BMSN1601– Anatomy – Part III (Physiology: L18, L19, L22, L26, L27, L28)

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| Introduction to The Endocrine System |

*# Gland: any specialized group of cells, makes and secretes a hormone*

◉ Hormones regulate the following body functions:

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| Mood | Sleep Cycle | Growth and Development |
| Metabolism and Energy Balance | Body Defense | Reproductive Process |

◉ Location of Major Endocrine Glands

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| Common Major Endocrine Glands | Pituitary gland |
| Pineal gland |
| Thyroid gland |
| Parathyroid gland |
| Hypothalamus |
| Thymus |
| Pancreas |
| Adrenal glands |
| Female Only: Major Endocrine Gland | Ovary |
| During Pregnancy Only: Major Endocrine Gland | Placenta |
| Male Only: Major Endocrine Gland | Testicle |

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| Secretion of Hormone – Mode of Action |

◉ Endocrine Glands has 3 Mode of Action to secret the hormone

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| Endocrine Signaling | Paracrine Signaling | Autocrine Signaling |
| ◉ Act on distant cells | ◉ Act on cells next to secreting cell | ◉ Act on cell that secreted them |
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| Exocrine Gland versus Endocrine Gland |

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| Endocrine | Exocrine |
| Do not have ducts (Ductless) | Do have ducts |
| Secret Hormone | Secret Sweat, Enzymes, Mucus, Sebum (皮脂) |
| Finally Carry to the ICF | Finally Carry to the outside of the body or into a body cavity |

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| Classification of Hormone – Structural Difference |

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| Amino acid derivatives (Amines) | Peptide and Proteins Hormone | Steroid (類固醇) |

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| Introduction to Amine Hormone (Amino acid derivatives) |

◉ Amine Hormones are **derivatives of the amino acid tyrosine**.

◉ Half-Life: minutes to few days

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| Amine Hormone | Thyroid Hormone | From **Thyroid Gland** |
| Epinephrine | From **Adrenal Medulla** |
| Norepinephrine |
| Dopamine | From **Hypothalamus** |

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| Introduction to Peptide Hormone |

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◉ There is a signal peptide in the polypeptide to tell the cell whether the Hormones:

▨ Should be encapsulated in cell

▨ directly release to the blood vessel

◉ The cell may secrete **multiple peptide hormones**—*derived from the same prohormone*—each of which differs in its

effects on target cells.

◉ Release the contents of the secretory vesicles by **exocytosis**

◉ Relative Half Life in Blood: minutes

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| Introduction to Steroid Hormone |

◉ Steroid Hormone are **derived from cholesterol (e.g.: cortisol)** and primarily produced by the:

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| Adrenal Cortex | Gonads (Testes / Ovaries) | Placenta (During pregnancy) |

◉ Vitamin D can be converted into active steroid hormone @ Liver / Kidney

◉ Steroid hormones **diffuse across the plasma membrane** into the circulation

▨ Reversibly **bound to carrier proteins such as albumin** in plasma

◉ **Synthesized in sER on demand** because of **longer half-life**

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| Summary of Amine Hormone, Peptide Hormone, Steroid Hormone |

◉ Do notice that: catecholamines and thyroid hormone are Amine Hormone

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|  | Major Form in Plasma | Location of Receptors | Rate |
| Peptides and catecholamines | Free | Plasma Membrane | Fast (minutes) |
| Steroids and thyroid hormone | Protein-bound | Intracellular | Slow (hours to day) |

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| Introduction to Some Important Hormone – Part I |

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| Introduction to Some Important Hormone – Part II |

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| Clinical Problem Related to Endocrine Disorders |

◉ Problems in the secreting gland, e.g. tumors, infection

◉ Problems in the **endocrine feedback system**, mostly **hypothalamic-pituitary axis**

◉ **Auto-immune disorders** (e.g. Type 1 diabetes mellitus)

◉ **Genetic disorders**

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| Case Study Related to Endocrine System – Menstrual Cycle |

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| In the proliferative phase (follicular phase), follicle-stimulating hormone (FSH) induces estrogen production by the ovary |
| Rising estrogen levels stimulate luteinizing hormone (LH) production, leading to ovulation |
| After ovulation, the corpus luteum produces estrogen and progesterone |
| In the absence of fertilization, corpus luteum decays. Estrogen and progesterone levels drop, which leads to uterus lining shedding and the onset of menses |

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| Introduction to Mechanism of Hormone Action |

◉ A hormone **can only trigger A SINGLE REACTION** in **SEPECIFIC CELLS**

*Hormone Receptors can also be triggered by the hormones which have high structural similarity hormone.*

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| Water-Soluble Hormone  (Peptides & Catecholamines Hormone) | Lipid-Soluble Hormone  (Steroid & Thyroid Hormone) |
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| ◉ Attach to the Membrane Protein and trigger series  Responses through Signal transduction.  ◉ Responses including:  ▨ Cytoplasmic Responses  ▨ Nuclear Responses | ◉ The Receptors are inside the Nucleus  ◉ Responses including:  ▨ Nuclear Responses [Controlling Gene Expression] |

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| 💦 | Supplementary Note:  ◉ Cytoplasmic Responses: Transport specific/some substance from intracellular vesicle release to the extracellular  fluid.  ◉ Nuclear Responses: Induce Gene Expression or Silencing Gene Expression. |

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| Hormone Interaction at Whole Body Level – Redundant Effect |

◉ **Safe-guard mechanism for very important metabolism**

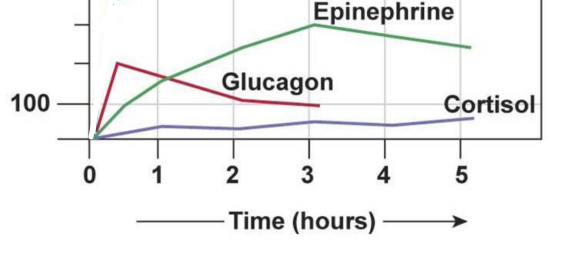
◉ **Produce synergistic outcome:**

combine action of redundant hormones to produce effects greater than the sum of their individual effects

◉ Definition: *Different hormones produce same effect*

◉ Case Study: Epinephrine, glucagon, and cortisol can all act on liver to increase blood glucose level. Although the result is

the same, the **mechanisms and time constant are different**.



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| Epinephrine (Adrenaline) | Glucagon | Cortisol |
| Amino Acid Derivative Hormone | Peptide Hormone | Steroid |
| ◉ Via Sympathetic Nerve System  🡪 Take times for Sympathetic Nerve  System to work. | ◉ Faster as 2 Responses are induced  (Cytoplasmic & Nuclear Response) | ◉ Only 1 Response is induced  (Controlling Gene Expression - Slow) |

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| Hormone Interaction at Whole Body Level – Reinforcement effects |

◉ Definition:

**Acts in different tissues to induce different responses which reinforce each other from perspective of body.**

◉ Case Study: Effect of Cortisol in Our Body

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| Pancreas | Adipose Tissue | Skeletal Muscle |
| Decrease Insulin Secretion | Increase break down of lipid | Increase break down of protein |
| * Maintain Blood Glucose Level | * Converting fatty acid into glucose in Liver | * Converting amino acid into glucose in Liver |
| **Blood Glucose Level is Increased** | | |

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| Hormone Interaction at Whole Body Level – Antagonistic effects |

◉ Definition:

**Hormones that act to return body conditions to within acceptable limits from opposite extremes**

◉ Case Study: Regulating Blood Glucose Level

▨ **Insulin decreases blood glucose level** whereas **glucagon increases blood glucose level**

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| Hormone Interaction at Whole Body Level – Permissive effects |

◉ Definition:

A Second Hormone can only affect the target cell   
if the **presence of primary (another) hormone is at certain concentration.**

◉ Case Study:

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| Estrogen induces the expression of progesterone receptor in uterus during proliferative phase.  ◉ Estrogen induces the **proliferation of uterine endometrium**  →Increase the thickness of the uterine wall  ◉ Progesterone induces the development of uterine endometrium, including blood vessels formation  →Prepare for implantation |

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| Summary of Hormone Interaction at Whole Body Level |

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| Type of Interaction | Definition | Example |
| Redundant effects | Combine action of redundant hormones to produce same effects which is greater than the sum of their individual effects | Effect of Epinephrine, glucagon, and cortisol on regulating (increasing uptake of) blood glucose level |
| Reinforcement effects | Acts in different tissues to induce different responses which reinforce each other from perspective of body. | Effect of Cortisol on Pancreas, Adipose and Skeletal Muscle. |
| Antagonistic effects | One hormone opposes the action of another in which case Hormones can act to return body conditions to within acceptable limits from opposite extremes | Interaction between Insulin and Glucagon to regulate blood glucose level to maintain homeostasis. |
| Permissive effects | The Concentration of one hormone controls the expression of receptor of another hormone. | Effect of Estrogen on the Receptor of Progesterone during development of uterine endometrium. |

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| Summary of Rhythms of Hormone Secretion |

◉ Hormone concentrations in blood plasma **fluctuate (波動) from minute to minute.**

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| Secretion | Definition | Example |
| Pulsatile secretion | Hormones **released in short bursts**, which is regulated by **physiological stimuli** (**In** **Most of Cases**) | Nutritional factors, Insulin |
| Diurnal secretion | Concentration of hormone fluctuate because of Circadian variation (昼夜节律). | Cortisol peaking shortly after waking, whereas melatonin peaking at night → Tell the cells what time it is |
| Cyclic secretion | Some hormones are secreted in complicated cycles with respect to some bodily events.   → Cyclic changes in hormonal levels control and orchestrate (編排) the events of the complicated cycle. | Secretion of Hormone during menstrual cycle. |

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| Summary of Regulation of Hormone Activity |

◉ Concentration of the hormone in the blood must be **returned to normal** after hormone has acted on target cells  
→ Prevent prolonged exposure of target cells to hormones.

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| Secretion | Definition | Example |
| Regulation of hormone receptors | **Internalization of receptor-hormone complex** can be used to reduce the number of receptors | **Growth hormone** downregulates receptors by targeting the receptor to degradation via internalization |
| Feedback Control - Negative Feedback | A negative way on the secretory cell to inhibit further hormone secretion | **Glucagon secretion** and blood glucose level |
| Feedback Control  - Positive Feedback | Broken of Positive Feedback Cycle | **Oxytocin** secretion during childbirth to cause contraction of uterine muscle |

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| Introduction to Thermoregulation |

◉ Different Type of Body Temperature

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| Body Core Temperature | Body Shell Temperature |
| ◉ Have a stable temperature (~37 ℃)  ◉ Can be measured:  ▨ under tongue  ▨ in ear canal  ▨ in rectum | ◉ Have a variable temperature (20℃ ~ 40℃)  ◉ Can be measured by IR thermometer gun |

◉ Circadian Rhythm (±0.5℃) & Thermoregulation

▨ Highest in late afternoon (4pm to 6pm)

▨ Lowest before dawn (4am to 6am)

◉ Aging & Thermoregulation [*Older is colder*]

▨ Aging lower the metabolic rate → The Heat release from the body is decreased → Body temperature is lower.

◉ More about Heat Balance

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| *Heat Production – Refer to Core Temperature* | *Heat Loss* |
| ◉ By-product of metabolism  ▨ A significant energy is given to the body as heat:  ◈ Nutrients are metabolized  ◈ ATP is reacted to ADP +Pi | ◉ By Radiation/[Conduction&Convection]/Evaporation   |  |  |  | | --- | --- | --- | | **(60%)** | (18%) | (22%) | |
| ◉ Factors which affect heat production:  ▨ Basal metabolism (Decreasing during Aging)  ▨ Increase of Muscle Activity  ▨ Release of Adrenaline (Thyroxine & epinephrine)  ▨ Diet-induced thermogenesis  ◈ Digestions, absorption and storage of food | ◉ Factors which affects loss of heat:  *When Body Temperature is HIGHER than environment*  ▨ Radiating Infrared rays from human body  ▨ Loss of heat by the Conduction to the Air/Object  *Body Temperature will always be lowered by*  ▨ Evaporation – Every moment:  ◈ Insensible water loss  ◈ Evaporation of Sweat |

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| Process of transferring heat to the Skin |

◉ Because of Rich Network of blood vessel (capillaries and arterioles) underneath the skin:

→ **Rate of Blood Flow into the skin vary significantly**

→ Heat is transferred / lost from internal body core to the skin **via circulation**.

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| Vasoconstriction of arterioles  (Decrease in diameter / 血管收縮) | Vasodilation of arterioles  (Increase in diameter / 血管擴張) |
| ◉ Blood flow is lowered  → **The Heat Loss Rate is reduced** | ◉ Blood flow is increased  → **The Heat Loss Rate is increased** |

◉ Insulating Properties of Skin

▨ **The skin and subcutaneous tissues (皮下組織) act together as heat insulator for the body**

→ Presence of Fat (Poor Heat Conductor)

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| Introduction to Core Temperature |

◉ Characteristic of Core Temperature

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| Impact rate of biochemical reactions | Impact rate of biochemical activity level |
| Biochemical reaction can be freed from fluctuating temperature of external environment | |
| Still can engage in most normal activities when there is significant change in external temperature | Ensure optimal temperature for biochemical reaction |

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| Introduction to Thermoregulatory capacity & Ambient Temperature |

◉ Definition of Thermoregulatory Capacity

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| 🎀 | Thermoregulatory Capacity is used to describe the ability to regulate the core temperature at a stable ‘set point’ over a wide range of Ambient Temperature.  → the heat gained / lost by the body would **overwhelm thermoregulatory capacity** @ Extreme Condition  → Resulting in hypothermia or hyperthermia |

◉ Definition of Ambient Temperature

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| 🕯 | Ambient temperature is the air temperature of the surrounding environment. |

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| Clinical Consequence of Large Elevations of Core Temperature |

◉ Large Elevations of Core Temperature is harmful & lethal.

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| Temperature (℃) | Consequence |
| 40~44 | ◉ Convulsions (抽搐)  ◉ Heat stroke  ◉ Multiple Organ failure  ◉ Brain lesions (腦部病變) |
| 38~40 | ◉ Hyperthermia (高溫症)  ▨ Usually caused by fever or strenuous exercise |
| 36~38 | *Normal Range* |
| 34~36 | ◉ Mild Hypothermia (輕度低溫症) |
| 30~34 | ◉ Impairment of temperature regulation  ▨ Fail to regulate the temperature  ▨ Decrease in Metabolic Rate |
| 27~29 | ◉ Cardiac fibrillation (心肌顫動) |

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| Thermoregulation in infants, adults and elderly |

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| Newborns / infants | Adults | Elderly |
| Do not readily shiver or sweat. | Can shiver or sweat. | |
| higher surface-to-mass ratio  → their core temperatures are more  prone to changes | Standard Surface-to-mass ratio | |
| Have many BAT | Very few amounts BAT (Brown Adipose Tissue) | |
| Good Ability to regulate Temp. | | Reduced ability to regulate Temp. |

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| Introduction to Thermoregulation – Homeostatic Control System |

◉ The body maintains a stable temperature by a homeostatic control system (**neural mechanism**).

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| Sensor | Control Center | Effectors |
| ◉ Peripheral Thermoreceptors  ▨ Detecting change in ambient  temperature.  ▨ Feedforward  ◉ Central Thermoreceptors  ▨ Found in **Deep tissue**  ▨ Found in **Hypothalamus** | ◉ Hypothalamus  ▨ Receive Signals from afferent  pathway.  ▨ Send Signals through efferent  pathway.  ◉ Signal are sent to:  ▨ cerebral cortex  ▨ motor neurons  ▨ Sympathetic nerves | ◉ Cerebral Cortex:  ▨ Elicits a sense of discomfort  → Induce Voluntary change in  the behavior.  ◉ Motor Neurons:  ▨ Induce Muscle shivering 📈  → muscle metabolic rate \* 2  ◉ Sympathetic nerves:  ▨ BAT (For Infant) 📈  → Abundant mitochondria → Stimulatedby  **norepinephrine**  ▨ Vasoconstriction 📈  → Skin Arterioles.  ▨ Eccrine sweat glands 📉  →Stimulated by **acetylcholine**  →Secretion of sweat  ▨ Vasodilation 📉  →Skin Arterioles. |
| Remarks:  1. Although Extreme Temperature induce pain receptors, they are not in homeostatic control system for thermoregulation.  2. Thermoreceptors are made up of:  i. **Warmth-sensitive neurons**  ii. **Cold-sensitive neurons**  *Increase Temp. excite i.*  *Decrease Temp. excite ii.* | Remarks:  1. The Signal sent can stimulate adjustment in heat production and heat loss. | Remarks:  1. Voluntary change in behavior including change in clothing, change in the current activity.  2. Muscle Shivering is rapid cycles of involuntary contractions and relaxations.  3. Newborn babies (< 6 months) are not able to shiver  4. **Norepinephrine** is a chemical secreted by **sympathetic noradrenergic neurons**, which stimulate *Brown Adipose Tissue* to **convert chemical energy to heat**.  5. **Norepinephrine** can also induce **Skin arterioles vasoconstricts and vasodilation.**  6. **Acetylcholine** is secreted by **sympathetic cholinergic neurons** |

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| Fever, Hyperthermia & Hypothermia |

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| Fever / Pyrexia | Hyperthermia |
| An increase in core body temperature **due to an elevation of the thermoregulatory set point** in the *hypothalamus*  (Body 自己要高温) | An increase in core body temperature above the set point, while the **set point itself did not change**  (Body 唔可以Regulate返正常Core Temperature) |
| ◉ Can be induced by bacterial / viral infection  ◉ In response to **exogenous pyrogens**  ▨ lipopolysaccharide from Gram-negative bacteria  ◉ In response to cytokines released by **macrophages** | ◉ Can be induced by:  ▨ Strenuous exercise  ▨ High ambient temperature  ▨ High ambient humidity  ◈ Decreased rate of evaporation of sweats |
| As a result:  **→ Production of PGE2 increases → Higher Set point** | As a result:  → The body loses water faster  → The body loses salt faster  ▨ Increased **aldosterone secretion** by **adrenal cortex**.  ▨ Sweating  → **Nausea & Collapse & Seizures & Delirium** → **Heatstroke**  ▨ Complete breakdown of thermoregulatory systems  (e.g. failure to sweat)  leading to continued increase in the core temperature. |
| **Antipyretic drugs** can inhibit the production of PGE2  ◉ Example: Aspirin or Ibuprofen |  |

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| Hypothermia |
| ◉ Can be induced by:  ▨ Prolonged immersion in cold water (high heat capacity)  ▨ Alcohol intoxication (**ingestion of alcohol causes vasodilation of skin blood vessels)**  ◉ Severe hypothermia can lead to **Impaired consciousness** or **cardiac arrest**. |