Physiology of Growth Hormone and Pituitary Dwarfism

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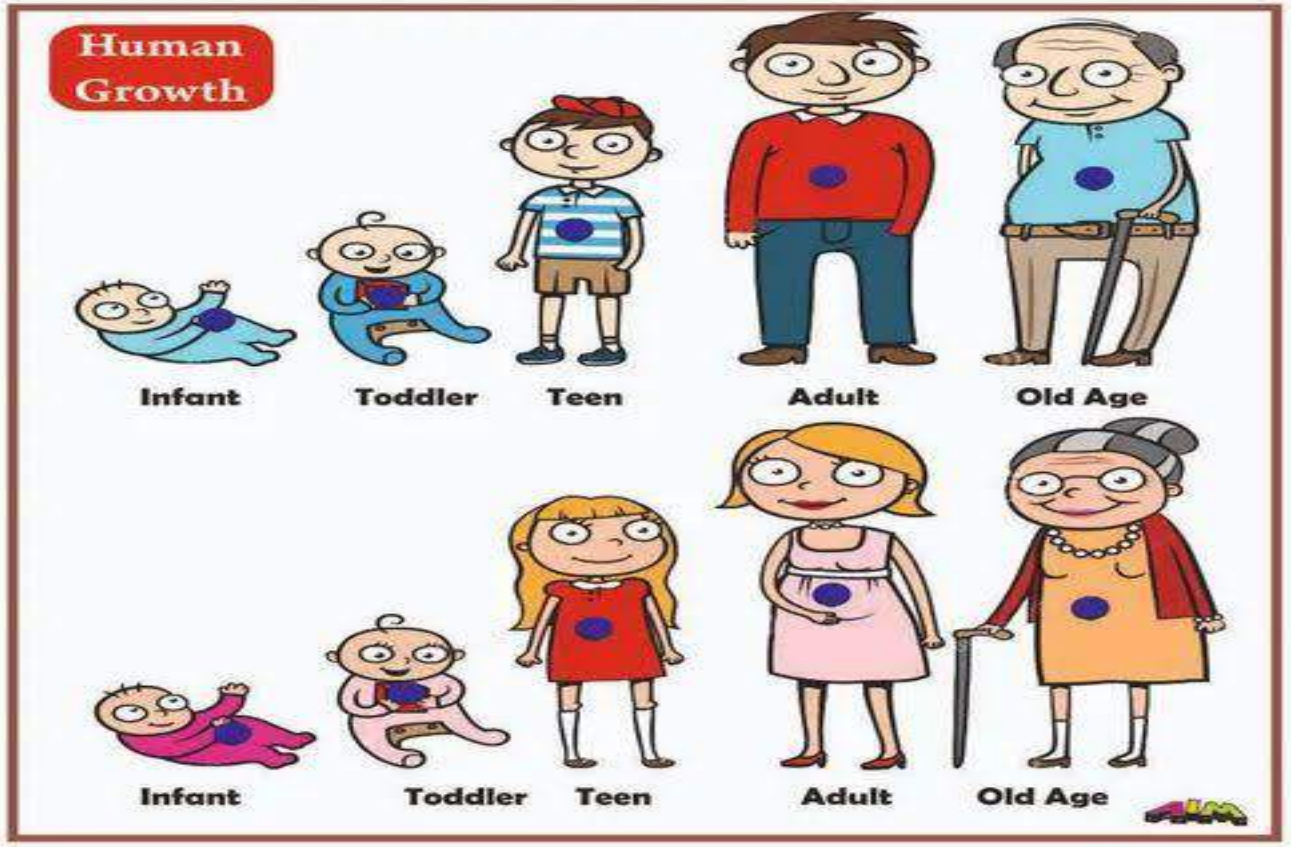
Hormones Having Growth Promoting Action

- Growth hormone
- Somatomedin C
- Insulin
- Thyroid hormone
- Androgen
- Estrogen



Growth hormone

Human growth hormone was first isolated and characterized in the 1950s primarily by

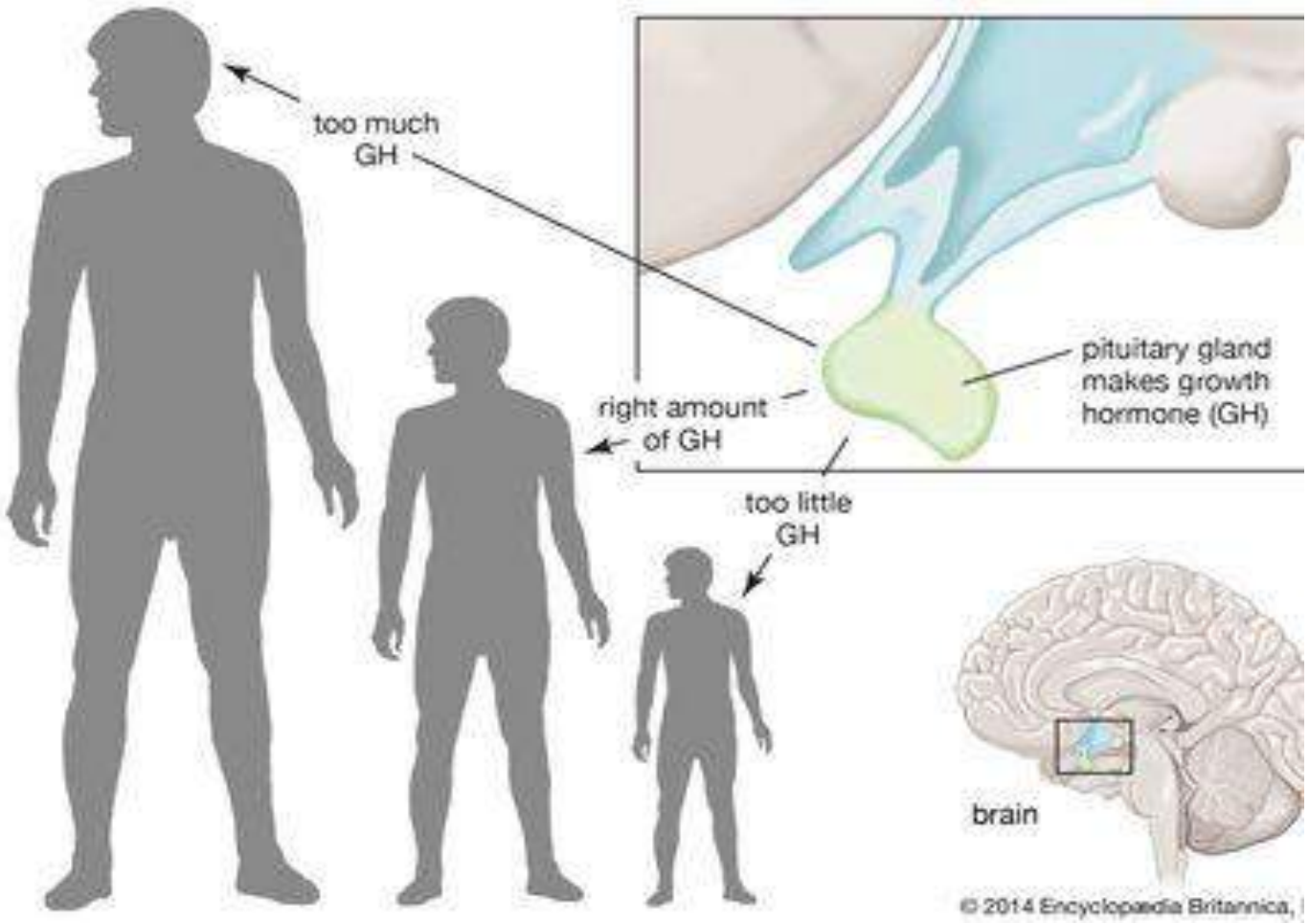
Choh Hao Li

and

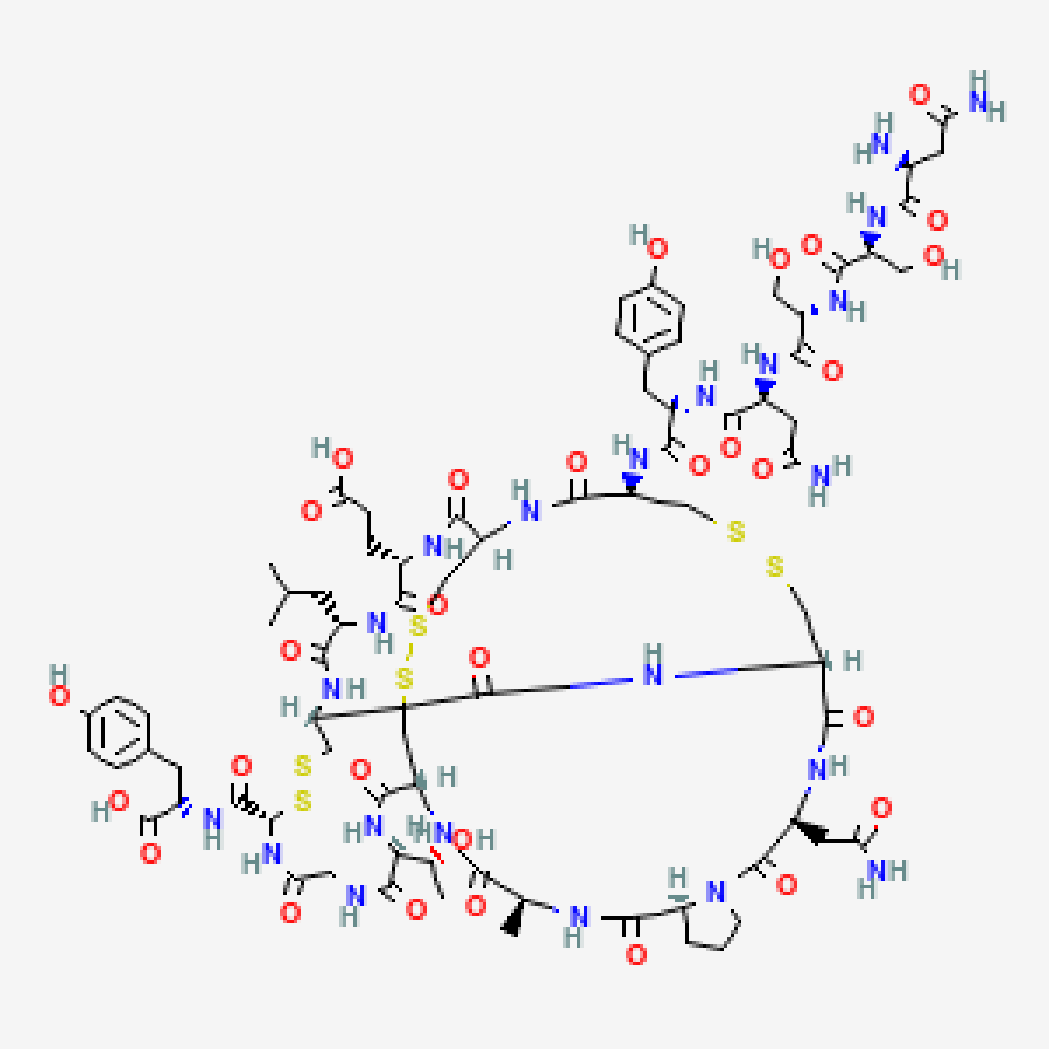
Harold Papkoff

at the university of California

- Growth hormone is an ancestral hormone, secreted episodically from somatotroph cells in the anterior pituitary
- Also called somatotrophic hormone or somatotropin



Chemical nature

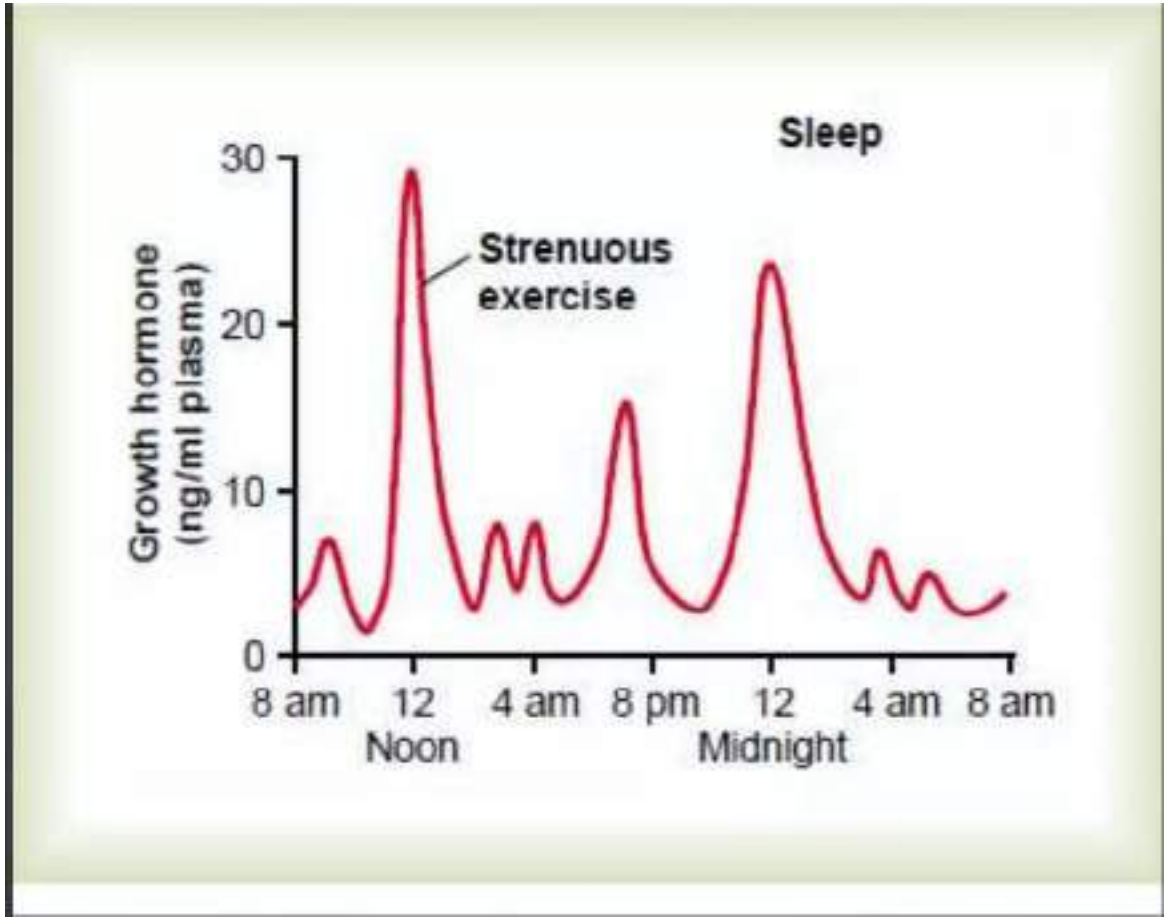


Protein hormone (191 AA)

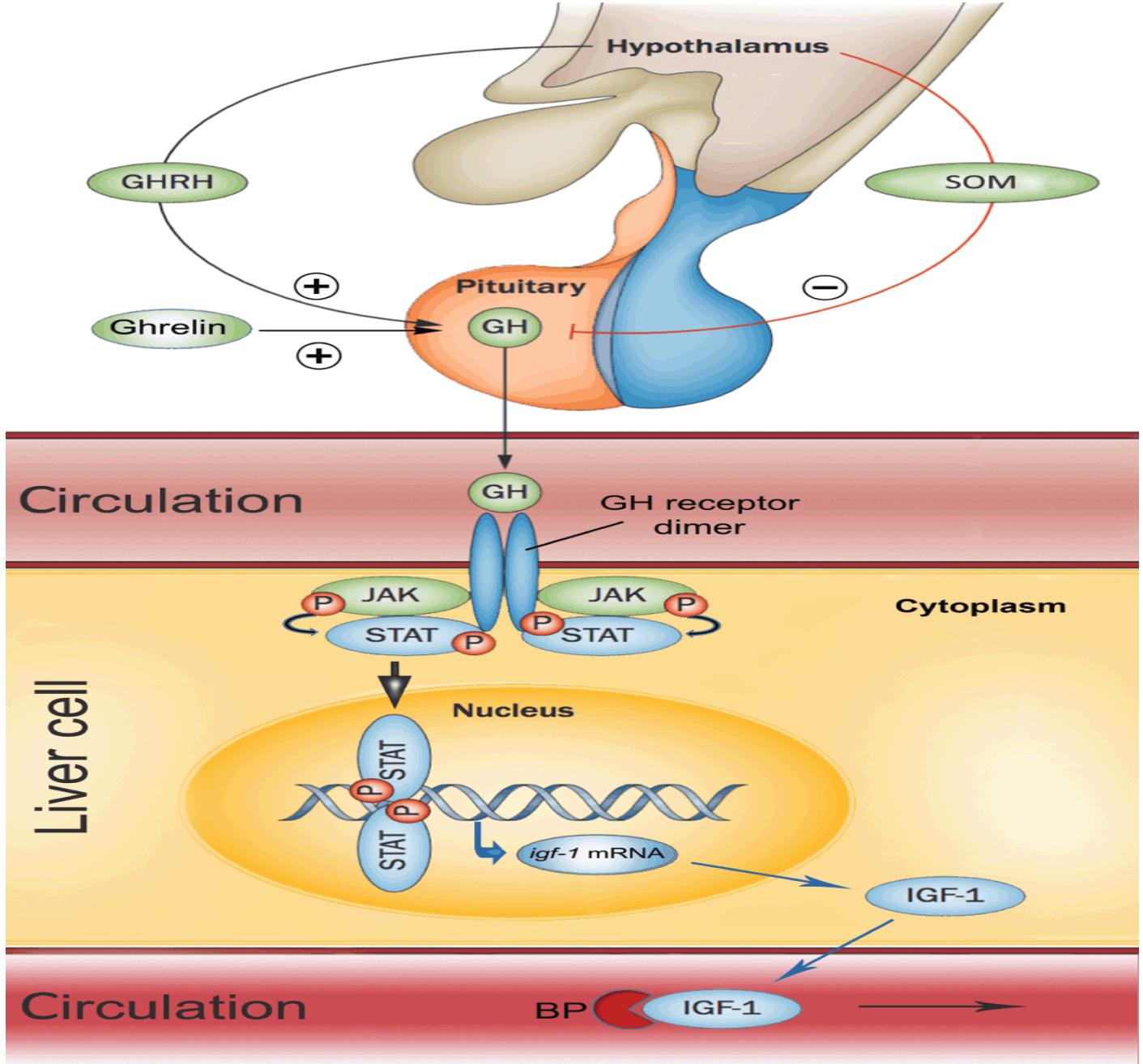
Pattern of secretion

- **Pulsatile fashion:**
  Every 1-2 hour interval , there is a rise in plasma GH level (10-20 pulses/day)

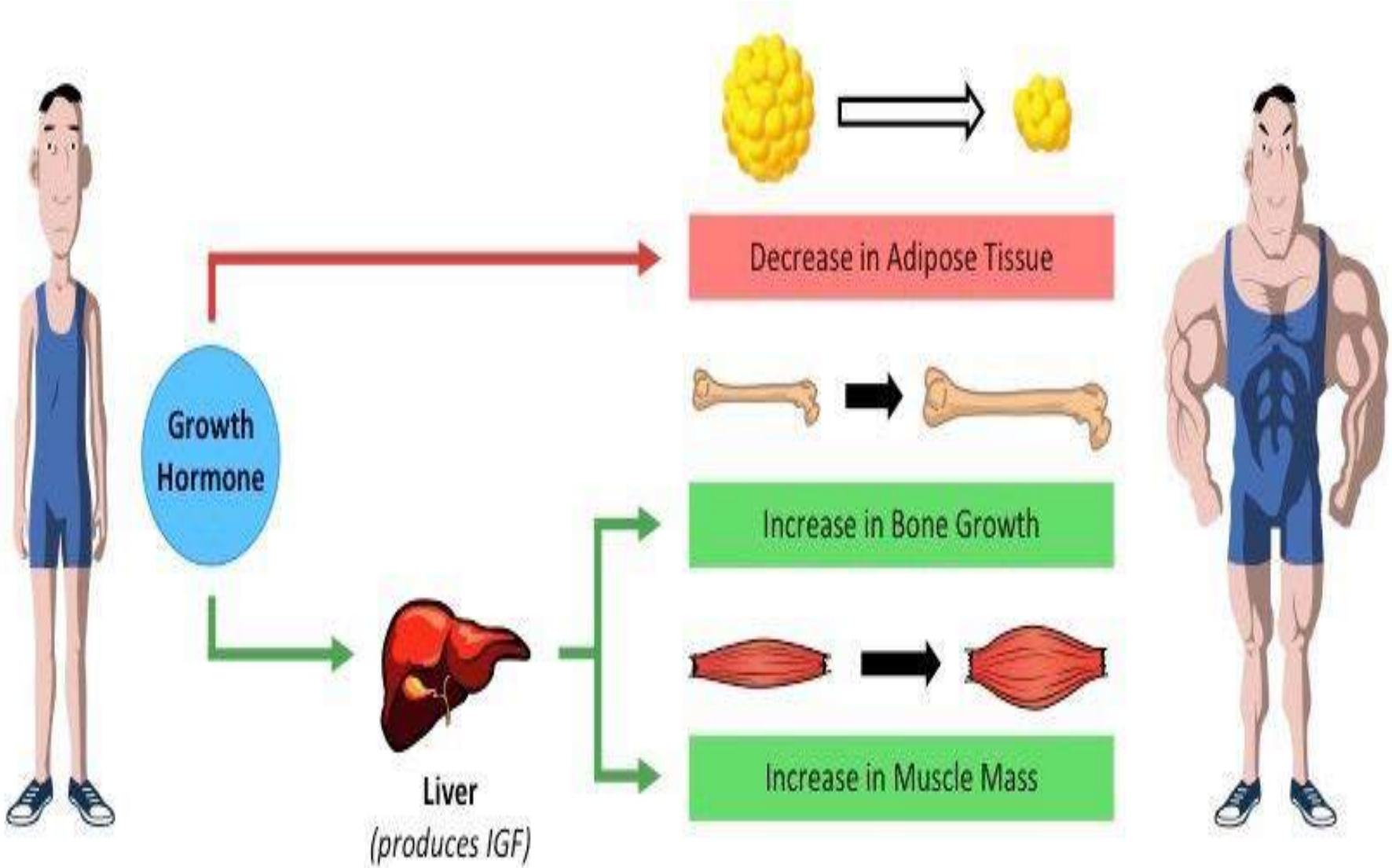
- **Diurnal variation in plasma levels of GH**
  The nocturnal peak occurs 1-2 hour after deep sleep



Mechanism of action of Growth hormone

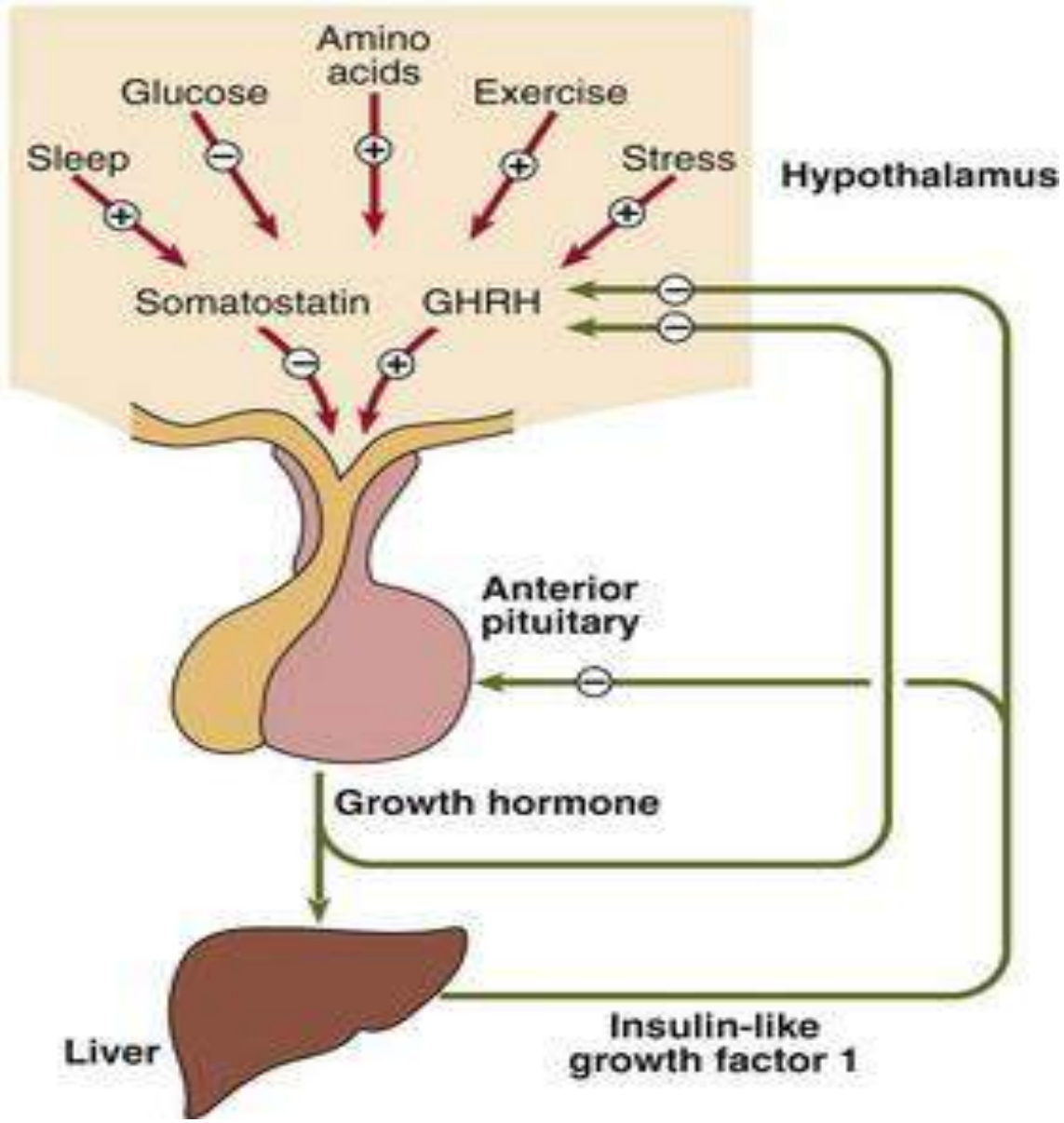


Mode of action of Growth hormone



Regulation of GH secretion

- Hypothalamic control
  - ✓ GHRH→ Increase GH
  - ✓ Somatostatin→ Decrease GH



Factors stimulates GH secretion

- Decreased blood glucose
- Decreased blood FFA
- Increased blood amino acids(arginine)
- Starvation or fasting, protein deficiency
- Trauma, stress, excitement, exercise
- Testosterone, estrogen
- Deep sleep (stages II and IV)
- GHRH
- Ghrelin

Factors inhibit GH secretion

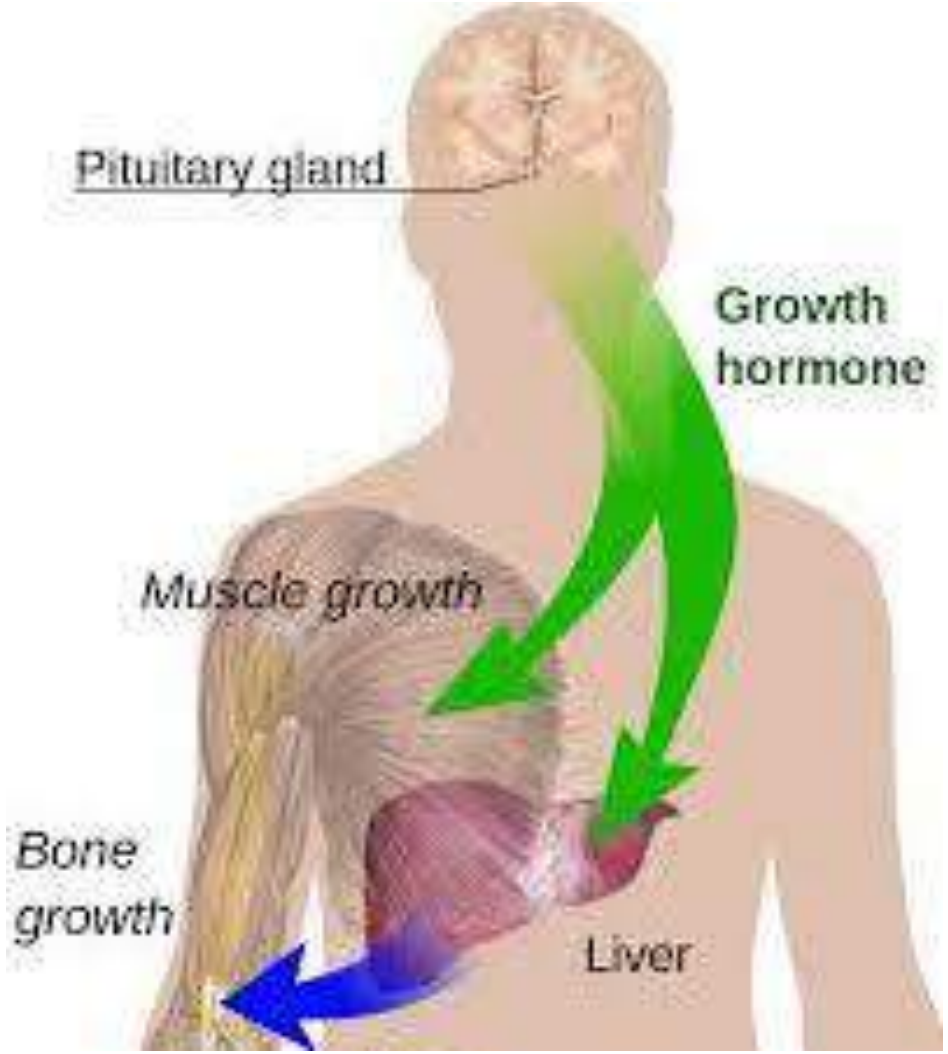
- Increased blood glucose
- Increased blood FFA
- Aging
- Obesity
- GHIH (somatostatin)
- GH (exogenous)
- Somatomedins (IGF)

Functions of Growth hormone

- On growth
- Metabolic functions

Growth-promoting actions

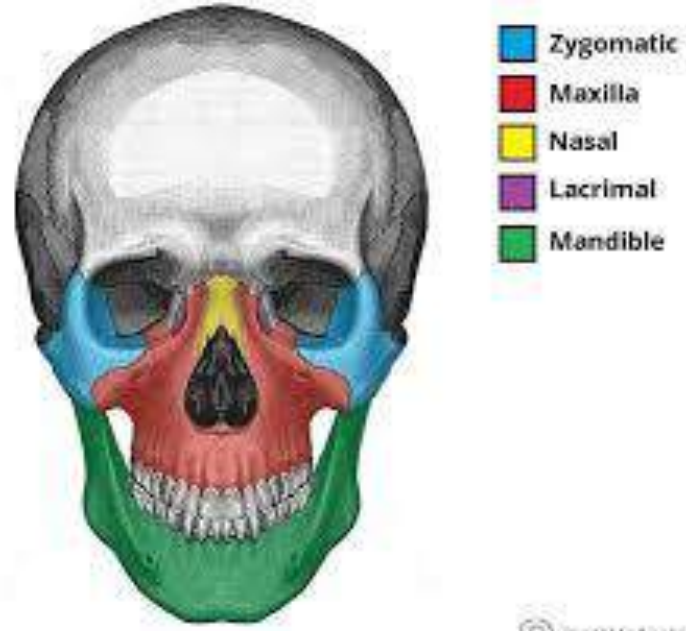
- It causes growth of almost all tissues of the body that are capable of growing.
  - Increased sizes of the cells due to protein deposition
  - Increased mitosis, with development of greater numbers of cells



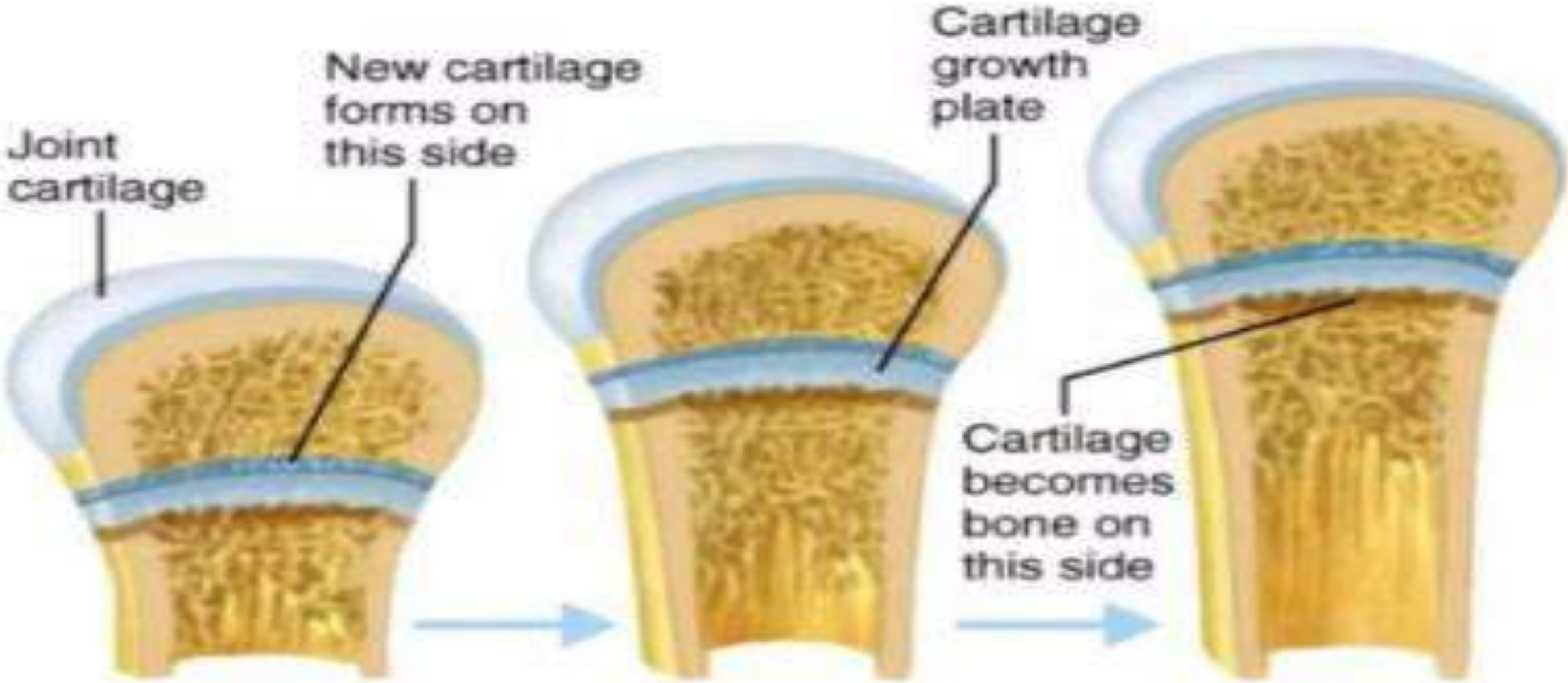
2 principles mechanism of bone growth in response to GH stimulation

➢The long bones grow In length (linear growth) at the epiphyseal cartilages.

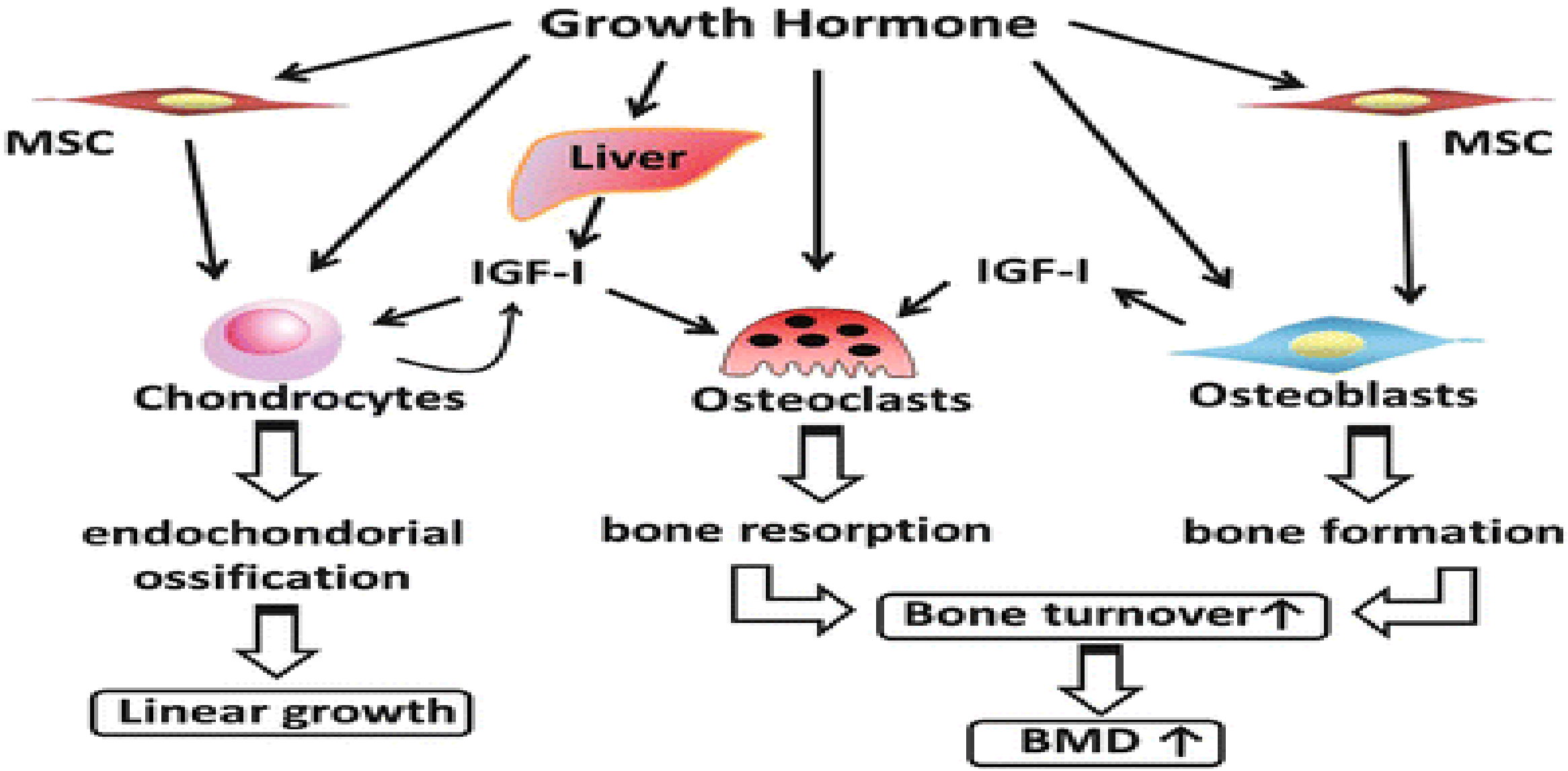
➢ Growth hormone strongly stimulates osteoblasts. So that bones can continue to become thicker throughout the life . This is especially true for the membranous bones.



Growth of long bone



Growth of membranous bone



Growth period

- **Growth during infancy:**
  - ✓ GH is unimportant for fetal development but most important for post-natal growth.
  - ✓ Secretion of IGF-I after birth is stimulated by GH

- **At the time of puberty:**
  - ✓ Anabolic effect of androgens.
  - ✓ In addition , the interaction between GH, sex hormone and IGF-I.
  - ✓ IGF-I reaches peak at 13-17 years of age

Cont.

- **Stoppage of linear growth**:

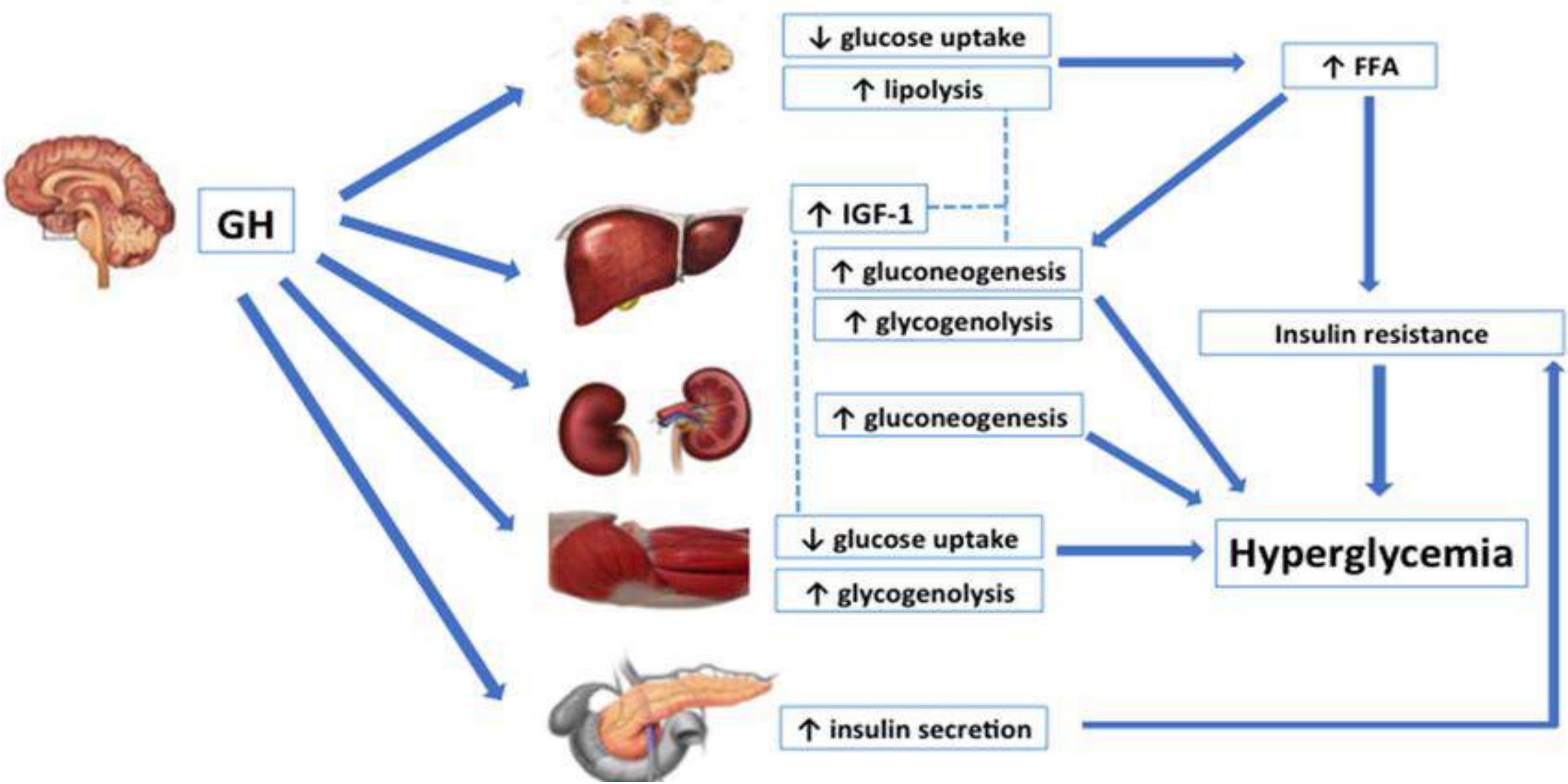
Estrogen induced epiphyseal closure.

Further rise in height is not possible after this phase

- Therefore , girls mature early as compared to boys. Due to this reason, sexual precocity is associated with dwarfism

Metabolic functions

Role of Growth Hormone in Carbohydrate metabolism

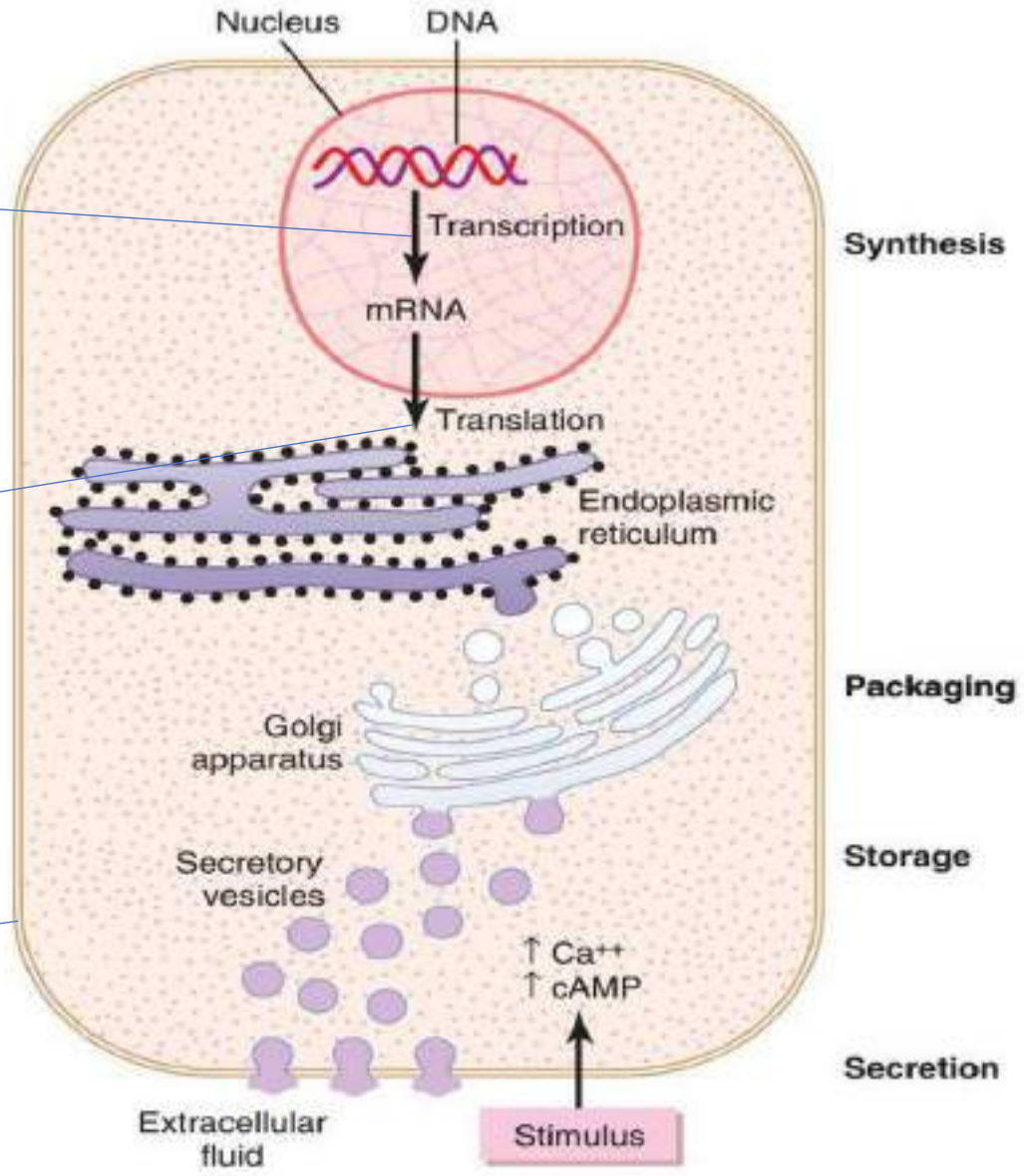


Role of Growth Hormone in Protein metabolism

Increased nuclear transcription of DNA to form RNA

Enhancement of RNA translation to cause protein synthesis by the ribosomes

Enhancement of amino acids transport through the cell membrane



Role of **Growth Hormone** in Lipid Metabolism

Lipolysis Stimulation

Growth hormone enhances the breakdown of triglycerides, thus increasing the availability of fatty acids for energy production.

Fatty Acid Oxidation

It stimulates the oxidation of fatty acids in various tissues, promoting the utilization of fats as an energy source.

Glucose-Sparing Effect

Growth hormone reduces the utilization of glucose, causing a shift towards using fatty acids for energy, consequently preserving glucose for essential functions.

Dwarfism

Dwarfism is a medical or genetic condition characterized by a short stature, generally defined as an adult height of 4 feet 10 inches (147 cm) or less.

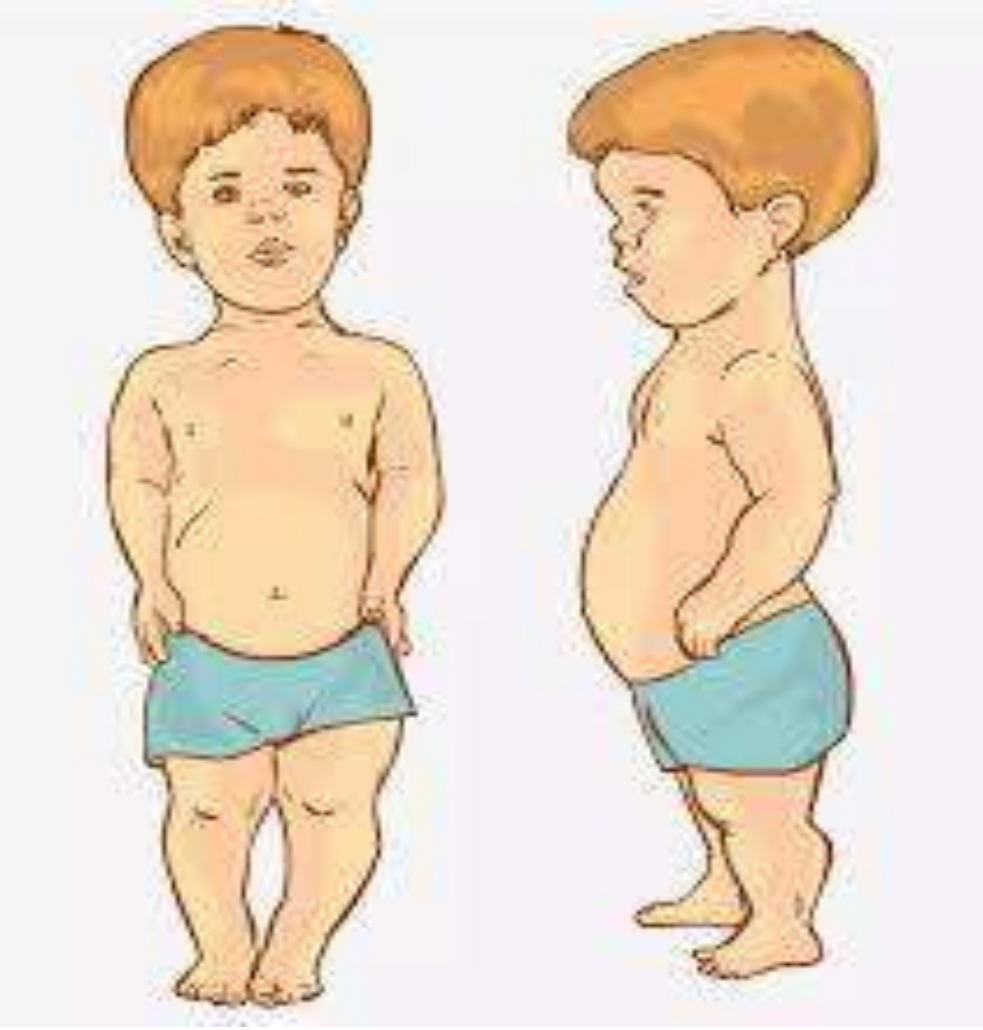
Causes of dwarfism

- GHRH deficiency (hypothalamic failure)
- Pituitary failure (↓ GH and IGF 1)-Pituitary dwarfism
- Unresponsive GH receptors (Laron dwarfism)
- Deficiency of IGF 1 (African Pygmy and Levi Lorain dwarf: GH ↑ or normal but IGF 1 ↓)

Other causes of dwarfism

Cretinism
Psychosocial dwarfism / Kasper Hauser syndrome
Achondroplasia (short limb but normal trunk)
Turner syndrome
Precocious puberty

- PITUITARY DWARFISM

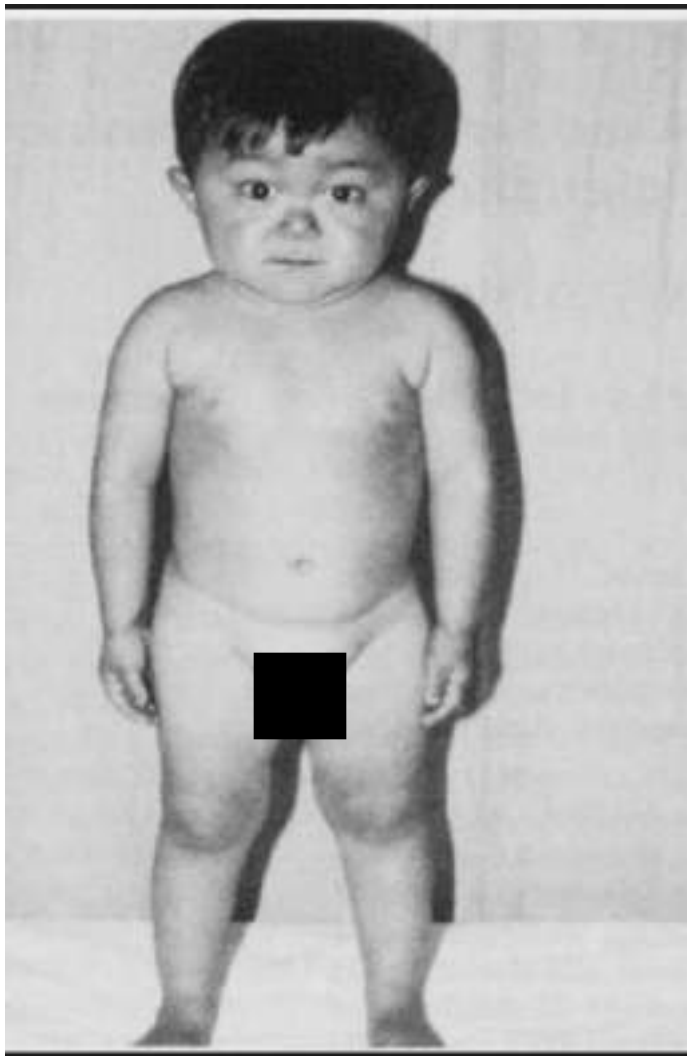


- LEVI LORAIN DWARFISM

Pituitary Dwarfism

Hyposecretion of GH before the bony fusion between shaft and epiphysis results in dwarfism. This is called **pituitary dwarfism**, characterized by the

- Stunted growth (short stature)
- Body developed to appropriate proportion to one another but rate of development is greatly decreased



Growth Hormone Deficiency in Children

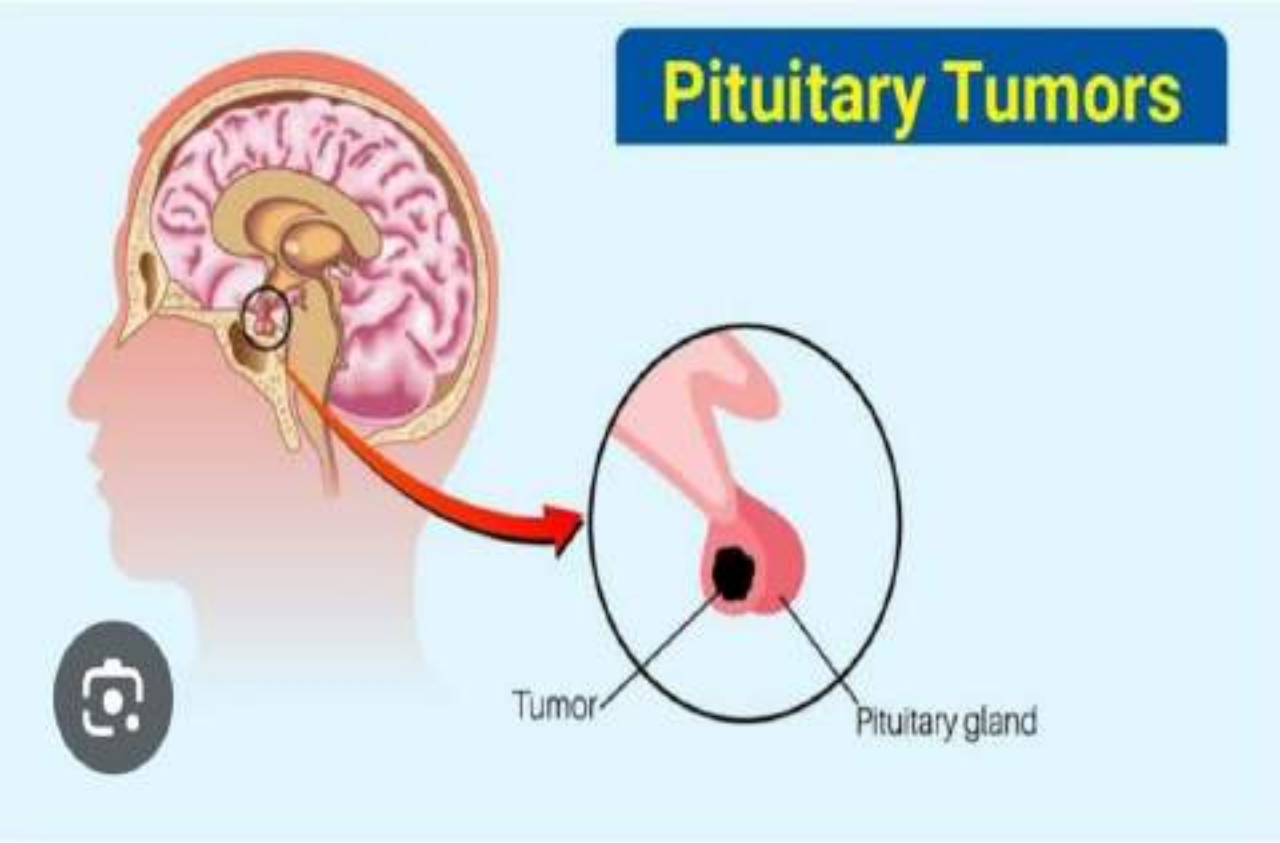
* Mid-facial crowding
* Round Facies
* Mild Obesity
* Immature facial appearance
* Depressed nasal bridge
* Frontal bossing
* Prominent philtrum
* High pitched voice
* Increased skin fold thickness
* Truncal Obisity
* Single central incisor
* Hypoplastic penis and scrotum

Pituitary Dwarfism in Adult

Decreased secretion of all anterior pituitary hormones.

Causes are:

1. Craniopharyngioma
2. Chromophobe tumors
3. Thrombosis of pituitary blood vessels



Some signs of hypopituitarism

Irregular periods.

Fatigue.

Short stature in children.

Decreased sex drive.

Loss of Muscle mass.

Can't make breast milk.

Approach to Treatment of Pituitary Dwarfism

Diagnosis:

- ✓ Growth charts(slow height progression)
- ✓ Serum GH, TSH, ACTH and Gonadotropins ➡ Low
- ✓ GH stimulation test
- ✓ MRI of the brain to examine the pituitary gland

Response to Treatment:

Requires hormone replacement for all missing hormones in addition to GH

Levi Lorain dwarfism

- Due to some congenital inability to synthesize significant amount of somatomedin C
- Some people (**pygmies of Africa**) develop small structure called **Levi Lorain dwarf**
- Plasma concentration of GH is normal or high
- Diminished plasma concentration of somatomedin C
- All body parts are developed in appropriate proportion to one another but the rate of development is greatly decreased

Approach to Treatment of Levi Lorain Dwarfism

Diagnosis:

- ✓ Serum Somatomedin C ➡ very Low

Response to Treatment:

- ✓ GH injections do NOT work
- ✓ Treatment is:
  IGF-1 replacement therapy
- ✓ Requires careful monitoring (blood sugar, growth response)

Prognosis

Pituitary Dwarfism

- ✓ Good prognosis if treated early
- ✓ Treatment with GH leads to:
  near-normal height
  normal physical development
- ✓ Delayed treatment reduces final height outcome
- ✓ Intelligence is usually normal

Levi Lorain Dwarfism

- ✓ Poorer prognosis compared to pituitary dwarfism
- ✓ Does not respond to GH
- ✓ Treatment with IGF-1 therapy results partial improvement only
- ✓ Final height often remains below normal
- ✓ Intelligence is usually normal

Take Home Message

- ✓ Growth Hormone is essential for normal physical growth in children
- ✓ Deficiency leads to pituitary dwarfism
- ✓ Individuals with dwarfism lead full, active lives and have typical intelligence.
- ✓ Size does not limit impact and they can achieve any dream.
- ✓ We should treat people with dwarfism as individuals, not a spectacle.


10

References

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THANK YOU