Pineal Gland
&
Thymus Gland

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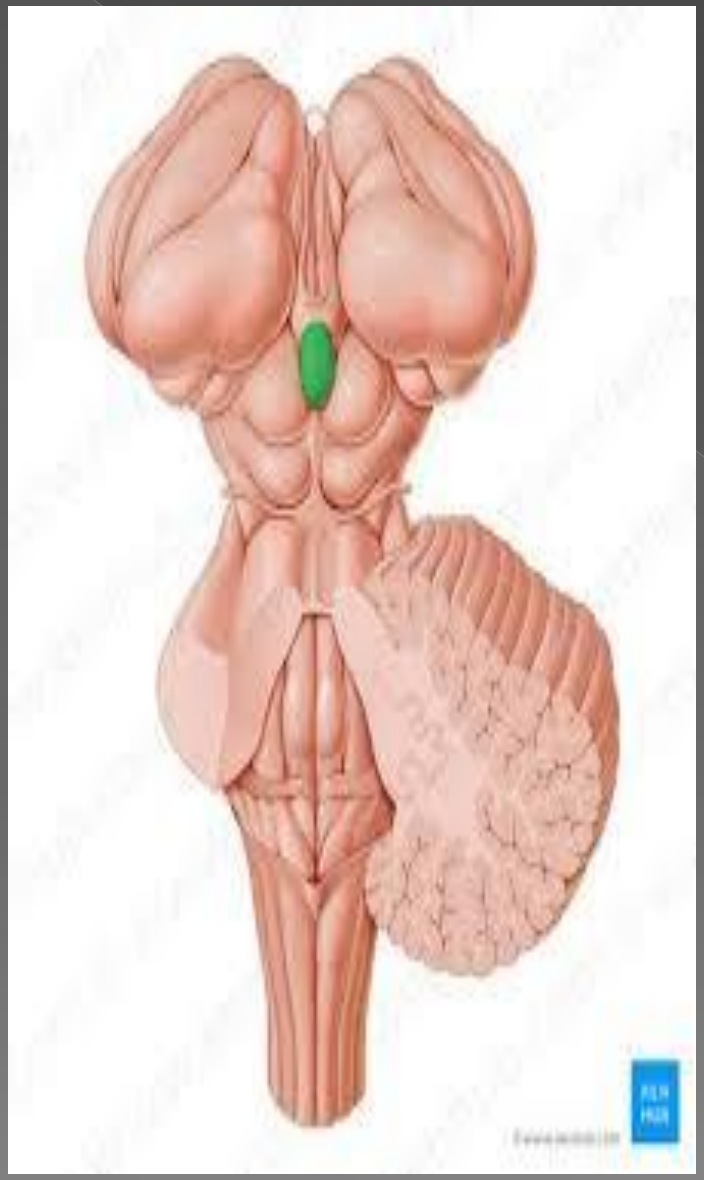
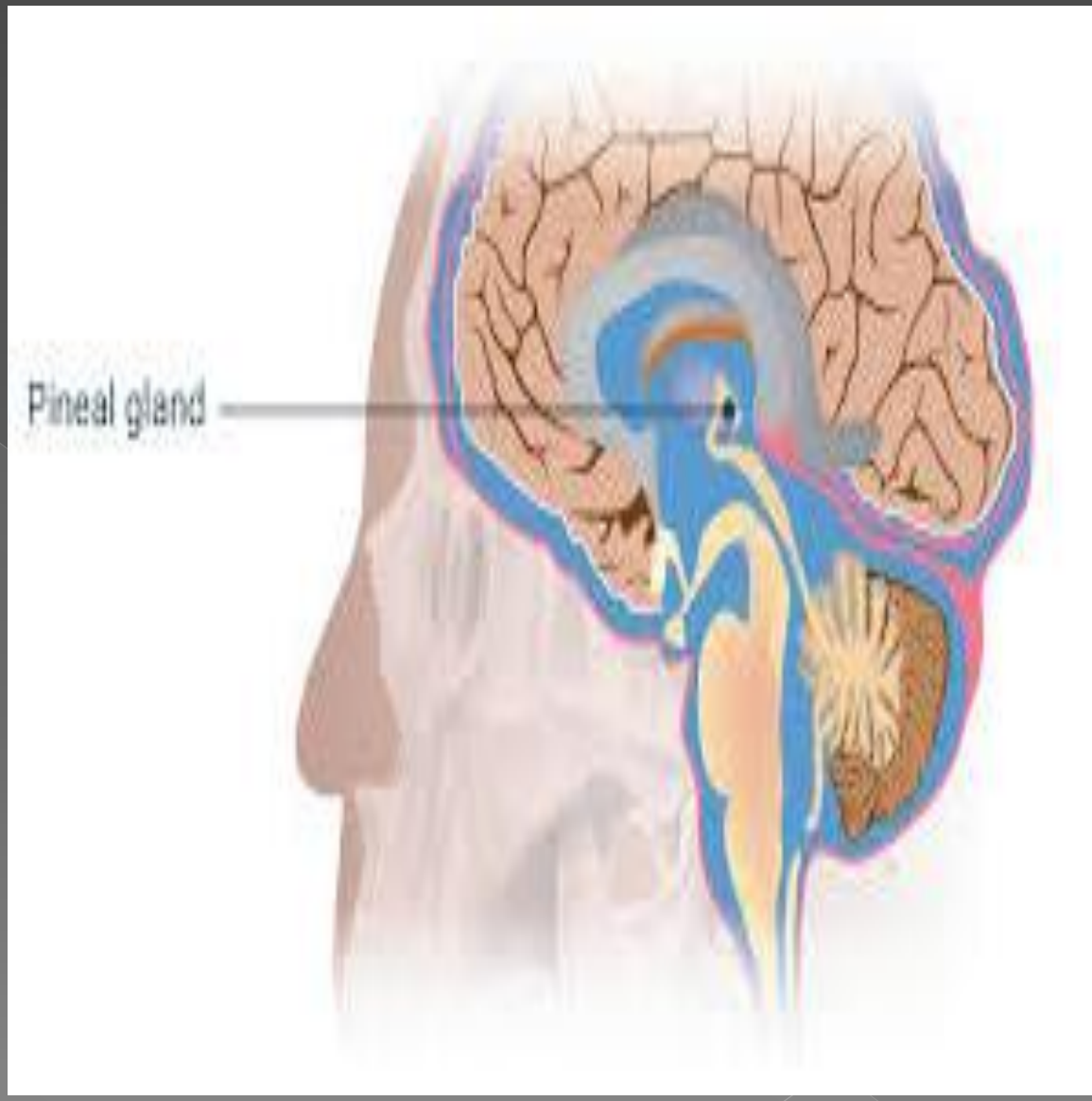
Lec 5

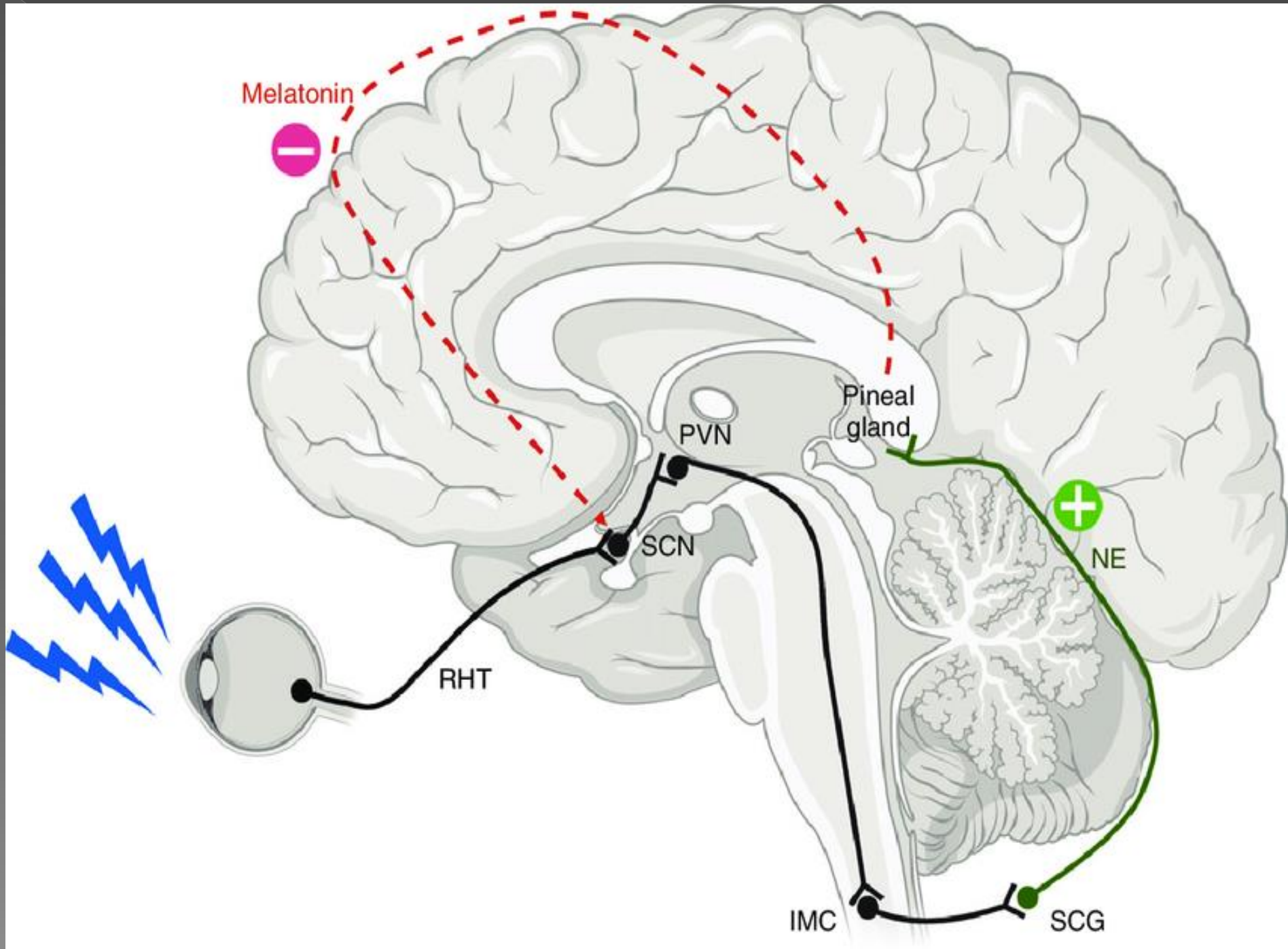
- Objectives:
- Define pineal gland &its location.
- Function of pineal gland.
- Dysfunction of pineal gland
- Definition &location of Thymus gland.
- Function of thymus gland.
- Dysfunction of thymus gland

- **The Pineal Gland**
- The pineal gland is a small, reddish-gray endocrine organ located near the center of the brain, in a groove between the two thalamic bodies.
- In humans, it measures about **8 mm in length** and is roughly the size of a pea.
- Histologically, the gland is composed mainly of **pinealocytes**, which are specialized secretory cells, and supportive **glial cells.**
- Functionally, the pineal gland acts as a link between the nervous and endocrine systems.
- It translates **sympathetic neural input** into **hormonal output**, primarily through the secretion of **melatonin**.




Pineal gland

- **Regulatory Pathway of Melatonin**
- **Light enters the Retina((which actually inhibits melatonin synthesis; darkness removes this inhibition)** → signal goes to the suprachiasmatic nucleus (SCN, hypothalamus biological clock).
- From the SCN → to the **paraventricular nucleus (PVN**, in the hypothalamus).
- **PVN** neurons send fibers down through the spinal cord to the superior cervical ganglion (SCG, in the neck, part of the sympathetic chain).
- The **SCG** releases **norepinephrine (NE**) → stimulates the pineal gland → secretion of melatonin


Melatonin
Pineal gland
PVN
SCN
NE
RHT
IMC
SCG

- Daylight **suppresses** melatonin secretion**,** while darkness **stimulates** it**.** Levels peak at night, promoting sleep, and fall during the day, maintaining wakefulness.
- Melatonin plays a central role in regulating **circadian rhythms** (wake–sleep cycles) and seasonal biological rhythm.
- Unlike most parts of the brain, the **pineal gland is not protected by the blood–brain barrier**.
- This allows it to have direct access to the systemic circulation and to rapidly release hormones, particularly **melatonin**, into the bloodstream.

- The pineal gland functions in close association with the **hypothalamus**, which regulates essential processes such as **thirst, hunger, sexual behavior, circadian rhythms, and aging-related biological timing**.
- With advancing age, **calcium salts and other mineral deposits accumulate** in the gland, a process known as **pineal calcification**.
- This is a common finding in the elderly and may reduce the gland's secretory activity.

Functions of the Pineal Gland

1. **Regulation of Circadian Rhythms**

- Secretes **melatonin** in response to light/dark cycles.
- Coordinates the body's biological clock (sleep–wake cycles).

2. **Seasonal (Photoperiodic) Rhythms**

- In humans, melatonin secretion varies with day length. During the longer nights of winter, melatonin secretion increases, while during the shorter nights of summer, secretion decreases.
- This seasonal variation may influence mood, leading to Seasonal Affective Disorder (SAD) — a type of depression that occurs during winter when daylight exposure is reduced.

3. **Neuroendocrine Regulation**

- Acts as a link between the **sympathetic nervous system** and the **endocrine system** by converting nerve signals related to light and dark into hormonal signals (melatonin).

4. **Antioxidant Role**

- Melatonin has strong antioxidant properties, protecting cells from free-radical damage.

5. **Role in Aging**: Melatonin secretion declines with age
6. **Reproductive Function**

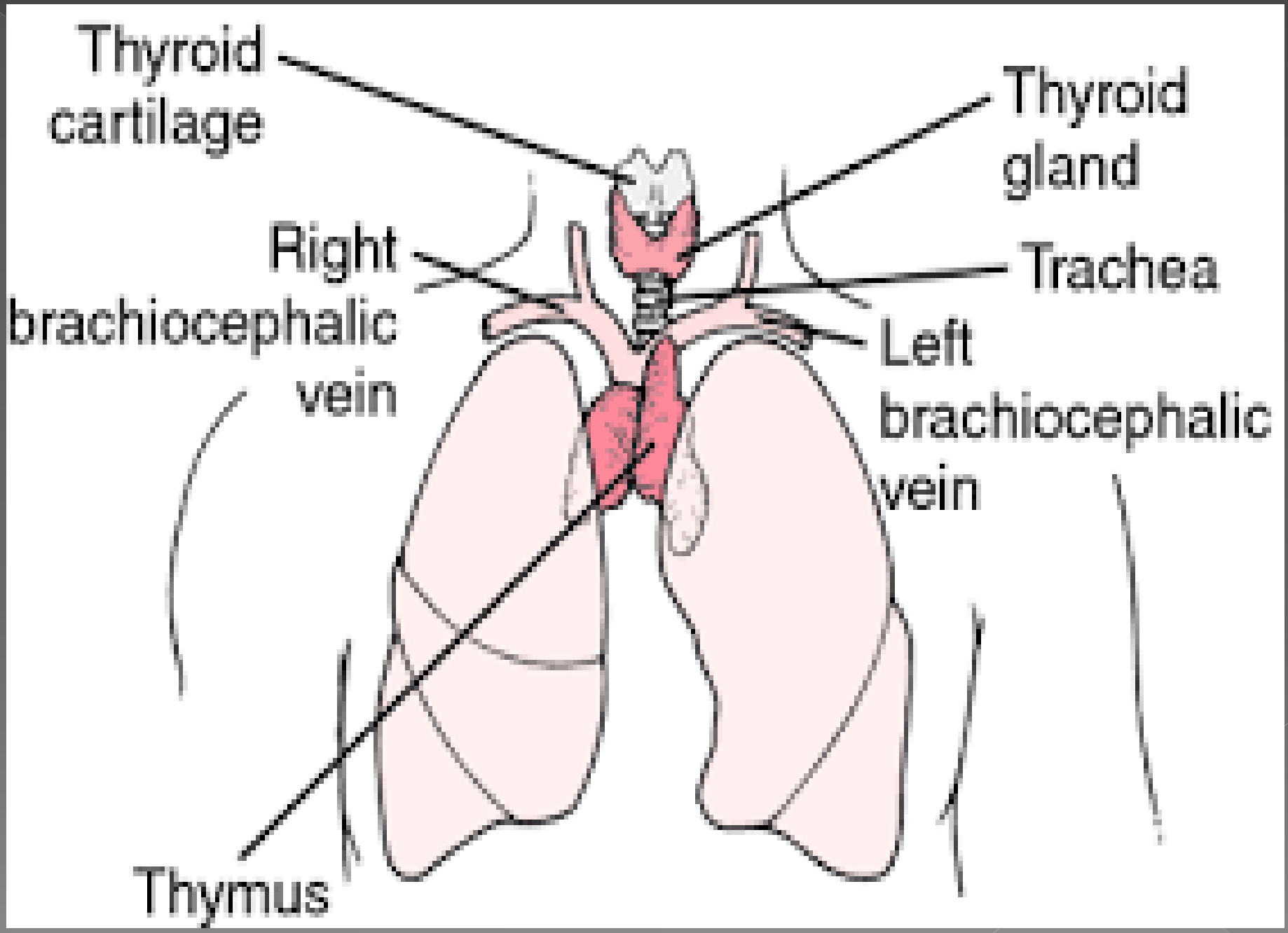
- Melatonin exerts an inhibitory effect on hypothalamic-pituitary-gonadal axis in children.
- By reducing GnRH and consequently gonadotropins (LH and FSH), it delays the onset of puberty.
- This inhibitory effect decreases with age, allowing sexual maturation.

Pineal Gland and Melatonin

Synthesis and Secretion

- Melatonin is synthesized in the **pineal gland** from the neurotransmitter **serotonin**.
- Its secretion follows a circadian rhythm and is mainly released into the **bloodstream**, with small amounts entering the **cerebrospinal fluid**.
- Although the pineal gland is the principal source, other tissues such as the **retina, gonads, skin, and immune cells** can also produce melatonin in smaller amounts.

- **Thymus Gland**
- The **thymus gland** is a specialized **primary lymphoid organ** essential for the development of the immune system.
- It is located in the **anterior superior mediastinum**, behind the sternum and in front of the heart.
- Structurally, the thymus consists of **two lobes**, each surrounded by a connective tissue capsule. Within each lobe, there is an **outer cortex**, rich in immature T-lymphocytes, and a **central medulla**, which contains more mature T-cells along with characteristic structures known as **Hassall's corpuscle.**


Thyroid cartilage
Thyroid gland
Right brachiocephalic vein
Trachea
Left brachiocephalic vein
Thymus

Thymus and T Lymphocyte Maturation

- The **thymus gland** plays a central role in the development and maturation of **T lymphocytes (T cells)**, which are crucial for adaptive immunity
- T-cell precursors arise from hematopoietic stem cells in the bone marrow. Immature cells migrate via blood to the thymus.

Thymic Education:

The thymus is essential for **T-cell education**:

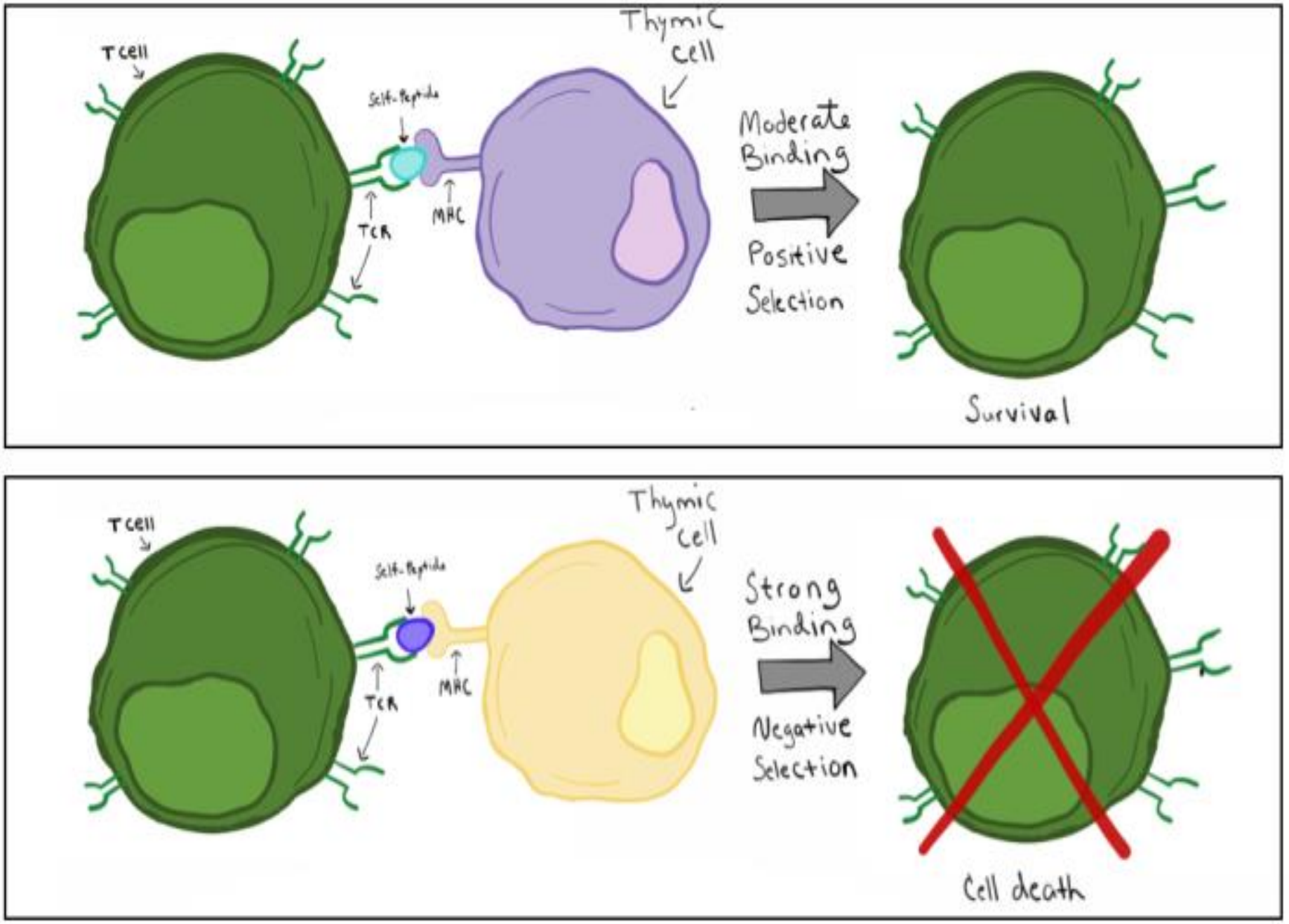
1. **Positive Selection (Cortex of Thymus)**

- Developing T cells are tested for their ability to recognize self–MHC molecules (Major Histocompatibility Complex).
- Only thymocytes whose TCRs bind moderately to self–MHC receive survival signals.
- Thymocytes that fail to recognize self–MHC undergo apoptosis (failure of positive selection).

- This process ensures that all surviving T cells will later recognize antigens only when presented on MHC molecules (MHC restriction).

2. **Negative Selection (in the medulla of thymus):**
    1. T cells that bind strongly to self-antigens presented on MHC are eliminated.
    2. This process prevents **autoimmunity**, ensuring self-tolerance.

- After these steps, only a small percentage (5–10%) of the original T cell precursors survive.


Thymic cell
T cell
Self-Peptide
TCR
MHC
Moderate Binding
Positive Selection
Survival
Thymic cell
T cell
Self-Peptide
TCR
MHC
Strong Binding
Negative Selection
Cell death

Exit of Mature T Cells from the Thymus

- **Mature but naïve T cells** ($CD4^+$ or $CD8^+$) leave the thymus once they finish positive and negative selection.
- Their exit is regulated by the **sphingosine-1-phosphate (S1P) gradient(is a lipid signaling molecule that is present at high concentrations in the blood and lymphatic fluid)**:
  - Low S1P inside the thymus, high S1P in blood/lymph.
  - T cells expressing **S1P receptor (S1PR1)** migrate along this gradient.

- **They enter the blood and secondary lymphoid organs (lymph nodes, spleen), where they await antigen exposure to complete functional activation.**
- **Outcome:**
- Surviving cells become mature but naïve $CD4^+$ or $CD8^+$ T cells, exit the thymus, then complete their functional maturation in secondary lymphoid organs such as lymph nodes to await antigen exposure.

Clinical Relevance

- **Congenital thymic defects** (e.g., DiGeorge syndrome) result in severe **immunodeficiency** due to lack of functional T cells.
- **Acquired or structural abnormalities** of the thymus can lead to impaired T lymphocyte maturation, resulting in immunodeficiency or, in some cases, autoimmune disorders due to failure of deletion of self-reactive cells.

- **Question:(Homework)**
- After puberty, the thymus undergoes involution and is largely replaced by adipose tissue. How is T-cell function maintained in adults despite reduced thymic output?