Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Obesity

Objectives :

1. Definition of obesity
2. Pathogenesis of obesity
3. Factors predisposing to obesity
4. Complications of obesity
5. Assessment and screening of obesity
6. Management of obesity

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Resources :

Doctor's slides + Team 436
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Same as 436 slides: Yes

Obesity

Definition:

- "Abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired" WHO
- Presence of an abnormal absolute amount or relative proportion of body fat.
- Obesity means excess accumulation of fat in the body
- 20% or more over an individual's ideal body weight
- Once it develops it is difficult to 'cure' and usually persists throughout life
- Obesity is usually diagnosed on the basis of calculation of:

  ➢ Body mass index (Weight in Kg / Squared Height in meter) it is the most practical measurement for obesity but not accurate (The classification of it you will found it on slide no.6)

  ➢ Measurement of waist-hip ratio

Classification of obesity regarding fat distribution:

Android (or abdominal or central, males)

- Collection of fat mostly in the abdomen (above the waist)
- apple-shaped
- Associated with insulin resistance and heart disease

Gynoid (below the waist, females)

- Collection of fat on hips and buttocks
- pear-shaped
- Associated with mechanical problems

IMP
Steps to evaluate someone with obesity:

1. Diagnose the disease : by doing Anthropometric measurement then decide if its central obesity or not.
2. Rule out secondary causes.
3. Rule out complications (because the management will change)
4. Start treatment

Prevalence:

- Well recognized as a serious and growing public health problem
- WHO estimates that over 1.7 billion people around the world are overweight, 310 million are obese
- Rates of obesity have tripled in the last 20 years in the developing world
- In US, 33.3 % of men and 35 % of women are obese in 2007
- 15-25 % of American children are obese
- In SA: study done between 1995-2000 in age group between 30-70 on 17000 subjects
- Prevalence of overweight: 36.9 % : 42% male, 31.8 % female
- Prevalence of obesity: 35.5 % , severe obesity 3.2 % with female of 44 %, male 26.4 %
- The prevalence of overweight and obesity was higher amongst a group of married women than among a group of single women in Saudi Arabia

Surrogate measures of adiposity

- Ideal body weight
- Weight
- Anthropometric measures
- Body mass index (BMI):
- Recommended by WHO
- Relatively reliable except in:
  Extremes of age or height
  Very fit individuals with muscular build

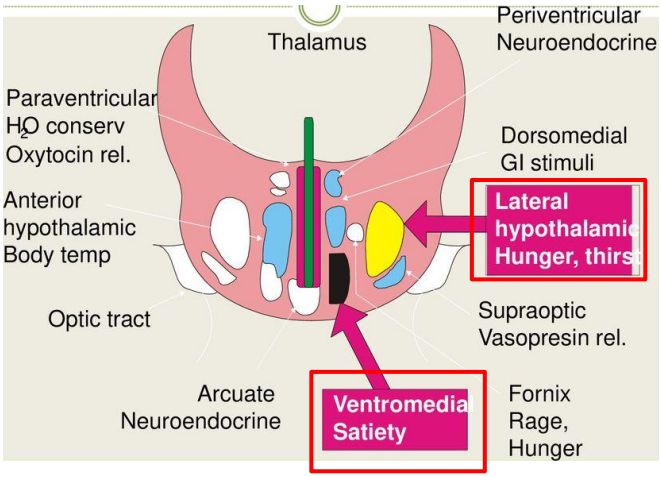
Mechanism of Obesity

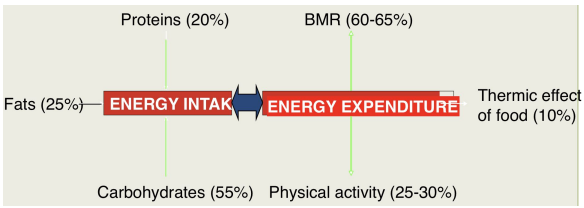
Food intake and utilization is regulated by:

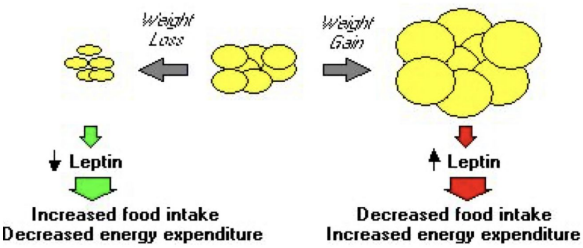
Hormones | Central nervous system | Neurotransmitters

- Signals from peripheries are carried out by neurotransmitters and hormones to CNS in presence or absence of food
- Signal from fat by hormone leptin to hypothalamus to reduce food intake and increase sympathetic activity and energy expenditure
- Gastric distension and contraction send signal for satiety and hunger
- Fall in blood sugar send signals to CNS for hunger
- Sympathetic activity from food thermogenesis leads to reduce food intake

Role of hypothalamus in mediation of hunger and satiety







Pathogenesis

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

- Control center for hunger and satiety

Endocrine disorders:

- Where are the hormones?

Hormone	Notes
Leptin	- Secreted from adipocytes - Acts on hypothalamus to decrease food intake and stimulate energy expenditure
Ghrelin	- Secreted in the stomach - Acts on hypothalamus to stimulate appetite - Peak before meal and decrease after

Obesity: How does it happen? And Predispose Factors

How does obesity happen?

Calories consumed not equal calories used
Over along period of time
Due to combination of several factors:

- Individual behaviors (10 % to BMI)
- Social interaction
- Environmental factors
- Genetic factors (40 % to BMI and adiposity) leptin deficiency.
  Note that the usual obese patient has leptin resistance not leptin deficiency .
- Neuroendocrine disease e.g. hypothyroidism
- Drug-induced e.g. SSRI "antidepressant"
- Dietary
- Reduced energy expenditure e.g. athletic got injury

Predisposing Factors of Obesity

Lifestyle:

- Sedentary lifestyle lowers energy expenditure
- 52 % of Saudi women are inactive, < 19 % doing regular physical activity
- Prolonged TV watching

Sleep deprivation:

- < 7 hours of sleep obesity
- Little sleep cause, little leptin secretion. Which increases Ghrelin secretion, that lead to have more appetite and CHO eating at night

Cessation of smoking:

- Average weight gain is 4 kg
- Due to nicotine withdrawal
- Can be prevented by calories restriction and exercise prograr

Social influences:

- Obese parents most likely to have obese children
- Obese individuals are surrounded by obese friends

Diet:

- Overeating, frequency of eating, high fat meal, fast food(> 2 fast food/wk)
- High carbohydrate and high fat diet
- Night eating syndrome: if > 25 % of intake in the evening

Energy expenditure:

- Resting metabolism
- Physical exercise
- Dietary thermogenesis (thermic effect of food)
- Adaptive thermogenesis

Table 1. Causes of Obesity

Excessive/inappropriate food intake
Sedentary lifestyle
Genetic disorders with obesity
Prader-Willi syndrome
Bardet-Biedl syndrome
Carpenter's syndrome (acrocephalopolysyndactyly type II)
Cohen syndrome
Endocrine disorders
Cushing's syndrome
Hypothalamic tumors/inflammation/trauma
Hypothyroidism
Polycystic ovary syndrome
Insulinoma
Drugs
Antipsychotics, especially atypical agents
Tricyclic antidepressants
Sulfonylureas
Insulin
β Blockers
Corticosteroids
Estrogen
Progestins

Health consequences of obesity

Greater BMI is associated with increased death from all causes and from CVD

Although overweight associated with decreased survival

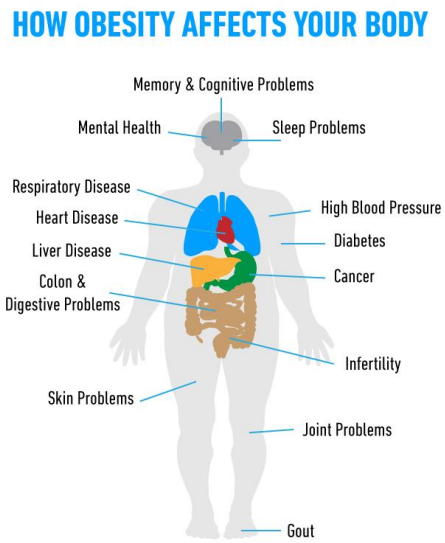
Each 5 kg/m2 increase in BMI was associated with significant increase in mortality related to:

- IHD and stroke
- Diabetes and non-neoplastic kidney disease
- Different types of cancer
- Respiratory disease
- Obesity is associated with reduction in life expectancy during adulthood

Increase in BMI is associated with increase in morbidity and CVD risk factors

For both men and women, increasing BMI was associated with higher death rates due to the following cancers:

- Esophagus
- Colon and rectum
- Liver
- Gallbladder
- Pancreas
- Kidney
- Non-Hodgkin lymphoma
- Multiple myeloma



Other consequences:

- Increase cost rate on obesity
- Increase number of sick leaves for obese subject
- Increase number of hospitalization
- Early age of retirement
- Increase cost of drugs for DM, CVD, GI disease
- Poor quality of life due to psychosocial issues

Central Obesity

Central or visceral obesity is associated with more metabolic disease:

- DM2
- Hypertension
- Dyslipidemia

? How to assess central or visceral obesity?

- MRI
- Dual X-ray absorptiometry (DEXA)
- Single CT slice L4/L5
- Waist: hip ratio
- Waist circumference the most practical

(Waist : hip ratio) is the narrowest circumference midway between the lower border of the ribs and the upper border of the iliac crest, taken from the side

Assessment and Screening

Screening of adults for obesity is important
With significant increase in morbidity and mortality
Although not in routine practice but it should be as a part of periodic health assessment
Screening:

BMI measurement | Evaluation of overall medical risks | Waist circumference

BMI measurement:

- Reliable, easy, correlated with percentage of body fat
- Guide for selection of therapy
- Varies among different races
- Recent WHO classification applied to whites, hispanics and black
- Asians are different: overweight BMI 23-24.9 kg/m2 and obesity by BMI > 25 kg/m2 IMPORTANT

Classification	BMI (Kg/m^2)	Risk of comorbidities
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal	18.5 - 24.9	Average
Overweight	25.0 - 29.9	Mildly increased
Obese class I	30.0 - 34.9	Moderate
Obese class II	35.0 - 39.9	Severe
Obese class III	≥ 40.0	Very Severe

Waist circumference:

- Measurement of central adiposity
- Associated with increased risk of morbidity and mortality
- Reflects visceral adiposity
- Increase risk of heart disease, DM, hypertension, dyslipidemia
- Important in identifying the risk in BMI 25-34.9 kg/m2
- Risk increase with WC > 88 cm in women, 102 cm in men
- Not useful if BMI > 35 kg/m2
- In Asian population risk starts with WC > 80 cm in Asian women and > 90 cm in Asian men

Identify the aetiology:

- Medical history is important
- Age at onset of obesity, course of it
- Eating habits, activity habits
- Past medical history
- Medications
- Cessation of smoking history
- Ethnic background
- Family history of obesity

Assessment and Screening

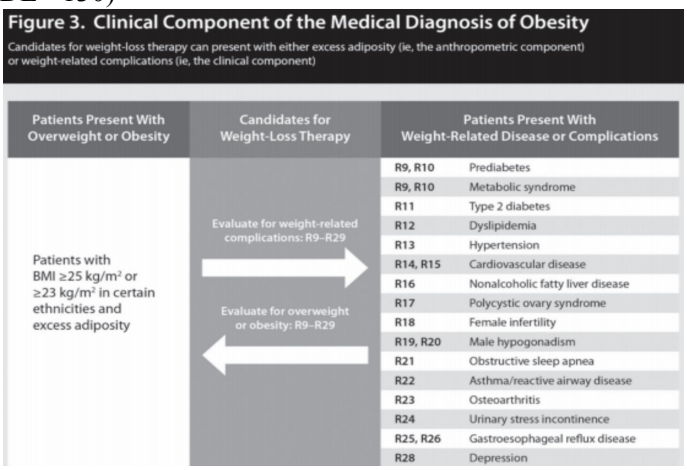
Assessment of risk status

- **Identify risk factors:**
  After BMI and WC, history
  BP measurement
  Fasting lipid profile
  Fasting blood sugar

- **Identify comorbidity:**
  Help to classify the risk of mortality
  Presence of atherosclerosis, DM2, HTN, dyslipidemia
  Sleep apnoea
  GI, osteoarthritis, gout

- **CVD risk factors that would affect mortality risk:**
  HTN
  DM2 (fasting blood glucose 110-125 mg/dl)
  Smoking
  Dyslipidemia (low HDL < 35 or high LDL> 130)
  Family history of premature CAD
  Physical inactivity

- **other risk factors:**
  Age of onset of obesity



Why is it important to look at it?

- It is a common disease with significant morbidity and mortality and without screening many high risk patients may not receive counseling about health risks, lifestyle changes, obesity treatment options, and risk factor reduction.
- Screening with BMI, waist circumference, and risk factor assessment is inexpensive and available to nearly all clinicians.
- Weight loss is associated with a reduction in obesity associated morbidity.

What will happen when lose weight?

- Weight loss of 0.5-9 kg (n=43,457) associated with 53% reduction in cancer-deaths, 44% reduction in diabetes associated mortality and 20% reduction in total mortality
- Survival increased 3-4 months for every kilogram of weight loss
- Reduced hyperlipidemia, hypertension and insulin resistance
- Improvement in severity of diseases
- Person feels ‘fit’ and mentally more active

Management

Lifestyle

Diet | **Exercise**

Medication

Surgery

Steps in treatment:

1. the foundation is a healthy lifestyle.
2. Refer to a dietitian.
3. Exercises (210 min/week) "it won't make the pt lose weight, exercises just for maintaining weight loss ".
4. Medications

Treatment Goal:

- Prevention of further weight gain
- Weight loss to achieve a realistic, target BMI
- Long-term maintenance of a lower body-weight this is the hardest part!

How much weight loss is significant?

A 5-10% reduction in weight (within 6 months) and weight maintenance should be stressed in any weight loss program and contributes significantly to decreased morbidity

The main interventions

The treatment of obesity comes in an arranged steps:
First: Lifestyle intervention (diet, exercise)
Second: Pharmacotherapy
Third: Surgical intervention

Life Style

Initial goal: 10% weight loss

- Significantly decreases risk factors

Rate of weight loss:

- 1-2 pound per week
- Reduction of calories intake 500-1000 calories/day

Slow weight loss is preferred approach

- Rapid weight loss is almost always followed by rapid weight gain
- Rapid weight loss is associated with gallstones and electrolytes abnormalities

Advices:

Aim for 4-6 months for weight loss
Average is 8-10 kg loss
After 6 months, weight loss is difficult

- Ghrelin and leptin effect
- Energy requirement decreased as weight decreases

Set goals for weight maintenance for next 6 months then reassess

Management

Lifestyle

Diet | **Exercise** | **Medication** | **Surgery**

Diet

- Indicated for all with BMI > 30 and those with BMI 25- 30 with comorbidities
- Teaching about food composition (fat, CHO, protein)
- Calories contents of food by reading labels
- Type of food to buy and to prepare

Careful Training in :

- Selection of lower fat, lower carb foods
- Modified food guide pyramid
- Increase fruits & vegetables
- Lower fat preparation techniques
- Estimation of portion size

Advices:

- Low calories diet-portion controlled
- Low fat diet
- Low CHO diet
- Mediterranean diet
- Average for women: 1000-1200 kcal/day
- Average for men: 1200-1600 kcal/day
- Adjust based on activity and weight

How much is 1200 calories?

- 1 big mac (580)
- 1 small fries (210)
- 1 small shake (430)

Then weight maintenance

How much should people eat?

Male	Age 20 - 49	2900 Kcal/day
	Age 50 +	2500 Kcal/day
Female	Age 20 - 49	2300 Kcal/day
	Age 50 +	1900 Kcal/day

Table 9. Association of Eating Patterns and Macronutrient Composition on Weight-Loss Efficacy

Eating Pattern or Macronutrient Change	Effect	Reference [EL]
Low glycemic index/load	↑ Endothelial function ↓ Glycemic variability Effects on energy expenditure Decreased adipocyte diameter No incremental effect on weight loss[1]	33 [EL 1; RCT], 34 [EL 1; RCT], 35 [EL 1; RCT, small N=13], 36 [EL 1; RCT]
Low carbohydrate	Improved glycemic status and lipids Improved other cardio-metabolic risk factors Improved renal function No incremental effect on weight loss (some studies show more short-term weight loss)[2]	37 [EL 4; NE], 38 [EL 1; RCT], 39 [EL 1; RCT], 40 [EL 1; RCT], 41 [EL 1; RCT], 42 [EL 1; RCT], 43 [EL 2; NRCT], 44 [EL 1; RCT], 45 [EL 1; RCT], 46 [EL 1; RCT], 47 [EL 1; RCT]
High protein	Longer benefit on WC, %fat Improved cardio-metabolic risk factors Decreased adipocyte diameter Animal (not plant) proteins associated with markers of inflammation Less relative loss of muscle mass No incremental effect on weight loss	33 [EL 1; RCT], 38 [EL 1; RCT], 45 [EL 1; RCT], 48 [EL 1; RCT], 49 [EL 1; RCT], 50 [EL 1; RCT], 51 [EL 1; RCT], 52 [EL 1; RCT], 53 [EL 1; RCT]
Moderate carbohydrate – moderate protein	Improved body composition, lipid, ppINS No incremental effect on weight loss	37 [EL 4; NE]. 54 [EL 1; RCT]
Low fat	Beneficial effects on lipids Benefits on lipids replacing with unsaturated fat Improved renal function No incremental effect on weight loss	37 [EL 4; NE], 41 [EL 1; RCT], 47 [EL 1; RCT], 55 [EL 1; RCT], 56 [EL 1; RCT]
High fat	With lactation: when hypocaloric, great weight loss compared with hypocaloric low-carbohydrate diet	57 [EL 2; PCS]
Mediterranean-style	Decreased risk certain cancers EVOO supplementation – no effect on weight Reduces cardio-metabolic risk factors and MetS Reduces markers of inflammation Improves hepatic steatosis and insulin sensitivity Improves renal function No incremental effect on weight loss	40 [EL 1; RCT], 58 [EL 1; RCT, post-hoc analysis], 59 [EL 2; PCS, post-hoc analysis], 60 [EL 1; RCT, secondary analysis], 61 [EL 2; PCS], 62 [EL 1; RCT], 63 [EL 1; RCT], 64 [EL 2; PCS], 65 [EL 2; PCS], 66 [EL 1; RCT]

Abbreviations: EL = evidence level; EVOO = extra-virgin olive oil; MetS = metabolic syndrome; ppINS = postprandial insulin response; WC = waist circumference.

[1] Incremental effect in comparison to a isocaloric control diet does not occur or is inconsistent.

[2] Short-term is <1 year.

Management

Lifestyle

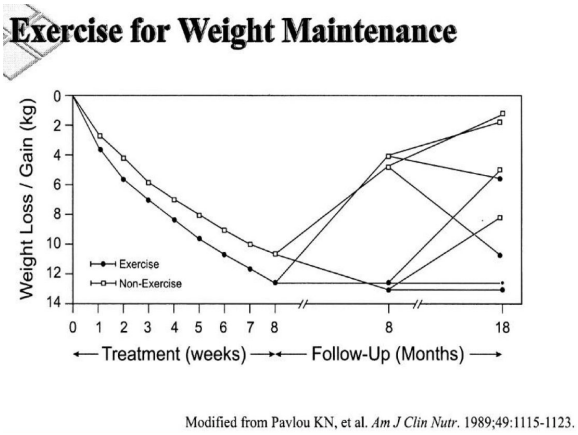
Diet | **Exercise**

Medication

Surgery

Exercise

- As integral part of weight loss
- Reduce risk of DM, heart disease, hypertension
- Alone is not helping
- Help to prevent weight regain



Modified from Pavlou KN, et al. *Am J Clin Nutr.* 1989;49:1115-1123.

advices:

Start slowly

- Change of daily living activities
- Avoid injury

Increase intensity and duration gradually

Long –term goal:

- 30-45 min or more of physical activity daily
- 5 or more days per week
- Burn 1000+ calories per week

Behavioral strategies

Keep agenda of diet and activity

- Set specific goals regarding: diet, activity related behavior
- Reminder system
- Reward yourself
- Don't deprive yourself, watch portion

Track improvement:

- Weight measurement on regular basis

Management

Lifestyle

Diet | **Exercise**

Medication

Surgery

Medication:

Average weight loss by medication **only** is 4-5 kg per year which is not effective.

Indicated in:

- BMI > 30
- BMI 27-30 with comorbidities
- Should not be used for cosmetic weight loss
- Used only when 6 months trial if weight and exercise fail to achieve weight loss

Sympathomimetics:

- Stimulate release of norepinephrine or inhibits its reuptake by nerve terminals
- Block serotonin and NE reuptake (sibutramine)
- Directly act upon adrenergic receptor
- Reduced appetite by early satiety

Pancreatic lipase inhibitor:

- Orlistat: inhibits fat absorption

Antidepressant

Antiepileptic

Diabetic drugs: metformin

Drugs approved by the FDA for treatment of obesity

Drug	Trade names	Dosage	DEA schedule
Pancreatic Lipase inhibitor approved for long-term use			
Orlistat	Xenical	120 mg three times daily before meals	-
Norepinephrine-serotonin reuptake inhibitor approved for long-term use			
Sibutramine	Meridia	5 to 15 mg/day	IV
	Reductil		
Noradrenergic drugs approved for short-term use			
Diethylpropion	Tenuate	25 mg three times daily	IV
	Tenuate Dospan	75 mg every morning	
Phentermine	Adipex	15 to 37.5 mg/day	IV
	Ionamin Slow Release	15 to 30 mg/day	
Benzphetamine	Didrex	25 to 50 mg three times daily	III
Phendimetrazine	Bontril	17.5 to 70 mg three times daily	III
	Prelu-2	105 mg daily	

UpToDate

***Orlistat**

- A lipase inhibitor, reduces the absorption of dietary fat
- Lowers Cholesterol (4-11%) & LDL (5-10%)
- Major C/I:
  - Chronic malabsorption syndrome
  - Cholestasis
  - Pregnancy and breastfeeding
- Dose:
  - 120 mg/ immediately before, during, or up to 1 hour after each main meal (up to max. 360 mg/day)
  - Max. period of treatment is 2 year

Management

Lifestyle

Diet | **Exercise**

Medication

Surgery

Surgery

Indicated in:

- Well-informed and motivated patients
- Have BMI > 40
- Acceptable risk of surgery
- Failed previous non-surgical method
- BMI > 35 with comorbidities like diabetes, sleep apnea, osteoarthritis, cardiomyopathy
- BMI 25-29.9 with WC > 102 cm in male and 88 cm in women
- Age 18-60
- Psychologically stable

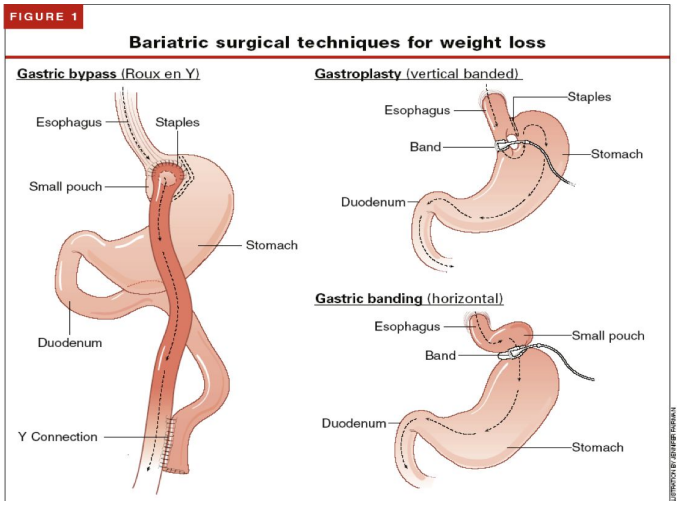
Restrictive-type of surgery:

- Vertical banded-gastroplasty
- Gastric banding

Malabsorptive and restrictive:

- Roux-en-Y gastric bypass
- Biliopancreatic diversion

Follow up is crucial



Summary

Obesity: “Abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired”

Predisposing Factors of Obesity :
1.Lifestyle
2. Sleep deprivation → less than 7 hours → ↓ leptin, ↑↑ Ghrelin → ↑ appetite
3. Cessation of smoking → due to nicotine withdrawal
4. Social influence (Obese parents most likely to have obese children)
5. Diet (Night eating syndrome: if > 25 % of intake in the evening)

Classification of obesity regarding fat distribution:

Android (males)	Gynoid (females)
• Collection of fat mostly in the abdomen (above the waist) • - apple-shaped • - Associated with insulin resistance and heart disease	• Collection of fat on hips and buttocks • - pear-shaped • - Associated with mechanical problems

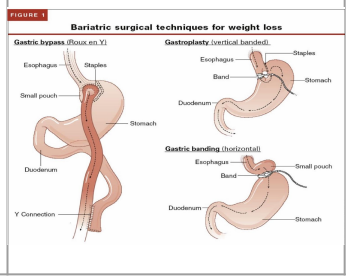
Hormones:

Leptin: from adipocytes, acts on hypothalamus to decrease food intake and stimulate energy expenditure.
Ghrelin: Secreted in the stomach, acts on hypothalamus to stimulate appetite, peak before meal and decrease after.

Screening for obesity

1.BMI measurement (underweight<18.5, normal 18.5-24.9, overweight 25-29.9, obese>30)
2. Waist circumference (Risk increase with WC > 88 cm in women, 102 cm in men)
3. Evaluation of overall medical risks

Management:

Diet	Exercise	Medications	Surgery
Indicated for all with BMI > 30 and those with BMI 25- 30 with comorbidities. -Average for women: 1000-1200 kcal/day - Average for men: 1200-1600 kcal/day	-30-45 min or more of physical activity daily. - 5 or more days per week. - Burn 1000+ calories per week.	Indication: BMI above 30, BMI 27-30 with comorbidities. Types: **Sympathomimetics** (sibutramine), **Pancreatic lipase inhibitor** (Orlistat), **antidepressants antiepileptic**, **diabetic drug** metformin	Indication: BMI above 40, BMI above 35 with comorbidities. 

Questions

1-Which of the following is the most common metabolic complications of obesity
A. Osteoarthritis .
B. Obstructive sleep apnea .
C. Colon cancer.
D. Diabetes mellitus.

2- Which one of the following is the best option in managing, 53 years old obese male with BMI=46 and known to have comorbidity such as DM and HTN ?
A. Lifestyle modification
B. Surgery
C. Medications such as sibutramine
D. Refer him to dietitian.

3- Which of the following is a healthy waist circumference for men and women?
A. Less than 94 cm and 80 cm respectively
B. Less than 65cm and 55cm respectively
C. Less than 102 cm and 88 cm respectively
D. Less than 70 regardless of gender

4- Which one of the following hormones suppresses the appetite?
A.Ghalin
B.Glycogen
C.Leptin
D.Somatostatin

5- choose the true statement about lower abdominal obesity?
A. also called apple shaped obesity
B. waist to hip ratio(<1.0 for women and <0.8 for men)
C. relatively common in females
D. associated with increase risk for coronary heart disease, stroke and DM

6- Which of the following is a contraindication for Orlistat ?
A- pregnancy
B- Cholestasis
C- Chronic malabsorption syndrome
D- All of the above

7- Which of the following is a Malabsorptive and restrictive type of surgery ?
A- Vertical banded-gastroplasy
B- Roux-en-Y gastric bypass
C- Biliopancreatic diversion
D- B&C

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