are polar

cannot enter cell

use "**second messenger**" to produce effect on target cells

hormones attaches to specific receptor site on target cell

triggers enzyme "**adenylate cyclase**"
(via G protein) to make "cyclic AMP" from ATP

cyclic AMP diffuses throughout cell and mediates target cell response to hormone

mainly by activating one or more different enzymes called "**protein kinases**"

each protein kinase has a specific substrate that it acts on:
→ enzyme activation or inactivation
→ cellular secretion
→ membrane permeability
→ gene activation or inhibition

Other Chemical Regulators

so far have studied two major types of regulatory molecules:
- **neurotransmitters & neuromodulators**
- **hormones**

defined mainly by function, location, and action

a 3rd class of regulatory molecules are distinguished by the fact that
- →they are produced in many different organs
- →generally active in same organ that produces them

= **paracrine regulators**

Paracrine Regulators

=eicosanoids
- produced in almost every organ and tissue of body except RBC's
- not officially part of endocrine system
- biologically active lipids
  - (modified fatty acids, not steroids)
- local regulators (= tissue hormones)
- made in small quantities
- short lived

mainly **prostaglandins** and **leukotrienes**

have wide variety of effects in various systems:
- immune response
  - →regulate inflammatory process
  - → role in pain, fever
- cardiovascular system
  - →role in blood pressure
  - →vasomotor system = distribution of bloodflow
- reproduction
  - →ovulation
  - → role in corpus luteum, endometriosis, PMS
  - →induce labor
- digestion
  - → inhibit gastric secretions
  - → intestinal peristalsis
- respiration
  - → constriction/dilation of blood vessels
  - → role in asthma
- clotting
  - eg thromboxane

→constricts blood vessels
→promotes platelet aggregations

urinary function
fat metabolism

Hormone Interactions

while each hormone has a specific function

hormones rarely act alone to maintain homeostasis

homeostasis usually involves several hormones working together in complex ways to regulate metabolic levels:

synergists → hormomes which tend to cause the same effect

eg. ADH & aldosterone

antagonists → hormones which produce opposite effects

eg. insulin & glucagon

permissive → hormones which only affect "preprimed" tissues

eg. progesterone

eg. Growth

Hormones that generally stimulate growth:

growth hormone

→stimulates growth of cartilage at epiphyseal plates

→ stimulates growth in all tissues
(except brain & reproductive organs)

→maintains adult tissues

thyroid hormones

→regulates the amount of energy available for protein synthesis

→esp skeleton and nervous sytem and brain

low TH: retards growth, childlike proportions
high TH: excessive growth, short stature,
demineralization in adults

mineralocorticoids

testosterone

→especially skeletal growth

Hormones that generally inhibit growth:

glucocorticoids

estrogen

<u>eg. Calcium Homeostasis:</u>

main hormones that maintain blood calcium levels:

PTH

→ stimulates osteoclasts
→ increases blood Calcium levels

Calcitonin

→ stimulates osteoblasts
→ decreases blood calcium

Estrogen & Testosterone

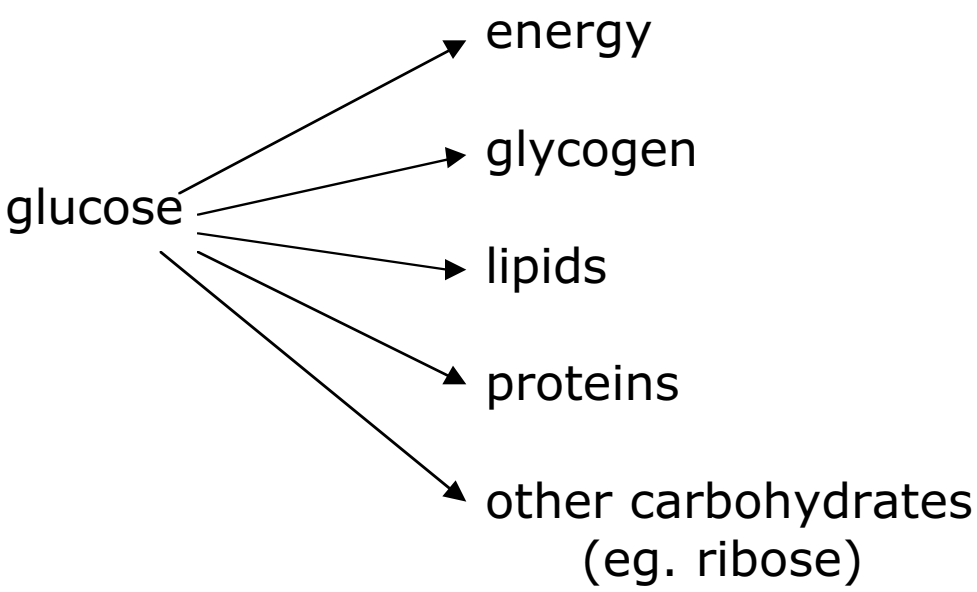
→ maintain bone density by
slowing osteoclast activity and
promoting osteoblast activity

eg. Carbohydrate Metabolism

one of best studied systems of hormone interactions

glucose is most utilized carbohydrate in body

circulates in blood until it is needed for any of several functions:



energy = with oxygen is converted to carbon dioxide and water

only energy source that the brain can use

storage = converted to glycogen
synthesis of other carbohydrates, proteins, lipids

several hormones from various glands play a direct role in glucose homeostasis

1. Insulin (Pancreas-Islet Cells)

accelerate transport of glucose into body cells
increases rate of utilization of glucose by body cells

→ lowers blood glucose levels

2. Glucagon (Pancreas-Islet Cells)

stimulates breakdown of glycogen in liver and
release of glucose into blood
also stimulates synthesis of glucose from lactic
acid, glycerol, etc (=gluconeogenesis)

→ raises blood glucose levels

3. ACTH (Anterior Pituitary)

tropic hormone that affects glucocorticoid production

4. glucocorticoids (Adrenal Cortex)

converts amino acids and fats to glucose in liver cells
excess glucose is released into blood

→ raises blood glucose levels

5. growth hormone (Anterior Pituitary)

shifts from glucose catabolism to fat catabolism
increases oxidation of fats; spares glucose

unused glucose is converted to glycogen to maintain normal glycogen
stores

excess glucose spills into blood

→ raises blood glucose levels

6. TSH (Anterior Pituitary)

tropic hormone that stimulates release of thyroid hormone

7. Thyroid Hormones (Thyroid)

may accelerate catabolism of glucose to cause lowered blood glucose
levels

or

or have other effects that raise blood glucose levels

8. Epinephrin (Adrenal Medulla)

stimulates breakdown of glycogen to glucose in muscle and liver cells

and release of glucose into blood

→ raises blood glucose levels

[but can also stimulate release of insulin by pancreas]

of all hormones listed only insulin is major "hypoglycemic hormone"

all others are mainly "hyperglycemic hormones"

Diabetes

diabetes is a general name for a group of diseases

two major varieties:
- diabetes insipidus
- diabetes mellitis (Types I & II)

Diabetes insipidus

a disease associated with Posterior Pituitary

deficiency in ADH causes low reabsorption of water

large volumes of dilute urine are produced:
(up to 10 gallons/day vs normal 1 qt/day)

leads to electrolyte imbalances etc

Diabetes mellitis

10 Million diabetics in US
40,000 die anually as result of disorder

effects:
- reduces life expectancy by ~1/3rd
- 25 x's greater rate of blindness
- 17 x's greater rate of kidney disease
- 17 x's greater rate of gangrene
- 2 x's greater chance of heart attack

may be triggered by:
- genetic factors
- environmental factors
- autoimmune disease
- pregnancy
- obesity

two kinds:
- 10% = Juvenile Onset Diabetes (Type I)
- 90% = Maturity Onset Diabetes (Type II)

Type I Diabetes

develops before the age of 20 years

is result of malfunction of Islet cells in pancreas
→dramatic decrease in the number of beta cells

insulin is not produced in sufficient quantities

in all body cells:
decreased glucose utilization
→ cells can take in only ~ $1/4^{th}$ normal amount of glucose

levels of glucose build up in blood
→ 3-10 times normal = hyperglycemia

since glucose can't be used alternate fuels are mobilized:

increased fat mobilization
fats in blood rise to up to 5x's normal
as cells shift to fat catabolism
→ produce ketone bodies
→ lower blood pH = acidosis
→ acetone breath
→ increased risk of atherosclerosis

without insulin to stimulate protein synthesis they are instead broken down and converted to glucose in cells
→ tissue wasting

high levels of glucose in blood lead to large quantities of glucose spilling into urine
→ diagnostic test for disease
(used to taste it, now have chemical indicators)
→ this draws large amts of water into urine

Type II

adult onset diabetes

body produces insulin but target cells don't respond
→receptor problem

related to obesity

possibly overstimulation of receptors
→they decline in numbers until cells don't respond

treatment mainly by dietary changes

eg. Fat Metabolism

fat is largest accessible store of energy in body

esp fat in liver and adipose tissues

glucose is most important precursor of fat

so regulation of fat is closely tied to glucose metabolism

1. **Insulin**
   → promotes fat synthesis by stimulating uptake of glucose by body cells

2. **Adrenalin**
   glucagon
   growth hormone
   } stimulate fat metabolism

eg. Protein Metabolism

1. Growth Hormone — accelerates movement of Insulin amino acids into cells
2. Testosterone — stimulates protein synthesis
3. glucocorticoids — release amino acids into blood
4. thyroxine — supports other activies that promote synthesis