

MEDICINE: OBESITY



Sources: Dr. Assim Alfadda's lecture, Dr. Aishah Ali Ekhzaimy's lecture, 427 Clinical Medicine Notes
429 Medicine Team
Questions? <http://ask.fm/TeamNotes429>

OBESITY

DEFINITION

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

WHO RECOMMENDED DEFINITION OF OBESITY (2000)

<u>Classification</u>	<u>BMI (kg/m²)</u>	<u>Risk of co-morbidities</u>
Underweight	<18.5	Low (but risk of other clinical problems increased)
Normal	18.5 – 24.9	Average
Overweight (pre-obese)	25 – 29.5	Mildly increased
Obese <ul style="list-style-type: none">• Class I• Class II• Class III	>30 <ul style="list-style-type: none">• 30 – 34.5• 35 – 39.9• >40	<ul style="list-style-type: none">• Moderately increased• Severely increased• Very severe increase

Remember:

$$\text{BMI Calculation (kg/m}^2\text{)} = \frac{\text{Weight (Kg)}}{\text{Height squared (meters)}}$$

PREVALENCE OF OBESITY

- Obesity is a 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 were obese in 2007
- Obesity increased from 5 to 10 % (1980 to 2008) in preschool children, from 5.6 to 19% in school age children, and from 5 to 18 % among adolescents in the US
- 15-25 % of American children are obese
- In SA: a study done between 1995-2000 in an age group between 30-70 on 17000 subjects revealed that:
 - The prevalence of overweight was: 36.9 %, 42% male, and 31.8 % female
 - The prevalence of obesity was: 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

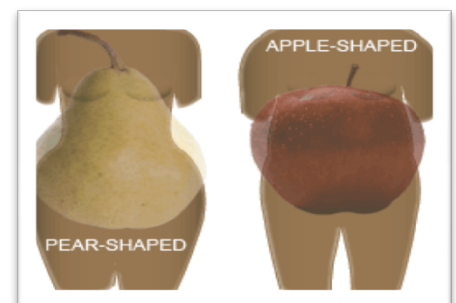
CLASSIFICATION OF OBESITY PER FAT DISTRIBUTION

1. Android (central, visceral, or abdominal obesity; apple shaped)

- Seen mainly in males
- Collection of fat mostly in the abdomen (above the waist)
- Associated with more metabolic diseases: insulin resistance and type 2 DM, hypertension and Dyslipidemia
- How to assess central obesity: waist circumference (the narrowest circumference midway between the lower border of the ribs and upper border of the iliac crest, taken from the side), waist: hip ratio, MRI (time consuming and expensive), DEXA (dual x-ray absorptiometry), or a single CT slice L4/L5

2. Gynoid (below the waist; pear shaped)

- Seen mainly in females
- Collection of fat on hips and buttocks
- Associated with mechanical problems



MECHANISM OF OBESITY: ETIOLOGY AND PATHOGENESIS

- Food intake and utilization is regulated by:
 - Hormones
 - Neurotransmitters
 - Central nervous system
- Signals from peripheries are carried out by neurotransmitters and hormones to CNS in presence or absence of food
- Gut to brain signaling: hypothalamic modulators of food intake

Orexigenic (increase food intake)	Anorexigenic (decrease food intake)
NPY	CCK
AGRP	INSULIN
GHRELIN	LEPTIN
MCH	GLP-1
GALANIN	CRH
OREXIN	α-MSH
NORADRENALINE	PPY 3-36
ENDOCANNABINOIDS	UROCORTIN
M, K OPIODS	CART
NEUROTRANSMITTERS	BOMBESIN

Remember:

- Leptin: secreted from adipocytes, acts on hypothalamus to decrease food intake and stimulate sympathetic activity and energy expenditure
- Ghrelin: a recently discovered Orexigenic hormone; secreted from the stomach and duodenum, acts on hypothalamus to stimulate appetite. It peaks before meals and decrease after. Has been implicated in both mealtime hunger and long-term regulation of body weight
- 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

ETIOLOGY AND PATHOGENESIS

- Multifactorial
- Biochemical/Dietary/behavioral pathways
- Imbalance between energy intake and energy expenditure
- Body weight is ultimately determined by the interaction of:
 - Genetic
 - Environmental and
 - Psychosocial factors
 - Acting through several physiological mediators of food intake and energy expenditure

ETIOLOGICAL CLASSIFICATION OF OBESITY

1. NEUROENDOCRINE DISEASES

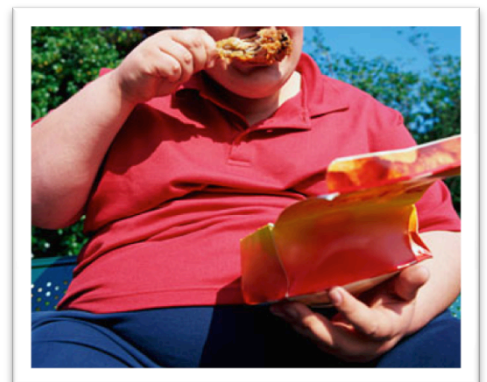
- Ventromedial hypothalamus damage: tumors, inflammatory lesions, or other hypothalamic diseases
- Cushing disease: GH deficiency, hypothyroidism

2. DRUG INDUCED

- Hyperinsulinism: insulin, sulfonylureas
- Antidepressants
- Antiepileptics
- Neuroleptics
- Steroids

3. DIETRY

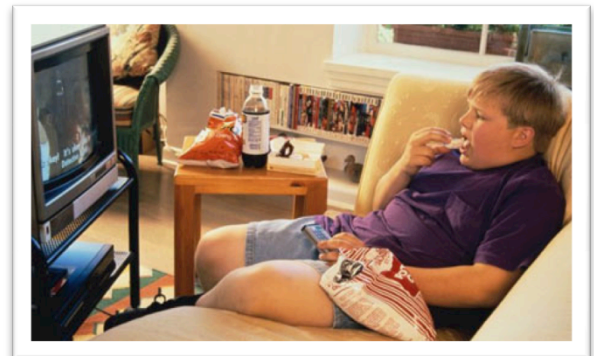
- High carbohydrate diet: surplus carbohydrate energy is NOT converted to fat. Instead, it will lead to accrual of body fat by sparing oxidation of dietary fat
- High fat diet:
(Clinical studies on humans)



- The body fat mass was positively correlated with intakes of total fat, saturated fatty acids, and monounsaturated fatty acids
- Body fat did not correlate with total energy intake in this study
- It was concluded that fat intake, independent of energy intake, may be associated with body fatness
- Thus, at a given level of energy intake, specific sources of energy in the diet may differentially affect weight gain (Epidemiological studies)
- The relationship between dietary fat and body weight is suggestive but not definitive
- Cross-sectional studies: positive relationship between dietary fat and body weight
- Longitudinal studies have shown inconsistent results, the reason for this inconsistency are not clear
- Several factors are involved: genetic, metabolic, physical activity, smoking habits, and behavioral factors (dieting in response to weight gain)

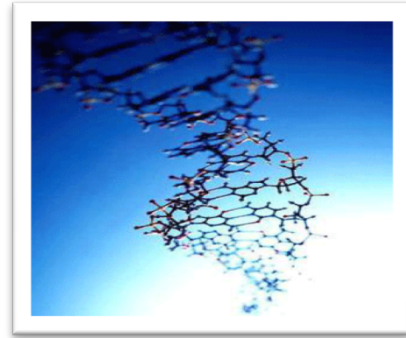
4. REDUCED ENERGY EXPENDITURE

- Resting metabolism
 - 800 – 900 kcal/m²/ 24hours
 - Females < males
 - Declines with age
- Physical exercise
 - ~1/3 of daily energy expenditure
 - Mostly easy manipulated
- Dietary thermogenesis (thermic effect of food)
 - Energy expenditure that follows the ingestion of meals
 - May dissipate ~10% of the ingested calories
 - In the obese, the thermic effects of food are reduced (especially in patients with diabetes)
- Adaptive thermogenesis
 - With acute over or under feeding
 - Shift in overall metabolism as large as 20%



5. GENETIC FACTORS

- Dysmorphic or syndromic obesity:
 - Bardet-Biel Syndrome
 - Alström Syndrome
 - Carpenter Syndrome
 - Cohen Syndrome
 - Prader-Willi Syndrome
- Single-gene cause of obesity:
 - Leptin and leptin gene deficiency (injection with leptin will decrease the appetite though some obese patients may have resistance to leptin)
 - POMC (pro-Orpio Melano Cortin) deficiency: hormone secreted by the arcuate nucleus- part of center of appetite in hypothalamus- inhibiting appetite
- Genetic defects with nonsyndromic obesity:
 - Ex. D elanocortin receptor system abnormalities: D C4R (D elanocortin-4 receptor) the receptor that POMC is acting on. This mutation is the most common mutation among the other mutations.
- Genetic susceptibility to obesity:
 - If both parents are obese ~80% of the offspring will be obese
 - If only one parent is obese ~10% of the offspring will be obese
 - Studies with identical twins reveal that hereditary factors account for ~70% and environmental factors (diet, physical activity or both) account for ~30% of the variation in the body weight

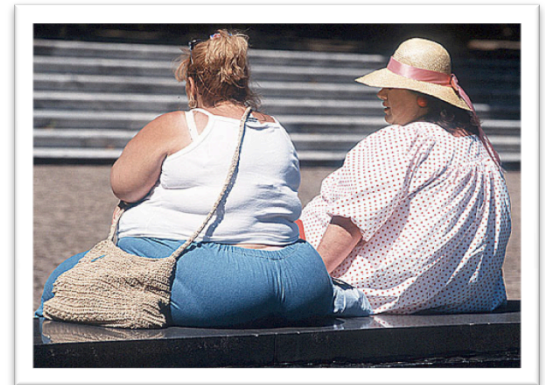


Note:

- The notion that obesity is a genetic disorder is misleading. The prevalence of obesity has increased markedly worldwide in recent years yet genes have not changed, changes occur with population when migrations occur
- Hence, phenotypic expression of genes for obesity is environmental specific. Obesity is a disorder of Gene-Environment interaction
- mGPD gene: the mGPD can be considered a spendthrift enzyme that significantly contributes to obligatory thermogenesis. The mGPD gene may play a role in the development of obesity if we consider the readiness with which some patients gain weight and the difficulties to lose weight when undergoing low calorie diets

PREDISPOSING FACTORS TO 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 leads to obesity
 - ↓ sleep leads to ↓ leptin, ↑↑ Ghrelin, hence ↑ 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 program
- 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)
 - Night eating syndrome: if > 25 % of intake in the evening



PHYSICAL EFFECTS AND HEALTH CONSEQUENCES OF OBESITY

- Obesity is associated with reduction in life expectancy during adulthood
- Hypertension
- DM type 2
- Coronary heart disease
- Gallbladder disease
- Certain cancers (in males: colorectal cancer / in females: breast cancer and endometrial cancer)
- Increase cost rate on obesity
- Increase number of sick leaves for obese subjects
- 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

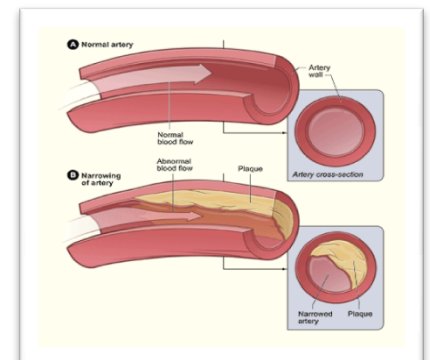


Table 2. Complications Associated with Obesity

Cardiovascular	Coronary artery disease, stroke, congestive heart failure, hypertension, dysrhythmias, pulmonary embolism
Pulmonary	Obstructive sleep apnea and obesity hypoventilation syndrome
Endocrine	Metabolic syndrome, insulin resistance, dyslipidemia, diabetes mellitus type 2, polycystic ovary syndrome
Gastrointestinal	Gallstones, abdominal hernia, nonalcoholic fatty liver disease, gastroesophageal reflux disease
Bone, joint, and skin	Osteoarthritis, low back pain, gout, acanthosis nigricans
Vascular	Venous stasis
Neurologic	Pseudotumor cerebri
Gynecologic/genitourinary	Stress incontinence, sexual dysfunction, abnormal menses

NOTE: Obesity is also associated with cancer of the esophagus, colon, pancreas, liver, prostate, breast, endometrium, cervix, and ovaries.

SURROGATE MEASURE OF ADIPOSITY

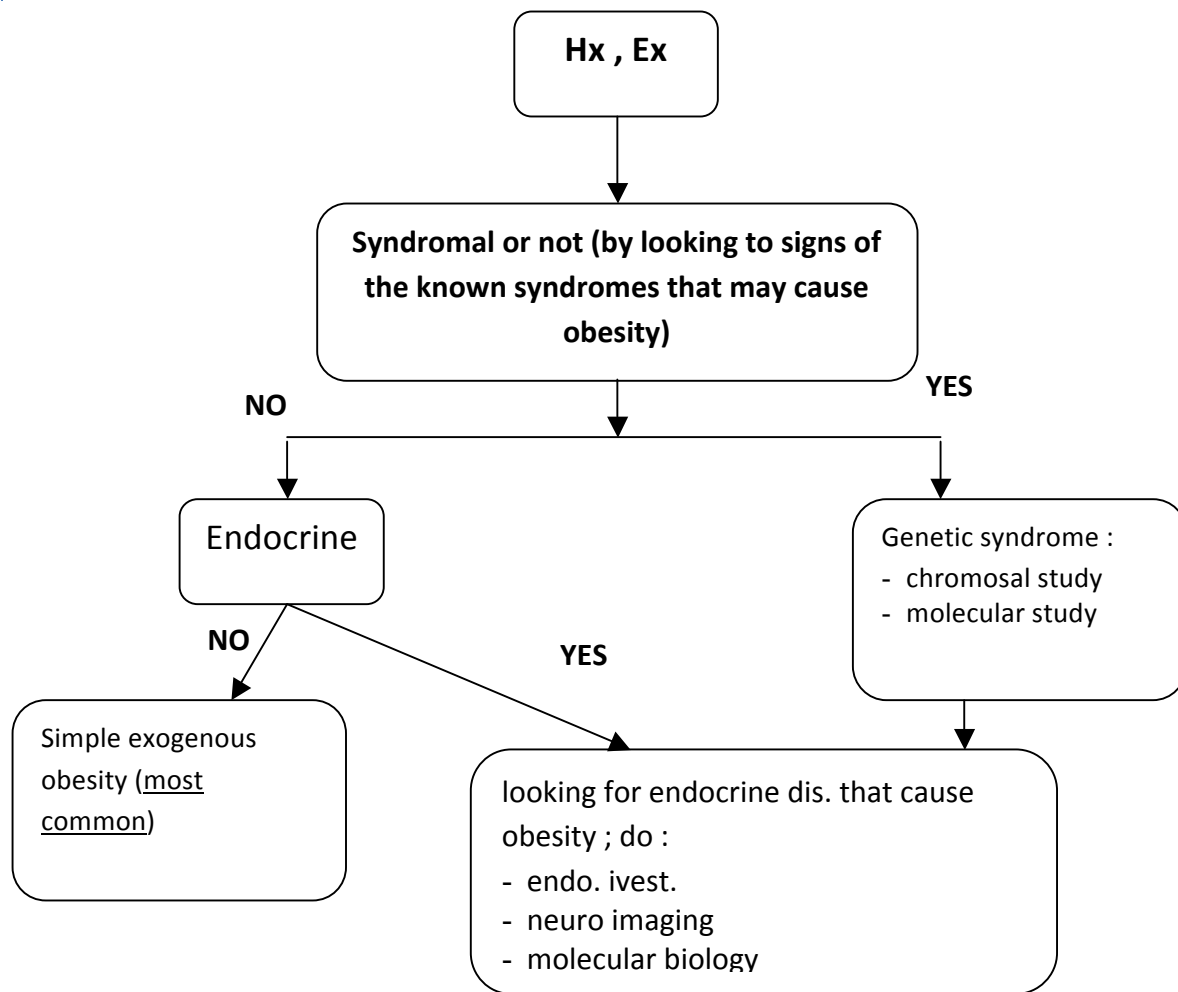
1. Ideal body weight
2. Weight
3. Anthropometric measures
4. Body mass index (BMI):
 - Reliable, easy, correlated with percentage of body fat
 - Guide for selection of therapy
 - Recommended by WHO
 - Varies among different races. Recent WHO classification applied to whites, Hispanics and black/Asians are different: overweight BMI 23-24.9 kg/m² and obesity by BMI > 25 kg/m²)
 - Relatively reliable except in:
 - Extremes of age or height
 - Very fit individuals with muscular build

SCREENING AND ASSESSMENT

- Screening of adults for obesity is important due to the significant increase in morbidity and mortality. Although it is not done in routine practice, screening for obesity should be as a part of periodic health assessment
- Screening:
 1. BMI measurement
 2. 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
 3. Evaluation of overall medical risks
- Identify etiology and assess:
 - Risk factors: After BMI and WC, history/BP measurement/Fasting lipid profile/Fasting blood sugar
 - Other risk factors: Age of onset of obesity
 - Comorbidities: Help classify risk of mortality/Presence of DM2, HTN, atherosclerosis, dyslipidemia/Sleep apnea/GI, osteoarthritis, gout

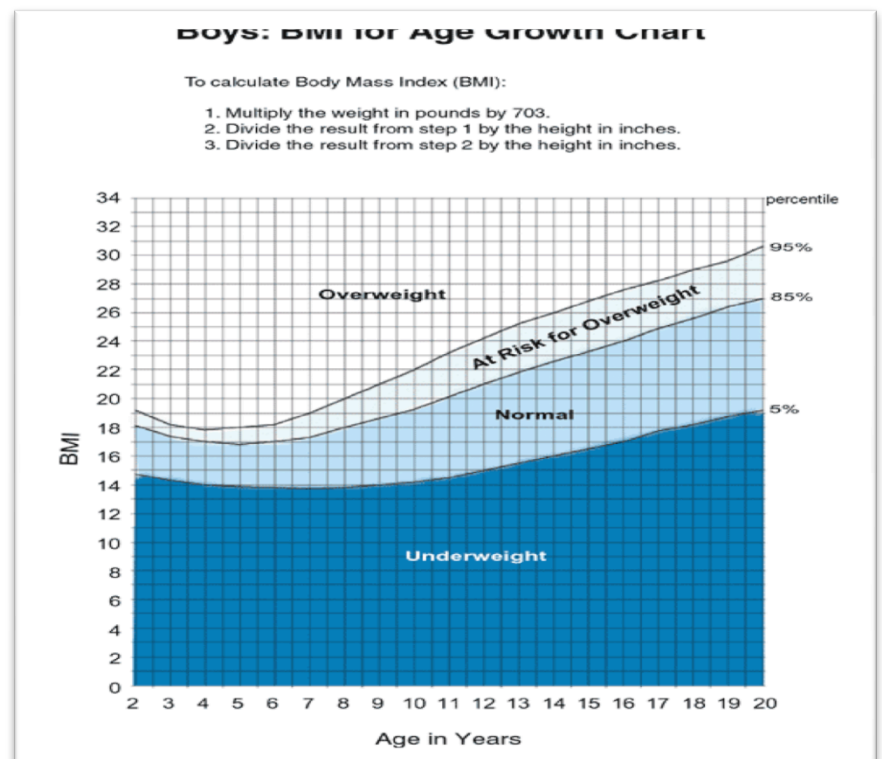
Height, in or cm	_____
Weight, lb or kg	_____
Calculated BMI, kg/m ²	_____
Waist circumference, in or cm	_____
Blood pressure SBP/DBP, mm Hg	_____
Fasting serum triglyceride, mg/dL or mmol/L	_____
Serum Hdl-cholesterol, mg/dL or mmol/L	_____
Fasting blood glucose, mg/dL	_____
Are there symptoms of sleep apnea?	_____
Are there medication(s) that increase body weight?	_____
Is there regular physical activity?	_____
Are there other etiologic factors?	_____

HOW TO ASSESS CAUSE OF OBESITY CLINICALLY



OBESITY IN CHILDREN

- Growth charts
- BMI-for-age reference charts



MANAGEMENT: BEHAVIOURAL, DRUGS, SURGERY

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

1. Behavioral (diet and exercise)

- Diet: Indicated for all with BMI > 30 and those with BMI 25- 30 with comorbidities
- 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
- 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
 - 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
- Dangers of Atkins diet
 - High saturated fat and cholesterol: CVD
 - High protein: decline in renal function, urinary calcium losses (osteoporosis)
 - Lack of fiber: increase colon cancer risk
 - Avoidance of carbs results in decreased intakes of essential vitamins (thiamin, folate, B6) and anti-oxidant phytochemicals
- Exercise:
 - Good to maintain muscle mass
 - Helps not to gain weight
 - But has little effect on reducing weight
 - Also, encourage pt. to change life-style
 - Also, ask family, friends to encourage and support pt.
 - Start slowly

- 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

- N.B. When you loose weight →you loose fat + protein (muscles) but when you regain weight you gain fat only→ become bag of fat!!!

2. Drugs

- 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
- Antidepressant
- Antiepileptic
- Diabetic drugs: metformin
- Pancreatic lipase inhibitor: Orlistat; inhibits fat absorption
- (Orlistat):
 - A lipase inhibitor, reduces the absorption of dietary fat
 - Lowers Cholesterol (4-11%) & LDL (5-10%)
 - It causes loss of 4 bonds in 4 weeks, if the loss is less than 4 it's mean the medication is not effective.
 - Major C/I:
 - Chronic malabsorption syndrome
 - Cholestasis
 - Pregnancy and breast feeding
 - Side effect:
 - Fecal incontinence



- Diarrhea "steatorrhea"
- Malabsorption of fat-soluble vitamins → "vit. Supplement"
- Dose:
 - 120 mg/ immediately before, during, or up to 1 hour after each main meal (up to max. 360mg/day)
 - Max. Period of treatment is 2 year

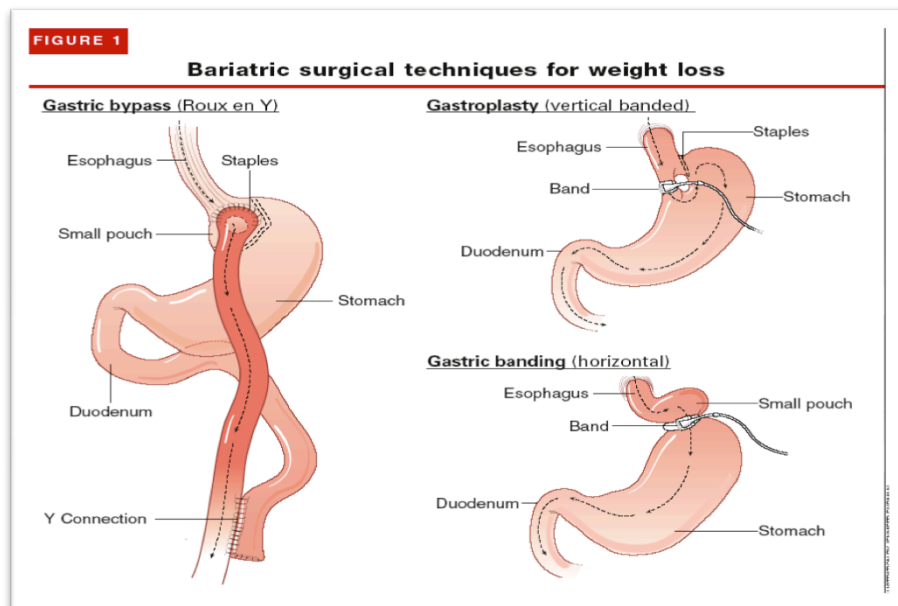
3. Surgery

- Considered for obesity of grade III or II with life-threatening complications. (Have BMI > 40/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
- Pt. Should be given a chance for dietary control, drugs (Failed previous non-surgical method)
- Needs multi-specialty team decision
- Pt. Should be followed-up, because it is associated with some complications.
- Two types:
 1. Restrictive "restrict Pt. to eat": e.g. banded gastroplasty:
 - Band placed over upper part of stomach.
 - More effective, less side effects: e.g. vomiting may be there.
 2. Malabsorptive "induce malabsorption of fat":

E.g. Roux-en-Y gastric bypass "gastrojejunostomy":

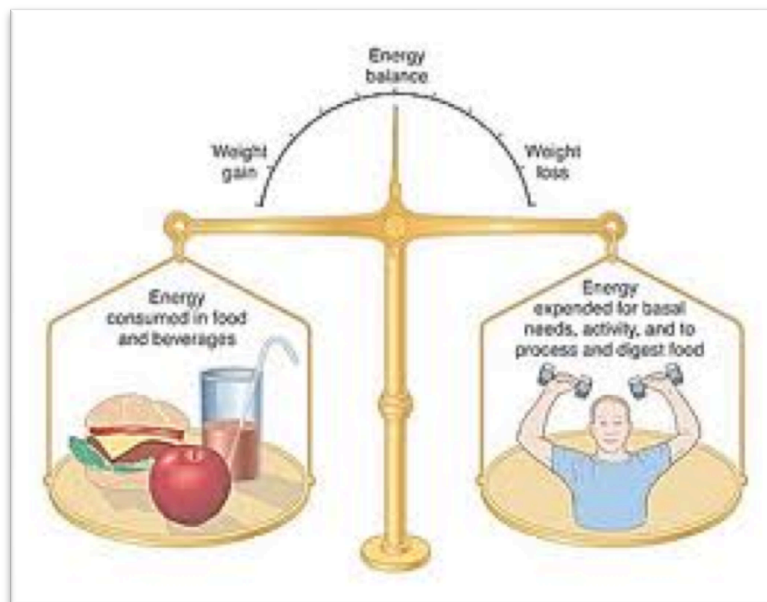
 - Results in nutrient deficiency (late complication)
 - Less effective

N.B: In bypass surgery there is more loss of weight than restriction surgery.



HEALTH BENEFITS OF WEIGHT LOSS

1. Survival increased 3-4 months for every kilogram of weight loss
2. Decrease CVD
3. Decrease glucose & insulin level
4. Decrease BP
5. Decrease LDL & Triglycerides, increase HDL
6. Decrease in severity of sleep apnea
7. Decrease symptoms of joint



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