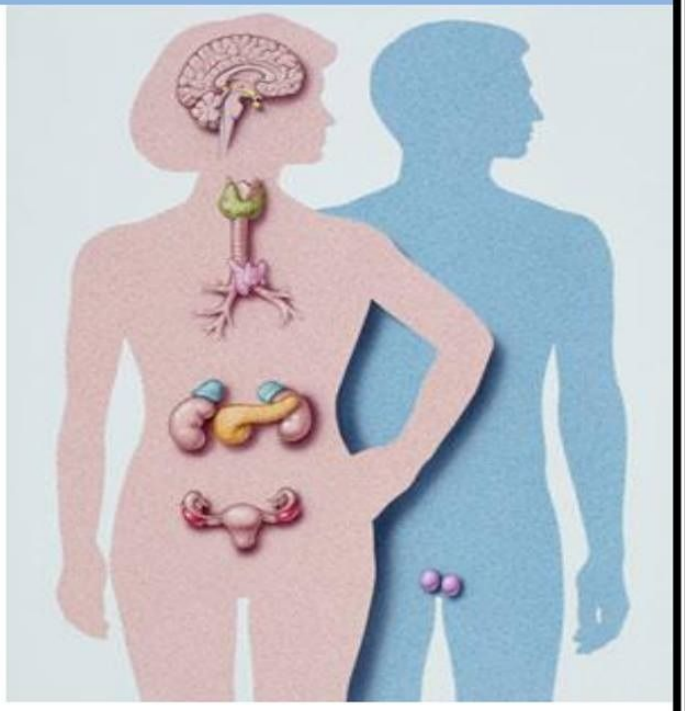
University of Jordan - Faculty of Medicine
(2013-19)

Medical Committee
The University of Jordan

Endocrine System



- ☐ Anatomy/Embryology/Histology
- ☐ Biochemistry
- ☐ Physiology
- ■ Pharmacology
- ☐ Pathology
- ☐ PBL

■ Slide ☐ Sheet ☐ Handout ☐ Other

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Date:

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Price:

Designed by: Zakaria W. Shkoukani

Pharmacology of Endocrine System

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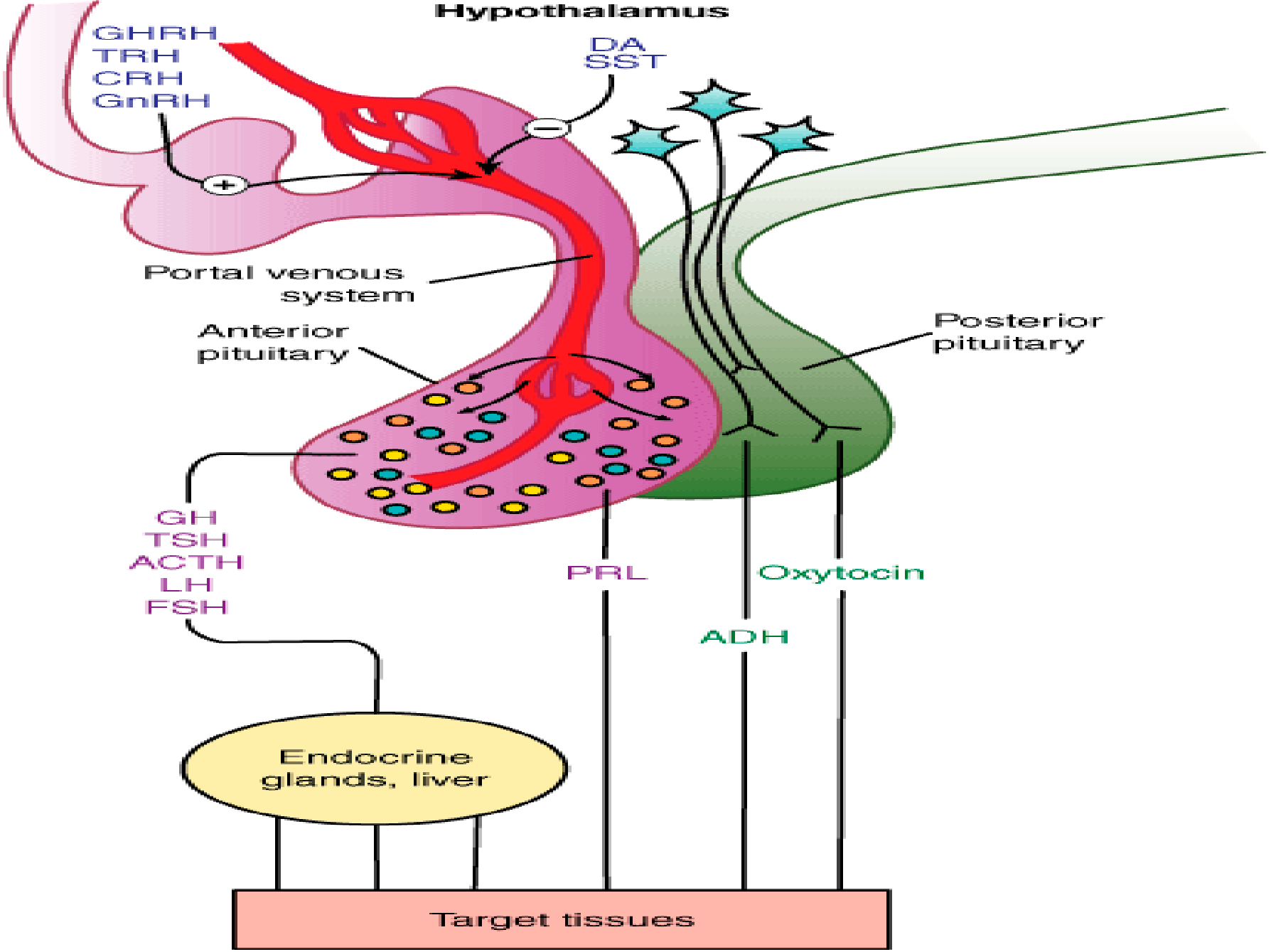
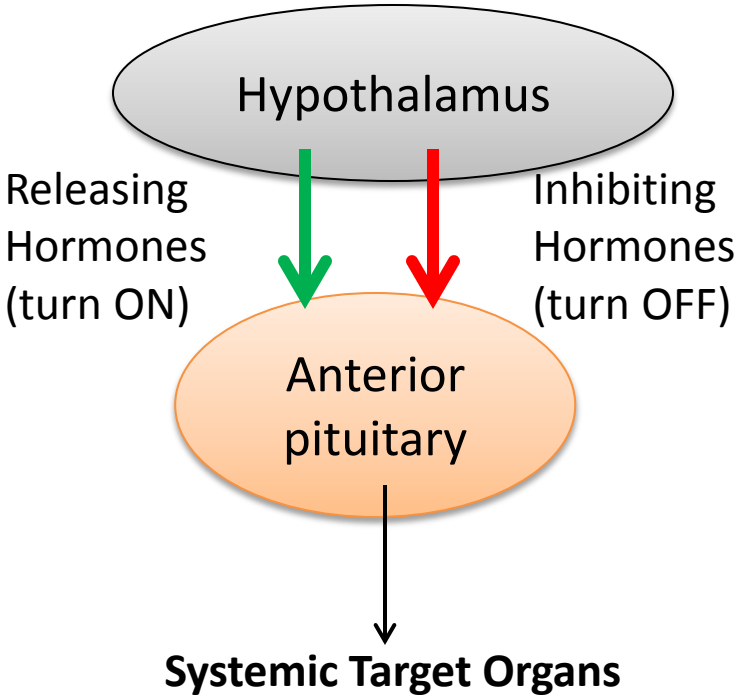
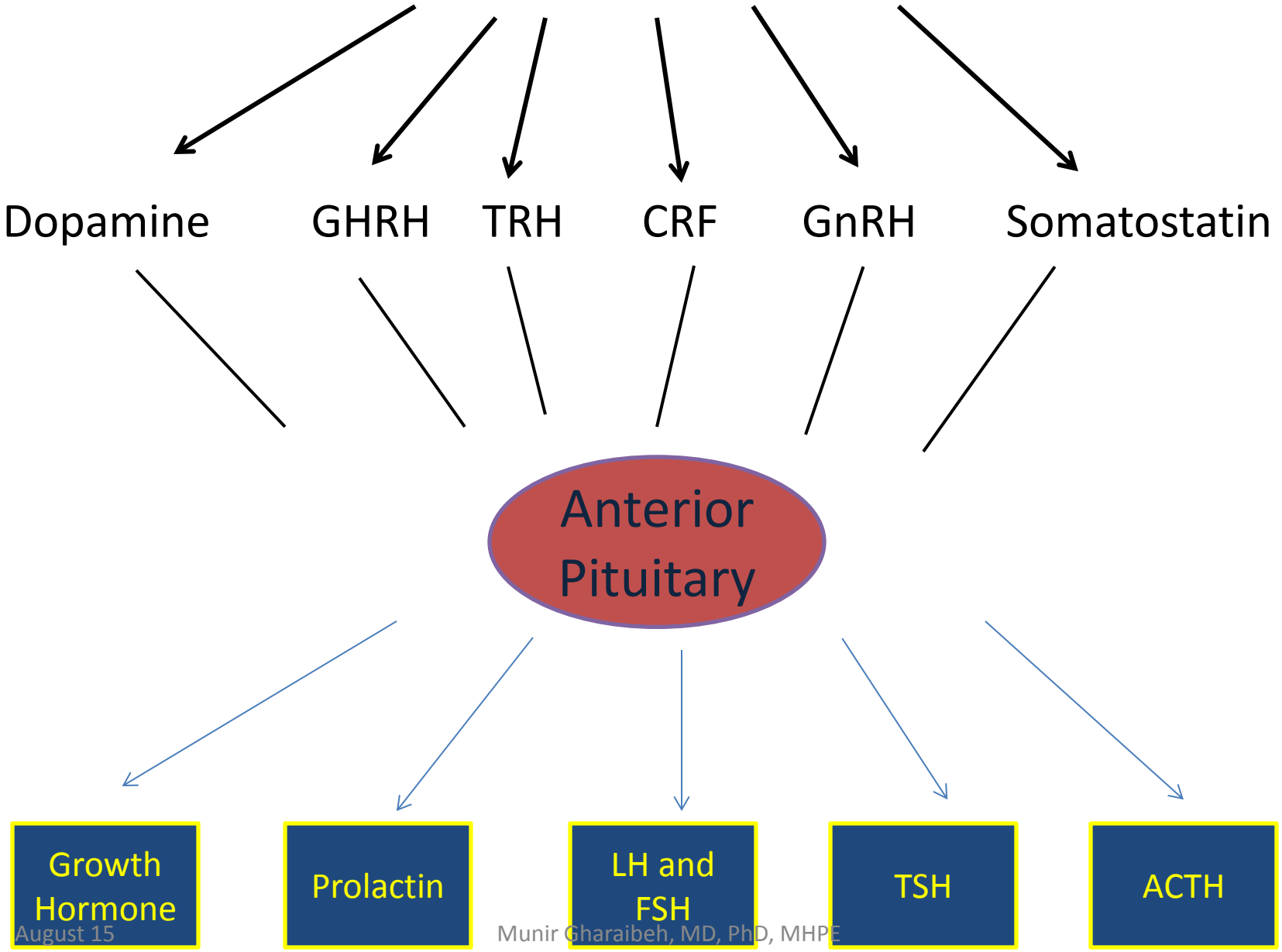


Hypothalamic Hormones

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



Hypothalamus



Hypothalamic Hormones

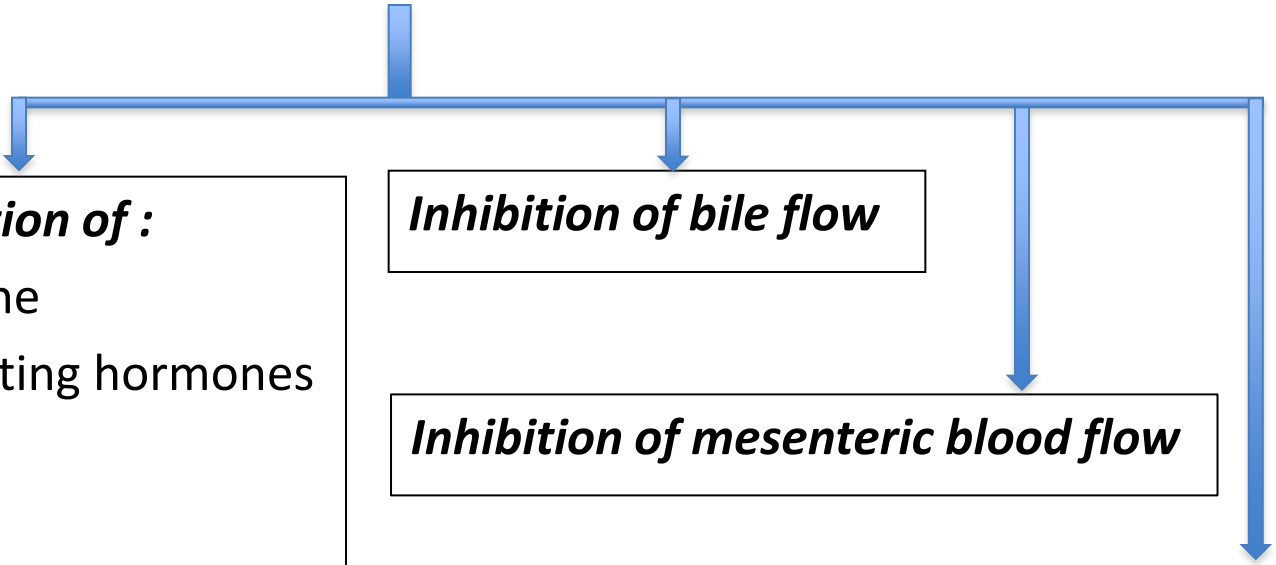
- **Dopamine**: inhibits the secretion of prolactin from the anterior pituitary gland
- **GHRH**: Growth Hormone-Releasing Hormone
- **Somatostatin**: inhibits the secretion of growth hormone
- **TRH:** Thyrotropin-Releasing Hormone, stimulates the release of thyroid-stimulating hormone and prolactin.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

Somatostatin

- Inhibits the secretion of growth hormone.
- 14-amino acid peptide
- Has very brief half-life in the serum, so clinically not feasible.

- **Octreotide:**
- An 8-amino acid analogue of somatostatin, so more stable.

Effects of Somatostatin



Inhibition of secretion of :

- Growth Hormone
- 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)*

- 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	Growth hormone	Liver, adipose tissue	Promotes growth (indirectly), control of protein, lipid and carbohydrate metabolism
	Thyroid-stimulating hormone	Thyroid gland	Stimulates secretion of thyroid hormones
	Adrenocorticotropic hormone	Adrenal gland (cortex)	Stimulates secretion of glucocorticoids
	Prolactin	Mammary gland	Milk production
	Luteinizing hormone	Ovary and testis	Control of reproductive function
	Follicle-stimulating hormone	Ovary and testis	Control of reproductive function
Posterior Pituitary	Antidiuretic hormone	Kidney	Conservation of body water
	Oxytocin	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**