# Practical endocrinology –First course

## Lecture- 2- ESTIMATION OF GH AND INSULIN


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|---|---|
| Sawa University | جامعـــــة ســـــــاوة الاهلية |
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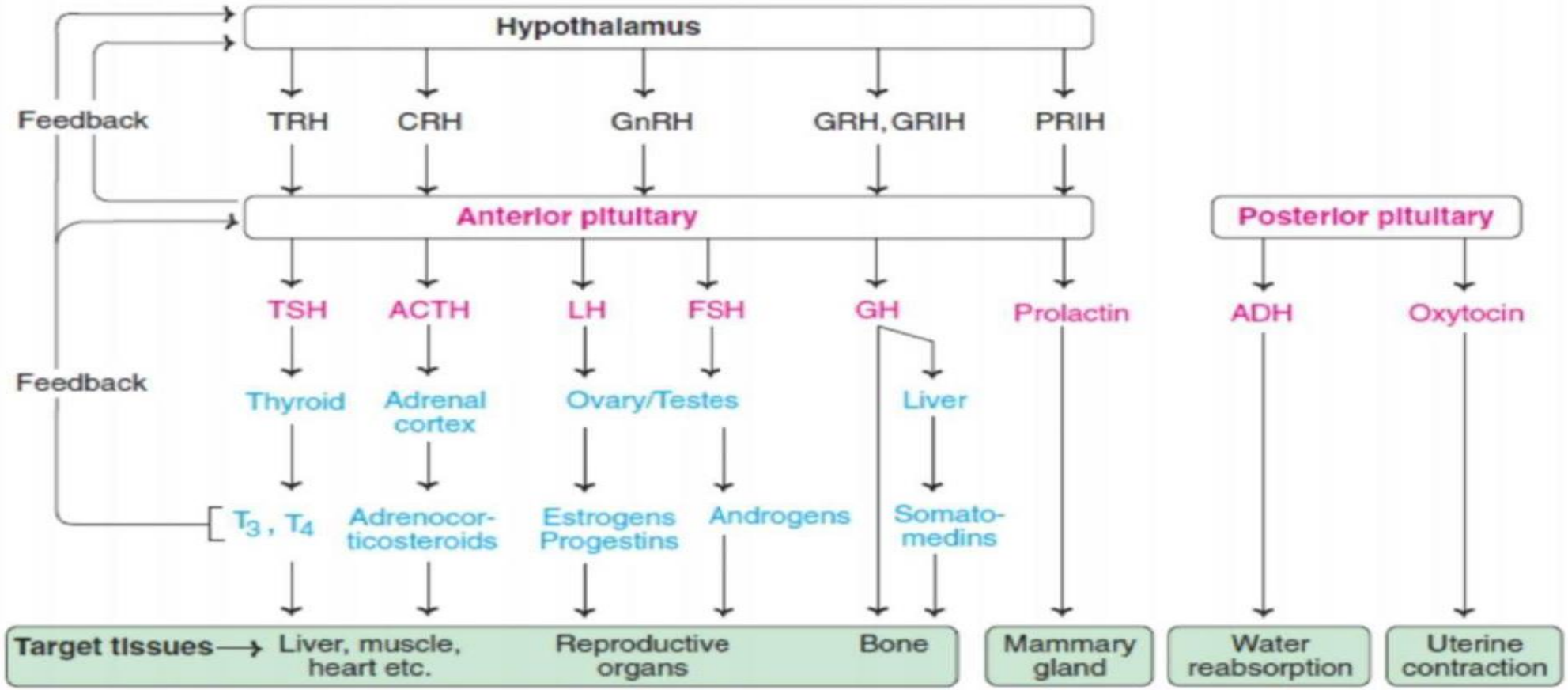
| Third Stage | المرحلـــــــــــة الثالثة |


الجانب العملي محاضرة رقم 2

Practical Lecture No. 2

تدريسي المادة : م. صكر عبد الكاظم صكر

## مخطط مهم جدا اضافي من عندي



# difference between somatostatin and somatomedin and somatotropin

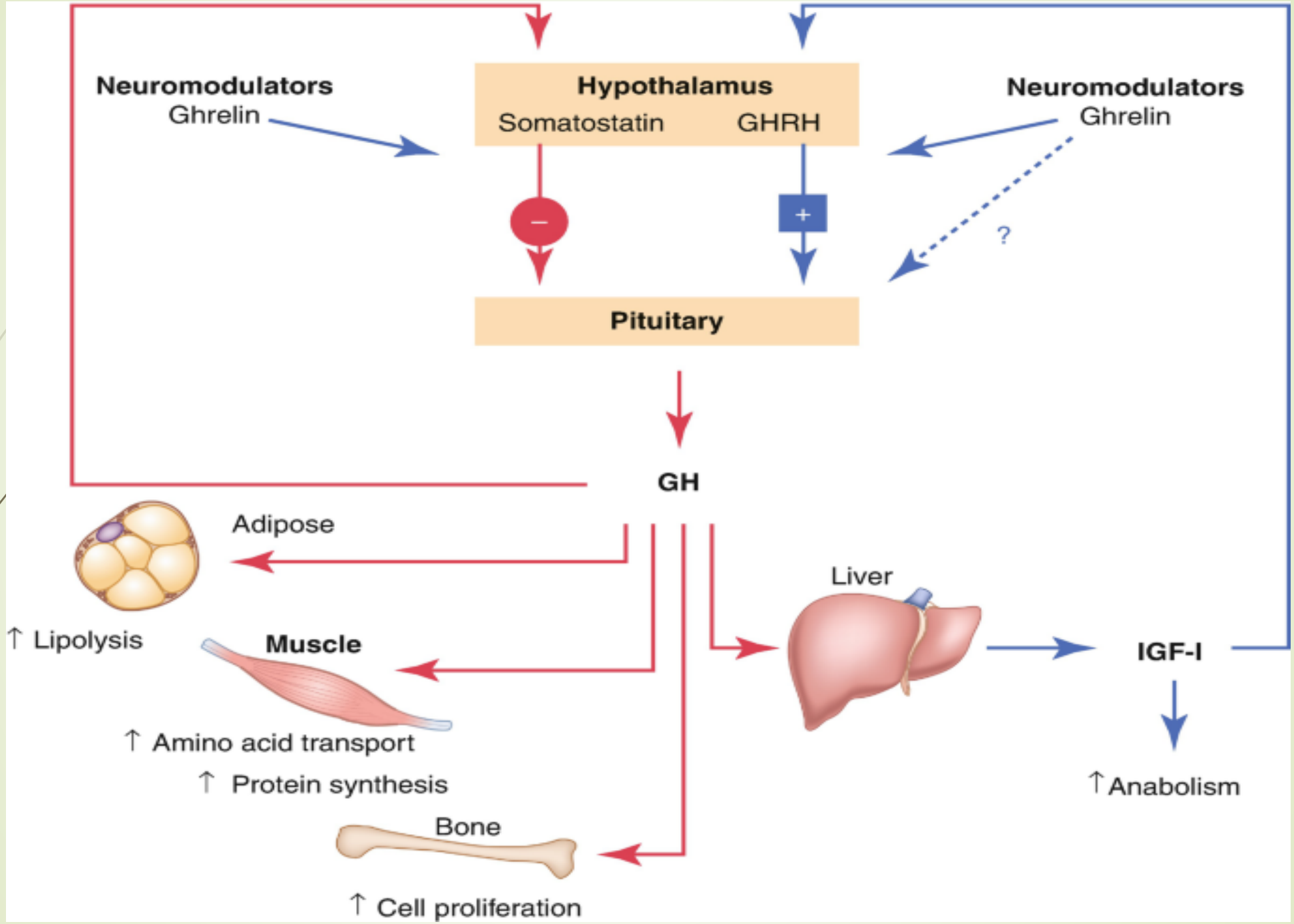
**Somatotropin**
is a growth hormone secreted by somatotrophs,

**somatostatin**

is a inhibitory factor secreted by the hypothalamus that inhibits somatotropin secretion

**somatomedin**

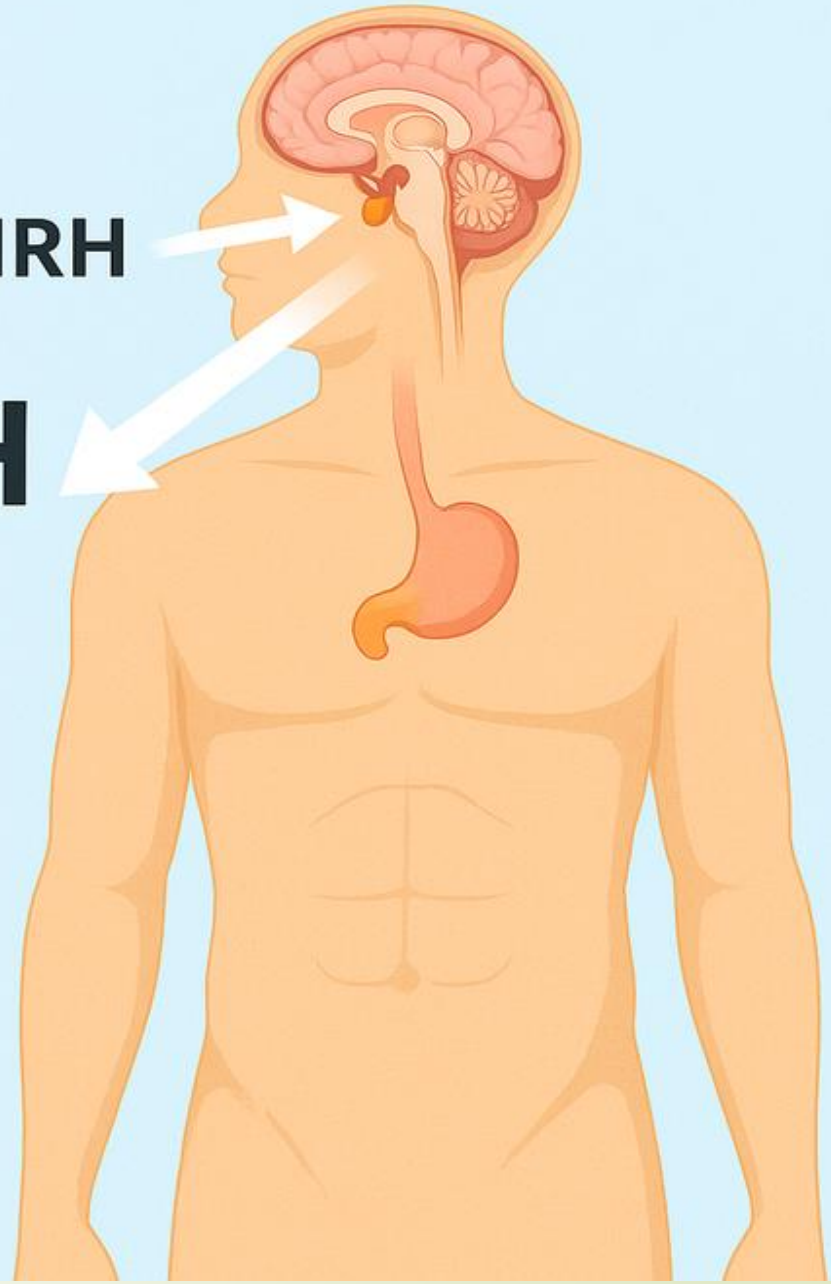
is defined as an insulin-like growth factor(**IGF-1**)


Neuromodulators
Ghrelin
Hypothalamus
Somatostatin
GHRH
Neuromodulators
Ghrelin
?
Pituitary
GH
Adipose
↑ Lipolysis
Muscle
↑ Amino acid transport
↑ Protein synthesis
Liver
IGF-I
↑ Anabolism
Bone
↑ Cell proliferation

# GROWTH HORMONE

- Muscle growth
- Bone growth
- Fat metabolism
- Tissue repair

REVOLUTION
HEALTH & WELLNESS



## A ) Growth Hormone (Somatotropin)

- The growth hormone (or somatotropin) is **produced by** **somatotropin**, **a special group of acidophilic cells** of anterior pituitary.
- ***Regulation of GH release***: ***Two hypothalamic factors play a prominent role*** in the release of growth hormones. ***These are***
  - the growth hormone releasing hormone (**GRH**) **that stimulates**
  - the growth hormone release-inhibiting hormone (**GRIH, somatostatin**) **that inhibits**.
- This, in turn, ***is regulated by*** **a feedback mechanism**.
- Growth hormone ***production is influenced by*** many factors such as ***sleep, stress (pain, cold, surgery), exercise, food intake etc.***
- ***It is observed*** that the **largest increase** in the **production of GH occurs** **after the onset of sleep**. This supports the adage "If you don't sleep, you won't grow.

# Regulation of Growth Hormone Secretion

- **Stimulators:**
  - Growth hormone-releasing hormone (GHRH) from the hypothalamus
  - Sleep, exercise, and fasting
  - Low blood glucose levels (hypoglycemia)
  - Ghrelin, a hormone secreted by the stomach

- **Inhibitors:**
  - Somatostatin (growth hormone-inhibiting hormone) from the hypothalamus
  - High blood glucose levels (hyperglycemia)
  - Insulin-like growth factor 1 (IGF-1) via negative feedback

**Biochemical functions of GH**: Growth hormone promotes growth, and also influences the normal metabolisms (protein, carbohydrate, lipid and mineral) in the body.

1. **Effects on growth**: As is obvious from the name, **GH is essential for the growth**. The growth-related effects of GH are mediated يتم التوسط through **insulin like growth factor I (IGF-I)** which **is also known as somatomedin C** (formerly **sulfation factor**), **produced *by liver***.

2. **Effects on protein metabolism**: Growth hormone has **an anabolic effect** on protein metabolism. *It promotes the uptake of amino acids into the tissues and increases the protein synthesis*. **The overall effect of GH is a positive nitrogen balance** that **leads to increase in body weight.**

3. **Effects on carbohydrate metabolism**: Growth hormone is **antagonistic to insulin and causes hyperglycemia. *GH increases gluconeogenesis, decreases glucose utilization***, **impairs glycolysis and reduces the tissue uptake of glucose**.

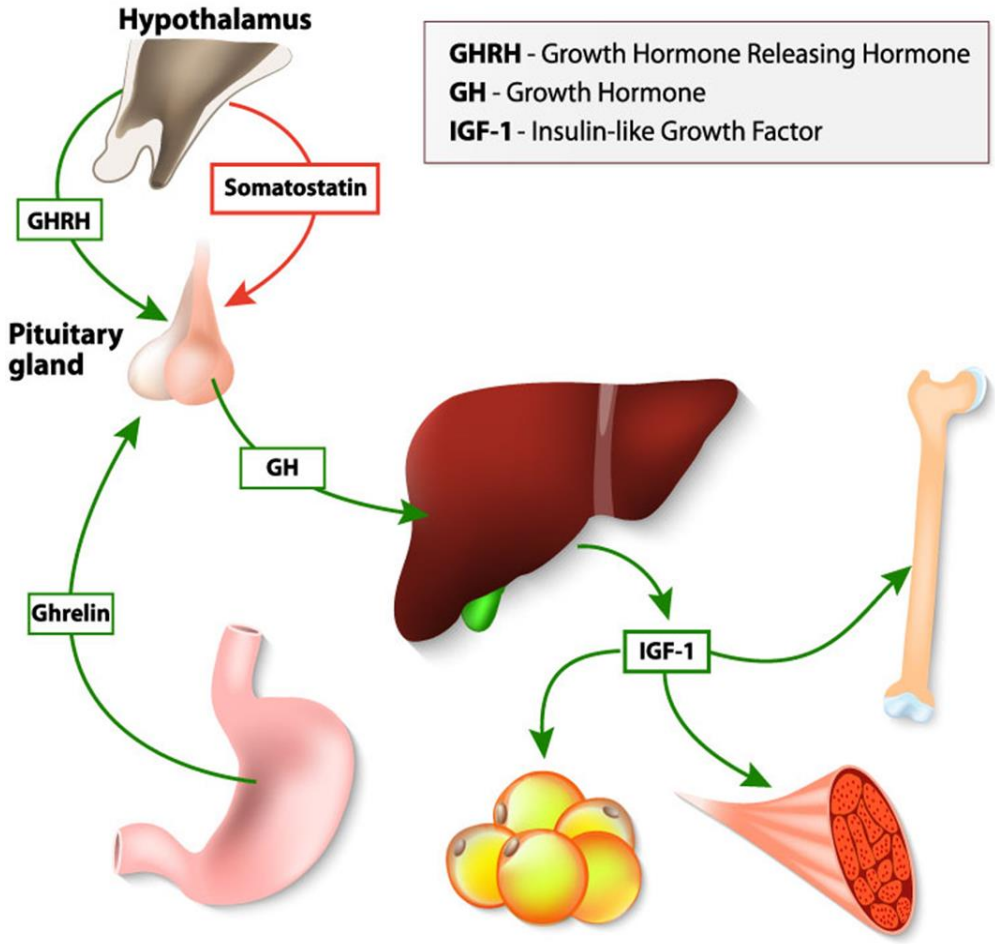
4. **Effects on lipid metabolism**: Growth hormone promotes **lipolysis in the adipose tissue** and **increases the circulatory levels of free fatty acids and their oxidation**. ***It increases ketogenesis, particularly in diabetes.***

5. **Effects on mineral metabolism**: Growth hormone promotes **bone mineralization and its growth**, ***as clearly observed in the growing children***.

# Insulin-like Growth Factor I (IGF-I)

- **Structure: IGF-I is a single-chain protein with structural similarities to insulin, hence the name.**
- **Production: It is primarily produced in the liver in response to stimulation by growth hormone (GH).**
- **Other tissues also produce IGF-I in smaller amounts.**
- **Roles of IGF-I**

1. **Growth and Development.**
2. **Enhances protein synthesis and inhibits protein degradation.**
3. **bone formation by stimulating osteoblast activity .**
4. **Neuroprotective Effects from apoptosis (programmed cell death).**



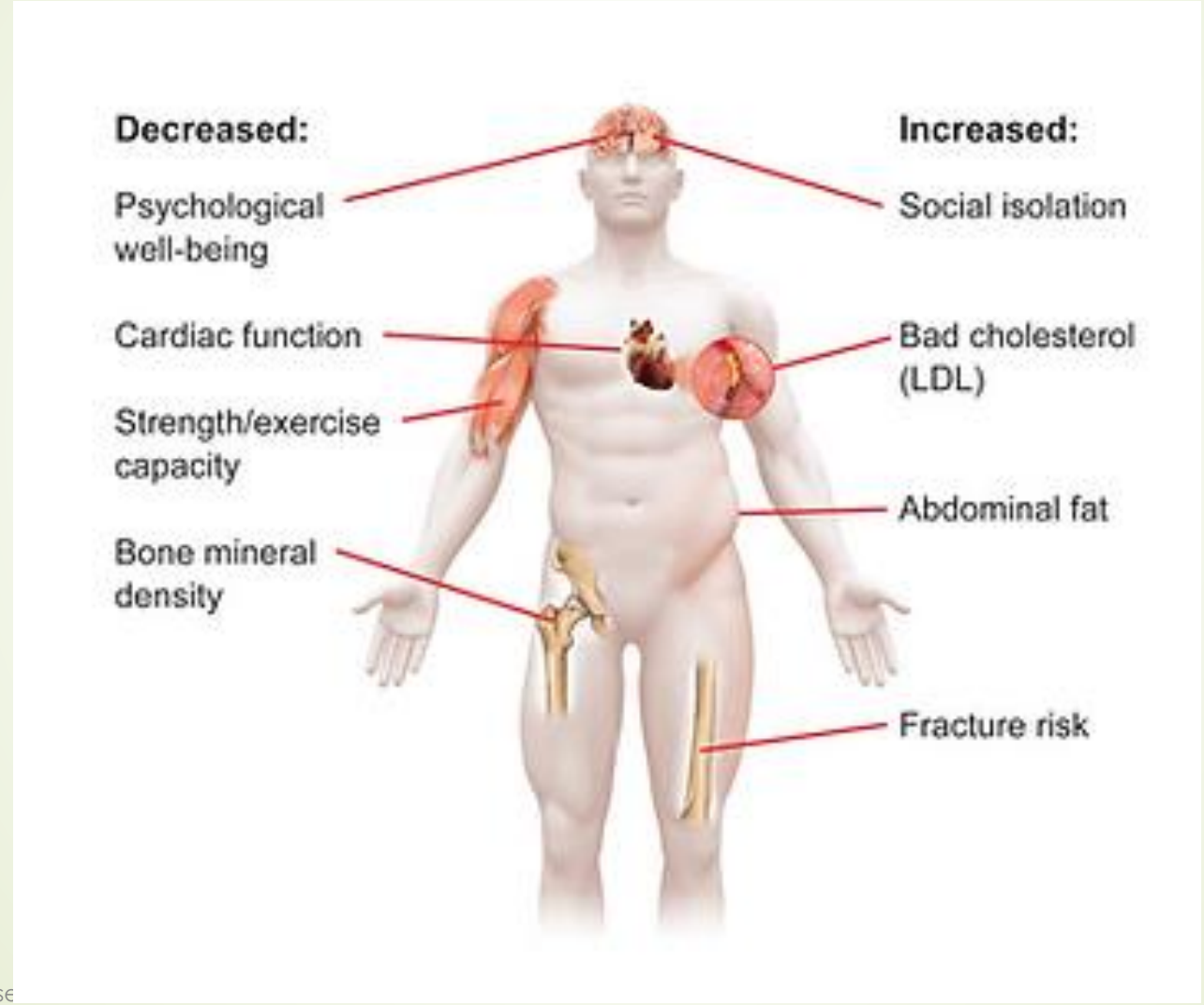
## Abnormalities of GH production

**Deficiency of GH**: Impairment in the secretion of growth hormone **in the growing age** causes **dwarfism.** التقزم.The *other deficiency metabolic effects* are not that serious in nature.

**Overproduction of GH**: Excessive production of GH causes **gigantism in children and acromegaly in adults**. This **usually occurs** in the **acidophil tumor of pituitary gland**. **Gigantism** is **characterized by** *increased growth of long bones* and this is observed **before the epiphyseal plates close**. قبل إغلاق الصفائح المشاشية

**Acromegaly** occurs **after epiphyseal closure** بعد إغلاق الصفائح المشاشية and is **characterized by** *increase in the size of hands, facial changes (enlarged nose, protruding jaw* تضخم الأنف وبروز الفك *), excessive hair, thickening of skin etc.*

# Diagnosis of the Adult Growth Hormone Deficiency



# diagnostic tests for growth hormone (GH) levels:

## 1. Basal GH Levels:

A. **Limitations:** Basal GH measurement is not a reliable diagnostic tool because GH is secreted in pulses, and levels can vary throughout the day, making it difficult to interpret accurately.

## 2. Stimulation Tests:

A. **Insulin-Induced Hypoglycemia:** This test stimulates GH secretion by inducing hypoglycemia through insulin administration. A normal response is an increase in GH levels.

B. **GHRH (Growth Hormone-Releasing Hormone) Administration:** Injecting GHRH can stimulate the pituitary to release GH, and the subsequent GH levels are measured to assess the pituitary's function.

## 3. Suppression Tests:

A. **Oral Glucose Tolerance Test (OGTT):** This test is used to diagnose acromegaly. In a healthy individual, glucose ingestion suppresses GH secretion. In acromegaly, GH levels remain elevated despite glucose intake. This lack of suppression indicates abnormal GH regulation.

1. **مستويات هرمون النمو الأساسية:**

**القيود:** لا يعد قياس مستويات هرمون النمو الأساسية أداة تشخيصية موثوقة لأن هرمون النمو يُفرز على شكل نبضات، وقد تختلف مستوياته طوال اليوم، مما يجعل تفسيره بدقة أمرًا صعبًا.

2. **اختبارات التحفيز:**

**انخفاض سكر الدم الناجم عن الأنسولين:** يحفز هذا الاختبار إفراز هرمون النمو عن طريق إحداث انخفاض سكر الدم من خلال إعطاء الأنسولين. والاستجابة الطبيعية هي زيادة مستويات هرمون النمو.

**إعطاء هرمون النمو المطلق:** يمكن أن يؤدي حقن هرمون النمو المطلق إلى تحفيز الغدة النخامية على إفراز هرمون النمو، ويتم قياس مستويات هرمون النمو اللاحقة لتقييم وظيفة الغدة النخامية.

3. **اختبارات التثبيط:**

**اختبار تحمل الجلوكوز عن طريق الفم (OGTT):** يستخدم هذا الاختبار لتشخيص ضخامة الأطراف. في الفرد السليم، يعمل تناول الجلوكوز على قمع إفراز هرمون النمو. في ضخامة الأطراف، تظل مستويات هرمون النمو مرتفعة على الرغم من تناول الجلوكوز. يشير هذا الافتقار إلى القمع إلى تنظيم غير طبيعي لهرمون النمو.

# Diagnostic Approaches

**GH Stimulation Tests:** Used to assess GH deficiency (e.g., insulin tolerance test).

**GH Suppression Tests:** Used to diagnose GH excess (e.g., oral glucose tolerance test).

**Measurement of IGF-1 Levels:** Reflects average GH activity.

### 1.Arginine Infusion Test:

- **Purpose**: Assesses GH secretion using arginine, which suppresses somatostatin (GH inhibitor)

### 2.Clonidine Stimulation Test:

- **Purpose**: Uses clonidine, an α2-adrenergic agonist, to stimulate GH secretion via the hypothalamus.

### 3.Glucagon Stimulation Test

**Purpose:** Assesses GH release by stimulating the hypothalamus-pituitary axis through glucagon administration.

## Therapeutic Applications

- **Recombinant Human Growth Hormone (rhGH):** Used to treat GH deficiency in children and adults
- **GH Antagonists:** Used to treat acromegaly (e.g., pegvisomant).

**1اختبار ضخ الأرجينين:**

الغرض: تقييم إفراز هرمون النمو باستخدام الأرجينين، الذي يثبط السوماتوستاتين (مثبط هرمون النمو)

**2اختبار تحفيز الكلونيدين:**

الغرض: استخدام الكلونيدين، وهو منشط لمستقبلات ألفا 2 الأدرينالية، لتحفيز إفراز هرمون النمو عبر منطقة تحت المهاد.

**3. اختبار تحفيز الجلوكاجون**

الغرض: تقييم إطلاق هرمون النمو عن طريق تحفيز محور تحت المهاد-الغدة النخامية من خلال إعطاء الجلوكاجون.

**التطبيقات العلاجية**

هرمون النمو البشري المؤتلف ( rhGH): يستخدم لعلاج نقص هرمون النمو عند الأطفال والبالغين

مضادات هرمون النمو: تستخدم لعلاج ضخامة الأطراف (مثل بيجفيسومانت).

# The normal range of growth hormone (GH)

- **Fasting/Non-Stimulated GH Levels:**

**Adults:**

Male: **< 5 ng/mL**

Female: **< 10 ng/mL** (higher in females **due to estrogen**)

**Children: 0–10 ng/mL**

**Newborns: 5–40 ng/mL** (higher **due to active growth**)

- **GH Stimulation Tests (Peak Values):**

**Adults:** > **5 ng/mL** is typically considered normal.

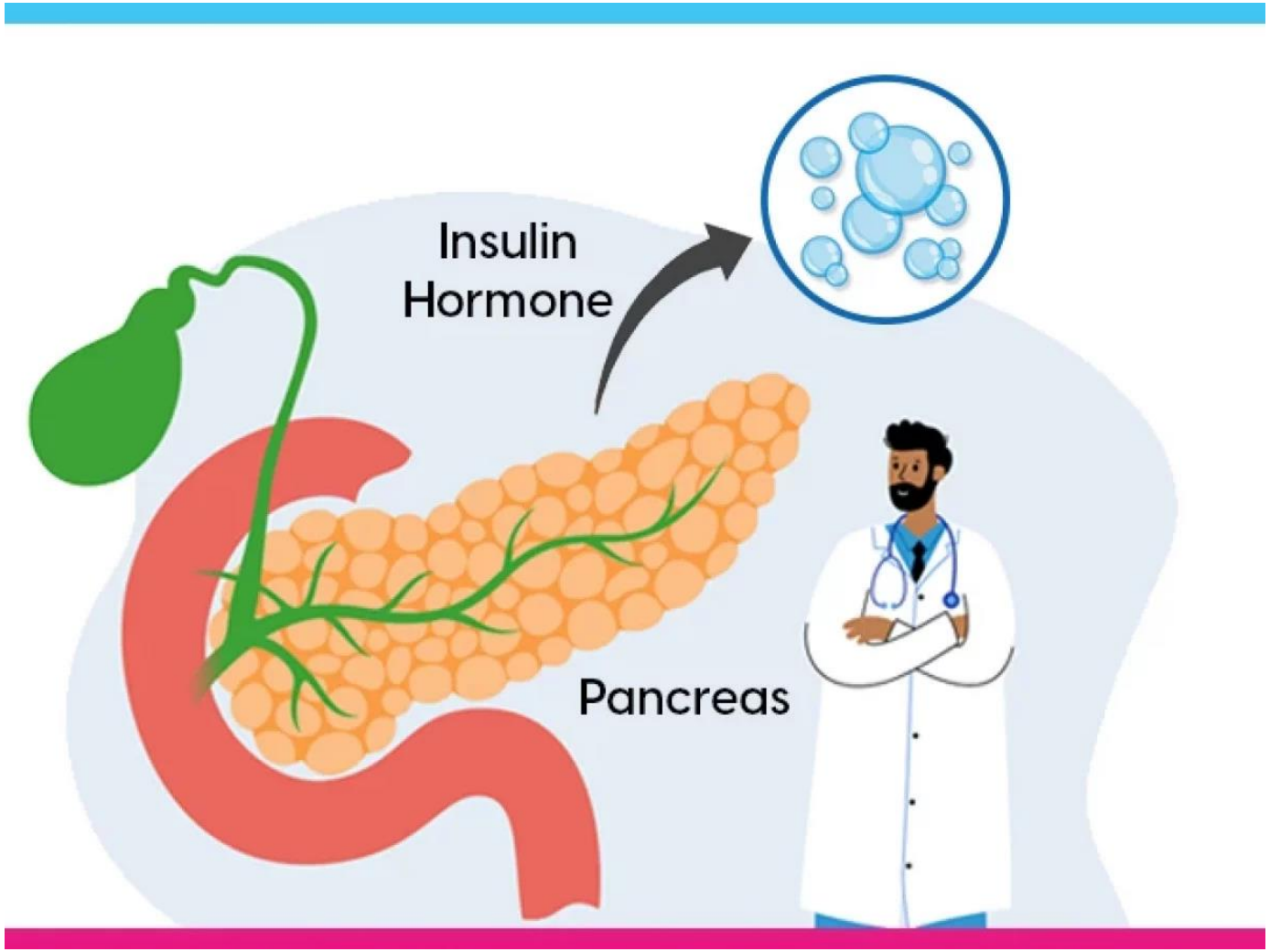
**Children:** > **10 ng/mL** is usually expected.

- **GH Suppression Tests (e.g., after glucose):**

Normal GH suppression: **< 1 ng/mL** (used to rule out acromegaly or GH excess).

- يستخدم لاستبعاد ضخامة الأطراف أو زيادة هرمون النمو

# INSULIN

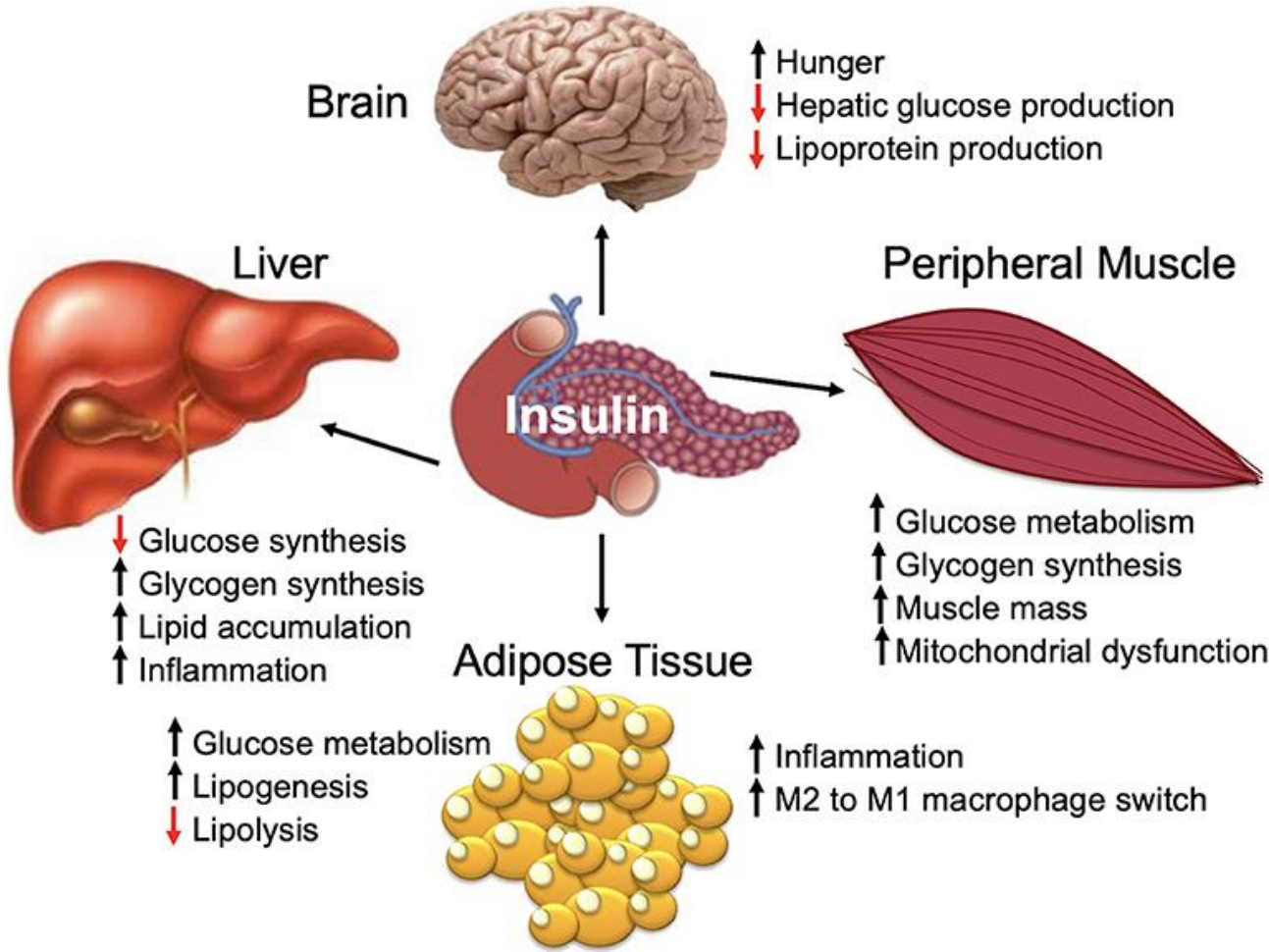


# Insulin

- Is ***a* protein hormone**, secreted by β-cells of islets of Langerhans of pancreas.
- composed of two polypeptide chains, called 'A'-chain and 'B'-chain, containing total of 51 amino acids. A chain contains 21 amino acids and B-chain contains 30 amino acids. Both the chains are held together by two S–S linkages.

- **Major target tissues of insulin are the**

1. Muscles.
2. Liver.
3. adipose tissue
4. Brain.



# Mechanism of action of insulin

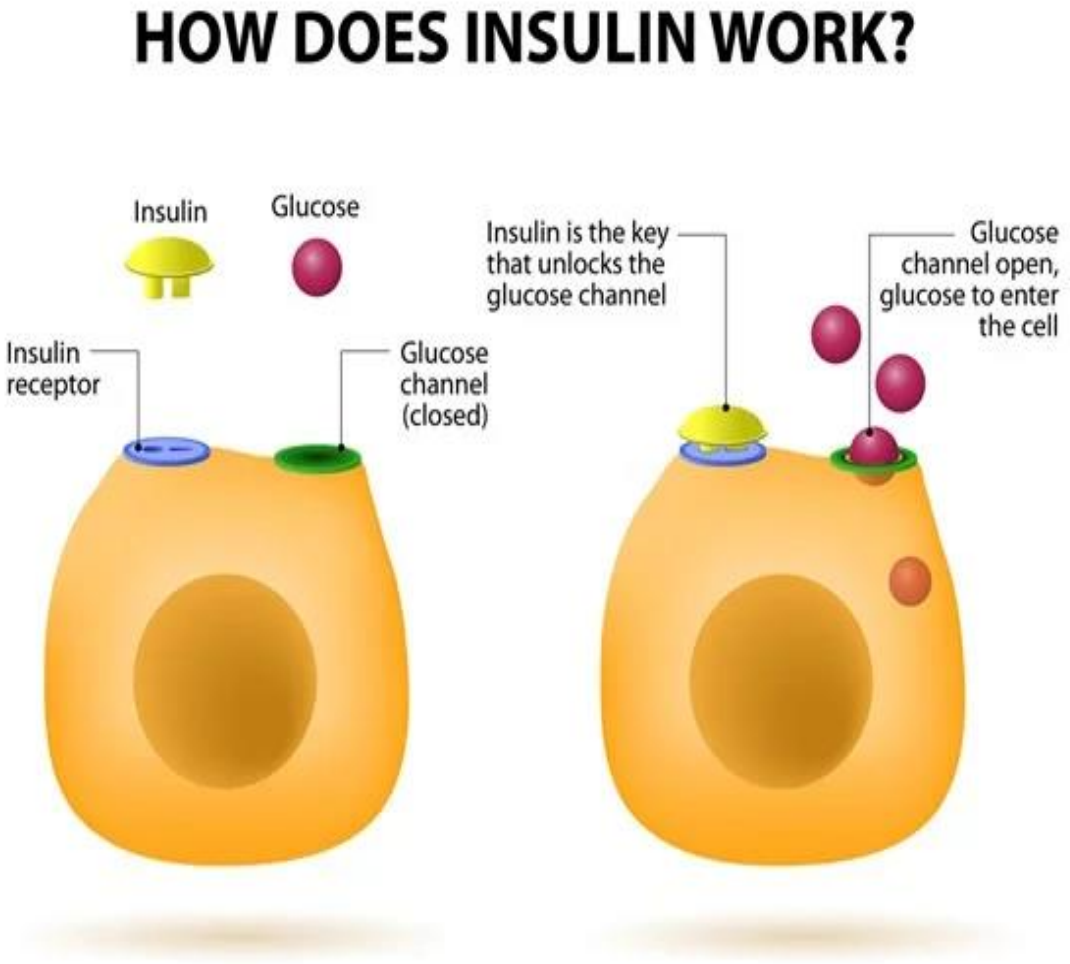
**Insulin binds to** specific plasma **membrane receptors** present on the target tissues, such as muscle and adipose. This results in a series of reactions ultimately leading to the biological action.

Three distinct mechanisms of insulin action are known.

**One** / Induction of transmembrane signals (signal transduction)

**second /** Glucose transport across the membrane via **GLUT4** transporters.

**Third/** Enzyme synthesis.



# Normal Range of Insulin Levels

Note: Ranges may vary slightly depending on the lab method and units used.

- **Fasting Insulin Levels:**
  Adults: 2–25 μU/mL (microunits per milliliter)
  Children: 3–20 μU/mL
- **Postprandial (2 hours after a meal):**
  Up to 50 μU/mL (higher due to insulin release after food intake)
- **Insulin Resistance (HOMA-IR):**
  Calculated using fasting glucose and insulin levels.
  A HOMA-IR value > 2.5 indicates insulin resistance.

**HOMA-IR = (Fasting Glucose (mg/dL) × Fasting Insulin (μU/mL)) ÷ 405**
(For glucose in mmol/L, divide by 22.5 instead of 405.)

# Clinical Applications

1. **Diagnosis of Diabetes:**
    1. Low fasting insulin levels may indicate Type 1 diabetes (absolute deficiency).
    2. High fasting insulin levels may suggest Type 2 diabetes (insulin resistance).
2. **Evaluation of Hypoglycemia:**

    Elevated insulin levels in the presence of low blood glucose indicate hyperinsulinemia, hypoglycemia.
3. **Management of Insulin Resistance:**

    Common in obesity, metabolic syndrome, and polycystic ovary syndrome (PCOS).
4. **Assessment of Beta-Cell Function:**

    Insulin levels are used to evaluate the pancreatic beta-cell reserve

**تشخيص مرض السكري:**

**قد تشير مستويات الأنسولين المنخفضة أثناء الصيام إلى الإصابة بمرض السكري من النوع الأول (نقص مطلق).**

**قد تشير مستويات الأنسولين المرتفعة أثناء الصيام إلى الإصابة بمرض السكري من النوع الثاني (مقاومة الأنسولين).**

**تقييم نقص سكر الدم:**

**تشير مستويات الأنسولين المرتفعة في وجود نسبة منخفضة من سكر الدم إلى فرط الأنسولين في الدم، ونقص سكر الدم.**

**إدارة مقاومة الأنسولين:**

**شائعة في السمنة ومتلازمة التمثيل الغذائي ومتلازمة تكيس المبايض (.PCOS)**

**تقييم وظيفة خلايا بيتا:**

**تستخدم مستويات الأنسولين لتقييم احتياطي خلايا بيتا البنكرياسية**