
كلية الطب /جامعة المستقبل


# Endocrinology

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Lec. 3

# Growth hormone

- Growth hormone (GH) is secreted by acidophilic somatotrophs in the anterior pituitary.
- It is a single-chain polypeptide of 191 amino acids (≈21.5 kDa).
- Plasma levels are <3 ng/mL in adults and ≈6 ng/mL in children/adolescents.
- About 50% circulates bound to a receptor-derived plasma protein, serving as a reservoir.
- GH has a half-life of ~20 minutes and is degraded mainly in the liver and kidneys.

# Effects Of Growth Hormone On Growth

- Growth hormone has widespread effects in the body.It plays a central role in overall body growth by stimulating cellular hypertrophy (increase in cell size) and enhancing mitotic activity, which leads to an increased number of cells.
- In addition, GH promotes the specialized differentiation of particular cell types, notably osteogenic cells involved in bone formation and myogenic cells that contribute to muscle development.

# Physiological Effect of GH:

## 1. Effect on Metabolism

GH Increases The Synthesis Of Proteins, Mobilization Of Lipids And Conservation Of Carbohydrates

### A. On Protein Metabolism

I. **Stimulation of Protein Synthesis**

- GH promotes **amino acid uptake** into cells, especially muscle and liver.
- Activates **ribosomal activity** → increases translation of mRNA into proteins.
- Enhances **transcription in the nucleus** → more mRNA production for structural proteins and enzymes.
- Net result = **increased protein synthesis** in almost all tissues

2.**Promoting anabolism of proteins indirectly**

GH increases the release of insulin (from β-cells of islets in pancreas), which has anabolic effect on proteins(?????????)

## 2. Effects of Growth Hormone on Fat Metabolism

- **Stimulation of Lipolysis:**
  1. GH promotes the breakdown of triglycerides in adipose tissue.
  2. This releases **fatty acids** into the blood, which become the main energy source for cells.
- **Protein-Sparing Effect:**
  1. By shifting energy production to fatty acids, GH **reduces the need to break down proteins** for fuel.
  2. This helps preserve proteins for **growth and tissue repair** rather than energy.
- **Excess GH (Above Physiological Levels):**
  1. The liver converts large amounts of fatty acids into **ketone bodies**, mainly:
     1. **Acetoacetic acid**
     2. **β-hydroxybutyric acid**
     3. **Acetone**
  2. High accumulation of these leads to **ketosis** (increased ketone bodies in blood)

- Accumulation of acetoacetic acid and β-hydroxybutyrate(ketones body) causes a **fall in blood pH → metabolic acidosis** (specifically, **ketoacidosis** in diabetes).

# 3. Effects of Growth Hormone on Carbohydrate Metabolism

1. **Anti-Insulin Effect:**
    1. GH decreases glucose uptake and utilization in muscle and adipose tissue.
    2. This action is opposite to insulin, so GH is considered **diabetogenic**.
2. **Increased Blood Glucose:**
    1. By reducing peripheral glucose use and stimulating gluconeogenesis in the liver, GH raises blood glucose levels.
    2. Chronic excess of GH (e.g., in **acromegaly**) may cause **hyperglycemia** and even **diabetes mellitus–like state**.
3. **Glycogen Storage:**
    1. Initially, GH promotes glycogen storage in tissues, but with prolonged excess it leads to impaired glucose tolerance

# Effects of GH on Bone

1. **Before Epiphyseal Closure (Childhood & Adolescence):**
    1. GH stimulates **chondrocyte proliferation** in the epiphyseal (growth) plates.
    2. Increases **chondrogenesis** → widening of plates.
    3. Promotes **new bone deposition** at the ends of long bones.Result → **linear growth in height**.
2. **After Epiphyseal Closure (Adulthood):**
    1. Linear growth is no longer possible.
    2. GH still stimulates **osteoblast activity**, causing thickening of bones (especially jaw, skull, hands, feet).This leads to **acromegaly** if GH is in excess.

# 3. Indirect Effect via IGF-1 (Somatomedins):

- **Somatomedins (insulin-like growth factors)** are small protein hormones structurally related to insulin. They are of two types.

a. **Insulin-like growth factor-I (IGF-I),(** which is also called somatomedin C )

- Somatomedin C (IGF-1) produced in the liver & locally in bone , binds tightly to plasma proteins, causing slow release and prolonged action on bones and protein metabolism, lasting up to ~20 Hr.

b. **Insulin-like growth factor-II** plays an important role in the growth of fetus(during fetal life).

# Effect of GH on Electrolytes:

- GH conserves $Na^+$ and $K^+$ by reducing their loss in urine and increases $Ca^{2+}$ absorption, ensuring that electrolytes are available in tissues for growth and bone development
- GH also

 Increases muscle mass through sarcomere hypertrophy.

 Stimulates the growth of all internal organs excluding the brain.

 Plays a role in homeostasis.

 Stimulates the immune system.

 Increases deiodination of T4 to T3.

Note: Growth hormone acts both directly (on fat, carbohydrate, and protein metabolism) and indirectly via IGF-1 (somatomedin C). Most of the growth-promoting effects on bone and tissues are mediated through IGF-1, while metabolic effects can occur without it

- GH secretion is pulsatile, peaking during deep sleep (stage III–IV NREM), with the largest burst in the first hour—about 70% of daily output.
- Each nocturnal pulse lasts 1.5–3 hours.
- GH itself has a short plasma half-life (20–30 min), but its effects persist because it stimulates hepatic IGF-1, which remains elevated for many hours ~20 h

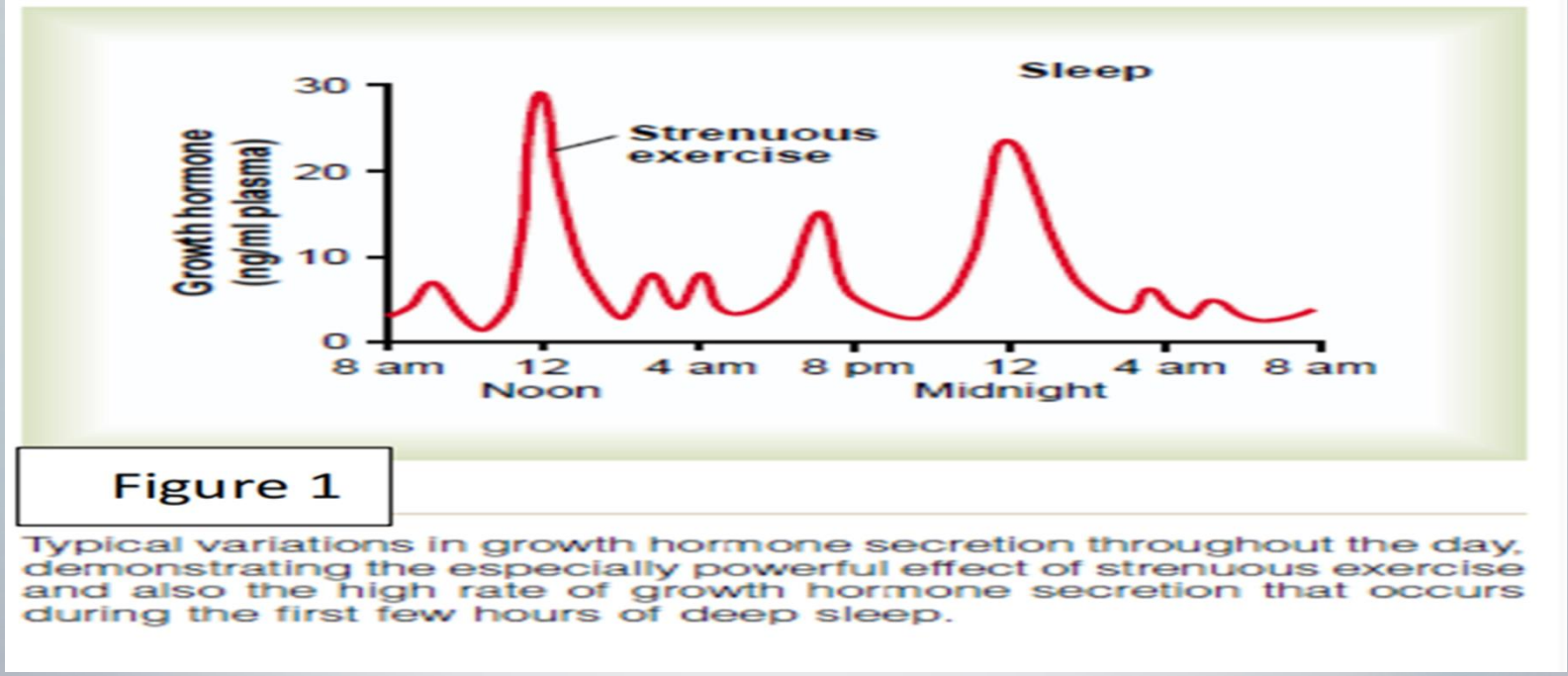



Figure 1

Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

## Growth Hormone Receptor.

- GH receptor is a transmembrane receptor.
- GH binds with the receptor situated mainly in liver cells and forms the hormone receptor complex which induces somatomedin secretion. Somatomedin in turn, executes the actions of growth hormone.
- **Regulation of GH Secretion.**

Growth hormone secretion is altered by various factors, however, hypothalamus and feedback mechanism play an important role in the regulation of GH secretion.

# GH Secretion is Stimulated by

- Hypoglycemia.
- Fasting and Starvation.
- Exercise.
- Stress and trauma.
- Initial stages of sleep.

## GH secretion is inhibited by:

- Hyperglycemia.
- Increase in free fatty acids in blood.
- Later stages of sleep .

**Regulation of Growth Hormone Secretion**

1. **Hypothalamic Control**

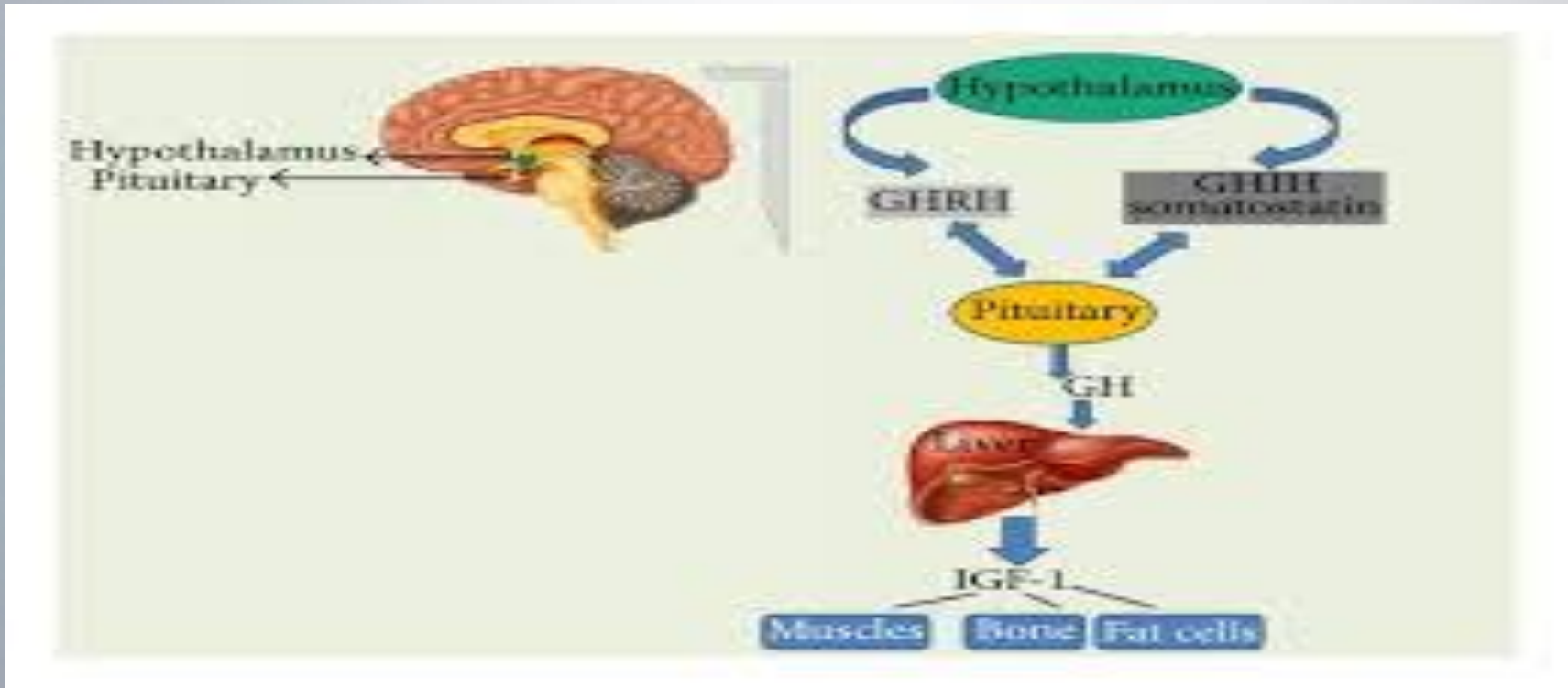
- **GHRH (Growth Hormone–Releasing Hormone):** Secreted by hypothalamic neurons.
- Stimulates somatotropes in the anterior pituitary to release GH.
- **Somatostatin (Growth Hormone–Inhibitory Hormone, GHIH**):Also secreted by hypothalamus.Directly inhibits GH secretion.Balance between them determines GH output.

2. **Ghrelin**: Secreted mainly by the stomach (also hypothalamus).

- Potent stimulator of GH release, acting synergistically with GHRH.
- Also plays a role in appetite regulation and energy balance.

## Feedback Control:

- GH inhibits hypothalamic GHRH.
- GH increases IGF-1, which: Directly inhibits GH secretion at the pituitary.
- Stimulates somatostatin release, adding further inhibition



# Gigantism

- Gigantism results from excessive secretion of growth hormone (GH) during childhood or early adolescence, prior to the closure of the epiphyseal growth plates. The most common cause is an adenoma of acidophilic cells in the anterior pituitary gland.
- Clinical Features:

1. Excess GH before epiphyseal closure causes extreme tall stature (7–8 ft),
2. Disproportionate limb elongation
3. Metabolic issues (hyperglycemia, glycosuria, pituitary diabetes)
4. Possible visual defects from pituitary tumor compression

# Acromegaly

**Cause**: Excess GH secretion in adults (usually from a pituitary acidophil tumor) after epiphyseal fusion.

## Features:

- Enlarged bones of face, hands, and feet; “acromegalic face” with coarse features, prognathism, and thickened skin.
- Kyphosis, enlarged visceral organs (heart, liver, spleen, lungs), and glandular hyperactivity.
- Metabolic effects: insulin resistance, type II diabetes, hypertension.
- Neurological/other: sweating, carpal tunnel syndrome, muscle weakness, headache, visual disturbances.

**Treatment:** Surgical removal of tumor; medical therapy with somatostatin analogs or dopamine agonists (e.g., bromocriptine) to suppress GH secretion.


A. Acromegaly

b. Gigantism

## Dwarfism (Hypoactivity of Anterior Pituitary)

- Definition: A childhood disorder due to reduced GH secretion, leading to stunted growth.
- **Causes:**

- Chromophobe tumor: Non-functioning pituitary tumor that destroys GH-secreting cells; most common cause.
- Panhypopituitarism: Deficiency of all anterior pituitary hormones → dwarfism with additional endocrine symptoms.
- **Sign and Symptom of Dwarfism:**
- Adult height usually ≤3 feet, with normal body proportions, slightly larger head, normal intelligence, and preserved reproductive function if only GH is deficient.
- **Diagnosis** requires stepwise evaluation, ending with GH stimulation tests to confirm pituitary response.

- **Pituitary insufficiency is accompanied by atrophy of the adrenal cortex, sensitivity to stress, growth inhibition, depressed thyroid function, hypoglycemia, pallor, and atrophy of the gonads.**
- **Pituitary insufficiency may be caused by tumors or, in women, by infarction following shock due to postpartum hemorrhage.**

**Dwarfism**