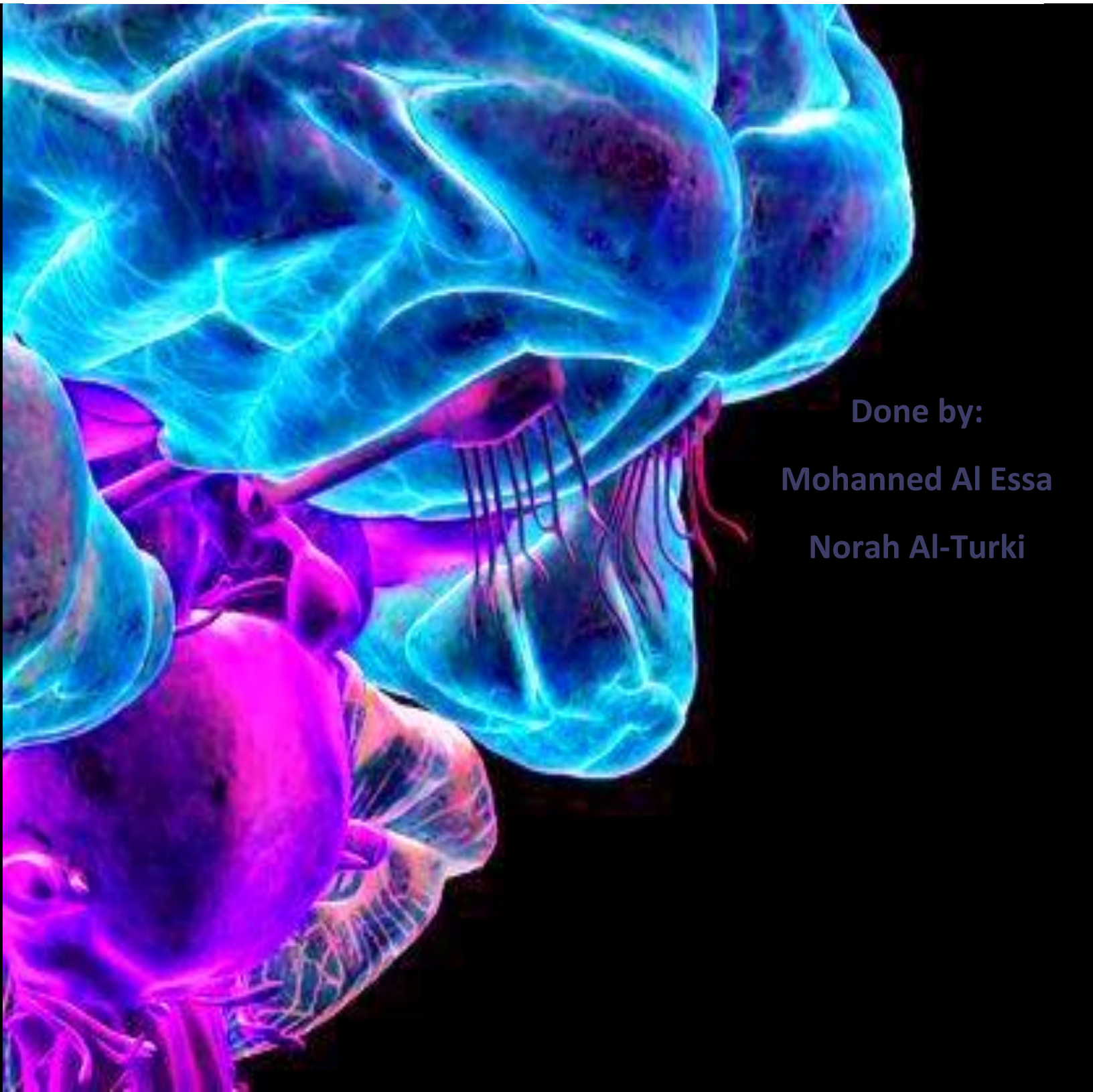# Obesity

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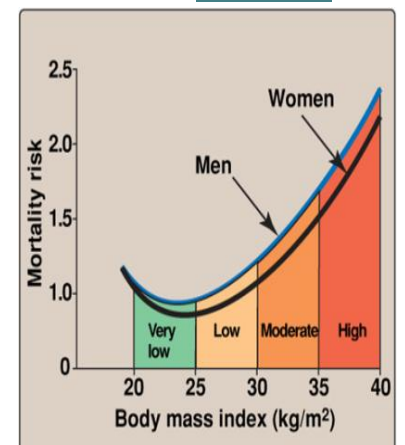
Mohanned Al Essa

Norah Al-Turki

- A disorder of body weight regulatory systems
- Causes accumulation of excess body fat
  - >20% of normal body weight "When the body weight is more than 20% of the normal range, it is called obesity".
- Obesity is associated with a high risk of:
  - Diabetes mellitus
  - Hypercholesterolemia
  - High plasma triglycerides
  - Hypertension
  - Heart disease
  - Cancer
  - Gallstones, arthritis, gout
  - Mortality

Body Mass Index (BMI):

- BMI is an indirect measure of obesity
  - **Why does the BMI considered as an indirect measure of obesity?**
  - because it measures the weight and height regardless to the muscle mass
  - For example, athletics may have high BMI (weight) though they are not obese.
  - **What is the direct measure of obesity?**
  - Dual-emission X-ray absorptiometry (DXA, previously DEXA) is a means of measuring bone mineral density (BMD). it measures total body composition and fat content with a high degree of accuracy
- Correlates height, weight and amount of body fat in an individual
  - BMI= weight(Kg)/ height(m^2)
- High BMI is associated with increased mortality risk
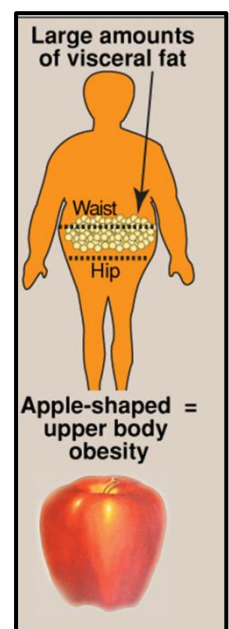
As the BMI increases, the mortality risk increases too. As you can see, the mortality risk is more/higher in men than women

	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

Anatomic differences in fat deposition

- Health risks depend on the pattern of fat deposition.
- **Android, "apple-shaped," or upper body obesity.**
- Excess body fat deposited in the central abdominal area
- Associated with risk of hypertension, insulin resistance, diabetes, dyslipidemia, and coronary heart disease
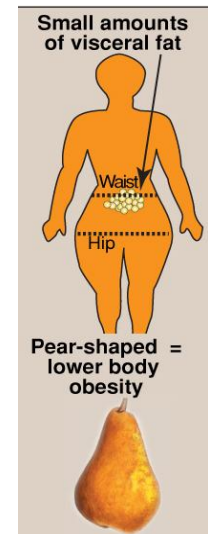
*How to measure the Android/apple-shaped obesity?
Waist to hip ratio: in women > 0.8, in men > 1

- **Gynoid, "pear-shaped," or lower body obesity**
- Fat deposited around the hips or gluteal region
- Associated risks are lower (almost the same as normal people)
- Waist to hip ratio: in women < 0.8 , in men < 1

Biochemical differences in Fat Deposits:

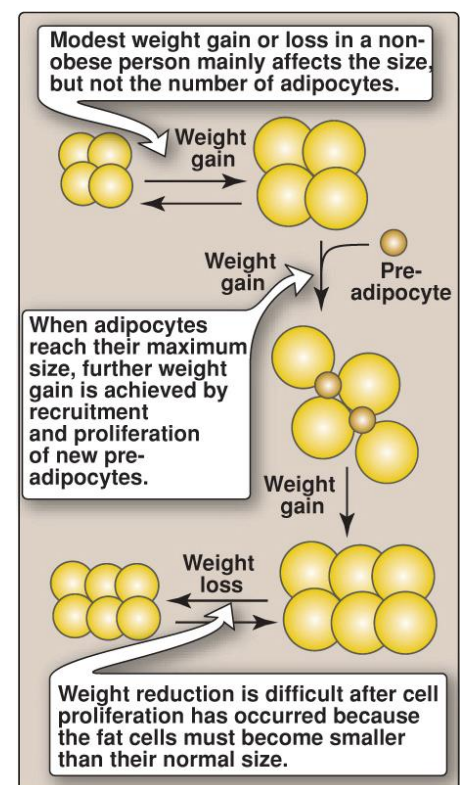| Abdominal fat	Gluteal Fat
Larger cells	Smaller cells
More responsive to hormones (easy to gain weight in the abdomen and easier to lose weight/fat from the abdomen)	Less responsive to hormones
Release substances via portal vein to the liver (that is why they are at higher risk of getting many diseases)	Release substances to circulation with no effect on the liver

Metabolic Changes in Obesity

- **Adipocytes send signals that cause abnormal metabolic changes such as:**
- Dyslipidemia
- Glucose intolerance
- Insulin resistance

Adipocytes:

- Triacylglycerols are deposited in adipocytes (fat cells)
- The cells increase in size, 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
- When a person is eating more than he/she is burning out, substances are going to be deposited as fat into adipocytes. Then, adipocytes start increasing in size, but there is a limit! (Increase in size)
- When it exceeds the limit, adipocytes will divide (increase in number) + there are stem cells in the body which are "Pre-adipocytes". They will be deposited into the adipocytes → increase in number. Now the person continues eats more and more, and these cells are getting bigger.
- When the patient wants to lose weight, it is way difficult because

there is more number in cells. Reduction in weight causes the cells to reduce the size NOT the number.

- That's why it is easier to re-gain the weight, because fat cells are already there.

Factors Contributing to Obesity:

- Genetic: familial tendency
- Environmental and behavioral
  - Sex: women more susceptible
  - Activity: lack of physical activity
  - Psychogenic: emotional deprivation/depression
  - Alcohol: problem drinking
  - Smoking "When people stop smoking, they usually gain weight"
- Drugs: e.g. antipsychotic drugs

> **Genetics** play a very important role in obesity.
> When both parents are obese → there is 70% – 80% chances their children are going to be obese
> When both parents are not obese → 9% chances that the children can be obese

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 behavior
  - Social interaction
  - Environmental factors
  - Genetics
- More in and less out = weight gain
- More out and less in = weight loss
- Hypothalamus
  - A control center for hunger and satiety
- Endocrine disorder
  - Hormonal imbalance

Hormonal Control:

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

Leptin:

- A protein hormone produced by adipocytes
- Required to keep the body weight under control
- Signals the brain about fat store levels

- 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

- The amount of Leptin in the body is proportional to the amount of fat mass.
- Signals the brain about fat store level (if there is enough fat, it tells the brain not to eat more.. If there is no fat, there will be decrease in the metabolism)
- In humans, it is not the deficiency of Leptin that caused the obesity; BUT it is the RESSISTANCE to the normal amount of leptin found in the body.
- Mutation in db gene causes leptin resistance in mice (this is in the mice, whereas in humans studies are still in progress)
db **gene:** is the name of the gene that encode leptin receptor (in mice).

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 the *db* gene causes leptin resistance in mice
- Leptin resistance may have some role in human obesity
  - Dieting decreases leptin levels
  - Reducing metabolism, stimulating appetite

Adiponectin:

- A protein hormone secreted by adipocytes **Exclusively**
- Promotes uptake and oxidation of fatty acids and glucose by muscle and liver (takes away the glucose and fatty acids from the circulation)
- Blocks the synthesis of fatty acids and gluconeogenesis by hepatocytes
- Increases insulin sensitivity / glucose tolerance
- Net effect is to increase the sensitivity to insulin, and improve glucose tolerance (that's why their defect is similar to insulin)
- Adiponectin levels are inversely correlated with body fat levels and directly with HDL levels
- Low levels are seen in metabolic syndrome and diabetes mellitus
- The more the patient is obese, the less they have Adiponectin and less HDL.
- In other words: ↑**obesity** → ↓adiponectin ↓HDL
- ↓**Obesity** → ↑adiponectin ↑HDL

Other Hormones

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

Cholecystokinin: Peptides released from the gut after a meal

- Sends satiety signals to the brain

Insulin: Promotes metabolism

Treatment Option:

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

Physical Activity

- Combined with healthy diet decreases obesity
- Reduces risk of heart disease and diabetes

Dieting

- Use of calorie-restricted diet

Drugs

Sibutramine

- An appetite suppressant
- Inhibits reuptake of both serotonin and norepinephrine (at the synaptic cleft, so that it makes them available at the synaptic cleft for longer duration)
- Serotonin and norepinephrine suppress appetite

Orlistat

- A pancreatic and gastric lipase inhibitor
- Decreases the breakdown of dietary fat
- Sibutramine + Orlistat has moderate effect on weight loss. If the patient did not lose weight in the first few months of using them, they should be discontinued.

Surgery

- Surgical procedures reduce food consumption in patients with BMI >40

- Used when other treatment options fail

Summary

- Obesity is defined as: 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 several diseases
- **Body Mass Index (BMI):**
- BMI is an indirect measure of obesity, it correlates height, weight and amount of body fat in an individual, High BMI is associated with increased mortality risk

Factors Contributing to Obesity:

- Genetic: familial tendency
- Environmental and behavioral
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- Drugs: e.g. antipsychotic drugs

Hormonal Control:

Leptin causes overweight mice to lose weight and maintain weight loss

Leptin Resistance caused by Mutation in the *db* gene causes leptin resistance in mice

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- A protein hormone secreted by adipocytes **Exclusively**
- Adiponectin levels are inversely correlated with body fat levels and directly with HDL levels
- Low levels are seen in metabolic syndrome and diabetes mellitus

Other Hormones **Ghrelin, Cholecystokinin, Insulin**.

Treatment Option:

Weight loss, Physical Activity, Dieting, Drugs, Surgery.