Endocrine

BIOCHEMISTRY

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The Endocrine System - An Introduction

Anything mentioned in the slides that wasn't mentioned by the doctor will be in [Square brackets, and in red]

Timestamps at the start of each topic will be in (brackets) next to the name of the topic, in case you want to go back to the video/lecture.

➢ *What is the endocrine system?*

- **The endocrine system** is a collection of ductless glands that secrete chemical messengers into the blood called hormones.

Other tissues that are not considered as endocrine glands, such as the **kidneys, liver, and heart,** may also secrete hormones.

"Endocrine" denotes internal secretion of biologically active substances.

"Exocrine" denotes secretion that occurs outside of body (e.g. sweat glands).

The word **"hormone"** is derived from the Greek word hormao meaning 'I excite or arouse'.

Hormones are defined as:
Substances released by endocrine glands and other tissues that are transported via the bloodstream to other tissues → where they can act to regulate specific functions and have certain effects on cells.

- *There are about 50 known hormones that exist in our body. With time, and thanks to the human genome project and further discovery initiatives, we are discovering more of these hormones.*

In order for hormones to be effective:

They must bind to receptors and cannot act on their own. **ONE EXCEPTION is Nitric Oxide,** which can be considered as a hormone *(To be discussed in the CNS).*

We will be focusing on the majority of hormones that bind to receptors.

TYPES OF HORMONES: *According to the type of receptor (03:00)*

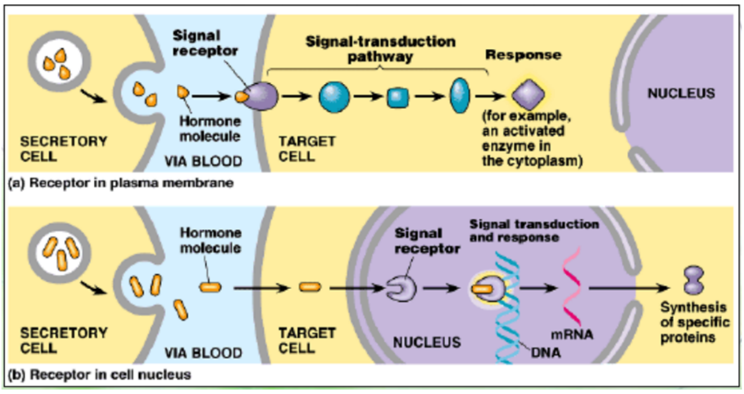
- Hormones can be classified into **two types** according to the *type of receptor to which they bind to.*

1. **Lipid-soluble hormones:**

They can diffuse through the plasma membrane → Bind to a receptor in the cell → The receptor-hormone complex binds to certain DNA regions (the complex acts as a transcription factor).

2. **Water-soluble hormones:**

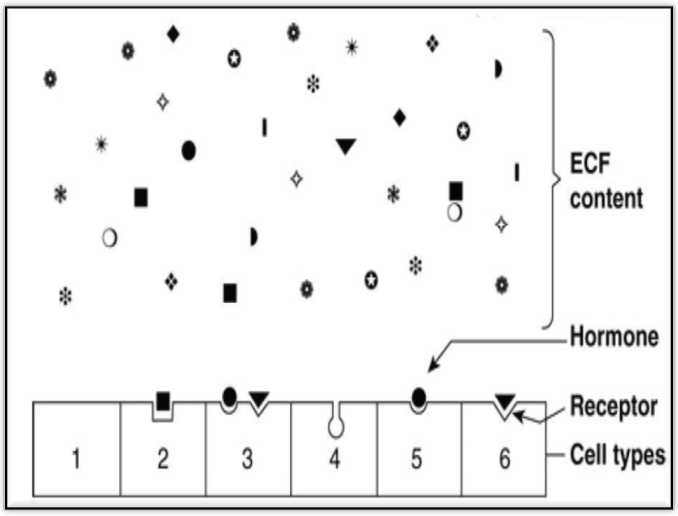
They are secreted by glandular cells → They then diffuse into the blood stream → They reach their destination (target cell) → They bind to the cell surface receptors → Transduce or transmit a signal into the cell → ACTION



- ***The barrier/challenge is:*** *the amount of hormone in the blood stream is minimal Atto- to Nano- molar range (10^{-18}* ***to*** *10^{-9}),* ***compared to structurally similar molecules*** *in the blood, like (sterols, amino acids, peptides, and proteins): that exist in the micro- to milli-molar (10^{-6} to 10^{-3} mol/L) range.*

This means that there's a minimal amount of hormone that must exert a strong and effective action in the body. How is this possible?

1. Binding of the hormone to the receptor must be specific
2. Must be saturable: There's a certain number of receptors that can bind to a certain hormone level. If the hormone level exceeds this specified level or limit, then not as much added action takes place.
3. The concentration of hormones that exist in the bloodstream is 20-folds more than the dissociation constant.



THE DISSOCIATION CONSTANT (Kd) (5:20)

If you look at the formula on the right,

H (Hormone) + R (Receptor) bind with a certain affinity and can dissociate as well.

$$H + R \underset{k-1}{\overset{k+1}{\rightleftharpoons}} H\text{-}R$$

$K_d = \{[H] X [R]\} / [H\text{-}R]$

- **The dissociation constant (K_d)** = the number of free molecules (free hormone H times free receptor R) / conc. of hormone-receptor complex (H-R)

- Usually Kd values are about 10^{-9}-10^{-11} M, and the concentration of hormones is usually 20 folds or 20 times more than the K_d (dissociation constant).

NOTE: The binding of the hormone to the cell surface receptor, as we've already mentioned, is very specific – there is no inaccuracy or imprecision.

There is one aspect that is important to biochemistry, endocrine glands, homeostasis and other biochemical reactions in the body - That is ***REGULATION.***

- *A massive amount of regulation takes place in the Endocrine System.*

<u>One example on regulation in the endocrine system is:</u>

→ The location or arrangement of glands in our body is NOT haphazard or random. On the contrary, the glands are organized in a certain way for a certain reason **(one of the reasons being to prevent the dilution effect of hormones in the body)**

<u>Examples on how the location of glands is NOT haphazard:</u>

1. **<u>Spermatogenesis</u>** occurs in the **seminiferous tubules**, which are ***<u>next to</u>*** the **Leydig cells**. The Leydig cells produce testosterone, which is required for the process of spermatogenesis.
2. **<u>Hepatic production of glucose:</u>** The level of glucose in the blood is regulated by the **liver**, which is under the control of two hormones: INSULIN and GLUCAGON. These hormones are produced in the **pancreas**, which is in ***<u>close proximity</u>*** to the **liver**.

- *Due to this close proximity, there is MINIMAL DILUTION OF THESE HORMONES.*

3. **The Hypothalamus and anterior pituitary** are in ***close proximity*** so that the regulatory hormones released by the hypothalamus can reach the pituitary gland ***nearby*** in high concentrations, via a special portal vascular system.
4. **The adrenal cortex** produces cortisol, which is required by the **adrenal medulla** for ***catecholamine synthesis***, reaching the medulla **(which is in close proximity to the adrenal cortex)** by a special portal vascular system.

NERVOUS VS/& ENDOCRINE SYSTEM (8:20)

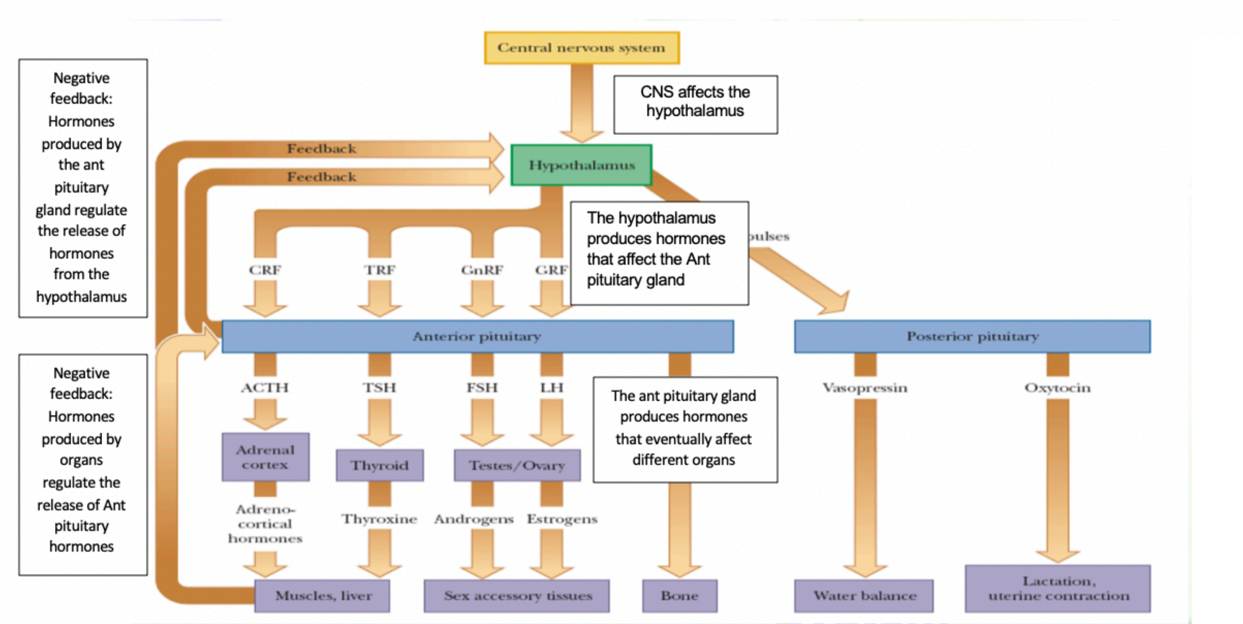
↳ *The endocrine system works in parallel and conjunction with the nervous system. So, the nervous system affects and regulates the endocrine system and vice versa.*

1. The CNS affects the hypothalamus
2. The hypothalamus produces a number of hormones: **Thyroid Releasing Factor (TRF), Gonadotropin Releasing Factor (GnRF), etc.**
3. These hormones affect the anterior pituitary → Stimulating the production of more hormones: **Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), etc.**
4. Eventually, these affect different organs.

By Negative Feedback:

The final hormones control the release of the early hormones.

5. *The **hormones** produced/released by **the affected organs** can **regulate** the release of **hormones** from the **anterior pituitary gland.***
6. *The **hormones** released from **the anterior pituitary gland** can also regulate the release of **hormones** from the **Hypothalamus.***



*The following table shows some differences & similarities between the Endocrine System and the Nervous System. **(IMP- Read it carefully)***

Criteria	Nervous	Endocrine
Range of effect	localized	widespread
Mediator	neurotransmitter	hormone
Effector cells	neurons	multiple tissues
Cellular targets	other neurons, muscle cells, glands	all tissues
Type of signal	chemical and electrical signals	chemical signals only
Mode of transmission	cell to cell only	Local and systemic
Onset of action	immediate response	gradual response (seconds – hours)
Duration of action	short lived (ms – minutes)	longer – lived effects (minutes – days)

Hormones are also classified into :-

1. True hormones:

- Secreted into the bloodstream by endocrine glands.

↳ thyroxine, epinephrine (adrenaline), estradiol, insulin.

2. Neurohormones:

- Secreted by nerve cells.
- [Many classic neurotransmitters (catecholamines, dopamine, acetylcholine, etc.) are similar to classic hormones with regard to synthesis, release, transport, and mechanism of action].
- They can affect other organs, like **muscles.**
- **Some of these hormones can act like neurotransmitters.**

↳ Catecholamines, dopamine, acetylcholine, etc.

<u>This depends on:</u>

1. The cell from which the hormones are released
2. The target cell (The ones they affect): different target → different action
3. Where they are secreted:

- Secreted into the vicinity: **Neurotransmitters**
- Secreted into the blood stream: **Hormones**

The following table shows some molecules that can act as hormones or neurotransmitters. *(The doctor said that it is important to know the names of the hormones, and that it isn't important to know exactly what they do, but we'll end up learning about the functions eventually in sections of this module or other modules...)*

Chemicals shared between Nervous and Endocrine Systems		
	as Neurotransmitter	**as Hormone**
Endorphins	**binds to pain receptors in brain**	**released from hypothalamus during times of stress**
Enkephalins	**blocks pain perception**	**blocks pain sensations**
Dopamine	**"feel good" neurotransmitter in limbic system & midbrain**	**inhibits secretion of prolactin**
Estrogen, Progesterone	**affects appetite center & body temp in hypothalamus and stimulates sexual arousal pathways**	**initiate secondary sex characteristics, follicular development & menstrual cycle**
Testosterone	**stimulates sexual arousal pathways and orgasm reflex**	**initiate secondary sex characteristics & spermatogenesis**
Norepinephrine, Epinephrine	**"feel good" neurotransmitter in limbic system and sympathetic branch**	**maintains sympathetic response**
Prolactin	**neurotransmitter in brain anterior pituitary**	**milk production**
Leutinizing Hormone	**neurotransmitter in brain anterior pituitary**	**maturation and development of reproductive system**

TYPES OF RESPONSES (12:10)

- *The type of response differs according to the hormone and the target cell.*

Communication between cells using hormones can be classified into:

1. **Endocrine mechanism** (classical hormones act via this mechanism)

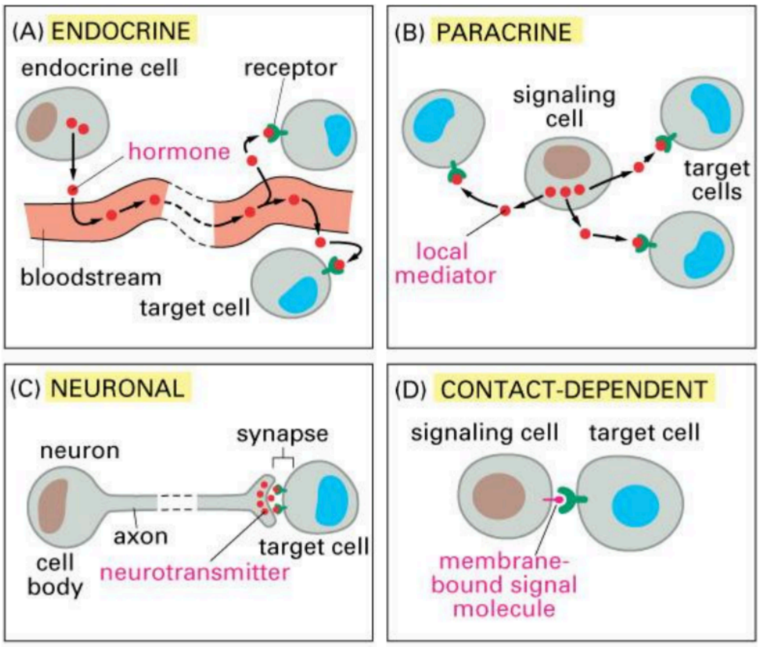
- The hormone is released into **the blood stream.**
- The hormone travels a **long distance (relatively).**
- The hormone affects a **target organ that is far away from the hormone-producing organ.**

2. **Paracrine mechanism:**

- **Two different cell types**, one is producing the hormone and the other is the target cell, but **BOTH** are in the same region/ vicinity.

3. **Autocrine mechanism**

- The released hormone **affects the same cell** that produced that hormone, OR
- The hormone affects a nearby cell of the **same type.**



4. **Neuroendocrine mechanism**

- Chemical communication between **nerve cells** and **distant target cells.**

Other less common mechanisms or responses:

5. **Intracrine mechanism**

- The hormone **IS NOT** released by the cell.
- The hormone acts **within** the cell itself (the signal is sent inside the producing cell itself).

6. **Juxtacrine mechanism**

- The hormone is bound to the cell surface.
- The hormone interacts with the receptor on a neighboring, juxtaposed cell.

7. **Pheromonal mechanism**

- Commonly found in **yeast.**
- Controls sensations and responses in a different organism rather than a cell.
- This also exists in humans. (Humans produce pheromones that give off a certain smell)

↳ *The pheromones will affect other human beings. The behavior/response is elicited by the other organism in front of that person (that's why we use perfumes and take a shower).*

LEVELS OF REGULATION (15:05)

It is very important to regulate hormones, and they are regulated at different levels.

They can be regulated at the level of:

1. Synthesis
2. Release
3. Transport in circulation
4. Metabolism
5. Delivery to the surface or interior of target cells
6. Intracellular signaling

THE TARGET CELL CONCEPT (15:38)

- *The target cell is the cell in which the hormone (ligand) binds to its receptor, regardless of the action.*
- *In our bodies, we have almost 200 types of differentiated cells, but only a few of them produce hormones.*
- *Every single one of the 75 trillion cells in a human are targets (can respond) to hormones.*
- So, there is a lot of diversity in the endocrine system. Therefore, it must be regulated very efficiently and meticulously.

- ☐ You can have one hormone bind to or affect **different cell types.**
- ☐ **A certain cell** can be affected by **several hormones**, producing **different** behaviors.
- ☐ **One hormone** can have **several effects** depending on:
  - The intracellular molecules that transmit the signal (mainly).
  - The receptor that it binds to.
  - The type of cell that it binds to.

Factors affecting the concentration of the hormone at the target cell

1. **The rate of synthesis and secretion of the hormone:**
   - The synthesis and secretion can be fast or slow.
2. **The rate of delivery (Proximity):**
   - How close the target cell is to the cell that produces the hormone (dilution factor).
   - Longer distance → Less effect (diluted effect) – Not a lot of the hormone reaches the target cell.
3. **Kd of the hormone-receptor complex**

- The dissociation constant measures the affinity of the hormone to the receptor.

4. **The rate of conversion of the hormone from its inactive form to its fully active form.**

- There could be a deficiency in the enzyme or process responsible for the conversion of the inactive hormone into its active form.

5. **The rate of clearance from the plasma.**

Factors affecting the target cell response

1. **The number, relative activity (affinity), and state of occupancy of receptors.**
   - You have a limited number of receptors that exist on the cell surface.
   - So, the response depends on how much hormone there is, the affinity of the hormone to the receptor, and the saturation level.
2. **The metabolism (activation / inactivation) of the hormone in the target cell:**
   - If we have a hormone that goes into the cell, will it be modified or not?
   - **Ex:** How are steroid hormones modified inside the cell?
3. **The presence of factors within target cells, that are necessary for the response.**
   - **Secondary messengers:** cAMP,cGMP, Calcium ions.
4. **Up- or down-regulation of the receptors upon interaction with the ligand.**
   - When the hormone binds to the receptor:
     - Some get internalized
     - Some get degraded
   - Desensitization: If we increase the number of hormone molecules that are bound to the receptor → internalization of the receptor occurs, which means that there are no available receptors on the cell surface for more hormone molecules to bind to. (There is a solution to this issue, which we will discuss at the end of this lecture)

BASIS OF CLASSIFICATION OF HORMONES (20:20)

Hormones can be classified into different categories according to a number of criteria:

- **Solubility**: *(lipid or water soluble)* -return to page 2-
- **Mechanism of transport** *(which depends on the solubility of the hormone)*
- **The chemistry of the hormone**: The structure *(for example: Is it a peptide, steroid or protein hormone?)*
- **Synthesis**

- **Processing and modification** *(some hormones are processed extensively while others are not)*
- **Pharmacology-based** *(we will not be discussing this point)*

SOLUBILITY*: (discussed on page 2 of this sheet)*

- **Water-soluble hormones:**
  1. Modified amino acids, proteins or peptides
  2. Eicosanoids

- **Lipid-soluble hormones:**
  1. Steroids
  2. Thyroid hormones
  3. Nitric Oxide

MECHANISM OF TRANSPORT: *Determined according to their solubility*

- **Water-soluble hormones:**
- Have no problem traveling by themselves in the bloodstream.
- **Lipid-soluble hormones:**
- Less soluble in blood.
- Need carriers in order to travel in the bloodstream.
- Most of them circulate in the blood as complexes, bound to **plasma globulins** or **albumin.** *(remember that albumin can bind to MANY molecules)*

FREE VS BOUND HORMONE:

- The free and bound hormones in the blood exist in equilibrium.
- The free hormone is the one that **is free to enter a cell** and **make it respond in a certain way.**
- **Biochemical assays** are important for:
- Determining the total hormone concentration
- Determining HOW MUCH of that hormone **IS FREE**
- Free hormone = Active hormone
- Measuring/determining the number of free hormone molecules is no easy task.

HALF-LIVES OF HORMONES

- Binding of hormones to different molecules or different carriers can affect their half-life (t1/2).
- A free hormone does not have a long t1/2.
- In general the t1/2 of:
- **Catecholamines from the adrenal medulla:** Seconds
- **Protein and peptide hormones:** Minutes

- **Steroids and thyroid hormone:** Long t1/2 (last for hours-days)
  - ➩ How come? They are bound, and therefore protected from enzymatic modification or clearance.

Factors affecting the target cell response

It's important to regulate the concentration of the hormone in the blood. This depends on:

1. **Rate of production:** Synthesis and secretion of hormones
2. **Rate of degradation and clearance**
3. **Rate of delivery:**
   - The dilution factor
   - The proximity of the gland/ producing cell from the target cell

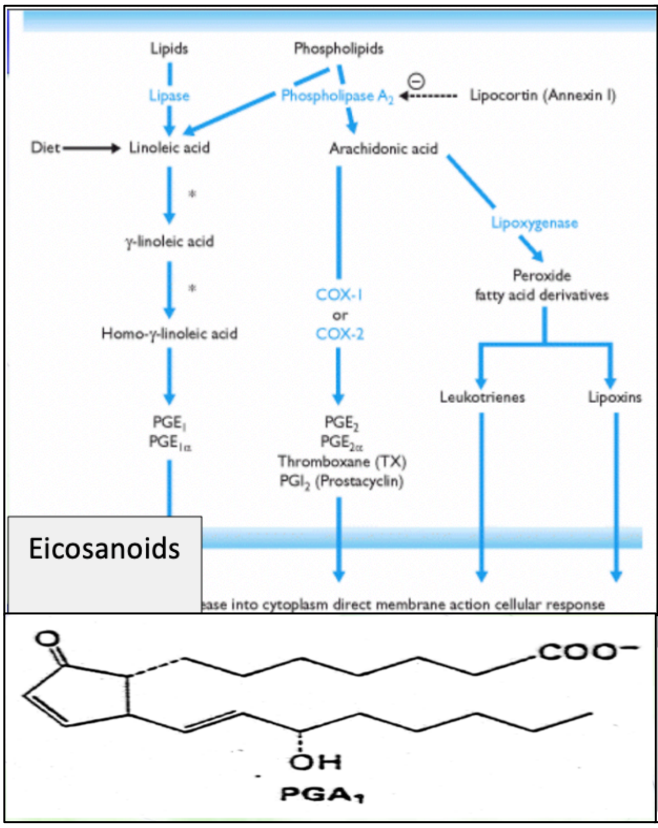
Other factors:

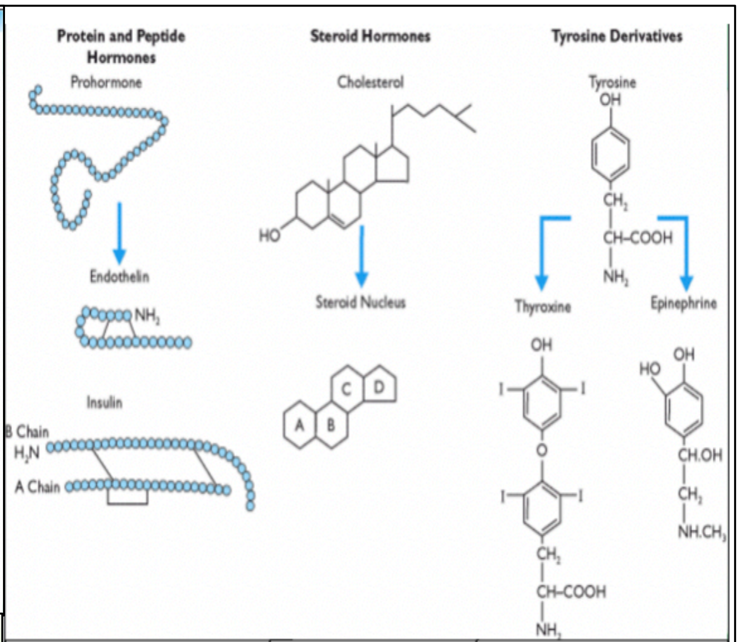
4. **Gender:** When taking a blood tests, there is a different range for hormone levels in males than that of the hormone levels of females.
5. **Age**
6. **Changes of the binding proteins**
7. **Developmental stage** (especially during the embryonic stage)
8. **Reproductive status:** Whether the person is reproductively active or not.
9. **Stage of temporal rhythm** for some hormones.

CHEMICAL CLASSIFICATION OF HORMONES

- **Peptides:** Small and large hormones. Peptides or polypeptides (3 to 100 AA's)
  - ➩ Insulin, glucagon, adrenocorticotrophic hormone (ACTH)
- **Amino acid derivatives:** Directly derived by modification of an amino acid such as epinephrine and thyroxine (made from tyrosine), and serotonin (5-hydroxytryptamine; made from tryptophan)
- **Steroids:** Derived from cholesterol by modification of the cholesterol ring system.
  - ➩ Estradiol, cortisol, calciferol (Vitamin D), and testosterone
- **Eicosanoids:** Derivatives of the unsaturated fatty acid, arachidonic acid.
  - ➩ Prostaglandins, leukotrienes, and thromboxane B
- **Gases:** Nitric oxide (NO) [produced and released by endothelial cells, synthesized by NO synthase (NOS), which catalyzes NAPDH-dependent oxidation of l-arginine. Also, CO.]

→ These figures show the previously mentioned chemical structures or classifications of hormones





Protein/peptide hormones with the sequence of amino acids	Steroid hormones derived from cholesterol	Amino acid derivatives like the Thyroid hormones, for example.

PROCESSING AND MODIFICATION *Can differentiate hormones from each other*

1. Hormones that are synthesized and secreted in their final form

- Aldosterone
- Hydrocortisone
- Estradiol
- Catecholamines (epinephrine & norepinephrine)

2. Hormones that are modified directly in the target tissue

- Insulin (synthesized as proinsulin and partially processed to insulin in the pancreas)
- [An extreme example: the products of the proopiomelanocortin (POMC) gene]

3. Hormones that are modified indirectly by non-target tissue

- Thyroxine – T4 is modified to T3 in the liver and pituitary gland.
- Testosterone (secondary sex tissues) – Testosterone is released from the source cells → reaches target cells where it is converted into dihydrotestosterone → released to the target cells.
- Vitamin D3 (from the skin)→ is converted to 25-hydroxycalciferol (in the liver) then to → 1,25-dihydroxycholecalciferol (in the kidney)

HORMONE SYNTHESIS (29:05)

↳ *Differs according to the type of hormones*

- Protein and peptide hormones
  1. **Alternative splicing**
  2. **Post-translational modification**
  3. **Early synthesis of a preprohormone:** Needs to be activated into its final form.
- Steroid hormones
- Amine hormones
- Eicosanoid hormones

SYNTHESIS OF PEPTIDE HORMONES (29:50)

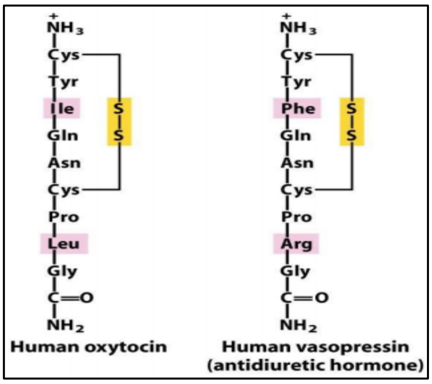
- **From precursor genes**
- **By** alternative splicing, post-translational modification, and synthesis of preproprotein hormone (which must be activated)

Alternative splicing:

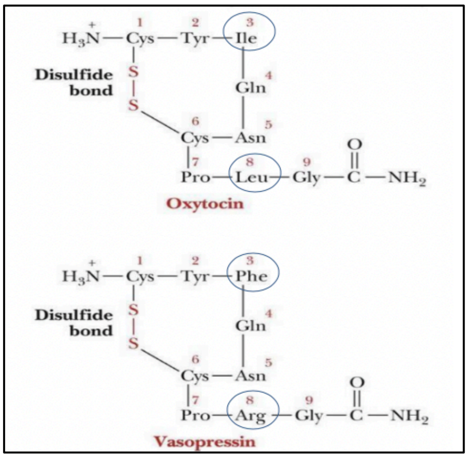
- As a result of alternative splicing of exons and post-translational modifications of the original amino acid sequence, more than one pro-hormone may be derived from a single gene.
- Alternative splicing and post-translational modification are typically tissue-specific.

Example #1 Vasopressin and Oxytocin:

- They are **9 amino acid** peptide hormones.
- They have almost identical primary structures of amino acid composition (except for positions 3 and 8).



- **The 3rd and 8th** amino acids are important for the activity of these hormones
  - **Oxytocin**- #3: Isoleucine, #8: Leucine
  - **Vasopressin**- #3: Phenylalanine, #8 Arginine
- [They are produced by different genes in hypothalamic neurons.]



Example #2 Calcitonin & calcitonin-gene related peptide (CGRP) – They are produced from the same gene but are alternatively spliced at the RNA level.

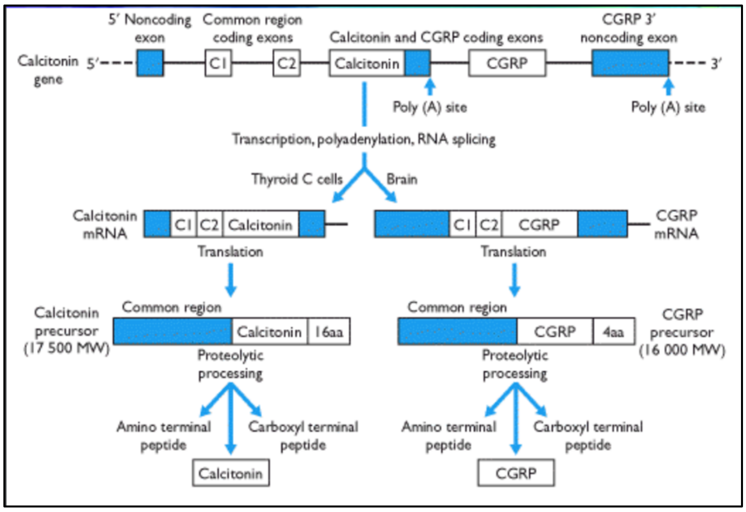
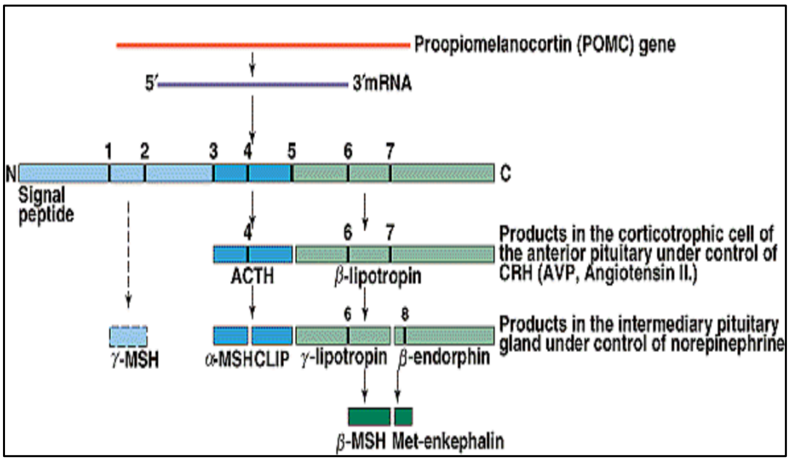


FIGURE: Notice that the **C1 and C2** exons are <u>shared among both hormones</u>, but the third exon differs from one hormone to the other. → **DIFFERENT HORMONES**

Example #3 Hormones that are produced from the Pro-opiomelanocortin peptide:



- It is a large peptide produced from a single gene → it is modified post translationally → cleaved into different biologically active peptide fragments → each peptide has a certain action.

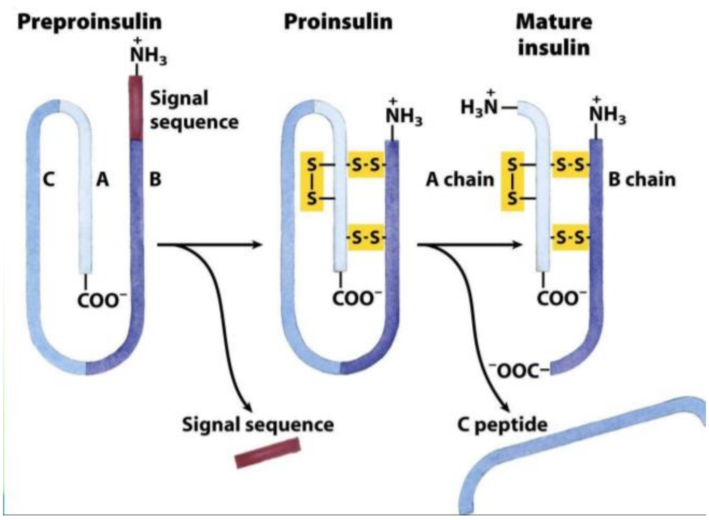
<u>The peptide fragments formed are:</u>

- **Adrenocorticotropic hormone (ACTH)** → Important for the production of cortisol
- **Enkephalins**
- **Endorphins**
- **Melanocyte stimulating hormone (MSH)** → For pigmentation of skin cells

Synthesis of a preproprotein hormone (Insulin and Glucagon)

1. They are produced on the surface of the endoplasmic reticulum.
2. They are internalized into the ER.
3. The pre-region is cleaved off (it is the signal sequence).
4. The prohormone is produced.
5. The prohormone is modified enzymatically (cleaved) into the active form of the hormone.

Ex: Preproinsulin



The insulin is produced from a single gene (single polypeptide) → disulfide bonds are formed → cleavage of the C peptide (C portion) → forming the final form of the Insulin molecule with the A and B chain

In our Molecular Biology course, we talked about cloning and how we can clone the different portions of genes in different bacteria → We can then combine the B and A peptides to form the final mature form of Insulin.

→ This table shows the differences in the structure or amino acid composition of these hormones.

Hormone	Structure
GHRH	44
TRH	3
GnRH	10
CRH	41
ADH	9
Vasopressin	9
Angiotensin I	10
Angiotensin II	8
Insulin	51
Glucagon	29

TRH is composed of **3 amino acids**, while **ADH** and **Vasopressin** are composed of **9 amino acids**. **Insulin**, on the other hand, is a **large protein molecule** (relatively).

– Don't memorize the numbers, just memorize which of them are large and which of them are small.

SYNTHESIS OF STEROID HORMONES (34:30)

- The synthesis of steroid hormones occurs in the mitochondria and smooth endoplasmic reticulum.
- They are synthesized from cholesterol.
- They require specific sequential enzymes that convert cholesterol into the appropriate steroid. **(they sequentially produce the steroid hormones)**
- These enzymes are expressed in different steroid-secreting cells.
- The expression of these enzymes is controlled by different **hormones (trophic hormones)** and/or other factors.

AMINE HORMONES (35:00)

- They are produced from amino acids. *(To be discussed later in the CNS)*
- **Ex:** Catecholamines, melatonin and serotonin are formed by side-chain modifications of either a single tyrosine or tryptophan.

EICOSANOID HORMONES (35:15)

- The eicosanoid family of hormones are formed **from lipids.**
- The eicosanoids consist of the **prostaglandins (PGs)**, **thromboxanes (TXs)** and **leukotrienes (LTs).**
- The principal eicosanoids are a group of molecules derived from the unsaturated 20-carbon fatty acid, **(arachidonic acid).**

PHARMACOLOGICAL CLASSIFICATION OF HORMONES (35:33)

Hormones act as:

1. Agonists (**glucagon and epinephrine**)
2. Antagonists (**insulin & glucagon**- the action of insulin is opposite that of glucagon)
3. Partial agonist-partial antagonists
4. Mixed agonist-antagonists *(we won't be talking about these in this module)*

HORMONE INTERACTIONS

Hormones rarely act independently, they work together to maintain homeostasis

The way they communicate can be classified into:

1. **Synergistic effect**
   - Hormones tend to cause the same final effect.
   - **ADH & aldosterone:** both have the same final effect.
   - **Estrogen and FSH** hormones are both needed in the ovaries for oocyte development.

2. **Antagonistic effect**
   - Hormones produce opposite effects.
   - An example is insulin and glucagon
   - **Insulin promotes synthesis of glycogen** by liver cells, while **glucagon stimulates the breakdown of glycogen** in the liver resulting in an increased serum glucose level.

3. **Permissive effect**
   - **Hormones only affect "preprimed" tissues.**

   - **We need a hormone to prepare** or prime the organ for the action of another hormone by:
     1) The permissive hormone stimulates the ***presentation of more receptors*** on the cell surface for another hormone.
     2) Sometimes the permissive hormone promotes the ***synthesis of enzymes*** needed for the expression/production of the other hormone.

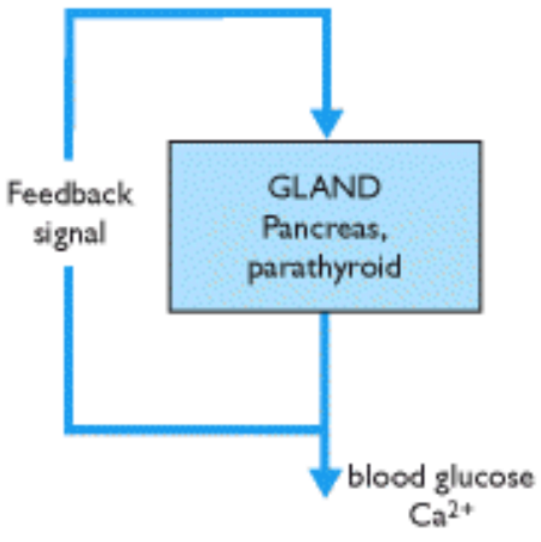
   - Also, can occur when **TWO** hormones act together to amplify the effect.
   - EXAMPLE: **Epinephrine** acts on fat cells to stimulate the breakdown of triglycerides for energy, but it doesn't that big of an effect. However, with the presence of **Thyroid hormone** (T3 and T4) and the same amount of **epinephrine** → A greater effect is brought about.

4. **Integrative effect**
   - Hormones produce **complementary effects** on different tissues, and they have the same end result.
   - EXAMPLE: **PTH and calcitriol** both increase the level of calcium in the blood.

FEEDBACK CIRCUITS (39:10)

- Mechanisms of regulating hormone release is important. **(VIA FEEDBACK CIRCUITS)**
- The final hormone controls/regulates the release of the early hormone.

- For example: ***Glucose and insulin***
  - The level of glucose can regulate how much insulin is released. HOW?



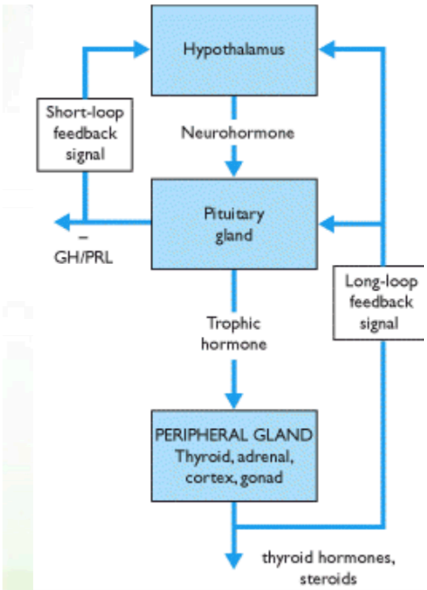
1. **Ingested lactose or sucrose** is absorbed in the intestine.
2. **Blood glucose level rises.**
3. This **increase in blood glucose** concentration stimulates the release of insulin from endocrine cells in the pancreas.
4. Insulin facilitates the **entry of glucose into many cells.**
5. Cells take up glucose and convert it into **glycogen.**
6. **Level of blood glucose falls.**

7. The stimulus for **insulin** release **disappears.**
8. **Insulin is no longer secreted.**

- A more complex feedback mechanism for the regulation of hormone release *(return to page 4):*
- Feedback loops involving the hypothalamopituitary axis that detects changes in the concentration of hormones secreted by peripheral endocrine glands.

RECALL:

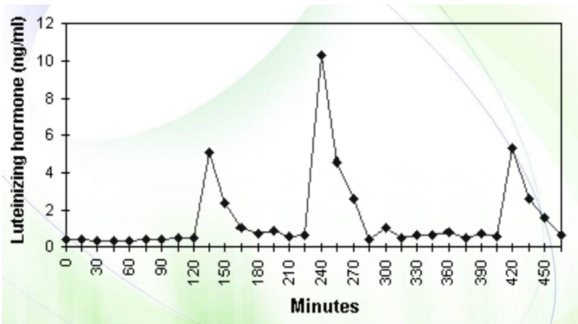
- Hypothalamic hormones are released → This affects the pituitary gland → The pituitary gland releases trophic hormones → These affect other peripheral glands → other hormones are released from the peripheral glands
- **By feedback inhibition**, the hormones produced by the pituitary gland can regulate the release of the hypothalamic hormones.
- And the peripheral hormones released inhibit the release of hormones from the pituitary gland and the hypothalamic gland as well.



MECHANISMS OF RELEASE: PULSATILE SECRETION (41:10)

The release of hormones isn't continuous, rather it occurs in **pulses**

- Each **pulse** has an amplitude and period.
- Groups of pulses have a frequency.
- Basal levels of hormone often reflect the spacing between pulses and its relation to hormonal clearance.
- Figure: **LH**, for example, increases reaching its peak, and then goes back down, then back up, and then back down, and so on. **Why does this happen?**



- The main reason is to **prevent desensitization** and **to reactive the signaling pathways** of these cells.
- When a hormone is being continuously produced/released → This hormone binds to the receptor → The receptor is internalized and gets degraded → This means there are no more receptors on the cell surface for the hormone to bind to → When the hormone disappears → the receptor reappears → the CYCLE continues.

→ **Being unsaturated all the time as we mentioned, is another way to prevent desensitization.**

Other examples of pulsatile secretion of glands:

- **Nerve impulses** to the adrenal medulla control the release of epinephrine.
- **Blood Ca++** regulates the secretion of parathyroid hormone.
- **ACTH** (hormone from the anterior pit. gland) stimulates the release of cortisol by the adrenal cortex.

[Elements of an Endocrine System] – <u>The last slide wasn't explained by the professor</u>

[Hormones are secreted by regulator cells in an endocrine gland, and transported to target cells, where signals are transduced via cellular molecules that include:

- Receptors
- Amplifiers (enzymes)
- Transducers (proteins and second messengers)
- Effector proteins]