BIOCHEMISTRY OF OBESITY

OBJECTIVES:
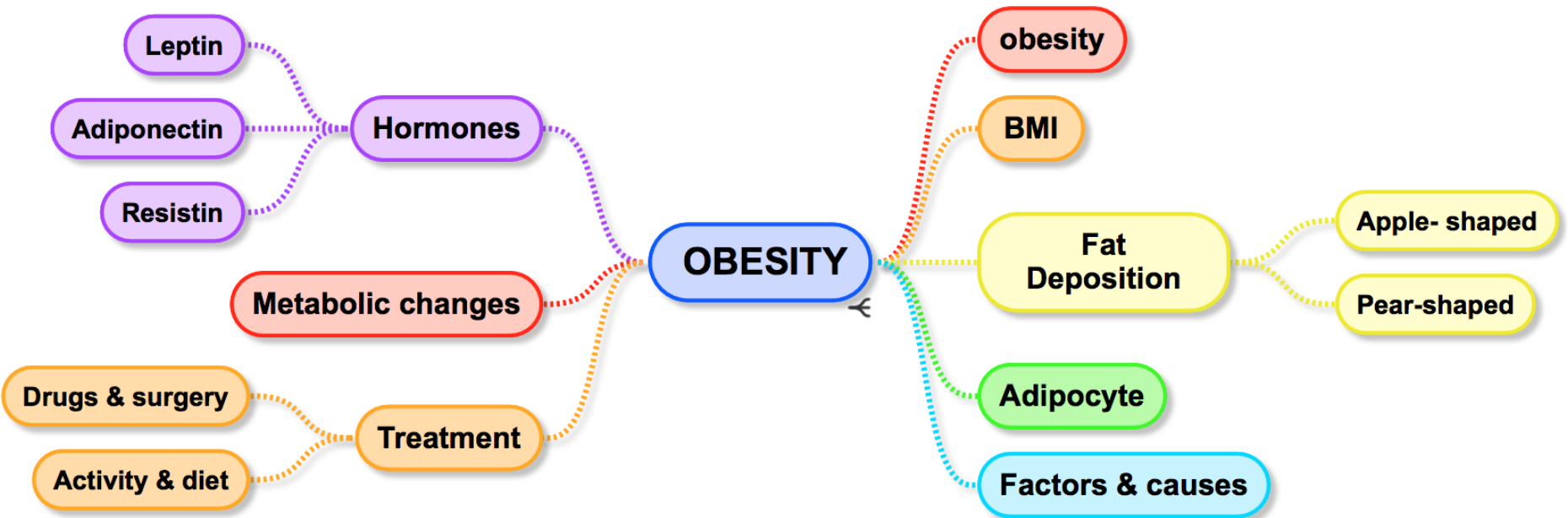
➢ Introduction

➢ 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

❖ **Important**   ❖ **Extra**   ❖ **Biochemistry Edit**

MIND MAP

INTRODUCTION

Obesity

A disorder of body weight regulatory systems .Causes accumulation of excess body fat(>20% of normal body weight)
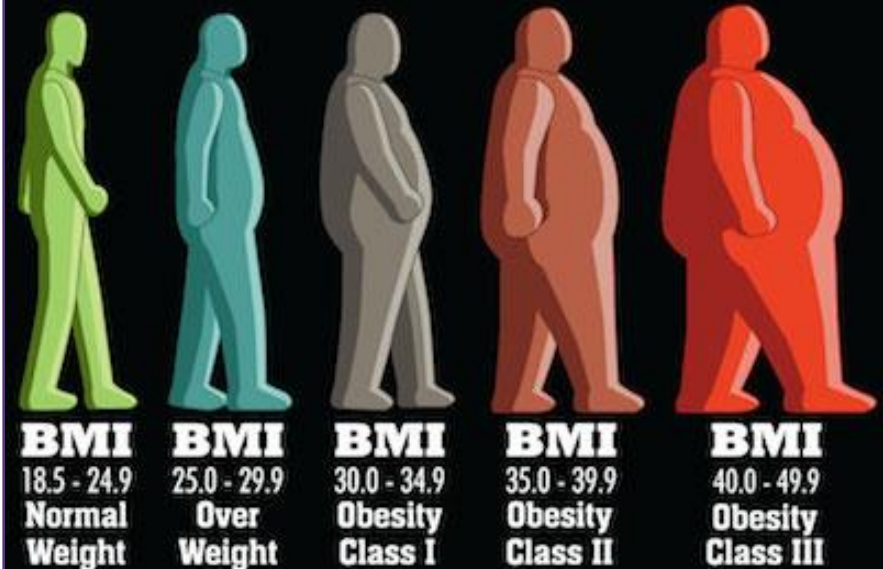
Obesity is associated with a high risk of:

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

(BMI)
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

BMI	BMI	BMI	BMI	BMI
18.5 - 24.9	25.0 - 29.9	30.0 - 34.9	35.0 - 39.9	40.0 - 49.9
Normal Weight	Over Weight	Obesity Class I	Obesity Class II	Obesity Class III

Different Fat Depots in the Body:

1-Subcutaneous Fat:
-The fat stored just under the skin in the abdominal and gluteal-femoral region.
-Constitutes 80-90% of the total fat in the body.
2-Visceral Fat: Composed of omental and mesenteric fat present in close association with digestive tract.

ANATOMIC DIFFERENCES IN FAT DEPOSITION

Android, (apple-shaped) or upper body obesity

- excess body fat deposited in the central abdominal area
- Large amounts of visceral fat.
- Associated with risk of hypertension, insulin resistance, diabetes, dyslipidemia, and coronary heart disease

Gynoid, (pear-shaped) or lower body obesity

- Fat deposited around the hips or gluteal region.
- Small amounts of visceral fat
- Associated risks are lower

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

Note: A waist-to-hip ratio of more than 0.8 for women and more than 1.0 for men is defined as "android". In contrast, a lower waist/hip ratio reflects a preponderance of fat distributed in the hips and thighs and is called "gynoid".

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
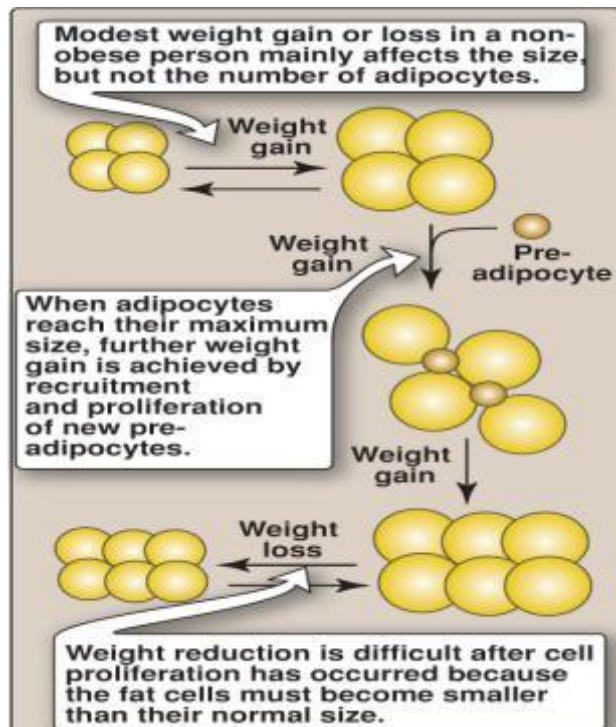
ADIPOCYTES

| Triacylglycerols (fats) are deposited in adipocytes (fat cells) which can increase in size up to a limit. | Prolonged overnutrition stimulates | Pre-adipocytes in adipose tissue | Proliferation / differentiation into mature fat cells | Increases adipocyte number |

Modest weight gain or loss in a non-obese person mainly affects the size, but not the number of adipocytes.

Weight gain

Weight gain — Pre-adipocyte

When adipocytes reach their maximum size, further weight gain is achieved by recruitment and proliferation of new pre-adipocytes.

Weight gain

Weight loss

Weight reduction is difficult after cell proliferation has occurred because the fat cells must become smaller than their normal size.

- Thus obesity is due to a combination of increased fat cell size (hypertrophy) and number (hyperplasia).

- Fat cells, once gained, are never lost

- Reduction in weight causes adipocytes to **reduce in size but not in number**.

Factors contributing to obesity

1. Genetic: familial tendency

2. Environmental and behavioral

   ❖ Sex: women more susceptible

   ❖ Activity: lack of physical activity

   ❖ Psychogenic: emotional deprivation/depression

   ❖ Alcohol: problem drinking

   ❖ Smoking: cessation of smoking

3. Drugs: e.g. tricyclic derivatives

Causes of weight Gain

1. **Energy imbalance**

   ❖ calories consumed not equal to calories used

2. **Over a long period of time**

3. **Due to a combination of several factors**

   ❖ Individual behaviors
   ❖ Social interactions
   ❖ Environmental factors
   ❖ Genetics

4. **More in and less out = weight gain**

5. **More out and less in = weight loss**

6. **Hypothalamus**

   ❖ control center for hunger and satiety

7. **Endocrine disorder**

   ❖ Hormonal imbalance
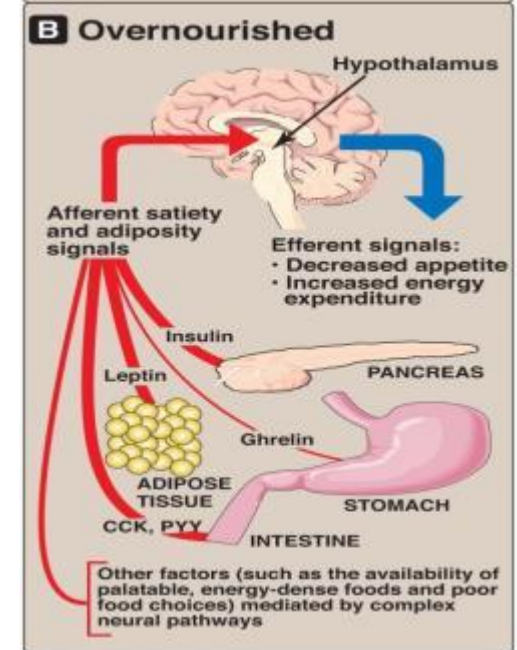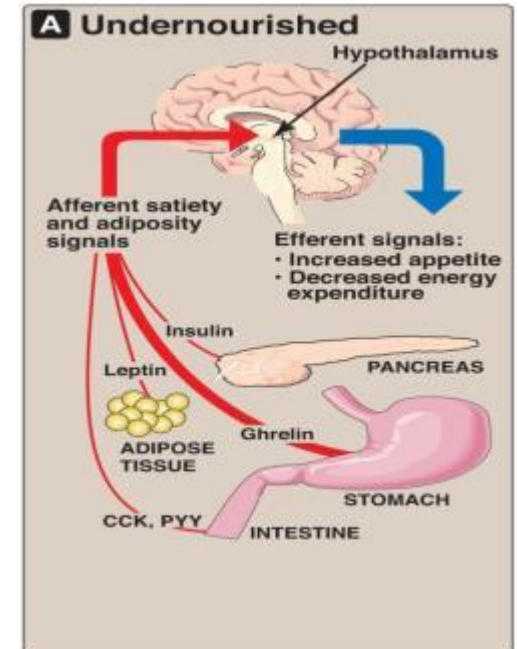
HORMONAL REGULATION

Appetite is influenced by:
- Afferent neural signals. (Vagal neurons)
- Circulating hormones. (e.g. Insulin,leptin,Ghrelin)
- 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

A) In a person who is undernourished (سوء التغذية) , Leptin, Insulin , CCK and PYY levels will be decreased , while the Ghrelin which is the hormone of hunger will increase influencing the hypothalamus causing it to release its effrent signals resulting in increasing Appetite and decreasing the expenditure of energy.

B) In a person who is overnourished Ghrelin hormone afferent will be decreased, while Leptin levels (which levels are parallel to fat stores) will be increased as well as Insulin, CCK and PYY, resulting in decreasing appetite and increasing the expenditure of energy.

A Undernourished
Hypothalamus
Afferent satiety and adiposity signals
Efferent signals:
· Increased appetite
· Decreased energy expenditure
Insulin
Leptin
PANCREAS
Ghrelin
ADIPOSE TISSUE
STOMACH
CCK, PYY
INTESTINE

B Overnourished
Hypothalamus
Afferent satiety and adiposity signals
Efferent signals:
· Decreased appetite
· Increased energy expenditure
Insulin
Leptin
PANCREAS
Ghrelin
ADIPOSE TISSUE
STOMACH
CCK, PYY
INTESTINE
Other factors (such as the availability of palatable, energy-dense foods and poor food choices) mediated by complex neural pathways

HORMONAL REGULATION

Leptin	Adiponectin	Ghrelin	Others
• Peptide hormone produced by adipocytes, it signals the brain about body fat stores and regulate their amounts by controlling appetite and energy expenditure.	• A protein hormone exclusively and abundantly secreted from adipocytes.	• Peptide Hormone secreted by stomach before the meals and drops after, it increase appetite and decrease energy expenditure.	• CCK: released from the Gut after a meal, Inducing satiety (as well as PYY)
• Leptin secretion is suppressed in starvation due to the depletion of fat stores , and enhanced in well-fed state.	• Promotes the uptake and oxidation of fatty acids and glucose by muscle and liver, and blocks the synthesis of fatty acids and gluconeogenesis by hepatocytes.	• The body step up ghrelin production in response to *weight loss*, so dieters have higher levels of it.	• Insulin: **High** in obese individuals, acts on hypothalamus to dampen[1] appetite. and promote metabolism.
• It is required to keep body weight under control.	• So it increase the sensitivity to insulin, and improve glucose tolerance.		
	• Its levels inversely correlated with body fat and parallel with HDL.		
	• Low levels in DM and metabolic syndrome		

Resistance to leptin has been found in obese humans, their leptin plasma levels are normal to their fat stores (but have no effect most likely due to the downregulation of receptors). Mutation in **db** gene (gene of leptin receptor) causes leptin resistance in mice. So leptin resistance may have role in obesity.

↑fat stores → Leptin secretion → Hypothalamus → ↓Appetite and ↑ energy expenditure
↓fat stores → suppressed leptin secretion → Hypothalamus → ↑Appetite and ↓energy expenditure

1. decrease

TREATMENT OF OBESITY

Obesity is thought to be a low grade chronic inflammation, Adipocytes send signals that cause abnormal metabolic changes such as : - dyslipidemia – Glucose intolerance – Insulin resistance , that's why it is important to treat obesity.

Weight loss **decreases risk factors for obesity Leading to:**

Lower blood pressure - Decreased serum triacylglycerol - Lower blood glucose levels - Increase in HDL levels - Decreased mortality - Beneficial changes in BMR - Decreased energy requirement
Slow weight loss is more stable

Life style
 - Physical activity combined with healthy diet decreases level of obesity & Reduces risk for heart disease and diabetes
- Dieting
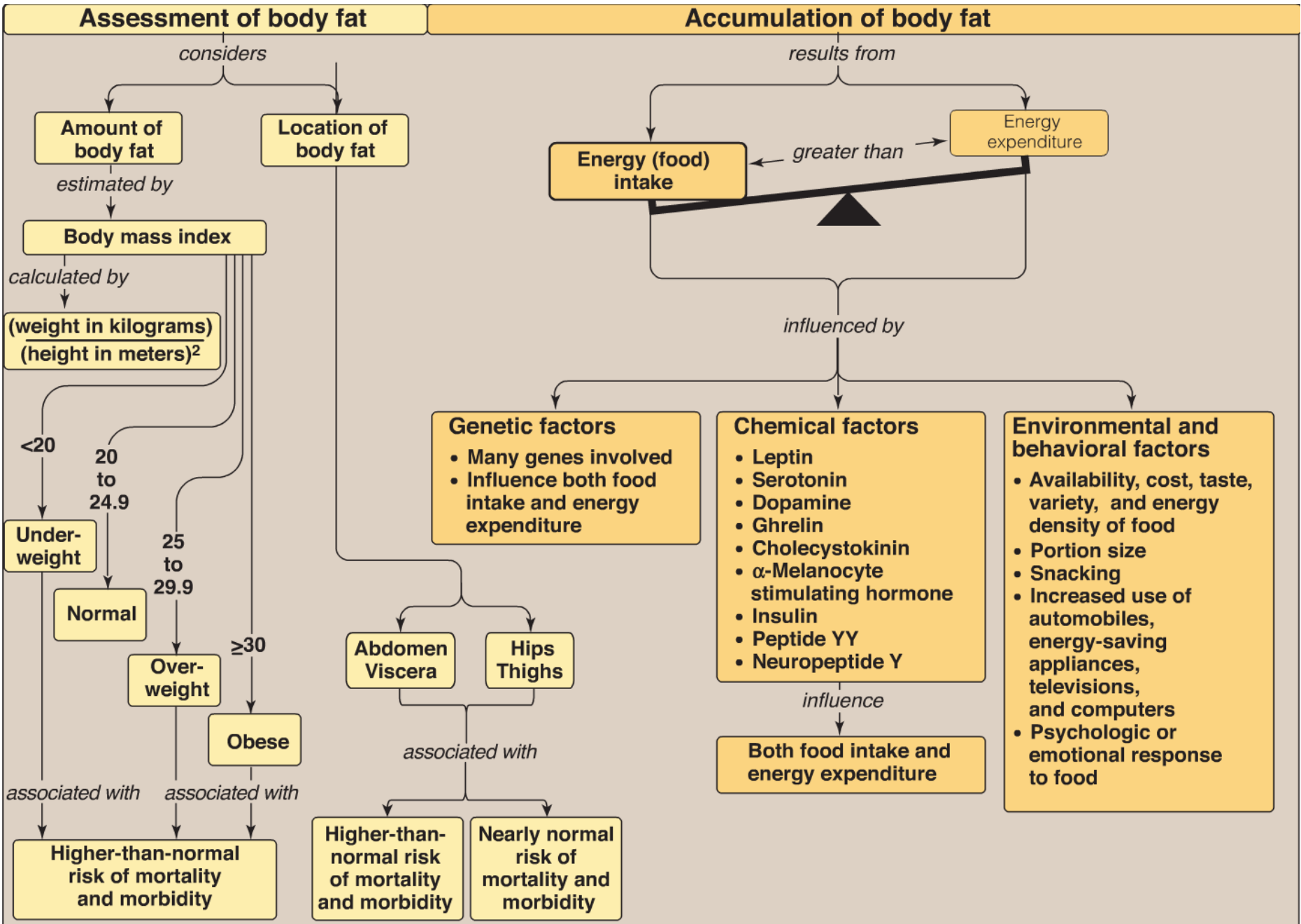Use of low-calorie diet & Restriction of excessive energy intake

Drugs
Orlistat : A pancreatic and gastric lipase inhibitor → Decreases the breakdown of dietary fat → it will not be absorbed and will be excreted.
Lorcaserin promotes satiety (selective serotonin agonist)

Surgery
Surgical procedures are designed to reduce food consumption in patients with BMI >40 , Used when other treatment options fail.

SUMMARY

Assessment of body fat

considers

- **Amount of body fat**
- **Location of body fat**

estimated by

Body mass index

calculated by

$$\frac{(\text{weight in kilograms})}{(\text{height in meters})^2}$$

- **<20** → **Under-weight**
- **20 to 24.9** → **Normal**
- **25 to 29.9** → **Over-weight**
- **≥30** → **Obese**

associated with → **Higher-than-normal risk of mortality and morbidity**

Abdomen Viscera / **Hips Thighs**

associated with

- **Higher-than-normal risk of mortality and morbidity**
- **Nearly normal risk of mortality and morbidity**

Accumulation of body fat

results from

Energy (food) intake ← *greater than* → Energy expenditure

influenced by

Genetic factors
- **Many genes involved**
- **Influence both food intake and energy expenditure**

Chemical factors
- **Leptin**
- **Serotonin**
- **Dopamine**
- **Ghrelin**
- **Cholecystokinin**
- **α-Melanocyte stimulating hormone**
- **Insulin**
- **Peptide YY**
- **Neuropeptide Y**

influence

Both food intake and energy expenditure

Environmental and behavioral factors
- **Availability, cost, taste, variety, and energy density of food**
- **Portion size**
- **Snacking**
- **Increased use of automobiles, energy-saving appliances, televisions, and computers**
- **Psychologic or emotional response to food**

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MCQS

1- Leptin is secreted from :
A) Stomach
B) Pancreas
C) Adipocytes
D) Hepatocytes

2- The majority of body fat is :
A) Subcutaneous
B) Visceral
C) Hepatic
D) Muscular

3- which of the following is a result of losing weight ?
A) High LDL levels
B) High HDL levels
C) High Blood pressure
D) High energy requirement

4- A 40 year-old woman who is waist to hip ratio is 1.05, which of the following is true about her ?
A) She has a normal number of adipocytes but larger in size .
B) She has an android body pattern.
C) She is not at high risk of developing DM or HTN.
D) She is expected to show high levels of adiponectin .

5- afferent signals of adiposity and satiety are integrated at :
A) Hippocampus
B) Thymus gland
C) Pituitary gland
D) Hypothalamus

1-c 2-a 3-b 4-b 5-d

SAQS

What are the most important factors contributing to obesity ?
1- Genetics 2- Life style 3- drugs

What are the hormone that found higher in a state of over nourishment ?
Leptin – CCK and PYY – Insulin

What is the ectopic fat ?
ectopic fat is defined by excess adipose tissue in locations not
classically associated with adipose tissue storage.

List the management options of obesity .
1- life style changes : physical activity & Diet
2- drugs : orlistat & lorcaserin
3- surgery

اللهم إني استودعك ما قرأت وما حفظت وما تعلمت فرده عند حاجتي
إنك على كل شيء قدير

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