Comparison of Nervous & Endocrine Systems

- **Neuroendocrine System**

  Nervous system controls through nerve impulses conducted by axons.

  Responses occur within milliseconds.

  Relatively local, specific effects. Stops when stimulus stops, adapts quickly.
Comparison of Nervous & Endocrine Systems

**Endocrine system** controls through hormones transported in the blood.

May have widespread general effects.

Responses occur after seconds to days & are more prolonged. Adapt slowly.
Endocrine Glands - General

– No ducts – secretion into fluid around cells diffuses into capillaries.

– Pituitary, thyroid, parathyroid, adrenal and pineal are examples.

– Many organs have partial endocrine function – hypothalamus, thymus, pancreas, ovaries, testes, kidneys, stomach, small intestine, skin, heart.
Endocrine System

- Hypothalamus
- Pineal body
- Pituitary
- Thyroid and Parathyroids
- Heart
- Thymus
- Adrenal gland
- Kidney
- Pancreas
- Ovary
- Testis
Endocrine Glands - General

- **Hormones** – long distance chemical messengers that travel in blood or lymph throughout the body.
Hypothalamus & Pituitary Glands

• **Anatomy**
  Hypothalamus floor and walls of third ventricle. Interfaces with ANS

Pituitary - Anterior [adenohypophysis]
  75% of gland – ectodermal origin

Regulated by “releasing” hormones from hypothalamus – no neural connection – joined through hypophyseal portal system.
Hypothalamus

Neurons that produce hormones released from posterior pituitary

Pituitary stalk

Anterior pituitary

Posterior pituitary
5 kinds of gland cells produce trophic hormones (affect other endocrine tissues).
  Somatotrophs (hGH)
  Thyrotrophs (TSH)
  Gonadotrophs (FSH, LH)
  Lactotrophs (Prolactin)
  Corticotrophs (ACTH, MSH)
Hypothalamus & Pituitary Glands


25%, ectodermal origin; stores and releases hormones – doesn’t make them

Ex. Oxytocin and ADH from hypothalamus
Hypothalamus

• In diencephalon – integrates nervous system & hormones & controls ANS.

• Synthesizes at least 9 hormones- 7 regulate the pituitary.

• Regulates growth and development, metabolism, homeostasis.
Hypothalamus

• Controls secretion of other hormones by other glands.

• Intimately in contact with pituitary by hypophyseal portal system [primary capillary plexus of infundibulum connected by hypophyseal portal veins with secondary capillary plexus in anterior pituitary.]
Hypothalamus Hormones

A. Growth Hormone Releasing Hormone (GHRH)

Target = anterior pituitary

Effect = stimulates release of growth hormone (GH)

Regulation = Plasma levels of glucose, fatty acids, and amino acids; sleep, ANS and other hormones.
Hypothalamus Hormones

• B. Growth Hormone Inhibiting Hormone (GHIH)
  Target = anterior pituitary

  Effect = inhibit release of GH

  Regulation = Plasma levels of glucose, fatty acids and aa's
Hypothalamus And Growth

- GHRH
- Pituitary
- Somatostatin
- IGF-1
- GH
- LIVER
- IGF-1 + IGF-BP1

Muscle growth
Femur growth

Fig. 30-1
Hypothalamus Hormones

C. Thyrotropin Releasing Hormone (TRH)
   Target = anterior pituitary gland
   Effect = stimulate release of Thyroid-stimulating hormone (TSH)
   Regulation = plasma levels of TSH and glucose; metabolic rate
Hypothalamus Hormones

• D. Corticotropin Releasing Hormone (CRH)

  Target = anterior pituitary gland

  Effect = stim. release of adrenocorticotropin hormone (ACTH)

  Regulation = blood glucose levels, stress, interleukin -1
Hypothalamus Hormones

E. Gonadotropin Releasing Hormone (GnRH)

Target = anterior pituitary gland

Effect = stimulate release of Follicle Stimulating hormone (FSH) & Luteinizing hormone (LH)
Hypothalamus Hormones

Regulation:
Females - plasma estrogen & progesterone levels;

Males – plasma testosterone levels
Hypothalamus Hormones

• **F. Prolactin Releasing Hormone (PRH)**
  
  Target = anterior pituitary gland

  Effect = stim. release of prolactin (PRL)

  Regulation = suckling
Hypothalamus Hormones

• G. Prolactin inhibiting Hormone (PIH)
  Target = anterior pituitary
  Effect = inhibit PRL release
  Regulation = suckling, plasma estrogen & progesterone levels
Hypothalamus Hormones

** 2 hormones are produced in the hypothalamus, & stored in special cells in the posterior pituitary.

- **H. Oxytocin (OT)** – from paraventricular nucleus
  Target = smooth muscle in uterus and breast

  Effect = contraction of muscle (labor, milk ejection, sexual arousal – “cuddle” hormone.)

  Regulation = hormonal changes during pregnancy, suckling
Hypothalamus Hormones

1. **Antidiuretic Hormone (ADH) [= vasopressin]**
   
   Target = kidney
   
   Effect = decrease sweat and urine output; constrict arterioles & increase blood pressure
   
   Regulation = blood osmotic pressure, stress, drugs [alcohol inhibits ADH].
Hypothalamus & Pituitary Hormones

- Oxytocin: Uterine muscles, Mammary glands
- ADH: Kidney tubules
- TSH: Thyroid
- ACTH: Adrenal cortex
- FSH and LH: Testes or ovaries
- Growth hormone (GH): Entire body
- Prolactin (PRL): Mammary glands (in mammals)
- Endorphins: Pain receptors in the brain
Pituitary Hormones

A. Human Growth Hormone (hGH) [Somatotropin]

Target = general [bones & skeletal muscles.]

Effect = ↑ production of insulin-like growth factors. ↑ cell growth & division; ↑ protein synthesis & fat catabolism, ↓ glucose catabolism

Regulation = GHRH, GHIH; also affected by stress, nutrition & sleep patterns.
Hypothalamus And Growth

- GHRH
- Somatostatin
- IGF-1
- GH
- Liver
- Femur growth
- Muscle growth

Fig. 30-1
Pituitary Hormones

• B. **Thyroid-stimulating Hormone (TSH)**
  
  Target = thyroid gland

  Effect = stim. secretion/release of T3 & T4

  Regulation = TRH
Pituitary Hormones

• C. Adrenocorticotropic Hormone (ACTH)
  Target = adrenal cortex
  Effect = stimulate glucocorticoids
  Regulation = CRH. Also affected by stress, hypoglycemia.
Pituitary Hormones

• D. Follicle-Stimulating Hormone (FSH)
  Target = gonads (ovary, testis)

Effect:
  Stimulates production of gametes
  (male & female)
Pituitary Hormones

Stimulates production of estrogen (female)

Regulation = GnRH, inhibin, estrogen (F) & testosterone (M)
Pituitary Hormones

E. **Luteinizing Hormone (LH)**

Target = gonads

Effect:

(F) stimulates ovulation, formation of corpus luteum and prod. of Estrogen & Progesterone.
Pituitary Hormones

(M) stimulates prod. of testosterone, LH also called interstitial cell stimulating hormone (ICSH) in male

Regulation = GnRH
Pituitary Hormones

• F. **Prolactin (PRL)** or Lactogenic Hormone
  Target = breast
  Effect = milk production
  Regulation = PRH, PIH, estrogen.
Pituitary Hormones

• G. Melanocyte-Stimulating Hormone (MSH)
  Target = melanocytes
  Effect = increases production of melanin; CNS neurotransmitter
  Regulation = MRH, MIH
Pituitary Hormones

• Control of Pituitary Secretion
  Timing & amount of secretion are regulated by hypothalamus, brain centers & feedback from target organs.
  Hypothalamus & Cerebral Control – releasing & inhibiting hormones. Brain monitors conditions & stimulates their release.
Pituitary Hormones

Neuroendocrine reflexes affect posterior lobe of the pituitary - in response to neurosensation [e.g., suckling].

Feedback from targets – negative feedback inhibition for the most part [note oxytocin response is positive].
Pineal Gland


  Cells = pinealocytes

Function – not clear

Produces melatonin [at night], & serotonin [by day] – may affect circadian rhythms, timing of puberty, & mood [SAD & PMS]
Thymus

- **Thymus** – over heart
  Functions in immunity, decreases in size with age.

  Produces thymopoietin & thymosin needed for T cell maturation.
Thyroid

• **General**
  
  Lateral lobes connected by isthmus anterior to trachea

  Follicles – made of follicular cells produce T3 & T4 upon TSH stimulation
Thyroid

Parafollicular cells – produce calcitonin

Hormones are stored in large quantities – only gland that does this - in colloid in follicle cavity.
Thyroid Hormones

• $T3, T4 \text{[main]}$

  Target – general

  Effect – regulate $O_2$ use, basal metabolic rate, growth & development - T3 more potent than T4

  Regulation – TSH from pituitary, TRH from hypothalamus
Thyroid Hormones

**Calcitonin**

Target – bone

Effect – inhibit osteoclasts, decrease Ca\(^{2+}\) release into blood, increase Ca\(^{2+}\) uptake into bone

Regulation – Ca\(^{2+}\) levels
Parathyroids

- Posterior surface of lobes of thyroid – 2/ side

- Hormone –
  \( \uparrow \) number & activity of osteoclasts.

Most important hormone in regulation of \( \text{Ca}^{2+} \) balance.
Parathyroids

↑ bone resorption, which ↑ blood Ca$^{2+}$ & HPO$_4^{2-}$

Kidney changes: ↑ rate of removal of Ca$^{2+}$ & Mg$^{2+}$ from urine & return to blood

Net effect – ↑ circulating Ca$^{2+}$ & ↓ HPO$_4^{2-}$
Parathyroids

Calcitonin is PTH antagonist

Also promotes formation of calcitriol from vitamin D, which increases rate of Ca$^{2+}$, Mg$^{2+}$, & HPO$_4^{2-}$ from GI

Control – Negative feedback via blood Ca$^{2+}$ levels
Hypocalcemia (low blood calcium) stimulates parathyroid glands.

Rising Ca\(^{2+}\) in blood inhibits PTH release.

PTH:
- Activates osteoclasts; calcium and phosphate ions released into blood.
- Increases calcium absorption from food.
- Promotes activation of vitamin D and increases calcium reabsorption.

Key:
- \(\cdot\cdot\cdot = \text{Ca}^{2+} \text{ ions}
- \(\bullet\bullet\bullet\bullet\bullet\bullet\) = PTH molecules

Bloodstream
Adrenal Glands

- **Adrenal Glands** – 1 on top of each kidney – 2 regions – cortex & medulla

**Adrenal Medulla**

Inner part of adrenal – not essential to life.

Chromaffin cells – sympathetic neurons specialized for hormone secretion.
Adrenal glands

Kidneys
Adrenal Glands

Produce catecholamines – epinephrine [80%] & norepinephrine – ANS sympathetic system [glycogenolysis, gluconeogenesis, glucose-sparing, etc.]

Link to cortex – under stress, catecholamine secretion stimulates corticosterone secretion.
Adrenal Glands

*Cortex* – 80-90%
Derived from mesoderm
Produce over 2 dozen steroid hormones essential to life from cholesterol.
Adrenal Cortex

3 zones:

Zona glomerulosa – outer zone
Produces mineralcorticoids – affect Na\(^+\) & K\(^+\)

Aldosterone – 95%
• Acts on kidney tubules
• Causes resorption of Na\(^+\) which also increases resorption of Cl\(^-\), HCO\(_3^-\) & H\(_2\)O
Adrenal Cortex

• Promotes secretion of $K^+$, which ↑ $K^+$ excretion

• Control – 4 mechanisms
  1. Renin-angiotensin pathway
     » Decrease in blood volume causes decrease in blood pressure.
     » This stimulates renin secretion by the kidney, which causes Angiotensinogen to be converted to angiotensin I in the liver.
Adrenal Cortex

» This promotes conversion to angiotensin II in the lung, which causes aldosterone secretion which ↑blood volume & ↑in blood pressure.

» A second target for angiotensin II is arteriole walls – they constrict which further increases blood pressure.
Adrenal Cortex

2. Plasma Na\(^+\) & K\(^+\) concentrations – \[^{\uparrow}\] inhibits, \[^{\downarrow}\] stimulates.

3. ACTH – in stress, causes \[^{\uparrow}\] aldosterone.

4. ANP – inhibits renin-angiotensin system.
Adrenal Cortex

Zona fasciculata → glucocorticoids regulate metabolism & resist stress

Cortisol [95%], corticosterone, cortisone,

Effects – stimulate:

Protein breakdown/construction

Gluconeogenesis
Adrenal Cortex

Lipolysis – breakdown of lipids

Stress resistance – ↑ glucose & Bp

Anti-inflammatory – ↓ mast cells which reduces release of histamine; also ↓ vessel permeability which reduces swelling, but also slows healing
Adrenal Cortex

Depression of immunity – helps with organ transplants

Control – negative feedback – blood levels of glucocorticoids ↓ → ↑ in CRH, which ↑ release of ACTH, which goes to cortex & ↑ glucocorticoid secretion.
Adrenal Cortex

Zona reticularis – produces androgens & some estrogens

This is not significant in males since the testes make more

In females – affect libido, increase axial & pubic hair,

Affect pre-pubertal growth spurt
Pancreas

• Endocrine & exocrine – posterior & slightly inferior to stomach

  Exocrine function – 98% – production of digestive enzymes by acinar cells

Endocrine function – Islets of Langerhans
Pancreas

3 main types of cells

\( \alpha \) – produce glucagon

\( \beta \) – produce insulin

\( \Delta \) – produce somatostatin
The image illustrates the anatomy of the pancreas, including the bile duct, pancreatic duct (duct of Wirsung), body of the pancreas, tail of the pancreas, common bile duct, plicae circulares, duodenum, duodenal papilla (papilla of Vater), and hepatopancreatic ampulla (ampulla of Vater). It also highlights the flow of digestive enzymes to the duodenum, acinar cells, capillary network, alpha cell, beta cell, delta cell, central duct, and islet of Langerhans.
Pancreatic Hormones

- Insulin

  **Target** – general

  **Effect** – ↓ blood glucose & ↑ diffusion of glucose into cells [not kidney, liver & brain], ↑ glycogenesis, ↑ uptake of amino acids & peptide formation (↓ gluconeogenesis), ↑ glucose change to fat & ↑ cellular respiration. ↓ glycogenolysis.
Pancreatic Hormones

Regulation – blood levels of glucose, amino acids & fatty a’s.
Pancreatic Hormones

- Glucagon
  Target – liver

  Effect: ↑blood glucose levels by stimulating gluconeogenesis & glycogenolysis.

  Regulation – blood glucose levels, ANS & Insulin
Pancreatic Hormones

- Somatostatin (GHIH)
  Target – digestive tract and pancreas
  Reduces acid secretion
  Inhibits secretion of glucagon
  Attenuates further insulin release
Ovaries

• Ovaries
  Estrogens [granulose cells of follicle & corpus luteum] & progesterone
  Regulate female reproductive cycle
  Maintain pregnancy
  Prepare mammarys for lactation
Ovaries

Develop and maintain secondary sexual characteristics

Inhibin – suppresses FSH
Testes

- Testes
  Testosterone – androgen [by interstitial cells]

Regulates production of sperm, sex drive
Testes

Regulates development of male secondary characteristics

Inhibin [by Sertoli cells]
Heart

• Heart – ANP

  Reduces blood volume, pressure & sodium concentration.

Inhibits aldosterone
Skin

- **Skin** – Cholecalciferol

  Inactive vitamin D formed by UV radiation → liver → kidney for full activation [calcitriol].

  Essential for calcium absorption from intestines.
Sunlight

Skin

7-Dehydrocholesterol

Cholecalciferol (vitamin D₃)

Liver

25-hydroxyvitamin D₃

k

1,25-dihydroxyvitamin D₃

Maintains calcium balance in the body

dietary intake

Vitamin D₃ (fish, meat)

Vitamin D₂ (supplements)
Others

- **Liver** – associated with production [often elsewhere] of 5 hormones – erythropoietin, angiotensin II, calcitriol, insulin-like growth factors I, Hepcidin [promotes uptake of iron]

- **Kidney** – Erythropoietin [Stimulates rbc production]. Calcitriol. Renin-angiotensin system
Others

• **GI** – Enteroendocrine cells
  Regulate digestive functions.

  Paracrines – local hormones.

• **Placenta** - Produces estrogen, progesterone, hCG.
Others

- **Adipose** –

  Leptin – secreted after glucose uptake – suppresses appetite.

  Resistin – an insulin antagonist.
Hormones & Their Actions

• **Chemistry**

Steroids
- Made from cholesterol nucleus with variable attachments.

- Glands – gonads and adrenal

- EX. Aldosterone, cortisol, vitamin D, androgens.
(a) Humoral

Capillary blood contains low concentration of Ca$^{2+}$, which stimulates...

Parathyroid glands

PTH

(1) secretion of parathyroid hormone (PTH) by parathyroid glands

(b) Neural

Preganglionic SNS fiber stimulates adrenal medulla cells...

Parathyroid glands

CNS (spinal cord)

Preganglionic SNS fiber

Capillary

(1) Preganglionic SNS fiber stimulates adrenal medulla cells...

(2) to secrete catecholamines

(c) Hormonal

The hypothalamus secretes hormones that...

Hypothalamus

Pituitary gland

Thyroid gland

Adrenal cortex

Gonad (Testis)

(1) The hypothalamus secretes hormones that...

(2) stimulate the anterior pituitary gland to secrete hormones that...

(3) stimulate other endocrine glands to secrete hormones
Hormones & Their Actions

Peptides and Proteins (3 – 200 amino acids)

– Synthesized in the rough endoplasmic reticulum. Some have CBH = glycoproteins - EX. – TSH, oxytocin, ADH, etc.
Hormones & Their Actions

Monamines - Amino acid – based

– Catecholamines – epinephrine, norepinephrine, dopamine from Tyrosine. Histamine from histidine. Serontonin, & melatonin from tryptophan.

– Thyroxine [thyroid hormones] - 2 iodinated tyrosine molecules coupled together. T3, T4
Hormones & Their Actions

• **Hormone synthesis**

Steroids – from cholesterol – vary in functional group attachments.

Peptides – transcription, translation, etc. → inactive preprohormone → RER → prohormone → Golgi → secretion
Hormones & Their Actions

Monamines – thyroxine example
Made from thyroglobulin – glycoprotein containing tyrosine – made by follicular cells.
1. Thyroglobulin is synthesized and discharged into the follicle lumen

2a. Trapping (active uptake) of iodide (I⁻)
2b. Oxidation of active form of iodine

3. Iodine enters follicle lumen where it is attached to tyrosine in colloid, forming DIT and MIT

4. Iodinated tyrosines are linked together to form T₃ and T₄

5. Thyroglobulin colloid is endocytosed and combined with a lysosome

6. Lysosomal enzymes cleave T₄ and T₃ from thyroglobulin colloid and hormones diffuse from follicle cell into bloodstream

Colloid in lumen of follicle

Capillary

Iodide (I⁻)

T₃

T₄

To peripheral tissues

Golgi apparatus

Rough ER

Thyroid follicle cell

Colloid

DIT (T₂) MIT (T₁)

Thyroglobulin colloid

Lysosome

T₃ T₄

T₃ T₄

T₃ T₄
Hormones & Their Actions

– Add 3 or 4 I’s
– Iodination process – $2I^- \rightarrow I_2$
– $I_2 + Tyr \rightarrow$ either 1 iodo or 2 iodo Tyr
– $T1 + T2 \rightarrow T3$
– $T2 + T2 \rightarrow T4$

Released from thyroglobulin by lysosomes

Transport – both carried in blood by thyroxin-binding globulin made in liver
Hormones & Their Actions

• **Hormone Transport**

Monamines & peptides are mostly hydrophilic, easily transported in blood.

Steroids & thyroid hormone are hydrophobic, moved by “transport” proteins – from liver.

Transport proteins also protect from degradation & elimination.
Hormone Receptors & Modes of Action

• **Hormone Target Cell Specificity**

  Receptors – proteins or glycoproteins, on target cells – other cells not affected.

  Constantly replenished
Hormone Receptors & Modes of Action

Response to hormone concentration –
Saturation – all are occupied. ↑ hormone will have no effect.

Control – “if a hormone is prevented from interacting with its receptors, it cannot perform its normal functions.”
Hormone Receptors & Modes of Action

Variable response – different cells may have receptors for the same hormone, but produce different responses to it.

EX. Insulin – In fat cells, it stimulates uptake of glucose & fat synthesis, in the liver it stimulates amino acid transport and glycogen synthesis, in the pancreas it inhibits glucagon-related reactions.
Hormone Receptors & Modes of Action

• **Steroids and thyroid hormone**
  
  Receptors are inside the target cell
  
  Action: Diffuse from blood through plasma membrane into cell.

  Bind to & activate receptors.
Activated receptor binds to DNA.

DNA is transcribed, & new mRNA is produced that directs synthesis of proteins, usually enzymes.
1. Binding of steroid hormone to receptor
2. Translocation of steroid-receptor complex to nucleus
3. Binding of complex to DNA regulatory site
4. Transcription
5. Translation

Source: “Module 6,” <http://www.thepeproject.net/>
Hormone Receptors & Modes of Action

• Thyroid hormone:
  In cell all is converted to T3.

  T3 binds to mitochondria to ↑ cellular respiration; binds to ribosomes & ↑ rate of protein synthesis; binds to DNA receptors ↑ transcription.
Hormone Receptors & Modes of Action

• **Peptides & catecholamines - Second Messenger Systems**

  Action [Ex. Glucagon]

  Hormone diffuses from blood to target cell & binds to membrane receptor.
Hormone Receptors & Modes of Action

This activates “G” proteins attached to the inside of the membrane, which activates adenylate cyclase (AC) also on the inside. AC converts ATP to cAMP in cytosol.

cAMP activates protein kinases (they add phosphates to proteins), either activating or inactivating the proteins.
G protein activation of adenylate cyclase

- Hormone binds to the receptor.
- The receptor stimulates the G protein, which activates adenylate cyclase.
- Adenylate cyclase converts ATP to cAMP.

**Key Components:**
- Receptor
- G protein (α, β, γ)
- Hormone
- Adenylate cyclase
- ATP
- cAMP
- GDP
- GTP
Hormone Receptors & Modes of Action

Control:

Phosphodiesterase inactivates cAMP

Increasing or decreasing cAMP.

Increases with ADH, TSH, ACTH, glucagon, epinephrine etc.

Decreases occur with GHIH, ANP.
Hormone Receptors & Modes of Action

• **Enzyme amplification** – one hormone molecule may activate many G’s, each of which may then activate many AC’s, each of which may produce many cAMPS, etc.
Hormone Receptors & Modes of Action

• **Modulation of sensitivity**
  
  **Down-regulation** – number of receptors ↓when concentrations of hormone are high – tissues become less sensitive.

  **Up-regulation** – number of receptors ↑when concentration of hormone ↓— tissue becomes more sensitive.
Hormone Receptors & Modes of Action

• **Half-Life, Onset, and Duration of Activity**

  Half-life – measures persistence of a hormone in circulation – usually a fraction of a minute to 30 minutes.
Hormone Receptors & Modes of Action

• **Hormone interactions:**

  **Synergistic** [works with another hormone for an effect] (ex: Testosterone needs FSH for normal sperm production)

  **Permissive** [enhances response to another hormone secreted later] (Ex: Thyroid hormone increases the effect of epinephrine)
Hormone Receptors & Modes of Action

• **Hormone interactions:**

• **Antagonistic** [one hormone reduces the effectiveness of a second hormone] (Ex: During pregnancy, progesterone inhibits uterine response to estrogen)
General Adaptation Syndrome [GAS]

• Response to prolonged, extreme or unusual stress

• Stressor – and disturbance – temperature, toxins, poisons, heavy bleeding, emotional upheaval
General Adaptation Syndrome [GAS]

- GAS – 3 stages
  1 – Alarm Reaction = Fight or flight
  Hypothalamus stimulates ANS & adrenal medulla → epinephrine/norepinephrine;
  Short lived
  Consumes glycogen stores
General Adaptation Syndrome [GAS]

2 – Resistance Stage [long-term]

Provide alternative fuels when glycogen has been depleted.

Dominated by cortisol. Cortisol counteracts insulin, contributes to causing gluconeogenesis. It also increases glycogen synthesis in the liver.
General Adaptation Syndrome [GAS]

Mediated by hypothalamus: CRH – stimulates ACTH production, which stimulates glucocorticoid [cortisol].

Fat breakdown, inhibits protein synthesis, immune response, etc.

If stress removed – body returns to normal.
Pituitary hormone in the bloodstream stimulates the outer part of the adrenal gland to release the stress hormone cortisol.

Sympathetic nervous system releases the stress hormones epinephrine and norepinephrine from nerve endings in the inner part of the adrenal glands.
General Adaptation Syndrome [GAS]

3 – Exhaustion – if stress continues past ability of Resistance Reaction to function → rapid decline & death [heart or kidney failure or overwhelming infection].
Stress

• **Stress and Disease** – stress can temporarily inhibit components of the immune system and produce gastritis, ulcerative colitis, irritable bowel syndrome, migraines, anxiety and depression.
Paracrines

• Eicosanoids – 20 C FA chains – derived from arachidonic acid in phospholipids in cell membranes. – Important considerations in pharmacology.
Endocrine Disorders

• **Homeostatic Imbalances – hypothalamus/pituitary**

  Hypersecretion of prolactin – may be due to adenohypophyseal tumors-
  inappropriate lactation, loss of menses, infertility.
Endocrine Disorders

Diabetes Insipidus – deficiency of secretion of ADH – Huge losses of urine, no sugar.

GH - Gigantism [hyper] & dwarfism [hypo]
Endocrine Disorders

• Homeostatic Imbalances – Thyroid

*Hypothyroidism* – myxedema – may be from thyroid defect or failed TSH or TRH release. Low metabolic rate, chills, thick dry skin, puffy eyes, lethargy.
Endocrine Disorders

If due to lack of I – can develop goiter.

Infantile version = cretinism – can be prevented with thyroid hormone replacement therapy, can’t be reversed.
Endocrine Disorders

*Hyperthyroidism* – Grave’s disease.
May be autoimmune disease.

Elevated metabolic rate, weight loss, rapid irregular heart beat, exophthalmos.
Endocrine Disorders

• **Homeostatic Imbalances – Adrenal Cortex**

Cushing’s Disease

Overproduction of glucocorticoids

Buffalo hump on back, edema, hypertension.

Due to steroid therapy or pituitary tumor.
Endocrine Disorders

Addison’s Disease – hyposcretion.
Fluid loss and hypotension.
Endocrine Disorders

• Homeostatic Imbalances – Pancreas
  Diabetes Mellitus – hyposecretion or hypoactivity of insulin.
  Elevates blood sugar levels, glycosuria, weight loss.

Ketoacidosis [from lipemia].
Endocrine Disorders

3 signs – polydipsia [excessive thirst], polyphagia [excessive hunger], polyuria [huge urine output].

Also hyperglycemia, glycosuria, ketonuria.
Endocrine Disorders

• Type I – insulin-dependent [juvenile].
  Involves depletion of beta cells.
  Requires insulin supplementation.
Endocrine Disorders

• Type II – non-insulin dependent [insulin levels are normal or elevated].
  Problem is insulin resistance.

  Adult-onset [40+].

  Associated with obesity.
Type 2 Diabetes: Insulin Resistance

Insulin receptors
Defect in signaling to Glut-4
Fat/muscle cells

Glucose transporters
Diminished glucose uptake
Endocrine Disorders

Fat catabolism $\rightarrow$ $\uparrow$ free FA’s $\rightarrow$ $\uparrow$ ketone bodies $\rightarrow$ osmotic diuresis, flushing of Na & K, acidosis $\rightarrow$ diabetic coma.
Endocrine Disorders

• Long-term degenerative effects on vascular and nervous system – compromised circulation → gangrene.

• Nerve damage → impotence, loss of sensation, etc.
Diabetic retinopathy

Diabetic gangrene
Endocrine Disorders

• Hypoglycemia – excess insulin, low blood sugar, anxiety, tremors, weakness.