

ENDOCRINE SYSTEM



LECTURE 9 :

Obesity

Objectives:

- Introduction
- Body Mass Index (BMI)
- Types of fat deposition in the body
- Metabolic changes in obesity
- Adipocytes (fat cells) and weight gain
- Hormones in obesity
- Leptin, adiponectin, ghrelin, cholecystokinin
- Treatment options

OBESITY

A disorder of body weight regulatory systems. It causes accumulation of excess body fat (>20% of normal body weight)

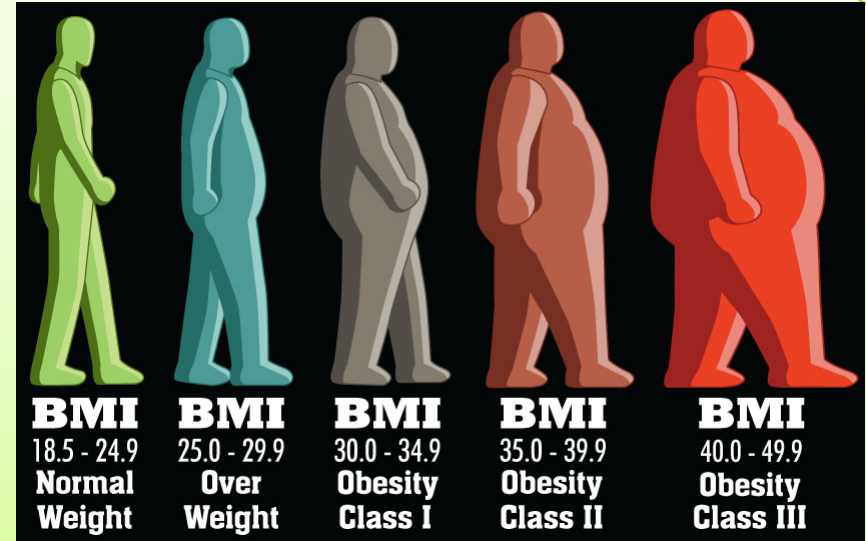
Obesity is associated with a high risk of:

- Diabetes mellitus
- High plasma triglycerides
- Heart disease
- Gallstones, arthritis, gout
- Hypercholesterolemia
- Hypertension
- Cancer
- Mortality

BODY MASS INDEX

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

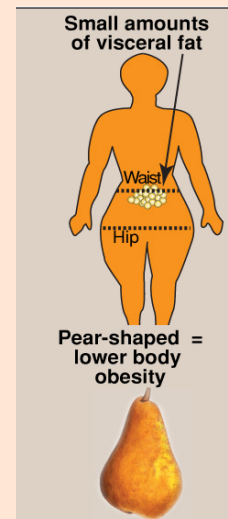
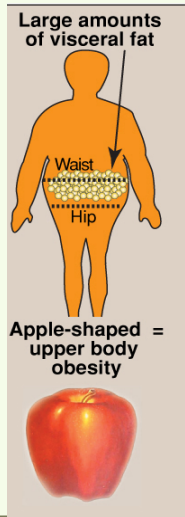
$$\text{BMI} = \frac{\text{Weight (Kg)}}{(\text{Height in metres})^2}$$



ANATOMICAL DIFFERENCE IN 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 (CHD)

- Gynoid, “pear-shaped,” or lower body obesity
- Fat deposited around the hips or gluteal region
- Associated risks are lower



Biochemical differences in fat deposits

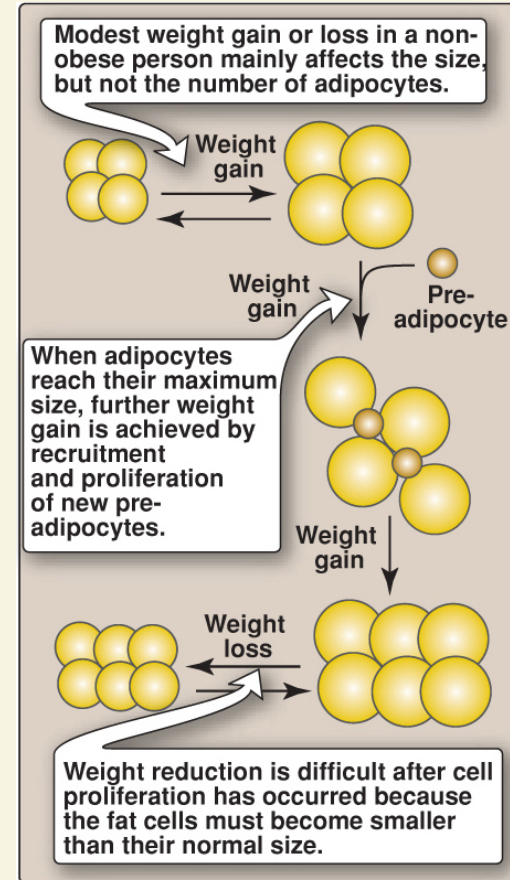
Abdominal fat	Gluteal fat
Smaller in size	Larger in size
More responsive to hormones	Less responsive to hormones
Release substance via portal vein to the liver	Release substance to circulation with no effect on the liver

Adipocytes & Metabolic changes in obesity

- Adipocytes **send signals that cause abnormal metabolic changes** such as:
 - Dyslipidemia** : ↑ triglycerides and LDL + ↓ HDL level.
 - Glucose intolerance**
 - Insulin resistance**: High Level Of TAG Induce Inflammation that triggers Release Of Specific Adibokines.
- 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**

Factors contributing to obesity

1. Genetic	Familial tendency	
2. Environmental	i. Sex	Women more susceptible
	ii. Activity	Lack of physical activity
	iii. Psychogenic	Emotional deprivation/depression
	iv. Alcohol	Drinking Problem
	V. Smoking	Smoking cessation
3. Drugs	e.g. Antipsychotic drugs	

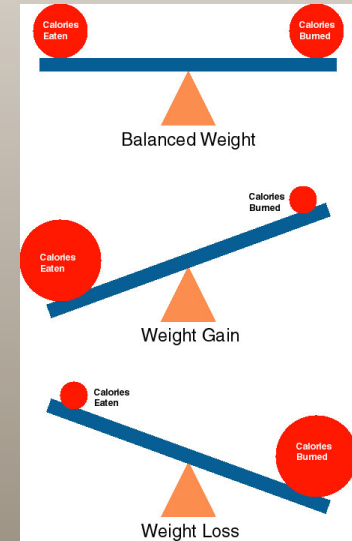


Causes of weight gain

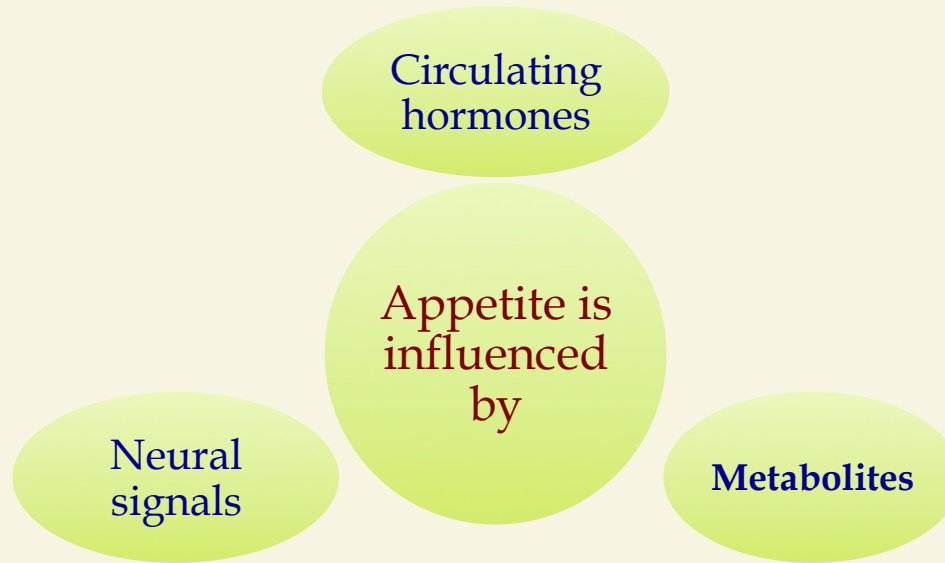
- 1. Energy imbalance:** calories consumed not equal to calories used over a long period of time.
- 2. Due to a combination of several factors**
 - Individual behavior
 - Social interaction
 - Environmental factors
 - Genetics :

More in and less out = weight gain
More out and less in = weight loss

- 3. Hypothalamus:** A control center for hunger and satiety
- 4. Endocrine disorder:** Hormonal imbalance



Hormonal control



- ❑ These signals cause the **release of hypothalamic peptides and activate neural signals**
- ❑ Adipocytes also function as endocrine cells, they release many regulatory molecules:
 1. **Leptin**
 2. **Adiponectin**
 3. **Resistin** (may cause insulin resistance observed in obesity)¹

1: Low levels of adiponectin and increased levels of resistin, may cause insulin resistance observed in obesity

LEPTIN

- ❑ A protein hormone produced by adipocytes, Required to keep the body weight under control
- ❑ FUNCTIONS: Regulates the amount of body fat by controlling appetite and energy expenditure
 1. Signals the brain about fat store levels
 2. Increases metabolic rate
 3. Decreases appetite in humans
 4. Causes and maintain loss of weight (in overweight mice)¹
- ❑ SECRETION :
 - ↑ In well-fed state (expansion of fat stores)
 - ↓ In starvation (depletion of fat stores)

Leptin Resistance

The receptor for leptin in the hypothalamus is produced by *db* gene



Mutation in the *db* gene causes leptin resistance in mice



It may have some role in human obesity :
Dieting decreases leptin levels
=> Reducing metabolism and stimulating appetite

1: Plasma leptin level in obese humans is usually normal for their fat mass

Adiponectin

- ❑ A protein hormone secreted by adipocytes
- ❑ Adiponectin levels are
 - ✓ Inversely correlated with **body fat levels**
 - ✓ Directly correlated with **HDL levels**
- ❑ Low levels are seen in: 1) **Metabolic syndrome** 2) **DM**

Functions of Adiponectin

Promotes uptake and oxidation of fatty acids and glucose by muscle and liver

Blocks the synthesis of fatty acids and gluconeogenesis by hepatocytes

Increases insulin sensitivity / glucose tolerance

OTHER HORMONES

Ghrelin:

❑ A **peptide hormone** secreted by **stomach**.

N.B: It has the complete opposite action of Leptin

❑ FUNCTIONS:

✓ Stimulates appetite

Secretion increases just before meals and drops after meals

✓ Increases food intake

✓ Decreases energy expenditure and fat catabolism

Secreted in response to: **weight loss**

The higher the weight loss, the higher the **ghrelin levels** (direct correlation)

Levels in dieters are higher after weight loss

Cholecystokinin

❑ **Peptide hormone** released from the gut **after a meal**

❑ FUNCTION:

Sends satiety signals to the brain

Insulin:

❑ Function:

Promotes metabolism

TREATMENT OPTIONS

Weight loss:

↓ Risk factors leading to:

↓ Blood pressure

↓ Serum triacylglycerols

↓ Blood glucose levels

↑ HDL levels

↓ Mortality

Beneficial changes in BMR

↓ Energy requirement

Slow weight loss is more stable



Physical Activity

+ healthy diet
= ↓ obesity

Reduces risk
of heart
disease and
diabetes



Dieting

Use of calorie-
restricted diet

Drugs

Orlistat

A pancreatic and
gastric lipase
inhibitor

=> ↓ the
breakdown of
dietary fat

Sibutramine

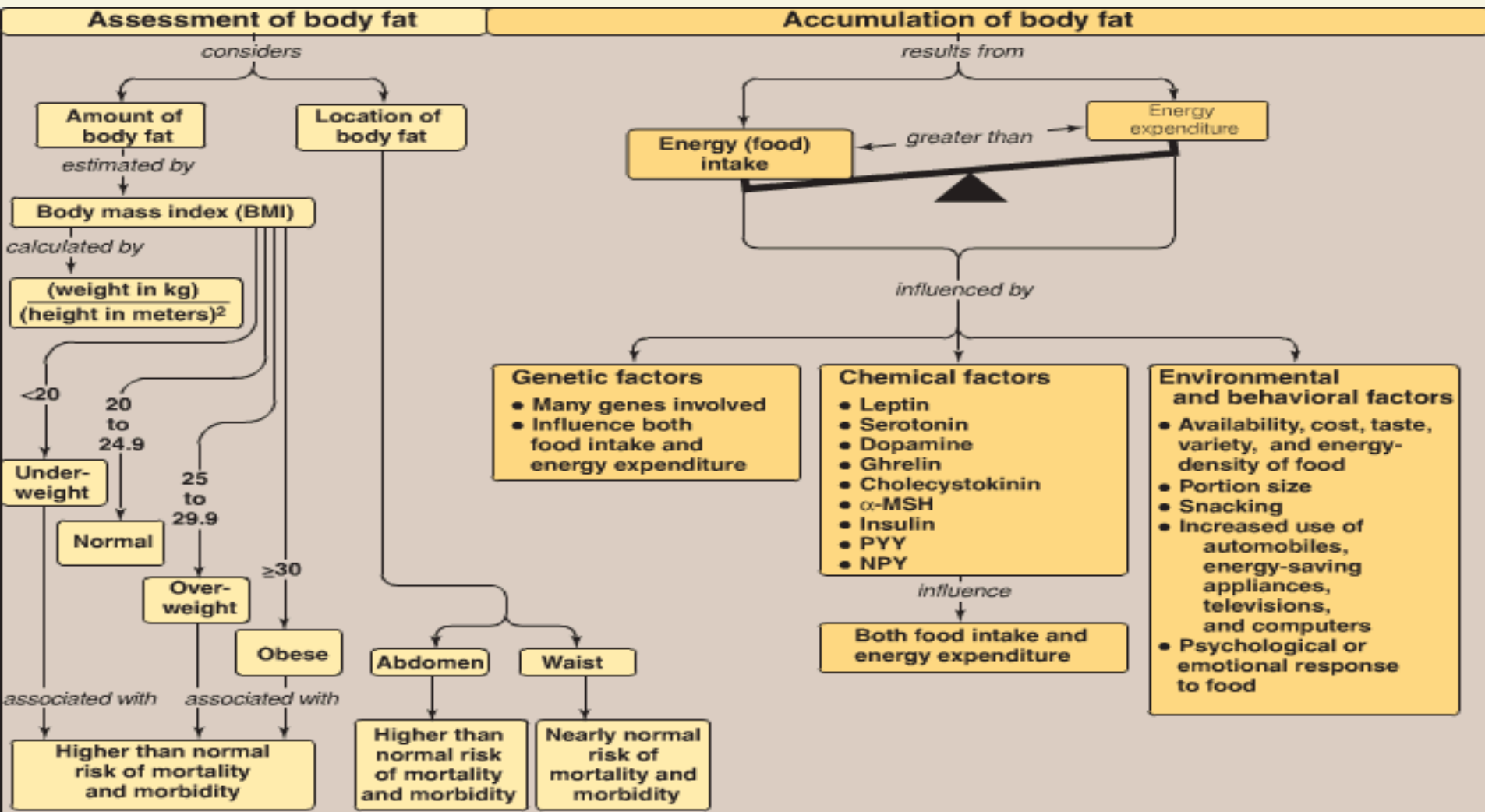
An appetite
suppressant
Inhibits the
reuptake of both
serotonin and
norepinephrine

Surgery

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

- Used when
other
treatment
options fail

Summary



TEST YOURSELF!

1: Which ONE of the following statements is NOT true regarding gluteal fat

- A- Less responsive to hormones
- B- Smaller in size
- C- Associated risks are lower
- D- Release substances in circulation

2: All the following metabolic changes occur in obesity except:

- A- Insulin resistance
- B- Glucose intolerance
- C- Protein catabolism
- D- High levels of LDL

3. Which one of the following is NOT produced by adipocytes

- A- Resistin
- B- Leptin
- C- Adiponectin
- D- CCK

4: During well-fed state, which one of the following hormones is secreted

- A- Leptin
- B- Adiponectin
- C- Ghrelin
- D- Glucagon

5: Which one of the following hormones is expected to be high in an individual who is undergoing calories-restricted diet and has lost 20 Kg:

- A- Leptin
- B- Insulin
- C- Ghrelin
- D- Glucagon

6. Leptin resistance is caused by:

- A- Fat deprivation
- B- db gene mutation
- C- Accumulation of body fat
- D- All the above

7. Which ONE of the following hormones send satiety signals to the brain

- A- Insulin
- B- Adiponectin
- C- Ghrelin
- D- CCK

8. The mechanism of action of Sibutramine is:

- A- Appetite suppressant
- B- pancreatic and gastric lipase inhibitor
- C- Inhibit reuptake of both 5-HT and NE
- D- A & C

Answers: 1) B 2) C 3) D 4) A 5)C 6) B 7) D 8) D

THANK YOU ...

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