Biochemistry of Obesity

Biochemistry Teamwork

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Biochemistry of Obesity:
Role of Hormones

What is Obesity?

- ✓ A disorder of body weight regulatory systems, which causes accumulation of excess body fat.
- ✓ >20% of normal body weight.

Example:
If a patient's normal weight is **50 Kg**. Then she gained **10 Kg (20% of her normal body weight)**, and her weight now is **60 Kg**. Now she's considered obese. Less than 60 she is **overweight** but **not obese**.

Obesity is associated with a high risk of:

- Diabetes mellitus
- Hypercholesterolemia (increased cholesterol in blood)
- High plasma triglycerides
- Hypertension
- Heart disease
- Cancer
- Gallstones, arthritis, gout
- Mortality

Obesity is **a chronic low-grade inflammation** → Increase the **risk of cancers due to release of cytokines by the adipocytes.**

Body Mass Index (BMI)

- ✓ BMI is an **indirect** measure of obesity. (more direct measure is **MRI**)

BMI doesn't exactly measure the fat. There are **body fat analyzers** available to measure the body fat.

- ✓ Correlates height, weight and amount of body fat in an individual
- ✓ High BMI is associated with increased mortality risk

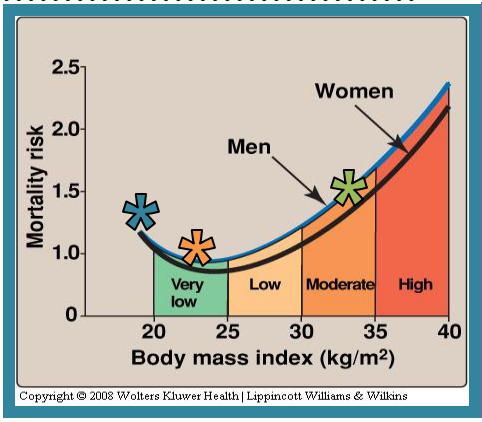
HOW TO CALCULATE BMI?

$$BMI = \frac{\text{weight (lb)} * 703}{\text{height}^2\ (\text{in}^2)}$$

OR

$$BMI = \frac{\text{weight (kg)}}{\text{height}^2\ (\text{m}^2)} \quad \text{(metric)}$$

	BMI	GRADE
UNDER WEIGHT	≤ 18.5 or 19.5	
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



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* Underweight → increased mortality risk

* Normal body weight → very low mortality risk

* BMI > 30 → increased mortality risk

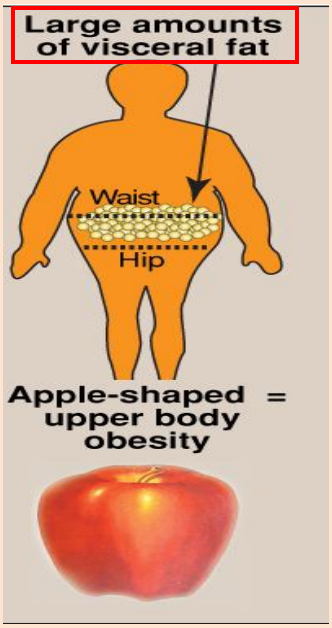
Body type should be taken in consideration. **Example:** if the patient is an **athlete**.

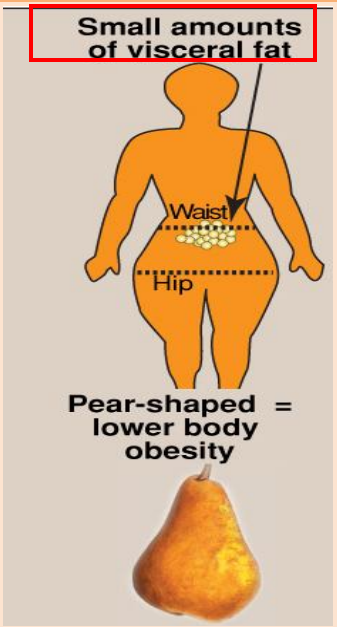
Anatomic Differences in Fat Deposition

✓ Health risks depend on **the pattern of fat deposition.**

Android, "apple-shaped," or upper body obesity	Gynoid, "pear-shaped," or lower body obesity
excess body fat deposited in the central abdominal area (mainly present in males)	**Fat deposited around the hips or gluteal region (hips&thighs). (mainly present in females)**
Associated with risk of hypertension, insulin resistance, diabetes, dyslipidemia, and coronary heart disease	**Associated risks are lower**

❖ This type of fat is more dangerous, because whatever is being released of adipocytes, is going directly to the liver by portal circulation





Biochemical Differences in Fat Deposition

	Abdominal fat (more in males)	Gluteal Fat (more in females)
Size of Adipocytes	Larger cells	Smaller cells
Range of the Turnover	Very high	-
Response to Hormones	More responsive to hormones	Less responsive
	Release substances via portal vein to the liver	Release substances to circulation with no effect on the liver

Because males' adipocytes are more responsive to hormones (more metabolically active), so when they start exercising and dieting, it is much easier for them to lose weight than females, whose fat is much resistant.

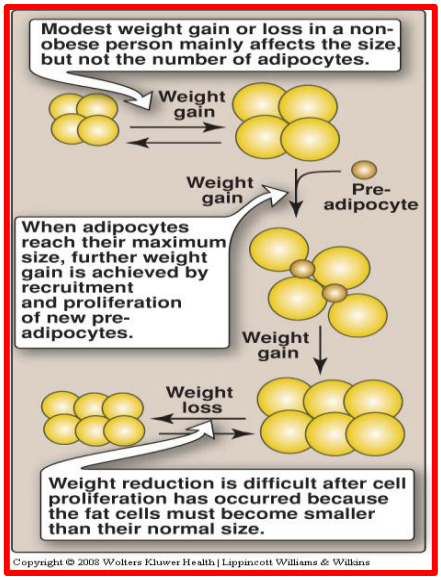
In females, the release of adipocytes is to the general circulation, with no direct effect on the liver → lower risks.

Adipocytes

- ✓ Triacylglycerols are deposited in adipocytes (fat cells).
- ✓ The cells increase in size and expand and divide.
- ✓ **Fat cells, once gained, are never lost.**
- ✓ In obesity adipocytes increase in number and size**.**
- ✓ Reduction in weight causes adipocytes to **reduce in size (not in number).**

That's why gaining weight is easier after losing weight. Because the number of adipocytes doesn't change, there is only reduction in size.

Preadipocytes: are present throughout adult life in adipose tissues and can proliferate and differentiate into mature adipocytes according to the energy balance.



Factors contributing to obesity

- ✓ **Genetic:** familial tendency.

For obese parents: 70-90% that their children will be obese.
For thin parents: Only 9% that their children will be obese.

- ✓ **Environmental and behavioral:**
  - **Sex:** women more susceptible.
  - **Activity:** lack of physical activity.
  - **Psychogenic:** emotional deprivation/depression.
  - **Alcohol:** problem drinking.
  - **Smoking:** cessation smoking.
- ✓ **Drugs:** e.g. tricyclic derivatives.

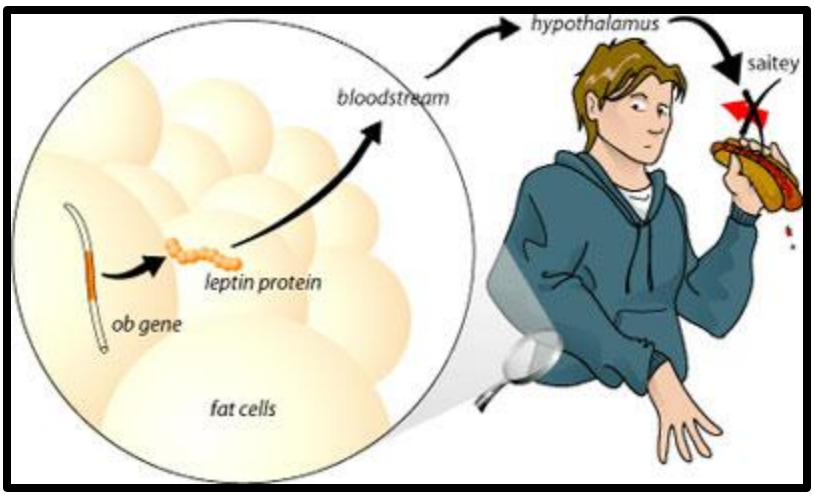
Causes of weight Gain

- **Energy imbalance**
  - **calories consumed not equal to calories used.**
- **Over a long period of time**
- **Due to a combination of several factors**
  - Individual behaviors.
  - Social interactions.
  - 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**

- ✓ **Appetite is influenced by:**
  - **Afferent neural signals**, **circulating hormones**, and **metabolites.**
- ✓ These signals cause the release of **hypothalamic peptides** and activate **efferent neural signals.**
- ✓ **Adipocytes** also function as **endocrine cells.**
- ✓ **They release many regulatory molecules:**
  - Leptin, adiponectin, resistin.
- ✓ **Adiponectin and resistin may cause insulin resistance observed in obesity.**

✓ Leptin:

- ✓ A protein hormone produced by adipocytes.
- ✓ **Functions:**
  - Required to keep the body weight under control.
  - Signals the brain about **fat store level** (sensor for the amount of body fat).
  - Regulates the amount of body fat by: **Controlling appetite and energy expenditure.**
- ✓ **Leptin secretion:**
  - Suppressed in starvation (depletion of fat stores).
  - Enhanced in well-fed state (expansion of fat stores).
- ✓ Leptin causes **overweight mice to lose weight and maintain weight loss.**



1- Leptin (appetite suppressor)

✓ **Leptin Resistance:**

- Leptin **increases metabolic rate** and **decreases appetite** in humans.
- Plasma leptin level in obese humans is usually **normal for their fat mass.**
- **Resistance to leptin** has been found in obese humans.
- The **receptor** for leptin **in the hypothalamus** is produced by ***db*** gene.
- 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**

That's why we can't see the functions of leptin in obese patients, although they have normal levels of leptin.

2- Adiponectin

- ✓ **Exclusively and abundantly** secreted hormone from the **adipocytes.**
- ✓ **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 (insulin-sensitivity), and **improve glucose tolerance**.
- ✓ Adiponectin levels are **inversely correlated with body fat percentage and parallels with the HDL level**.
- ✓ **Low levels** are seen in **metabolic syndrome** and **diabetes mellitus**.
- ✓ With obesity the levels of Adiponectin goes down.

Other Hormones: Ghrelin (The Hunger Hormone)

Ghrelin: A peptide hormone secreted by stomach

- **Stimulates appetite**
- Secretion **increases just before meals and drops after meals**
- **Increases food intake**
- **Decreases energy expenditure and fat catabolism**
- 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**

Other Hormones

- ✓ **Cholecystokinin**: Peptides released **from the gut after a meal,** satiety signals to the brain.
- ✓ **Insulin:** **Promotes metabolism.**

Metabolic Changes in Obesity

- ✓ **Adipocytes send signals that cause abnormal metabolic changes such as:**
  - Dyslipidemias: High triglycerides and low HDL level.
  - Glucose intolerance: Because of insulin resistance, there is build-up of glucose.
  - Insulin resistance

Weight loss

- ✓ **Decreases risk factors.**
- ✓ **Leads to:**
  - Lower blood pressure
  - Decreased serum triacylglycerols
  - Lower blood glucose levels
  - Increase in HDL levels
  - Decreased mortality
  - Beneficial changes in BMR
  - Decreased energy requirement

- ✓ **Slow weight loss is more stable**

Treatment options

- ✓ Physical activity combined with healthy diet decreases level of obesity
- ✓ Reduces risk for heart disease and diabetes
- ✓ Dieting
- ✓ Use of calorie-restricted diet
- ✓ Restriction of energy intake
- ✓ **Drugs:** e.g.: **Orlistat** :
  - A pancreatic and gastric lipase inhibitor
  - **Decreases the breakdown of dietary fat** (Preventing the further gain of fat)
- ✓ **Surgery:**
  - Surgical procedures are designed to reduce food consumption in patients with **BMI >40**
  - Used when other treatment options fail

SUMMARY

- A disorder of body weight regulatory systems, which causes accumulation of excess body fat.
- Obesity is associated with a high risk of several chronic diseases, such as: DM, HTN.
- BMI is an **indirect** measure of obesity.
- Health risks depend on **the pattern of fat deposition.**
- **Fat cells, once gained, are never lost.**
- **Factors contributing to obesity:** Genetic factors, environmental factors and drugs.
- **Causes of weight gain:** energy imbalance and due to combination of several factors, such as: social interactions.
- **Appetite is influenced by:**
  - Afferent neural signals, circulating hormones, and metabolites
- Leptin **increases metabolic rate** and **decreases appetite** in humans.
- Adiponectin levels are **inversely correlated with body fat percentage and parallels with the HDL level**.

QUESITIONS

Q1: Which one of the following is not secreted by adipocytes?

A. Leptin
B. Adiponectin
C. Ghrelin

Q2: One of the following acts as appetite stimulating hormone:

A. CCK
B. Insulin
C. Ghrelin

Q3: Regarding leptin which of the following is not true?

A. Regulate the amount of body fat
B. When depleted, the result is losing weight
C. Acts on hypothalamus

Case Question4:

A 40-year-old woman, 155 cm tall and weighing 85.5 kg, seeks your advice on how to loss weught. Her waist imeasured 104 cm and her hips 99 cm. A physical examination and blood laboratory data were all withn the normal range. Her only child, who is 14 years old, her sister, and both of her parents are overweight. The patient recalls being obese thoughout her chidhood and aldolescence. Over the past 15 years she had been on seven different diets for periods of 2 weeks to 3 months, losing from 2-7 kg. On discontinuation of each diet, she regained weight, returning to 84-86 kg. Which of the following best describes this patient?

A. She is classified as overweight.
B. She shows an "apple" pattern of fat distribution.
C. She has approximately the same number of fat cells as a normal-weight individual, but each adipocyte is larger.
D. She would be expected to show lower than normal levels of circulating leptin.
E. She would be expected to show lower than normal levels of circulating triacylglycerol.

Answers:
Q1: (C)
Q2: (C)
Q3: (B)
Q4: (B)