Biochemistry Team 435

جامعة الملك سعود
King Saud University

OBESITY: ROLE OF HORMONES

* Please check out this link to know if there are any changes or additions.

Revised by
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Color index: Important | Doctors notes | Further explanation.

OBJECTIVES:

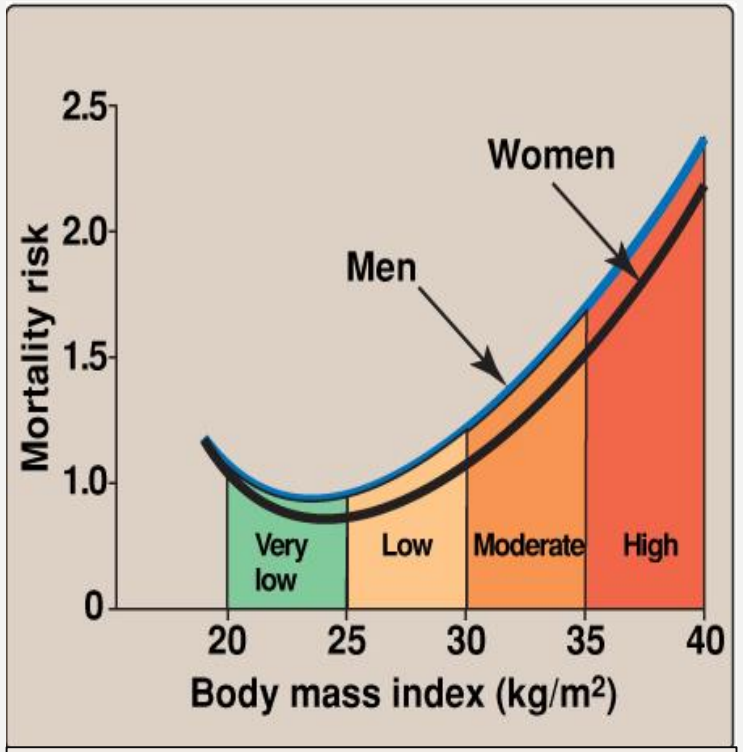
Unknown ☹ .

Obesity

- A disorder of body weight **regulatory systems.**
- Causes accumulation of **excess** body fat **>20%** of normal body weight

Obesity is associated with a high risk of:	**Diabetes mellitus**
	Hypercholesterolemia
	High plasma **triacylglycerols**
	Hypertension
	Heart disease
	Cancer
	Gallstones, arthritis, gout
	Mortality

Dyslipidemia (hypercholesterolemia & high plasma triglycerides) can lead to hypertension, heart diseases & cancer as well



- As the BMI increases, the mortality risk becomes greater.
- Risk factor are more common in men!

Note: obesity is considered as a disease. Also, it gives rise to other disorders such as those above.

Your Body always tries to maintain your weight! So when you're gaining weight its counter mechanism for that will suppress hunger and increase metabolic rate, returning to its original weight.
If you're losing weight the opposite should happen. It will try to increase appetite and decrease BMR.

Causes of weight Gain

- **Energy imbalance**
  - calories **consumed** not equal to calories **used**
    - Over a **long** period of time
      - (if it was over a short period of time, the body can regulate it.)
- **combination of several factors**
  - **Individual behavior**
  - **Social interaction**
    - People who are sociable they go to occasions more frequently and accordingly they eat more
  - **Environmental factors**
  - **Genetics**
- **More in and less out = weight gain**
  - More out and less in = weight loss
- **Hypothalamus**
  - **Control center** for hunger and satiety
- **Endocrine disorder**
  - Hormonal **im**balance

Video

Factors contributing to obesity

Genetic: familial tendency

Sex: women more susceptible

Activity: lack of physical activity

Psychogenic: emotional deprivation/ depression

Alcohol: problem drinking

Smoking: cessation of smoking

Drugs: e.g. tricyclic derivatives

- Genetic factors.
- Environmental and behavioral factors.
- Drugs.

Note: Most important is the environmental and behavioral

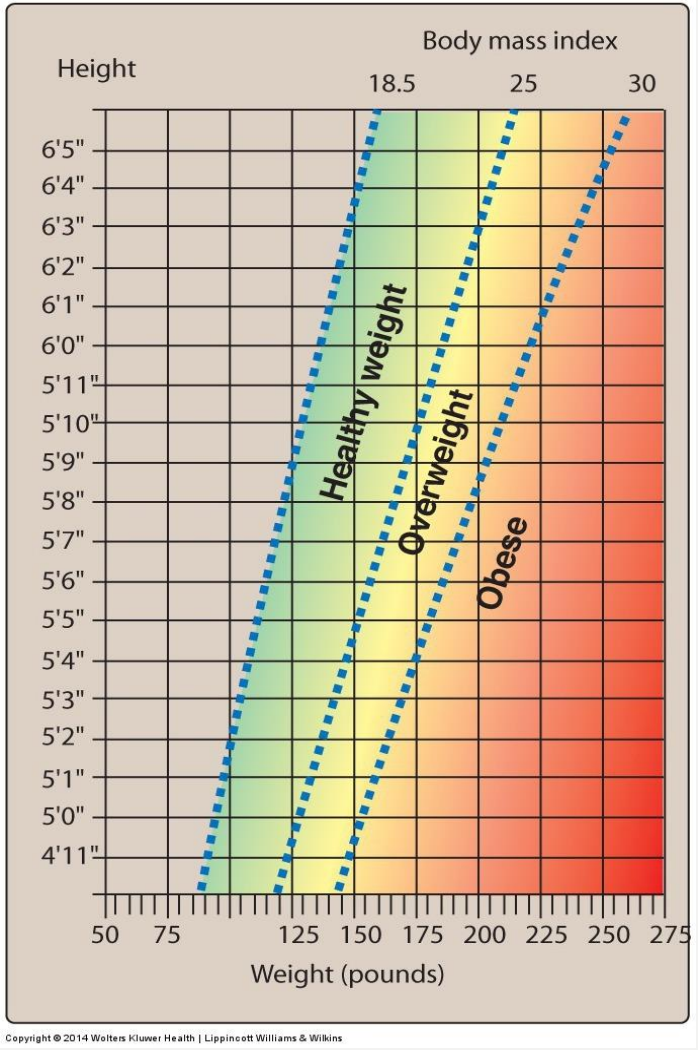
Ectopic fat

- Excessive calories that cannot be stored in adipose tissue "**spill over**" into other tissues such as **muscle** and **liver**.
- It is called "ectopic fat" that is strongly associated with **insulin resistance**.

Body mass index (BMI).

- **BMI** is an **in**direct measure of obesity provides a measure of relative weight, adjusted for height.
- **Correlates: height** , **weight** and amount of **body fat** in an individual

	BMI	GRADE
UNDER WEIGHT	≤ 18.5	
NORMAL	18.5 – 24.9	
OVER WEIGHT	25.0 – 29.9	
OBESE	30.0 – 34.9	I
OBESE	35.0 – 39.9	II
HIGHLY OBESE	≥ 40	III



Note: This way correlate well with most population except for some like **athletes**, they have lots of muscle mass which adds to their weight.

BMI= (weight in kg)\(Height in meters)2

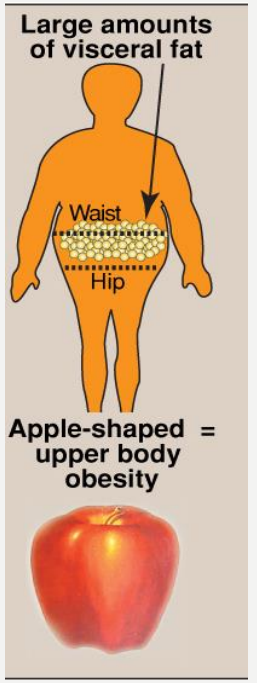
Anatomic differences in fat deposition

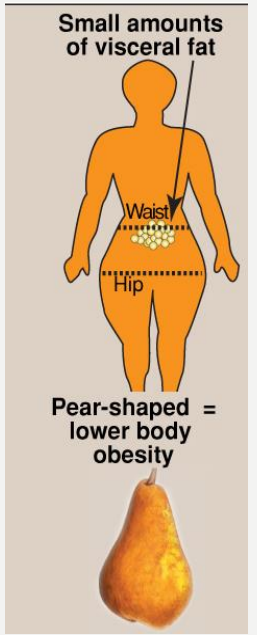
- Health risks depend on the pattern of fat deposition:

	Android obesity:	Gynoid obesity:
Known as:	"apple-shaped," central, or upper body obesity	"pear-shaped," or lower body obesity
Location of body fat deposition:	In the **central abdominal area**	Around the **hips** or **gluteal region**
Associated with risk of:	➢ Hypertension. ➢ Insulin resistance. ➢ Diabetes. ➢ Dyslipidemia. ➢ Coronary heart disease.	Associated risks **are lower**.
More common in:	**Men**	**Women**

Central obesity has high mortality risk in comparison to lower body obesity. In fact, some researchers believe that lower body obesity is **protective** against heart diseases!!

Adipose tissue is considered an endocrine gland, higher deposition of fat would send inflammatory signals to the body that disturbs the organs function.





Fat deposits

Note: Subcutaneous fat is **less** harmful than visceral fat

❖ Different fat deposits in the body:

Subcutaneous Fat	Visceral Fat
The fat stored just **under the skin** in the **abdominal** and **gluteal-femoral region**	Composed of **omental** and **mesenteric** fat present in close association **with digestive tract**
Constitutes **80-90%** of the total fat in the body	When the subcutaneous tissue is fill. The fat is deposited in viscera

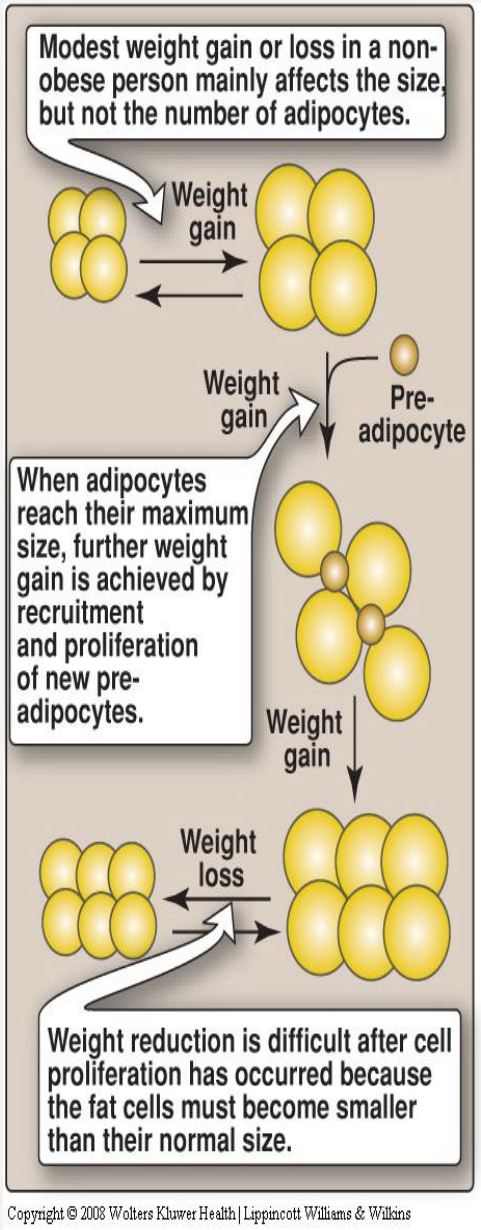
❖ Biochemical differences in fat deposits:

Abdominal fat	Gluteal Fat
Smaller cells	**Larger** cells
More responsive to hormones** (both **visceral** and **subcutaneous**).	***Less** responsive to hormones.
Release substances via **portal vein** to the **liver** (harmful)	Release substances to **circulation** with **no** effect on the liver

*More prone to synthesize and store triglyceride & are very resistant to fat breakdown & aren't removed easily.
That is why it's more easier for men to lose weight because they usually gain fat around their abdomen which respond more to hormones & release fatty acids faster than gluteal region.
**if there was insulin-resistance these adipocytes which are in the abdominal region are the most responsive to lipolysis. So they'll start mobilizing and secreting lipids.

adipocytes

Triacylglycerols are **deposited** in adipocytes (fat cells) which can **increase in size** up to a limit → **Prolonged** over-nutrition → **Stimulates Pre-adipocytes** in adipose tissue → **Proliferation / differentiation** into **mature fat cells** → **Increases** adipocyte **number**



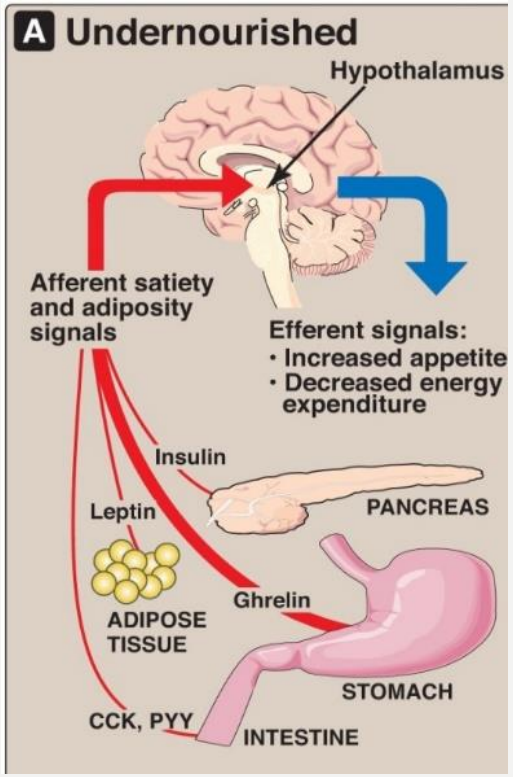
- Thus obesity is due to a combination of increased fat cell **size** (**hypertrophy**) and **number** (**hyperplasia**)
- Fat cells, once gained, are **never lost**. (but actually they do have a life span which is 10 years ☺!)
- Reduction in weight causes adipocytes to reduce **in size not in number**. That's why we can gain the lost weight again easily.

بالبداية الترايجليسرولز بتترسب بالأنسجة الدهنية وهلترسب بيكبر حجم النسيج (هايبروتروفي) لحد مايوصل لحجم معين!
بعدها بتتحفز البري اديبوسايتس وبتكبر وبيصير لها دفرنشيشن (زيادة بالعدد= هايبربلازيا)..
اذا الاوبيزتي هي عبارة عن هايبروتروفي + هايبربلازيا للخلايا الدهنية

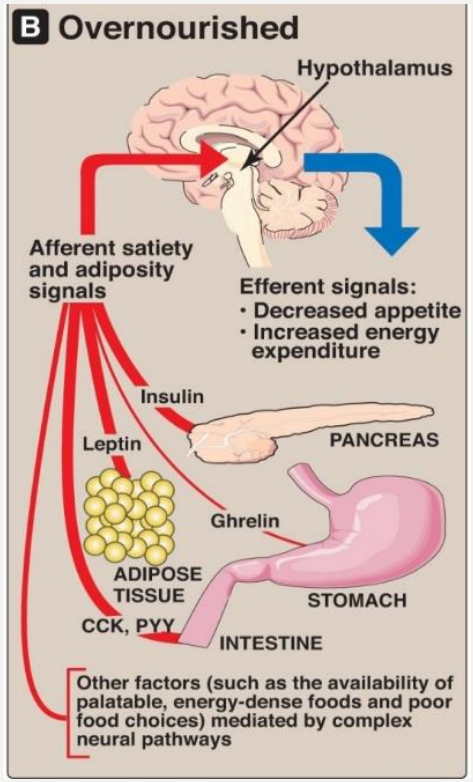
Hormonal control

❖ **Appetite is influenced by:**

1. **Afferent neural signals**, **circulating hormones** and **metabolites**
   - These signals cause the release of **hypothalamic peptides** and activate **efferent** neural signals
2. **Adipocytes** also function as endocrine cells. (What are hormones released by adipocytes?)
   - they release many regulatory molecules: **Leptin, adiponectin, resistin**



A) In an undernourished person, Leptin, Insulin , CCK and PYY levels will be low , but Ghrelin which is the hormone of hunger will increase causing the hypothalamus to release efferent signals leading to increasing Appetite and decreasing expenditure of energy.



B) In an over nourished person, Ghrelin hormone will be low, while Leptin, Insulin, CCK and PYY are increased , leading to decreased appetite and increased expenditure of energy.

Hormonal regulation

Leptin | **Adiponectin** | **Others:**

Leptin:

- A **protein** hormone produced by **adipocytes** that is required to keep the body weight under control
  - ✓ Signals the brain about **fat store level**
- **Regulates the amount of body fat by:**
  - **Controlling appetite and energy expenditure.**
- **Leptin secretion:**

suppressed	Enhanced
Starvation (depletion of fat stores)	**well-fed state** (expansion of fat stores)

- Leptin causes **overweight mice to lose weight** and maintain weight loss.

Leptin resistance

- Leptin increases metabolic rate and decreases appetite in humans.
  - ✓ Plasma leptin level in obese humans is usually **normal** for their fat mass. Which is something bad.
- **Resistance to leptin has been found in: obese humans.**
- **Mechanism?** The receptor for leptin in the hypothalamus is produced by ***db* gene** and mutation in **db gene** causes leptin resistance in mice.
- **Leptin resistance may have some role in human obesity**
  - **Dieting** decreases leptin levels
  - **Reducing metabolism, stimulating appetite**

Leptin makes a person stop eating, and it's the hormone for you to lose weight.

Leptin signals delay for 20 minutes in average, that's why if u stopped eating in the middle of a meal and waited for a couple of minutes u may feel full.

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Hormonal regulation

- Leptin
- Adiponectin
- Others:

Adiponectin:

- A **protein hormone** exclusively and abundantly secreted from **adipocytes.**
- **Effects:**
  - **promotes** the uptake and oxidation of **fatty acids** and **glucose** by **muscle** and **liver**
  - **Blocks** the synthesis of **fatty acids** and **gluconeogenesis** by **hepatocytes**

Net effect is to increase the sensitivity to insulin, and improve glucose tolerance

- ✓ Adiponectin levels are inversely correlated (علاقة عكسية) with body fat percentage and parallels with the **HDL level**
- ✓ Low levels are seen in **metabolic syndrome** and **diabetes mellitus**

Hormonal regulation

Leptin | **Adiponectin** | **Others:**

Ghrelin	Cholecystokinin	Insulin:
A **peptide** hormone secreted (in between meals) by **stomach**	**Peptide**.	-
Secretion increases just **before meals** and drops **after meals**	released from the gut **after a meal**	-
Stimulates appetite. ▪ **Increases** food intake ▪ **Decreases** energy expenditure and fat catabolism	**Satiety signals to the brain**	**Promotes metabolism**
Levels in dieters are higher after weight loss " The body steps up ghrelin production in response to weight loss. **The higher the weight loss, the higher the ghrelin levels**"	-	-

In people who lose their weights in a short period of time, ghrelin will ↑ → more appetite. So if u lose your weight slowly it'll "remember" ur current weight as a "checkpoint" and tries to return to it if needed.

Video

Metabolic changes in obesity

Adipocytes send signals that cause abnormal metabolic changes such as:

- **Dyslipidemia**
- **Glucose intolerance**
- **Insulin resistance**

Old theory says: don't eat so you lose weight. But as long as making yourself hungry decreases body expenditure, it causes weight gain

Benefits of weight loss in obesity

- **Lower** blood **pressure**
- **Decreased** serum **triacylglycerol**
- **Lower blood glucose levels**
- **Increase** in **HDL** levels
- **Decreased mortality**
- **Beneficial changes** in **Basal metabolic rate (BMR)**
- **Decreased energy requirement**

Treatment options :

Physical activity combined with healthy diet decreases level of obesity and reduces risk for heart disease and diabetes

- **Dieting**
- ✓ **Use of low-calorie diet**
- ✓ **Restriction of excessive energy intake**

Drugs

- **Orlistat**
  - A **pancreatic** and **gastric lipase inhibitor**
  - Decreases **the breakdown of dietary fat**
- **Lorcaserin**

promotes satiety

Surgery

Surgical procedures are designed **to reduce food consumption in patients with BMI >40**

Used when other **treatment options fail**

Check your understanding!

Q1: Hunger and satiety are both regulated by the:

A. GIT reflexes
B. Hypothalamus
C. Cerebellum
D. None of the above

Q2: Low levels of ectopic fat are associated with developing Insulin resistance.

A. True
B. False

Q3: The obesity pattern found mostly in men, known as "apple-shaped," or upper body obesity is called

A. Android Obesity
B. Gynoid Obesity
C. Central Obesity
D. A + C

Q4: Most of the fat in the body is stored as

A. Visceral Fat
B. Gluteal Fat
C. Subcutaneous Fat
D. Abdominal Fat

Q5: Development of Obesity is due to ……. of fat cells

A. Hypertrophy (ONLY)
B. Hyperplasia (ONLY)
C. Hypertrophy & Hyperplasia

Q6: Rebound weight gain after weight loss is due to fat cells only decreasing in size after weight loss, not in number.

A. True
B. False

Q7: Mutation in the db gene causes resistance to which of the following hormones?

A. Leptin
B. Adiponectin
C. Resistin
D. Ghrelin

Q8: Which hormone causes increases sensitivity to insulin?

A. Leptin
B. Adiponectin
C. Resistin
D. Ghrelin

1.B 2.B 3.D 4.C 5.C 6.A 7.A 8.B

Check your understanding!

9: Ghrelin levels are most likely highest in:

A. A person who has lost 8kg of weight over a month, and has just eaten
B. A person who has gained 10kg of weight over 2 weeks, and has just eaten
C. A person who has lost 6kg of weight over 3 weeks and hasn't eaten all day
D. A person who has lost 9kg of weight over 2 months, and is about to eat

10: High levels of Ghrelin hormone will cause

A. Increased energy expenditure and fat catabolism
B. Decreased energy expenditure and fat catabolism
C. Increased energy expenditure, and decreased fat catabolism
D. Decreased energy expenditure, and increased fat catabolism

11: Orlistat causes weight loss by

A. Inhibiting Salivary a-amylase
B. Inhibiting Pancreatic lipase
C. Inhibiting Gastric lipase
D. B + C

12: Surgery would be the most likely used in the case of:

A. A Moderately obese patient
B. A sedentary patient with a BMI of 33
C. A morbidly obese patient with a BMI of 42
D. None of the above

13: Which hormone is released by the gut after a meal, sending satiety signals to the brain?

A. Ghrelin
B. Leptin
C. Cholecystokinin
D. Adiponectin

9.D 10.B 11.D 12.C 13.C

Done by:

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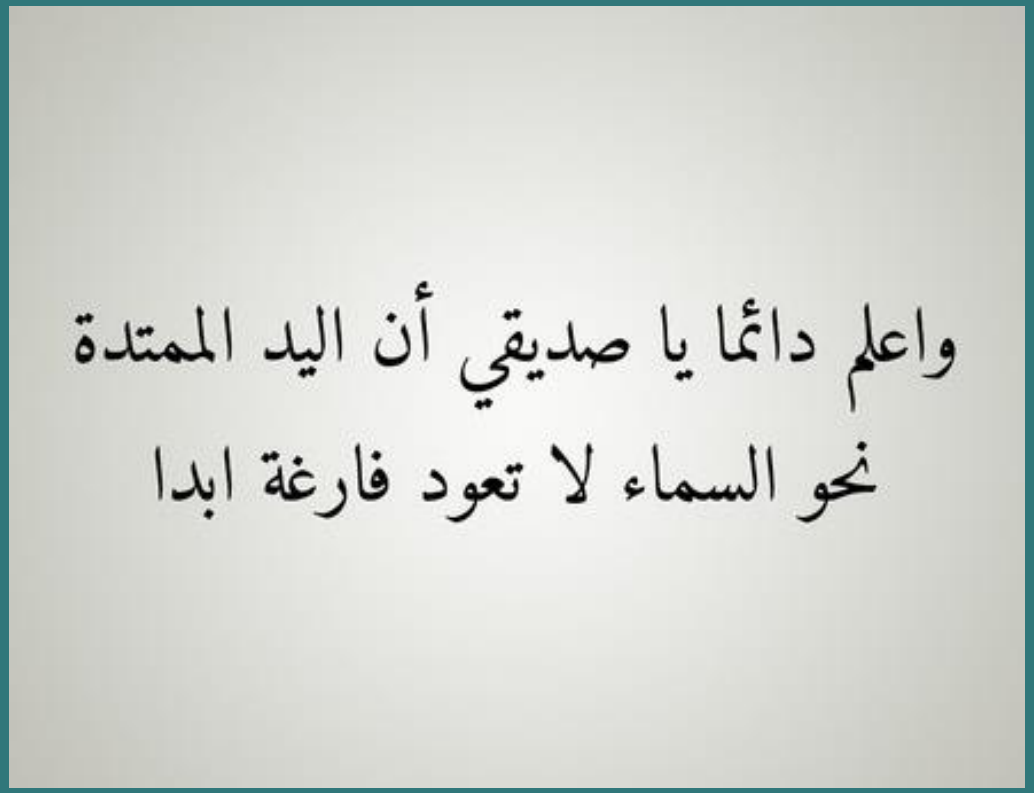

Resources:

- 435's slides and notes.
- Biochemistry: Lippincott's illustrated reviews - 6th edition .

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