

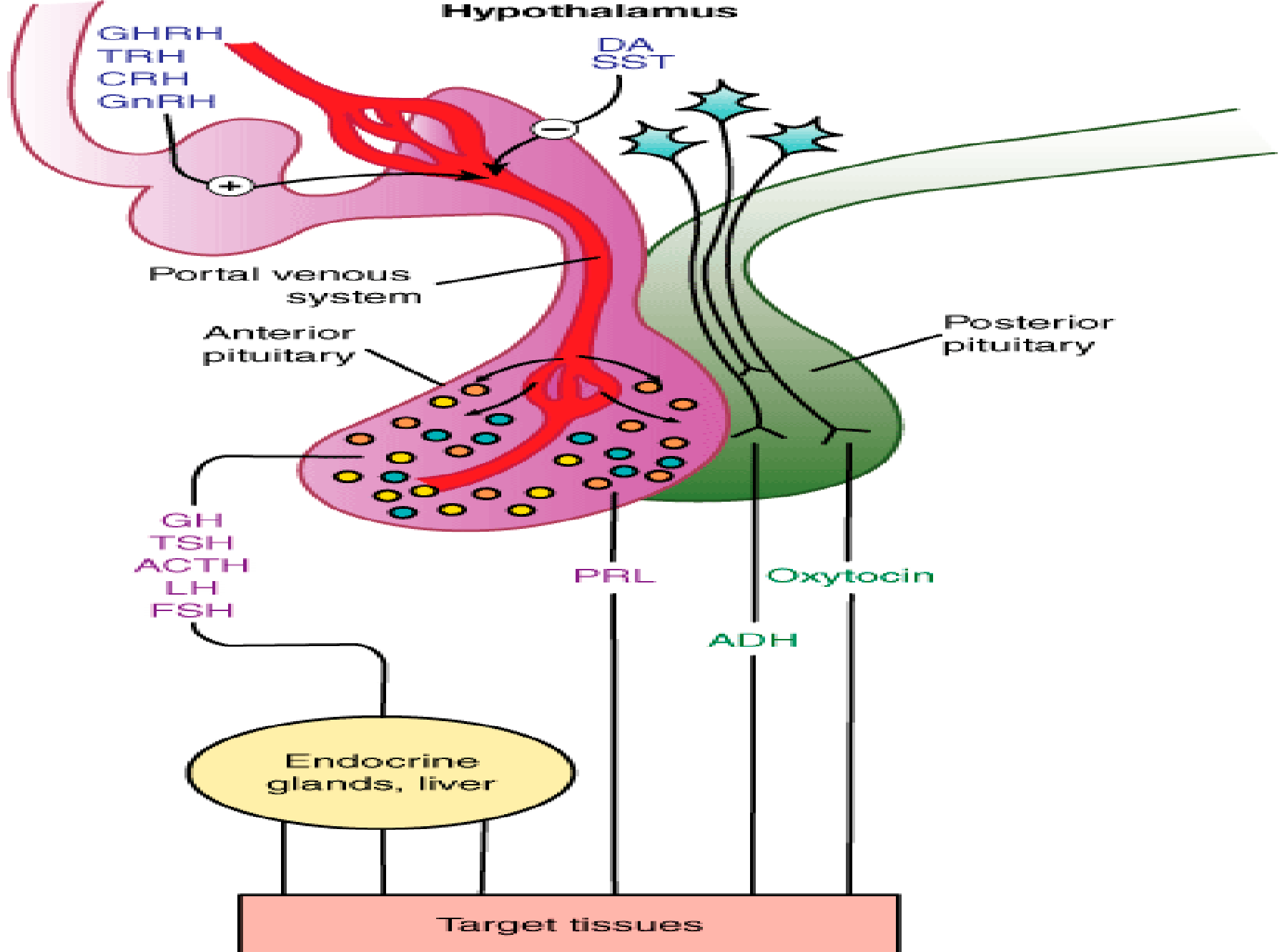
# **Pharmacology of Endocrine System**

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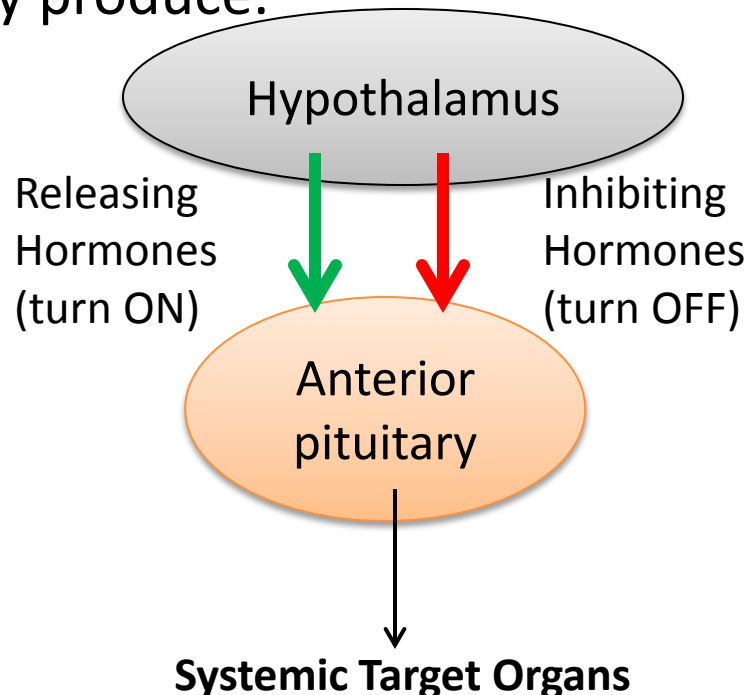
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# Hypothalamus

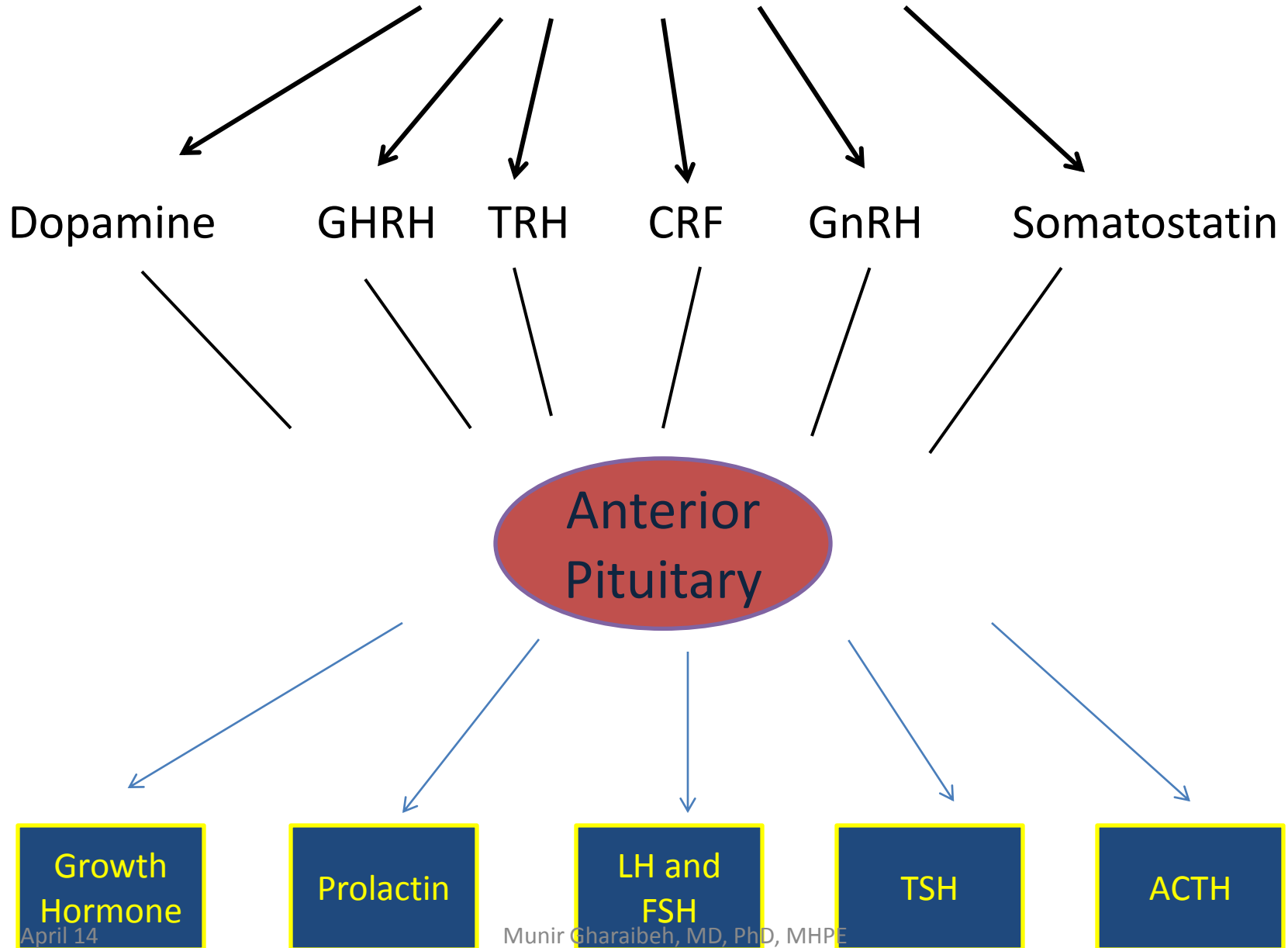


# Hypothalamic Hormones

- Hypothalamic releasing and inhibiting hormones are carried directly to the anterior pituitary gland via adenohypophyseal portal vasculature.
- Specific hypothalamic hormones bind to receptors on specific anterior pituitary cells, modulating the release of the hormone they produce.



# Hypothalamus



# Hypothalamic Hormones

- **Dopamine:** inhibit the secretion of prolactin from the anterior pituitary gland
- **GHRH:** Growth Hormone-Releasing Hormone
- **Somatostatin:** inhibits the secretion of growth hormone
- **TRH:** Thyrotropin-Releasing Hormone, stimulates the release of thyroid-stimulating hormone and prolactin. (Protirelin)
- **CRF:** Corticotropin-Releasing hormone, stimulates ACTH release
- **GnRH:** Gonadotropin-Releasing Hormone

# Somatostatin

- Inhibits the secretion of growth hormone
- Primarily a 14-amino acid peptide
- Have very brief half-life in the serum  
————→ So Not Useful Clinically.....
- **Octreotide:** An 8-amino acid analogue, so  
**More Stable.**



# Effects of Somatostatin

## ***Inhibition of secretion of :***

- Growth Hormones
- Thyroid-stimulating hormones
- Prolactin
- ACTH
- Insulin
- Glucagon
- Pancreatic polypeptide
- Gastrin
- Cholecystokinin
- Secretin
- Vasoactive intestinal peptide
- Exocrine pancreas secretion

***Inhibition of bile flow***

***Inhibition of mesenteric blood flow***

***Decreased gastrointestinal motility***

# Octreotide (*Sandostatin, LAR*)

- Depot injection (Monthly).
- Used to treat **Acromegaly**
- Other uses:
  - Counteract diarrhea associated with neuroendocrine tumors such as insulinomas or carcinoid tumors.
  - Control severe diarrhea associated with AIDS that doesn't respond to other treatments.
- Side effects:
  - Gastrointestinal discomfort.
  - Decreased glucose tolerance.
  - Formation of gallstones.



# **Gonadotropin-Releasing Hormone (GnRH) or Gonadorelin**

- Stimulates the production of Luteinizing hormone (LH) and Follicle stimulating hormone (FSH) from anterior pituitary.
- Released in bursts at regular intervals (every 2 hours).
- Has very short half-life (7 minutes)
- The response to GnRH ( or its analogues) depends on the concentration and mode of administration.
- Pulsatile administration doesn't have the same effect as continuous administration

# **Biological actions of GnRH**

## **Agonists and Antagonists**

DRUG	DOSE and Regime	EFFECT
Agonist	Low, pulsatile	Pituitary and gonadal stimulation
Agonist	High, constant	Pituitary and gonadal stimulation followed by suppression for 2 weeks
Antagonist	Constant	Pituitary and gonadal suppression

Part of the desensitization of GnRH is caused by a decreased number of pituitary receptors.

# Lutrepulse (agonist)

- Lutrepulse, (Gonadorelin) is used to cause ovulation in women who do not have a period. (when FSH and LH are low)
- Administered intravenously, in pulses, through a pump.
- Used for women who are not producing enough GnRH.

# **Gonadotropin Suppression**

- **Leuprolide**
- **Goserelin**
  - Stable potent derivatives of GnRH.
  - Long acting agents.
  - Suppress gonadotropin production(after initial stimulation)
  - Used as palliative treatment for reduction of prostate cancer growth.
- **Ganirelix:**
  - Is an antagonist given by monthly injections.
  - Used to prevent premature ovulation in women undergoing ovarian stimulation as part of fertility treatment.

	Hormone	Major target organ(s)	Major Physiologic Effects
Anterior Pituitary	<u>Growth hormone</u>	Liver, adipose tissue	Promotes growth (indirectly), control of protein, lipid and carbohydrate metabolism
	<u>Thyroid-stimulating hormone</u>	Thyroid gland	Stimulates secretion of thyroid hormones
	<u>Adrenocorticotrophic hormone</u>	Adrenal gland (cortex)	Stimulates secretion of glucocorticoids
	<u>Prolactin</u>	Mammary gland	Milk production
	<u>Luteinizing hormone</u>	Ovary and testis	Control of reproductive function
	<u>Follicle-stimulating hormone</u>	Ovary and testis	Control of reproductive function
Posterior Pituitary	<u>Antidiuretic hormone</u>	Kidney	Conservation of body water
	<u>Oxytocin</u>	Ovary and testis	Stimulates milk ejection and uterine contractions

# **Anterior Pituitary Hormones**

- Anterior pituitary hormones are released in a pulsatile manner.
- Secretion varies with time of day or physiological conditions such as exercise or sleep.
- Understanding the rhythms that control hormone secretion leads to better uses of hormones in therapy.

# **Growth Hormone (Somatotropin)**

- 191- amino acid peptide.
- Required during childhood and adolescence for attainment of normal adult size
- Has important effects throughout postnatal life on lipid and carbohydrate metabolism, and on lean body mass.
- Effects are primarily mediated via insulin-like growth factor 1 (IGF-1, somatomedin C) and, to a lesser extent through insulin-like growth factor 2 (IGF-2).

# Growth hormone deficiency (Pituitary Dwarfism)

- Individuals with congenital or acquired deficiency of GH during childhood or adolescence fail to reach their predicted adult height and have disproportionately increased body fat and decreased muscle mass.
- Also, these individuals have disproportionate delayed growth of skull and facial skeleton giving them a small facial appearance for their age.
- Adults with GH deficiency also have disproportionately low lean body mass.





# Dental Manifestations (Dwarfism)

- The maxilla and mandible of affected patients are smaller than the normal and the face appears smaller with the permanent teeth showing a delayed pattern of eruption .
- Often the shedding pattern of deciduous teeth is delayed for several years, and also the development of roots of permanent teeth appears to be delayed.
- Dental professionals may be the first health care providers to see the signs and symptoms of growth disorders, and thus have the first opportunity to correctly diagnose this serious disease.

# Dwarfism



**Delayed eruption of teeth**



**Microdontia**

- The dental arch gets smaller than normal; it cannot accommodate all the teeth, thus irregularity of teeth develops.
- The roots of the teeth are also shorter than normal in dwarfism.

# **Somatotropin (*Humatrope*)**

- A recombinant form of growth hormone (GH).
- Has the same amino acid sequence.
- Administration: subcutaneously (SC) in the evening.

# Clinical Uses of Somatotropin

- Mainly used in growth failure of pediatric patients.
- Other effects include :
  - Improved metabolic state, increased lean body mass, sense of well-being in adults with GH deficiency.
  - Increased lean body mass, weight, and physical endurance and wasting in patients with HIV infection
  - Improved gastrointestinal function in short bowel syndrome in patients who are also receiving specialized nutritional support

# Gigantism

- Gigantism is the childhood version of growth hormone excess and is characterized by the general symmetrical overgrowth of all body parts



# Acromegaly



- A chronic metabolic disorder in which there is too much growth hormone and the body tissues gradually enlarge.
- Excess secretion occurs after epiphyseal plate closure at puberty.
- Usually results from pituitary tumor (adenoma).
  1. Treatment of choice is surgical removal of the tumor
  2. Octreotide