The Endocrine System

no clear distinction between nervous and endocrine systems

= neuroendocrine system

they are intimately interrelated

→ complement each other
→ two ends of a single spectrum

<table>
<thead>
<tr>
<th>The Neuroendocrine System</th>
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<tbody>
<tr>
<td>Nervous System</td>
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<tr>
<td>Targeted effects</td>
</tr>
<tr>
<td>Targets: neurons, muscle cells or glands</td>
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<tr>
<td>Transmission by nerve impulses</td>
</tr>
<tr>
<td>immediate response (ms to seconds)</td>
</tr>
<tr>
<td>Short lived (ms to minutes)</td>
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<tr>
<td>Both</td>
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General Characteristics of Hormones

1. a chemical is considered a hormone if it is secreted and transported in the blood

same chemical can also be a neurotransmitter, or
lymphokine, etc

the major hormones are secreted from ductless glands directly into blood

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
   receptor can be on the surface of the target cell or inside the target cell
   target cells respond only to specific hormones

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

   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;

8. Hormones don’t accumulate in blood
   those that bind to target cells are destroyed
   → half-life ~ seconds ~ 30 minutes
   excess are continually cleared by liver and kidney
   therefore for prolonged effect
   → hormones must be continuously secreted

(exocrine vs endocrine glands)

all major endocrine glands are richly supplied with blood capillaries

2. most, if not all, organs produce hormones
   "officially" the endocrine system consists of several major glands
   and many minor glands

3. Hormones are secreted in response to specific stimuli
   3 mechanisms: neural, humoral, hormonal

A. Humoral
   hormones secreted in direct response to changing blood levels of certain chemicals in blood
   affect endocrine gland directly

B. Neural
   hormones secreted due to direct nervous stimulation

C. Hormonal
   Anterior Pituitary = master gland
   secretes several hormones that control the secretion of other endocrine glands
   → Tropic Hormones

4. Many endocrine glands secrete more than one hormone
   hormones can be secreted independently of one another
**Major Endocrine Glands**

**Pituitary Gland (=Hypophysis)**
small but extremely important structure
attached to a stalk (infundibulum) at base of hypothalamus
housed in sella turcica of sphenoid bone
consists of two separate glands

**Anterior Pituitary Gland**
master gland
secretes tropic (or trophic) hormones:

a. **Thyroid Stimulating Hormone (TSH)**
   → stim development and secretions from thyroid gland

b. **Adrenocorticotropic Hormone (ACTH)**
   → normal growth and development of adrenal cortex

c. **Follicle Stimulating Hormone (FSH)**
   in women: stimulates follicles to begin growing to ovulation
   in men: stimulates development of seminiferous tubules and sperm cells

d. **Leutinizing Hormone (LH)**
   → in women:
      final maturation of follicle
      stimulates formation of corpus luteum
      [a temporary endocrine gland of pregnancy]
      promotes secretion of progesterone
   → in men:
      stimulates interstitial cells to secrete hormone = testosterone
   if pituitary gland is removed by radiation or surgery, need hormone treatment rest of life or some other glands will shut down

in addition to tropic hormones, Ant Pit also secretes some other (nontropic) hormones:
e. **Growth Hormone (GH)**
   promotes growth of bone and soft tissue
   stim protein synthesis
   amt of GH secreted decreases with age

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<th>during childhood</th>
<th>→ gigantism</th>
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| HYPOSECRETION of GH | during childhood | → dwarfism |

f. **Prolactin (PRL; = Lactogenic Hormone)**
affects female:
   → induces breast development during pregnancy
   → initiates milk secretion after childbirth
   prl release is stimulated by suckling
   no significant functions in males

**Posterior Pituitary Gland**
hormones released by direct nervous stimulation of posterior pituitary

a. **Antidiuretic Hormone (ADH, =vasopressin)**
   (=against production of urea)
   ADH is released whenever receptors indicated dehydration
   ie. decreases urine output conserves water

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b. **Oxytocin**
   (=swift childbirth)
   stimulates contraction of uterine muscles during labor
   causes milk ejection into ducts as result of nursing infant [let down reflex]
   triggered by neural stimulus: sucking
   functions in "societal memory": affects ability to recognize & trust others
   [deficiency may be correlated with autism]
Pineal Gland
located behind the midbrain and 3rd ventricle
attached to roof of third ventricle
not sure of all its functions in humans but seems to
regulate cyclic activities
Rene Descartes (1596-1650) thought it was the seat of
the human soul
is light sensitive → monitors photoperiod
a. Melatonin
main hormone it secretes is melatonin
light suppresses production
dark stimulates production
→ secretion rises at night, fluctuates seasonally
and with changing day length
in lower animals it helps regulate cyclic activities:
hibernation
estrous
migraton
In humans:
→ may help regulate menstrual cycle
→ inhibits onset of puberty in males
may be related to seasonal affective disorder and
PMS

Thymus
a temporary endocrine gland
behind sternum, below thyroid
large in fetus and child
maximum size at puberty
degenerates in adult (replaced with fat)
functions as endocrine gland and as part of immune
system
secretes thymosin and related hormones
→ stimulates development of lymphatic organs
→ induces maturation and development of WBC's
particularly T-lymphocytes

Thyroid Gland
the largest endocrine gland in adults
surrounds trachea just below larynx
consists of 2 lobes → usually described as butterfly
shaped
Hormones:
a. Thyroid Hormones (T3, T4)
activated by TSH from Ant Pit
contain Iodine atoms
98% of body’s Iodine is in the thyroid gland
inadequate iodine in diet → goiter
thyroid hormones help to regulate metabolism
in all cells:
→ increases metabolic rate & ATP production
→ increase oxygen consumption and bld O2 levels
→ promotes maturation and development of the
nervous system
→ increases protein synthesis
→ help maintain normal reproductive function
many environmental stimuli can inhibit
secretions of this gland:
cold temp, physical stressors, noxious stimuli
HYPERSECRETION of Thyroid Hormones
Graves disease
up to 30% increase in Metabolic Rate
Δ appetite
weight loss
nervous irritability
HYPOSECRETION of Thyroid Hormones
During growing years
cretinism
low metabolic rate
retarded growth and sexual devel
often mentally retarded
As adult
Myxedema
loss of mental and physical vigor
weight gain
thickened skin
b. Calcitonin
decreases blood Ca++ / promote bone
deposition by inhibiting osteoclasts
stimulating osteoblasts
its effects are significant only in children,
negligible effect in adults
HYPOSECRETION of Calcitonin
can cause rickets in children
(but usually due to Ca++ or Vit D deficiency)
Parathyroid Glands

small round bodies attached to the posterior surfaces of the thyroid gland
usually 4 or 5, but varies

a. Parathyroid Hormone (PTH)

helps maintain homeostasis of blood calcium
antagonist to calcitonin
raises blood Ca^{++} levels:
  \rightarrow\text{promotes Ca^{++} absorption by kidney tubules and intestine}
  \rightarrow\text{stimulates osteoclasts to dissolve bone}
  \text{since bone contains both calcium and phosphorus this releases both into blood}
Calcium homeostasis is important in:
  \text{neuromuscular function}
  \text{blood clotting}
  \text{synapses to activate certain enzymes}
  \text{affects cell membrane permeability}
surgical removal of thyroid gland requires PTH hormone replacement therapy if all parathyroids are removed at the time

Pancreas

both an \textit{exocrine} and \textit{endocrine} gland

exocrine (98\% of mass of pancreas):
  \text{secretes digestive enzymes}
endocrine (<2\% of mass of pancreas):
  \text{contains clusters of endocrine cells}
  = \textit{Islets of Langerhans}
  \text{(~1 Million clusters; each up to several 1000 cells)}
humoral regulation: monitors blood glucose conc & amino acid levels
mainly secretes:
  \textit{insulin}
  \textit{glucagon}
\}\text{regulate blood sugar levels}
both are proteins

a. Insulin

levels rise immediately after a meal
  \rightarrow\text{moves glucose, amino acids and fatty acids out of blood, into cells (except liver cells)}
  \rightarrow\text{lowsers blood glucose concentrations}

Diabetes

diabetes is a general name for a group of diseases

two major varieties:
  \text{diabetes insipidus}
  \text{diabetes mellitis (Types I & II)}

\text{Diabetes insipidus}

a disease associated with Posterior Pituitary
deficiency in ADH causes low reabsorption of water
large volumes of dilute urine are produced:
  \text{(up to 10 gallons/day vs normal 1 qt/day)}
leads to electrolyte imbalances etc

\text{Diabetes mellitis}

most common of all endocrine disorders
  \rightarrow18.2 \text{ Million (2004) diabetics in US,}
  \text{5-6 Million more may be borderline diabetics}
diabetes is 7th leading cause of death & leading cause of blindness in US
  \rightarrow40,000 die annually as result of disorder
diabetes is a group of disorders characterized by high blood glucose concentrations
caused by:
- inadequate insulin secretion by beta cells in Islets = Type I
- lack of response by target cells to insulin = Type II

10% = Juvenile Onset Diabetes (Type I)
90% = Maturity Onset Diabetes (Type II)

**Type I: Insulin Dependent Diabetes Mellitus**

usually develops during adolescence

is an autoimmune disorder triggered by 2 factors:
1. genetic component → susceptibility
2. environmental component → still unknown, may be viral

results in malfunction of Islet cells in pancreas:
- dramatic decrease in the number of beta cells
- insulin is not produced in sufficient quantities

results in all body cells (target cells):
- decreased glucose utilization
- levels of glucose build up in blood

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 amounts of water into urine

**Type 2, Non Insulin Dependent Diabetes Mellitus**

target tissues become less responsive to insulin = insulin resistance

causes are poorly understood:
most are obese → but its not obesity per se seems to be a strong genetic component also associated with a sedentary lifestyle

**Immediate (Acute) Complications** of both forms

hyperglycemia, ketoacidosis, electrolyte imbalances (as cations such as Na⁺ and K⁺ accompany ketones into urine)

**Chronic Secondary Complications**

often involve gradual changes over years

most common changes occur in vascular system
1. narrowing of large blood vessels in brain, heart and lower extremities → can result in stroke, heart attack or limb loss
2. lesions in microvasculature are common leads to development of scar tissue → especially affect kidneys and eyes
3. impaired nerve function esp autonomic fibers and peripheral sensory fibers leads to altered GI, bladder function and impotence and loss of sensation esp in lower limbs

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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

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Adrenal Glands

on top of kidneys
divided into cortex and medulla which function as two separate glands

Adrenal Cortex
cortex = outer layer of adrenal gland
→ comprises 80 – 90% of adrenal gland
absolutely essential for life
regulated mainly by ACTH from Ant. Pituitary
secretes 30 - 50 different hormones
all hormones secreted by adrenal cortex are steroids
all are made from cholesterol
these hormones can be categorized as 3 different kinds:

a. Mineralocorticoids (90% = aldosterone)
   → aldosterone increases salt and water reabsorption by kidneys
   maintains constant blood Na⁺ levels
   by reabsorbing Na⁺ in kidney if needed

b. Glucocorticoids (95% = cortisol (hydrocortisone))
   affect every cell in body
   secretion follows circadian rhythm
   → highest ~8:00am; lowest ~12:00am
   1. generally raise blood glucose levels:
   2. inhibit inflammation and tissue destruction
   also immunosuppressive
   3. additional effects on
      blood pressure
      immunity
      wound healing
      fetal development of brain and lungs

HYPOSECRETION of Mineralocorticoids
Addison’s Disease
Kennedy had mild form
low ACTH may also produce this symptoms:
   bronzing of skin
   kidney impairment
   water retention
   increased blood pressure
   weight loss
   apathy
   cannot cope with stress
   immunosuppression
   hypoglycemia
   lethargy and muscle weakness

HYPOSECRETION of Mineralocorticoids
Cushing’s Syndrome
weaks skin and muscles

C. Sex Hormones (=gonadocorticoids; eg. DHEA, estrogen, progesterone, testosterone)
   androgens:
      promote protein synthesis
      normally not masculinizing
   female hormones:
   
   HYPERSECRETION of gonadocorticoids
   women in early puberty:
   adrenogenital syndrome
   masculinizing effect

Adrenal Medulla

unlike cortex, is not essential for life
secretes epinephrine and norepinephrine (=catecholamines)
also neurotransmitters of sympathetic NS
→ affect same structures as sympathetic NS:
   heart
   smooth muscle
   glands
serves to prolong or increase effects initiated by sympathetic NS.
Ovaries & Testes
endocrine and reproductive function
secrete steroid hormones
the same gonadotropins that are found in adrenal cortex
affect development and maturation of reproductive organs and reproductive behavior

Steroid Abuse
Taking large amounts of Androgens (steroids):
has negative feedback effect on FSH & LH
→ almost shuts down
decreased sperm production
temporary or permanent sterility
increased cancer risk
also when large amounts are take some is transformed into estrogen
→ breast enlargement

Minor/Temporary Endocrine Glands

Kidneys
secrete most (85%) erythropoietin
→ stimulates RBC production in bone marrow

Liver
secretes ~ 15% of body’s erythropoietin
stimulates RBC formation

Heart
atria contain some specialized muscle cells that secrete Atrial Natriuretic Peptide (ANP)
→ reduces blood volume, pressure, Na⁺ conc

Stomach & Duodenum
mucosal lining secretes several hormones to help control digestion:
gastrin
enterogastrone
secretin
cholecystokinin

Adipose Tissue
releases leptin
after uptake of glucose and lipids which is converted to fat
leptin binds to CNS neurons in hypothalamus
→ produces sensation of satiety

Placenta
acts as temporary endocrine gland during pregnancy
releases 3 hormones:

a. chorionic gonadotropic hormone (CGH)
→ maintains hormonal activity of ovary
pregnancy test

b. estrogens & progesterone

regulates secretion of:
gastric juices
pancreatic enzymes
bile