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 system 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
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
      \( \rightarrow \) 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
   \( \rightarrow \) some hormones provoke immediate response
   \( \rightarrow \) 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
    \( \rightarrow \) half-life \( \sim \) seconds – 30 minutes

    excess are continually cleared by liver and kidney

    \( \rightarrow \) effects may disappear rapidly as blood levels drop
    or may persist even though blood levels are low

    therefore for prolonged effect
    \( \rightarrow \) 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
  \( \rightarrow \) intracellular receptors

hormone enters cell and binds to receptor and activates it

hormone/receptor complex inters nucleus
  \( \rightarrow \) binds to a protein on chromosome
  \( \rightarrow \) 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:
  \( \rightarrow \) enzyme activation or inactivation
  \( \rightarrow \) cellular secretion
  \( \rightarrow \) membrane permeability
  \( \rightarrow \) 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 3\textsuperscript{rd} class of regulatory molecules are distinguished by the fact that 
\rightarrow they are produced in many different organs 
\rightarrow 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
\rightarrow regulate inflammatory process 
\rightarrow role in pain, fever

cardiovascular system
\rightarrow role in blood pressure 
\rightarrow vasomotor system = distribution of bloodflow
reproduction
\rightarrow ovulation
\rightarrow role in corpus luteum, endometriosis, PMS
\rightarrow induce labor
digestion
\rightarrow inhibit gastric secretions 
\rightarrow intestinal peristalsis
respiration
\rightarrow constriction/dilation of blood vessels 
\rightarrow role in asthma
clotting
\rightarrow 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** → hormones 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 system 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**
**eg. Calcium Homeostasis:**

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
- glycogen
- lipids
- proteins
- other carbohydrates (eg. ribose)

**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 mellitus (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 mellitus**

10 Million diabetics in US
40,000 die annually as result of disorder
effects:
  reduces life expectancy by $\sim 1/3^{rd}$
  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**

devolves 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\textsuperscript{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

\textbf{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 activities that promote synthesis