TOPIC VII: THE ENDOCRINE SYSTEM

Learning Outcomes: Upon completion of Topic VII (7), you should be able to

a) Describe the major functions of the endocrine system.
b) Define the terms hormone, hormone receptor and target cell.
c) Compare and contrast the location of target cell receptors for fat and water soluble hormones.
d) Compare and contrast the mechanisms of action of plasma membrane hormone receptors and intracellular (nuclear) hormone receptors.
e) Explain the functions of second messenger systems.
f) Describe the various signals that trigger hormone secretion (e.g. humoral substances, the nervous system, other hormones).
g) Use parathyroid hormone, insulin and thyroid hormone to describe negative feedback regulation of hormone secretion.
h) Describe the general adaptation syndrome in response to stress.
i) Describe the major hormones released during the alarm reaction and describe their actions.
j) List the major hormones released during the resistance reaction and describe their actions.
k) Describe the endocrine control of spermatogenesis, and the functions of testosterone.
l) Describe the four major hormones involved in female reproductive cycles, and explain the function of each.
m) Define ovulation, and explain the role of luteinizing hormone (LH) in ovulation.
n) Describe endocrine regulation of oogenesis, follicular/luteal development and the ovarian cycle.
o) Name the phases of the uterine cycle, and describe the anatomical changes in the uterine wall that occur during each phase.
p) Describe the correlation between the uterine and ovarian cycles.
q) Describe the function and mechanism of action of oral contraceptives, implants and the morning after pill in contraception.
r) Describe the general structure and functions of the placenta.

A) System Overview

- regulates growth, reproduction, metabolism (long-term events)
- glands and tissues secrete hormones which travel in blood to target cells (= cells with specific receptors for that hormone)
- bind to receptors + change cell activity
- receptors (proteins) found:

1) on the cell membrane
2) intracellular (nuclear)

B) <u>Hormone Types</u>

1) <u>Water Soluble Hormones</u>
- peptides, proteins, catecholamines (= 1st messenger)
- steps:
  a) hormone binds to cell membrane receptors (do not enter cell for their actions)
  b) hormone-receptor complex activates membrane proteins e.g. G-proteins
  c) G-proteins then activate 2nd messenger systems
    e.g. cAMP, Ca^{++}

- example using cAMP (cyclic adenosine monophosphate) as 2nd messenger
  a) hormone binds to cell-surface receptor and activates G-protein(s)
  b) G-protein activates adenylate (adenylyl) cyclase (membrane protein)
  c) adenylate cyclase converts ATP to cAMP (= second messenger)
    ∴ ↑ [cAMP]
  d) cAMP activates protein kinases (in cytosol)
  e) protein kinase acts on (phosphorylates) other proteins to alter their activity
    ∴ changes cell activity

    e.g. epinephrine on liver cells (activates cAMP)
      - causes breakdown of glycogen to glucose → released to blood

- Why use 2nd messenger systems?
  a) hormone can't enter cell (water soluble)
  b) rapid acting (enzymes already present - just activate)
  c) 1 hormone molecule → many enzyme molecules activated → multiplies signal
  d) limited - messenger broken down or removed
    e.g. cAMP broken down by phosphodiesterase in cell

2) <u>Lipid Soluble Hormones</u>
- steroids (e.g. cortisol) and thyroid hormones
- trigger protein synthesis
  - takes time ∴ slow but long lasting response
- steps for action:
  a) enter target cell and bind to <u>intracellular (nuclear)</u> receptors in cytosol or nucleus
  b) hormone-receptor complex binds to a specific region on DNA (activates genes)
    → starts gene transcription
    - produces messenger RNA (mRNA)

c) mRNA attaches to ribosomes to produce proteins (translation)

C) <u>Regulation of hormone secretion into blood</u>

- stimuli acting on an endocrine gland may be:

1) Humoral Stimulus

→ stimulus = ions/nutrients

e.g. 1: ↑ blood glucose (after eating carbs)

- pancreatic β cells (Islets of Langerhans) detect glucose and release insulin → ↓ blood glucose (-ve feedback)

e.g. 2: ↓ blood Ca^{++}

→ parathyroid gland detects low Ca^{++} + releases parathyroid hormone (PTH) → ↑ bone resorption (breakdown) by

a) ↑ osteoclast activity

b) ↓ osteoblast activity

→ ↑ blood Ca^{++} (-ve feedback)

2) Neural Stimulus

e.g. 1: heart rate (HR)

resting HR
↓ "surprise!!"
SNS - preganglionic directly to
↓ nt = ACh
adrenal medulla
↓ Epinephrine + NE
↑ HR + force of contraction

* moving out of homeostasis in a controlled manner

e.g. 2: uterine contraction → hypothal → post pituitary
↓
oxytocin

+ve feedback

3) Hormonal Stimulus

e.g. Metabolism

low metabolism
↓ + = stimulates

hypothalamus: - = inhibits
thyrotropin releasing hormone (TRH)
- ↓ +
ant. pituitary
thyroid stimulating hormone (TSH)
- ↓+
thyroid gland
thyroxine (T_4)
↓
T_4 to T_3 (in target tissue or liver)
↓
↑ metabolism (overall –ve feedback)

Insert MyFigures Topic VII #1 Control of thyroid hormone secretion

D) <u>Stress</u>

- any extreme external or internal stimulus e.g. surgery, infections, strong emotions, exams
- triggers a set of body changes called the General Adaptation Syndrome
- all co-ordinated directly or indirectly by the hypothalamus
- Phases:
  1) <u>Phase 1: Alarm Reaction (Fight or Flight Response)</u>
     - immediate = NS

     CNS (sensory input - detect change)
     ↓
     Hypothalamus (RAS (reticular activating system)∴ ↑ alertness)
     ↓
     SNS → adrenal medulla
     ↓ ↓
     Organs epinephrine (epi) + NE
     (prolongs fight or flight response)

     - effects of NS and hormones:
       a) ↑ blood glucose (energy)
          - SNS inhibits insulin release
          - Epi, NE trigger conversion of glycogen to glucose in the liver

b) ↑ HR, force of contraction
c) ↓ blood flow to skin, abdominal viscera
∴ more available to skel. and cardiac muscle + brain
(O_2 + glucose to working organs)
e) ↓ digestion, urine production

2) <u>Phase 2: Resistance Reaction</u>
- long term ⇒ endocrine
- permits recovery from 1) (tissue repair etc)
or
- response to longer term stress (e.g. starvation)
- hypothalamic hormones initiate phase 2

Hypothalamus

growth hormone releasing hormone (GHRH) ↓ ↓ ↓

↓ ↓ ↓ corticotropin releasing hormone (CRH)

Ant. Pituitary

↙ ↘

Growth hormone (GH)

adrenocorticotropic hormone (ACTH)

↓

Adrenal Cortex

↓

cortisol (glucocorticoid)

- GH
a) stimulates growth (protein production, cell reproduction)
- Cortisol
a) released within 30 sec. of the stress <u>but the response</u> not for hours – steroid hormone - acts at nuclear receptors
b) inhibits insulin release

- release of hormones causes:
a) ⇑ blood glucose:
- liver stimulated to produce new glucose from fats and later from proteins
- little insulin (because of inhibition), so glucose not taken up well, especially by skel. muscle (at rest) + adipose tissue ∴

i) glucose spared for use by NS
ii) metabolism of non-nervous tissue directed to fats for energy (control = GH, cortisol)
- if stress continues, cortisol inhibits GH release and proteins are then also used

iii) Overall: ↑ blood fa and aa → energy (except brain)

b) inhibition of: immune system, bone formation, formation of CT (delayed healing)

c) release of aldosterone + antidiuretic hormone (ADH)
→ reduces salt + water loss at kidney to maintain blood vol.

- Long term effects:
  - ↓ weight, ↑ bp, ↑HR, immune suppression (cortisol), ↓ bone density, ↑ risk of type 2 diabetes (because of ↑ blood glucose)

Insert MyFigures Topic VII #2 Regulation of adrenal cortex secretion

3) <u>Phase 3: Exhaustion</u>
- results from:
  a) depletion of body resources i.e. lipid reserves
  b) loss of K^+ (aldosterone effect)
  c) damage to organs (heart, liver, kidneys)

E) ♂ <u>Reproductive Hormones:</u>

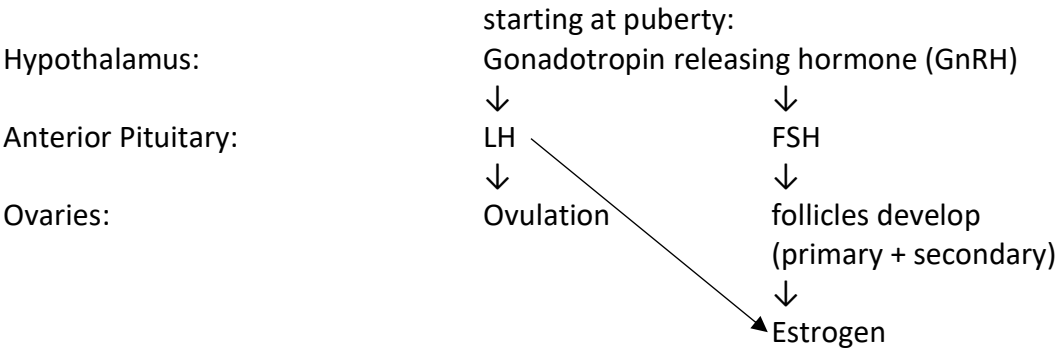
	starting at puberty:		
Hypothalamus:	Gonadotropin Releasing Hormone (GnRH)		
	↓	↓	
Anterior Pituitary:	LH	FSH	
	↓	↓	
Testes:	Testosterone (Leydig cells)	→	spermatogenesis (in seminiferous tubules)

<u>Functions of Testosterone:</u>

1) development of organs of ♂ reprod tract + 2^o sex characteristics
2) stimulates bone growth at epiphyseal plate (converted in bone to estrogen (E)

to stop growth = closure of plate)
3) promotes protein anabolism
4) directly stimulates spermatogenesis

F) ♀ **Reproductive Hormones**



1) FSH:
- stim - 1^o to become 2^o follicle
- inhibited when ↑ Progesterone (P) (∴ FSH ↑ when P ↓)

2) LH:
- stimulates estrogen production from theca + granulosa cells of follicle
- surge in LH → ovulation and then formation of corpus luteum from remnants of follicle
- in follicular phase - E from 2^o follicle rises for a few days → stim. LH release (via GnRH) → stim. follicle to ↑ E secretion etc (+ve feedback) → leads to LH surge
- luteal phase - P inhibits LH release

3) Estrogen:
- required for ovulation
- development of 2^o sex characteristics
- stim. growth of, + maintains, endometrium
- ⇑ bone growth, closure of epiphyses

4) Progesterone (P):
- from corpus luteum
- prepares uterus for pregnancy

G) **Ovarian/Uterine Cycle** (~ 28 days)

1) Days 1 – 14

a) Ovary: Follicular (preovulatory) phase

Early on: P low ∴ LH, FSH secreted - some 1^o follicles → 2^o follicles due to FSH

- follicles secrete E ∴ blood E rises

Later on: one (usually) 2^o follicle becomes vesicular follicle

b) Uterus: (at same time as (a))

i) Menstrual phase (days 1-5):

- stratum functionalis shed (outer layer of endometrium) + denuded areas bleed

∴ menstrual flow = blood, cells, secretions

ii) Proliferative phase (days 6-14):

- E → repair + proliferation of stratum functionalis (due to mitosis in stratum basalis)

2) <u>Day 14: Ovulation</u>

- due to LH surge
- LH triggers:

a) completion of meiosis I → 2^o oocyte

b) rupture of vesicular follicle with release of 2^o oocyte

3) <u>Days 15-28</u>

a) Ovary: Luteal phase

- high P from corpus luteum inhibits GnRH (∴ LH + FSH) ∴ no follicles develop

b) Uterus: Secretory phase

- P from corpus luteum:

i) prepares endometrium for implantation - becomes vascular, thick + stores glycogen

ii) inhibits uterine contractions

4) <u>If fertilization occurs:</u>

a) placenta secretes human chorionic gonadotropin (hCG)

- hCG maintains corpus luteum (similar structure to LH)

b) corpus luteum → P, E

- for about 6 weeks, then placenta takes over (secretes P, E)

c) FSH, LH inhibited by high P (no new follicles develop)

5) <u>If NO fertilization:</u>

a) corpus luteum → corpus albicans (no hCG, low LH)

b) ∴ P, E ⇓ ∴

i) no longer inhibit LH, FSH → LH, FSH ↑

ii) no longer maintain endometrium → menstruation

H) <u>Contraceptives</u>:

1) Oral contraceptives:
- high E + P → inhibit GnRH secretion ∴ low FSH, LH (mimics luteal phase)
- no follicle maturation, no ovulation

2) Implants – e.g. progestin – similar mechanism to oral contraceptives

3) Morning after pill
- high E and progestin or progestin only (= Plan B)
- prevents implantation, ovulation or fertilization

I) <u>Placenta</u>
- formed from chorion (fetus) and endometrium (maternal)
- blood vessels of mother and fetus in close proximity (no blood mixing)
- functions:
    1) exchange site:
        - gases, nutrients/wastes, hormones, antibodies (passive immunity)
        - drugs e.g. alcohol, morphine, nicotine
        - viruses - measles, polio
    2) secretes hormones:
        a) E + P
        b) hCG
            - maintains corpus luteum for ~ 6 weeks post-fertilization
            - detected by pregnancy tests
            - stim. testosterone secretion by fetal testes