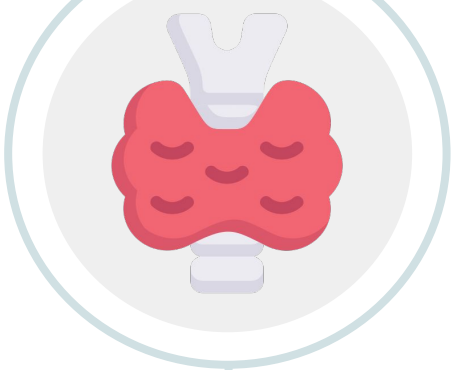
Obesity



Objectives :

- ★ Know why do we study obesity.
- ★ Learn what is obesity.
- ★ Know what is the impact of obesity in Saudi Arabia.
- ★ Know the Body weight regulations
- ★ Know how to manage an obese individual
- ★ Know the obesity-related complications
- ★ Learn the effective preventive strategies for obesity

Editing file

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Introduction

Definition [1]

- **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.
- Not all obese people eat more than the average person, but all obviously eat more than they need.

◀ Obesity is a chronic disease [2] and health issue

- **Obesity is one of the five most important health concerns worldwide,** the present obesity epidemic is mainly due to **changes in lifestyle behaviour**

WOF
World obesity federation

"The World Obesity Federation takes the position that obesity is a chronic, relapsing, progressive disease process and emphasizes the need for immediate action for prevention and control of this global epidemic"

OC
Obesity Canada

"Obesity is characterized by excess body fat that can threaten or affect your health. Many organizations including the Canadian Obesity Network, now consider obesity to be a chronic disease."

AMA
American medical association

"American Medical Association recognizes obesity and overweight as a chronic medical condition (de facto disease state) and urgent public health problem…and work towards the recognition of obesity intervention as an essential medical service…"

EASO
European association for the study of obesity

"A progressive disease, impacting severely on individuals and society alike, it is widely acknowledged that obesity is the gateway to many other disease areas…"

FDA
The US food and drug administration

"Obesity is a chronic relapsing health risk defined by excess body fat"

RCP
Royal college of physicians (UK)

"Obesity is a chronic progressive disease caused by an imbalance between energy intake and energy expended, with a wide range of damaging effects on the body."

AOASO
Asia Oceania association for the study of obesity

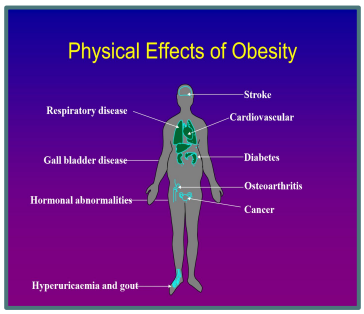
"We hereby propose a concept for international recognition of a pathological state (obesity disease) in which a person suffers health problems caused by or related to obesity thus making weight loss clinically desirable and requiring treatment as a disease entity"

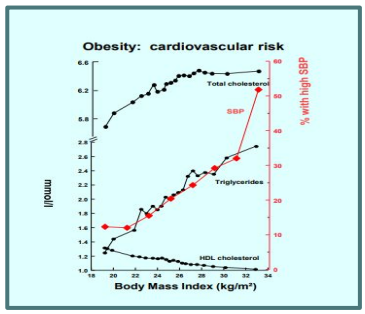
1- Obesity can be healthy or unhealthy
2- Because it is associated with CVS and psychological complications

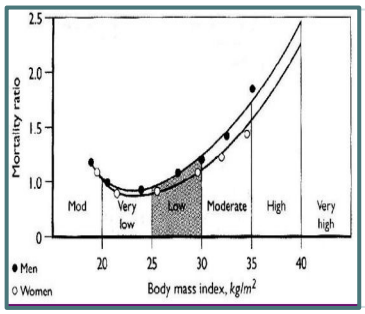
Introduction *cont.*

◀ "ABCD" Diagnostic term

- **"ABCD" Diagnostic term for obesity as a chronic disease state:**
  - Obesity : **A**diposity **B**ased **C**hronic **D**isease
- Mechanical complications e.g. obstructive sleep apnea, osteoarthritis
- Cardiometabolic complications including:
  - hypertension, dyslipidemia, hyperglycemia
- Psychological changes
- The neuroendocrine and metabolic causes of accumulation of excess fat mass
- The development of adipose tissue dysfunction
- The metabolic and neuroendocrine complications of obesity



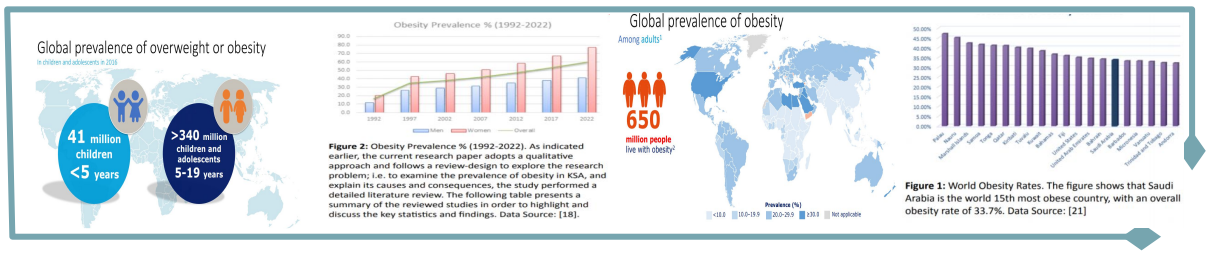




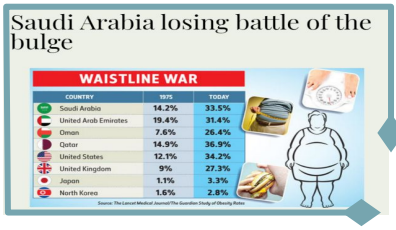
classical "J" shape, on the Y axis is the mortality rate and on the X axis is the BMI, if the BMI is very low or High (>30) patient will have increase in mortality rate

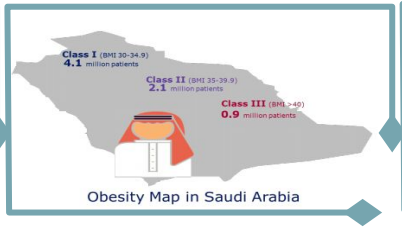
◀ Prevalence

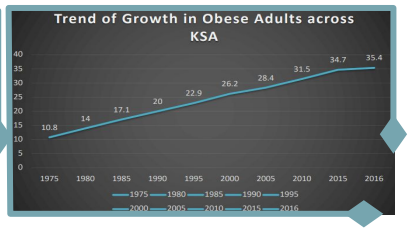
- **Globally :**
  - ❑ There is an increase in the prevalence of obesity worldwide, more than 650 million live with obesity.



- **Saudi Arabia :**
  - ❑ Highest rates of obesity, higher in women. Rates are expected to increase to 59% by 2022
  - ❑ The prevalence of obesity In KSA has increased to 33.5% it was 14.2%







- Recently, there is an increased incidence of T2DM in the pediatric age group due to increased obesity

Introduction *cont.*

◀ Surrogate measures of adiposity

- We can measure fat in our body by different ways and some of them are possible, difficult, time consuming, expensive, inappropriate to use in this field.

01 **BMI** — It is the practical thing to use, but not the best.

02 **Ideal body weight**

03 **Anthropometric measures**

04 **Weight**

◀ Body Mass index (BMI):

Body Mass index (BMI):

- Body mass index (BMI) is a simple index of weight-for-height that is used to classify obesity in adults: **BMI ≥ 30kg/m².**
- Recommended by WHO
- **Relatively reliable except in:**
  - ★ Extremes of age or height
  - ★ Very fit individuals with muscular build
- Production of ethnic-specific cut-points is very important for BMI, body fatness, morbidity and mortality
- Additional interim cut-point of BMI of 23 kg/m 2 or greater to indicate overweight in Asian populations and a BMI of 25 kg/m 2 to represent a higher level of risk equivalent to obesity

WHO recommended definition of obesity (2000)		
Classification	**BMI(kg/m2)[1]**	**Risk of comorbidities**
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal range	18.5 - 24.9	Average
Overweight (Pre-obese)	>25.0 25-29.9	Mildly increase
Obese (BMI >30)		
Obese Class I	30-34.9	Moderate
Obese Class II	<35-39.9	Severe
Obese Class III	>40.0	Very severe

◀ Waist circumference (measure of visceral obesity)

Waist circumference:

- The easiest way to assess obesity is by measuring the narrowest circumference midway between the lower border of the ribs and the upper border of the iliac crest, taken from the side, it's even considered to be one of the vitals signs to measure in patients with metabolic diseases
- Waist circumference helps to screen health risks of obesity and overweight
- This risk goes up with a waist size that is greater than 35 inches for women or greater than 40 inches for men
- Variable depending on the race
- An increase in waist circumference will lead to a rise in the risk of complications like cardiometabolic complications

Population	Risk of metabolic complications of obesity	
	Increased	**Substantially Increased**
Caucasian (WHO)[2]		
Men	>94 cm (37 in)	>102 cm (40 in)
Women	>80 cm (35 in)	>88 cm (35 in)
Asia (IASO/IOTF/WHO)		
Men		>90 cm
Women		>80 cm
China (WGOC)		
Men		>85 cm
Women		>80 cm

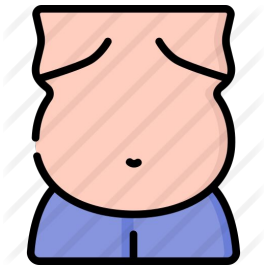
1- cutoff points depend on the ethnicity, in this table the cutoff points are from the west. In japan, china, south korea the cutoff points are lower than those mentioned. We use this in KSA but we need more studies to make sure that we follow the correct cut-off points
2- we follow this one

Introduction cont.

◀ Central Obesity

Males slides

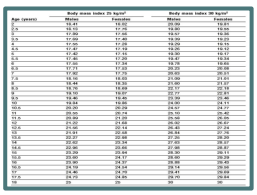
- **Central or visceral obesity is associated with more metabolic disease and complications:**
  - DM2
  - Hypertension
  - Dyslipidemia
- We can measure central or visceral obesity by:
  - MRI
  - Dual X-ray absorptiometry (DEXA)
  - Single CT slice L4/L5
  - **Waist: hip ratio**
  - **Waist circumference** (the most practical way and most effective)

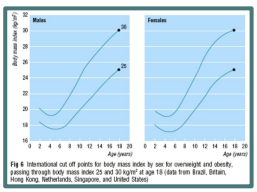


- A central distribution of body fat (a waist/hip circumference ratio of >1.0 in men and >0.9 in women) is associated with a higher risk of morbidity and mortality than is a more peripheral distribution of body fat (waist/hip ratio <0.85 in men and <0.75 in women).
- This is because fat located centrally, especially inside the abdomen, is more sensitive to lipolytic stimuli, with the result that the abnormalities in circulating lipids are more severe.

◀ Obesity in children

- Assessing obesity in children is an issue due to the presence of a 3rd factor (Growth hormone) that affect children weight, for that growth charts are created, though it is not that accurate, it can give a close representation of the expected weight that a child may get in certain age.
- Growthcharts
- BMI-for-age reference charts
- "International standard"BMI-for-age :- -
  - Cole et al. (BMJ 2000; 320:1240-1243) - Combined sample of seven countries
  - By tracking the percentile representing a BMI of 25 kg/m2 and 30 kg/m2 at 18 years back through to birth.
  - It's use will provide a standard definition and enable meaningful comparisons to be made between countries.





Mechanism of Obesity

Food intake and utilization is regulated by

- **Hormones**
- **CNS** (Hypothalamus)
- **Neurotransmitters**

1

Signals from peripheries from the stomach when you full are carried out by neurotransmitters and hormones to CNS in presence or absence of food

2

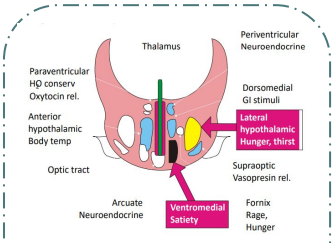
Signal from fat by hormone leptin to hypothalamus to reduce food intake and increased sympathetic activity and energy expenditure

3

Gastric distension and contraction send signal for satiety and hunger

4

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

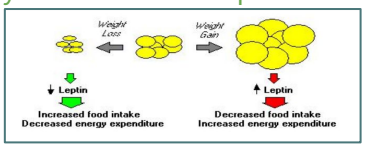
Mechanism of obesity

◄ Hypothalamic modulators of food intake

Males' slides	
Orexigenic (Increase Appetite)	**Anorexigenic (Decrease Appetite)**
NPY	CART
AGRP	CCK
MCH	CRH
Galanin	a-MSH
Orexin	**Insulin**
Ghrelin The hormone of hunger	**GLP-1**[1]
Noradrenaline	PYY 3-36
Endocannabinoids	**Leptin**
m, κ Opioids	Urocortin
Neurotransmitters	Bombesin

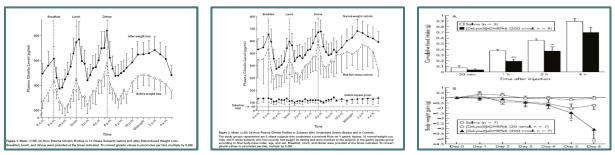
Leptin [3]

- Leptin from adipocytes acts on hypothalamus to decrease food intake and stimulate energy expenditure
- Plasma levels of leptin are very high, correlating with the BMI.
- Weight loss due to food restriction decreases plasma levels of leptin.
- Deficiency or resistance to leptin leads to obesity

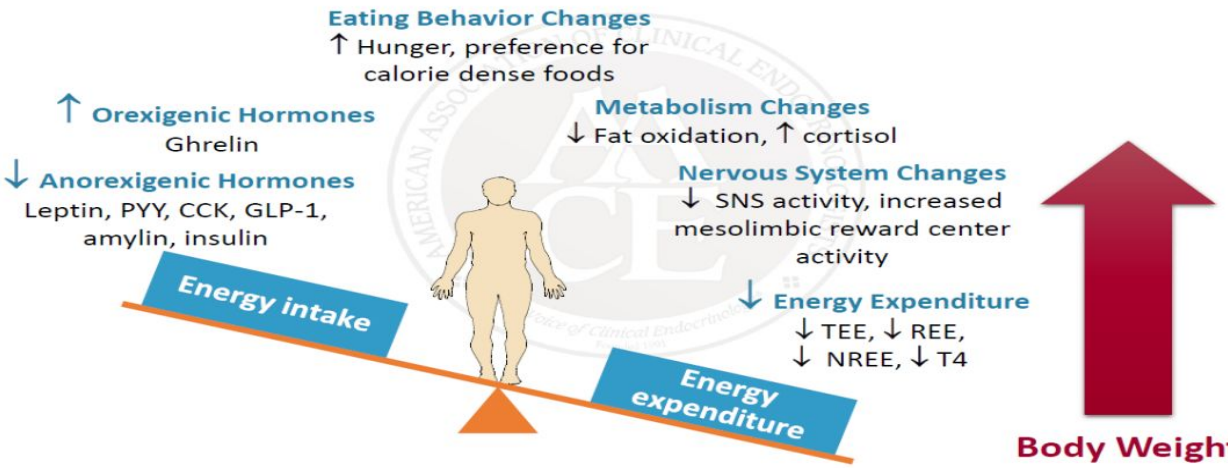


Ghrelin

- Ghrelin is a recently discovered orexigenic hormone (an obesity hormone) .
- **Increase with hunger decrease with eating**
- Secreted primarily by the stomach and duodenum, and acts on hypothalamus to **stimulate appetite**
- Has been implicated in both mealtime hunger and the long-term regulation of body weight.



◄ Adaptations to weight loss (obesity protects obesity)



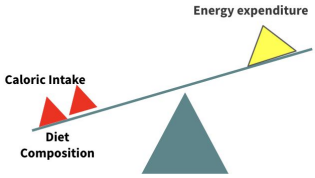
1- Famously known hormone that decrease food intake, on of the medications used to treat obesity is **Liraglutide** (Saxenda) which is a GLP-1 agonist.

2- The ob gene is found on chromosome 7 and produces a 16 kDa protein called leptin. In the ob ob mouse, a mutation in the ob gene leads to production of a non-functioning protein. Administration of normal leptin to these obese mice reduces food intake and corrects the obesity. A similar situation has been described in a very rare genetic condition causing obesity in humans, in which leptin is not expressed.

3-Leptin is a satiety hormone that is secreted from adipose cells to act on the hypothalamus to suppress appetite and decrease food intake, obese people have decreased levels of leptin or increased with resistance "not functioning on receptors"

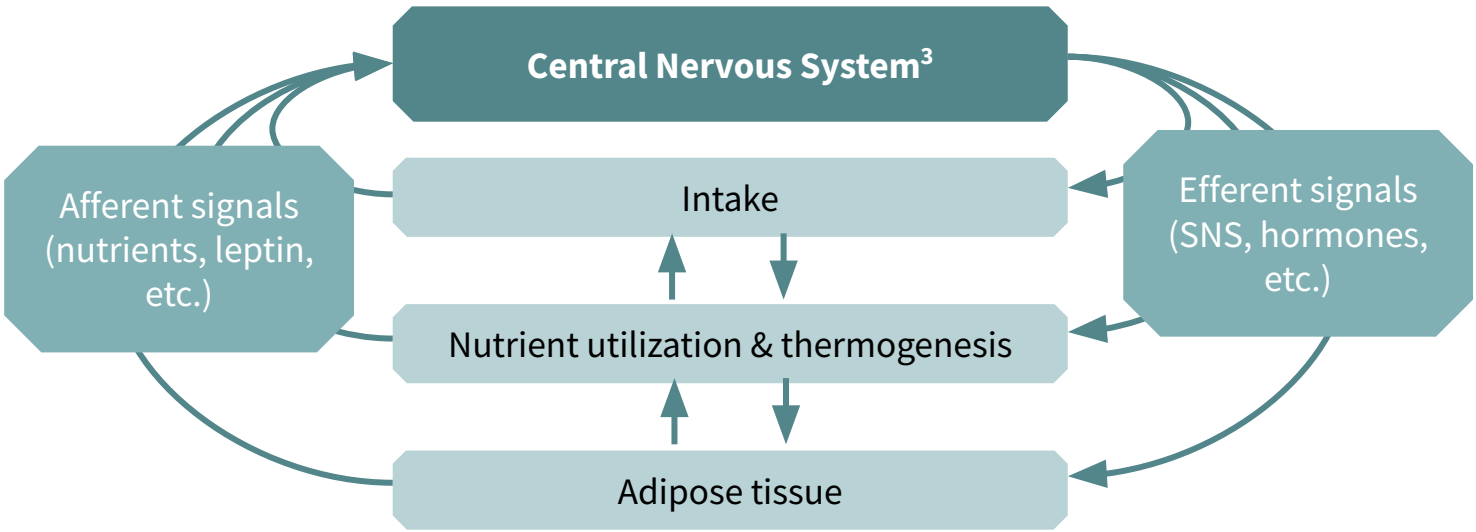
Etiology and pathogenesis

◄ Etiology & Pathogenesis



- **Multifactorial**
- **Biochemical/Dietary/behavioral pathways.**
  - Some individuals eat more during periods of heavy exercise or during pregnancy and are unable to get back to their former eating habits. The increase in obesity in social class 5 can usually be related to the type of food consumed (i.e. food containing sugar and fat). Psychological factors and how food is presented may override complex biochemical interactions.
- **Imbalance between energy intake and energy expenditure**
  - Energy balance is determined by several variables, including **basal metabolic rate (BMR)**[1], **appetite**, **diet** and **physical activity**[2].
  - It has been shown that obese patients **eat more than they admit to eating,** and over the years, a very small daily excess of intake over expenditure can lead to a large accumulation of fat.

Body weight and composition regulation:



◄ Obesity: How does it happen?

1 **Calories consumed not equal calories used over a long period of time**

2 **Due to combination of several factors:**

1) Individual behaviors (10 % to BMI)
2) Psychosocial factors
3) Environmental factors
4) Genetic (40 % to BMI and adiposity)
5) Acting through several physiological mediators of food intake and energy expenditure

1- BMR in obese subjects is higher than in lean subjects, which is not surprising since obesity is associated with an increase in lean body mass.
2- Obese patients tend to expend more energy during physical activity as they have a larger mass to move. On the other hand, many obese patients decrease their amount of physical activity.
3- Obesity can be considered as a neuroendocrine disorder because a lot of the afferent and efferent signals that control appetite are regulated by the CNS which will decide if you need to eat or not. if the thermostat isn't functioning in the brain very well; the Patient will feel hungry all the time. And if not perfectly working in the peripheral tissue there will be alot of accumulation of fat instead of burning it

Etiology and pathogenesis *cont.*

◀ Etiological classification of obesity

1 Neuroendocrine disease

- **Ventromedial hypothalamus damage:**
  - Tumors e.g. Insulinoma
  - Inflammatory lesions
  - Other hypothalamic disease, especially head trauma which affect the centers in hypothalamus
  - **hypothalamic obesity**: caused by neuroendocrine tumor, **radiation**[1] **to the hypothalamus or pituitary gland** and infiltrative disease to the neuroendocrine glands.
- **Cushing disease, Hypothyroidism and Polycystic ovary syndrome**

2 Drug-induced ★

- **Hyperinsulinism**
  - Insulin
  - **Sulfonylureas e.g.(Glibenclamide, Diamicron)**
- **Antidepressants**
- **Antiepileptics (phenytoin)**
- **Neuroleptics**
- Estrogen and progestins
- Antipsychotics (especially atypical agents)
- Beta Blocker
- **Corticosteroids**

Medication	Weight Gain Associated With Use	Alternatives (Weight Reducing in Parentheses)
Diabetes medications	Insulin, sulfonylureas, TZDs, mitiglinide, sitagliptin?[a]	(Metformin, acarbose, miglitol, pramlintide, exenatide, liraglutide, SGLT-2 inhibitors)
Hypertension medications	α-Blocker?, β-blocker?	ACE inhibitors?, calcium channel blockers?, angiotensin-2 RAs
Antidepressants and mood stabilizers	Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine, fluoxetine?, sertraline?, paroxetine, fluvoxamine	(Bupropion), nefazodone, fluoxetine (short term, sertraline, <1 year)
Oral contraceptives	Depot progesterone	Barrier methods, IUDs

Category	Drugs that cause weight gain	Possible alternatives
Conventional antipsychotics	Thioridazine	Haloperidol
Atypical antipsychotics	Olanzapine, Clozapine, Quetiapine and Risperidone	Ziprasidone, Aripiprazole
Lithium	Lithium carbonate	
TCA	Amitriptyline, Clomipramine, Doxepin. Imipramine, Nortriptyline	Protriptyline
SSRI	Paroxetine	Other SSRIs (e.g. Fluoxetine (Short term, Sertraline, <1yr)
Atypical antidepressants	Mirtazapine	Bupropion, Nefazodone
Anticonvulsant drugs	Valproate, Carbamazepine and Gabapentin	Topiramate, Lamotrigine, Zonisamide
Antidiabetic drugs	Insulin, Sulfonylureas, Mitiglinide and Thiazolidinediones, sitagliptin?	Metformin, Alpha-glucosidase inhibitors (e.g. acarbose, miglitol), Liraglutide, SGLT-2 inhibitors
Serotonin and histamine antagonist	Pizotifen	
Antihistamines	Cyproheptadine	
Beta blockers	Propranolol, Atenolol and Metoprolol	ACEI?, CCB?, Angiotensin-2 RAs
Steroid hormones	Glucocorticoids	
	Progestins: Megestrol acetate, OC[1] (Medroxyprogesterone acetate aka depot progesterone)	Barrier methods, IUDs

1- Patient was lean and was diagnosed with germinoma which required surgery on the brain + radiation to the hypothalamus and pituitary which results in gaining weight after radiation and also complicated with diabetes.

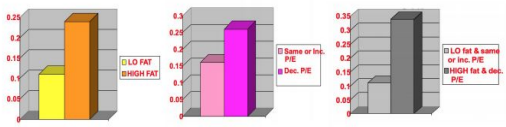
Etiology and pathogenesis *cont.*

◀ Etiological classification of obesity *cont.*

3 Dietary obesity

- **High carbohydrate diet**
  - This one is mainly responsible for obesity in Riyadh
- **High fat diet**

Change in BMI (kg/m2) from 1989 to 1991

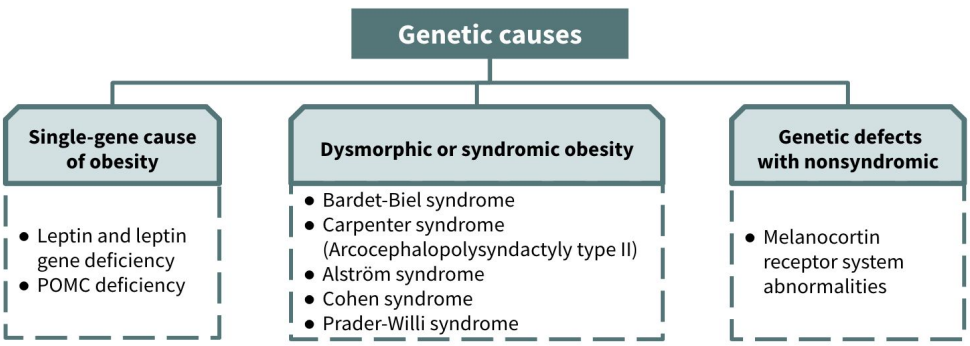


4 Reduced energy expenditure

- **Resting metabolism:**
  - 800 to 900 kcal/m2/24hr
  - Females <Males
  - Declines with age
- **Physical exercise:** **this one you can control**
  - ~ 1/3 of daily energy expenditure
  - Most easily manipulated
- **Dietary thermogenesis (thermic effect of food):**
  - Energy expenditure which follow the ingestion of meal
  - May dissipate ~ 10% of the ingested calories
  - In the obese, the thermic effects of food are reduced (especially in patients with diabetes) and post-obese subjects.
  - **Adaptive thermogenesis:**[1]
  - With acute over – or underfeeding
  - Shift in overall metabolism as large as 20%

5 Genetic factors in obesity

- **Genetic susceptibility to obesity:**
  - If both parents are obese ~ 80% of the offspring will be obese
  - If only one parent ~ 10% of the offspring will be obese
  - Studies with identical twins: - Hereditary factors account ~ 70%
  - Environmental (diet, physical inactivity, or both) account ~ 30% of the variation in the body weight
- **The notion that obesity is a genetic disorder is misleading:**
  - The prevalence of obesity has increased markedly, world-wide, in recent years, yet genes have not changed.
  - Changes occur within population when migration occurs.
  - Phenotypic expression of genes for obesity are environment specific
  - Obesity is a disorder of gene-environment interaction



1- Brown adipose tissue in animals, when stimulated by cold or food, dissipates the energy derived from ingested food into heat. This can be a major component of overall energy balance in small mammals but the effect is likely to be very small, and of doubtful clinical significance in adult humans, even though brown adipose tissue is found in humans.

Etiology and pathogenesis

◀ Other factors predisposing to obesity:

01 Lifestyle

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

02 Diet

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

03 Cessation of smoking[1]

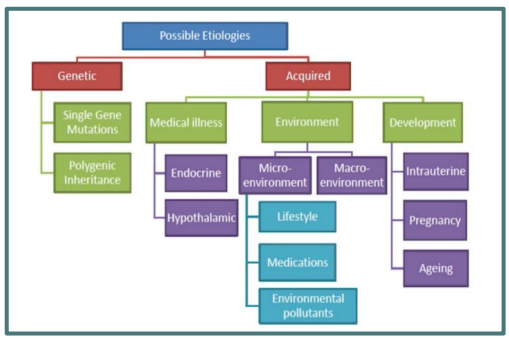
- Average weight gain is 4 kg
- Due to nicotine withdrawal
- Can be prevented by calories restriction and exercise program

04 Social influences

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

05 Sleep deprivation

- < 7 hours of sleep ⟶ obesity
- ↓ sleep ⟶ ↓ leptin, ↑↑ Ghrelin ⟶ ↑appetite and CHO eating at night



◀ Contributors to obesity

01 Sociocultural :

- **Preference for foods high in fat and/or carbohydrate**
- **Large portion sizes (value meals)**
- **Work-life circumstances :**
  - Sedentary occupations and leisure activities
  - Heavy time commitments to work,social, and family obligations
  - Sleep deprivation

02 Environmental :

- **Community design infrastructure not conducive to physical activity:**
  - Lack of safe, convenient areas for outdoor activities
  - Distances between home and work/shops too far for walking
  - Lack of public transportation
  - Ubiquity of escalators, elevators, etc
  - Weather

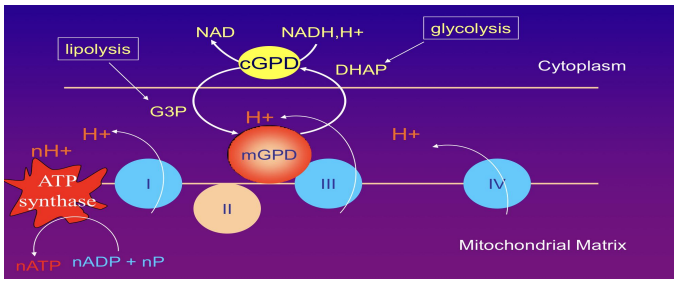
1-Nicotine suppresses appetite, the weight gain after cessation can be avoided by the exercise

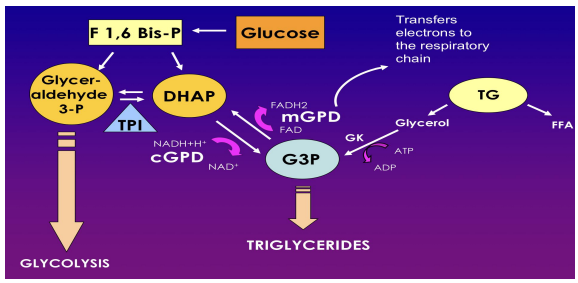
Dr's study on G3PD gene

Title and objectives of the study

- **Title:**
  - Metabolic consequence of deleting the mitochondrial Glycerol 3-phosphate dehydrogenase gene in mice
- **Objectives:**
  - We studied the consequences of deleting the mGPD gene regarding:
    - Responses to fat- or carbohydrate-rich diets.
    - Tolerance and responses to caloric restriction and fasting.

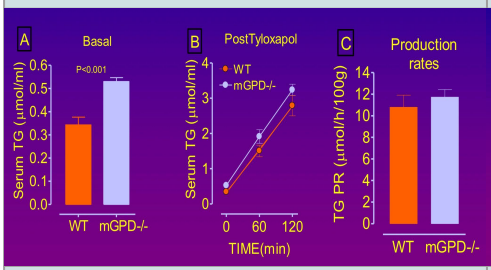
The NADH Glycerol 3-Phosphate Shuttle[1]



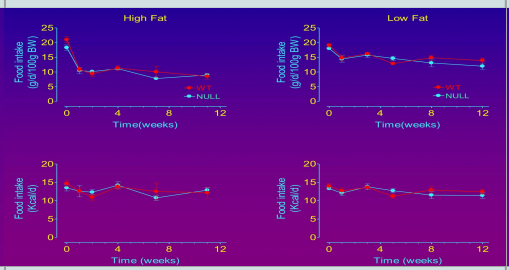


Results

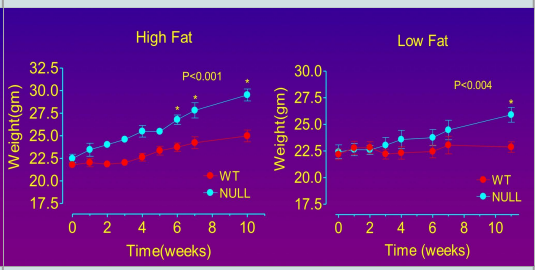
Serum Triglycerides



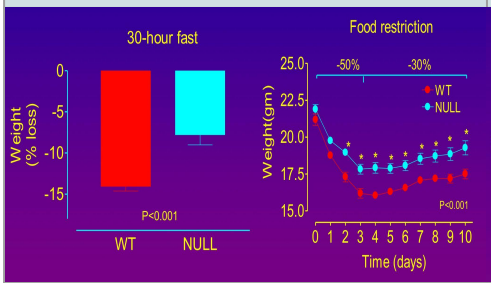
Food intake



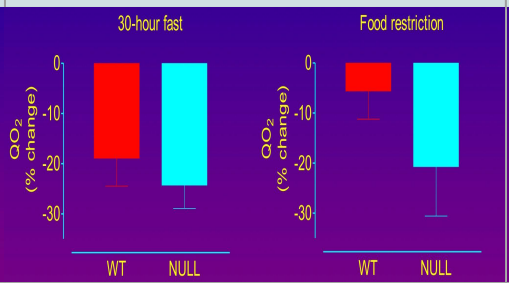
Body weight



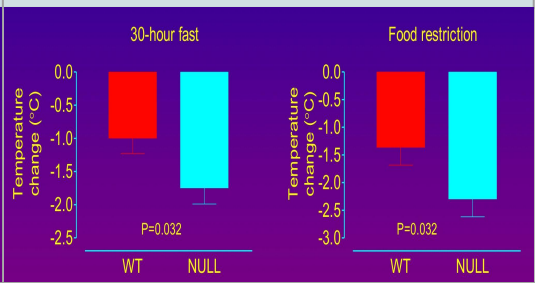
Weight loss



Change in energy expenditure



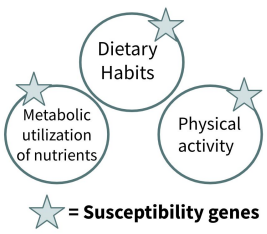
Core temperature change at 22C



Conclusion

- The **mGPD** can be considered a **spendthrift enzyme**[2] 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 weight when undergoing a low calorie diets

Factors participating in body-weight maintenance

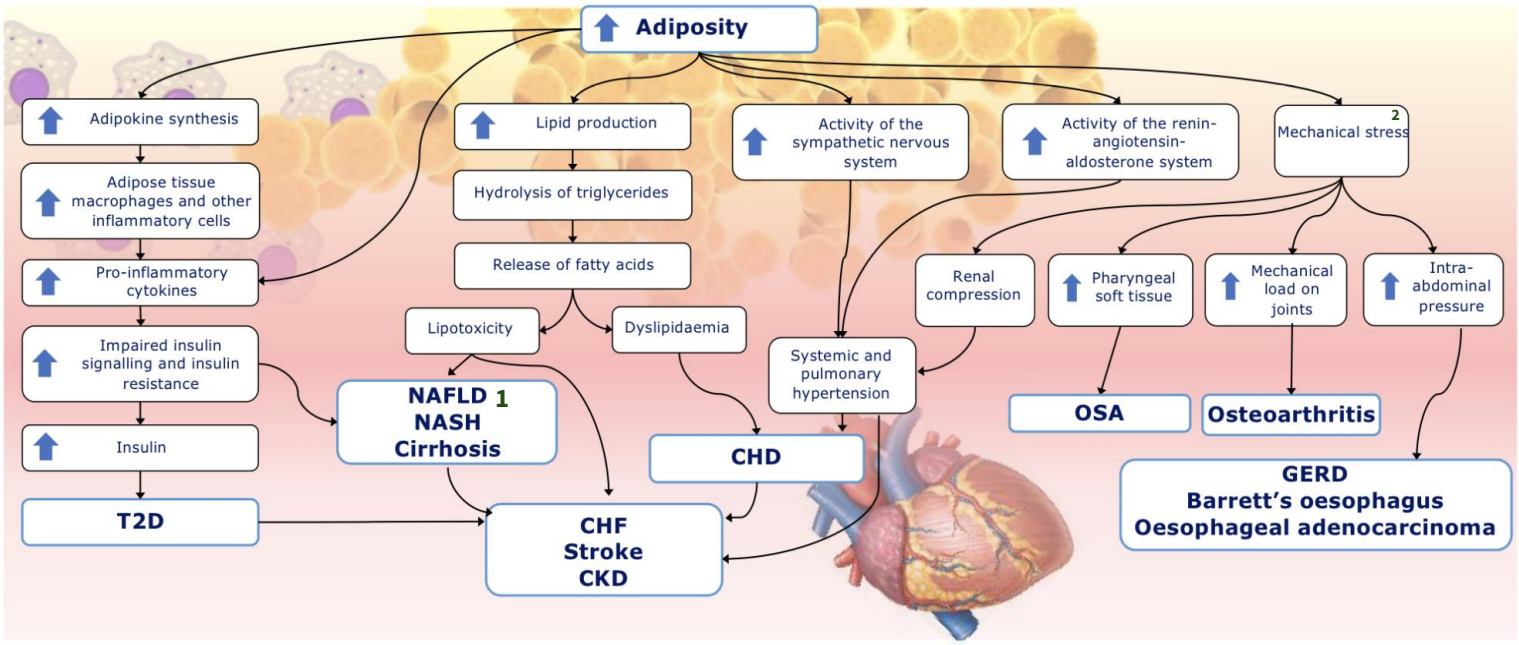


1- NADH glycerol 3-phosphate shuttle is present in the mitochondria, it's responsible for the end ATP synthase and the generation of ATP.
2- Is an enzyme that help in storing fat or carbs, when the intake is reduced it will help in to reduce calorie expenditure by reducing body temperature making the mice feel cold.

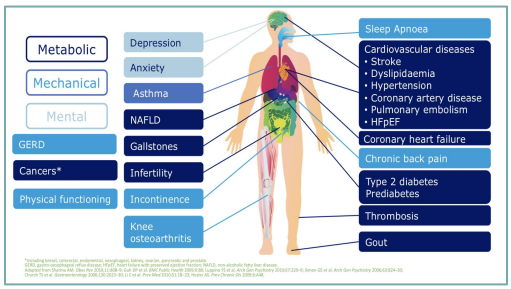
Complications of obesity

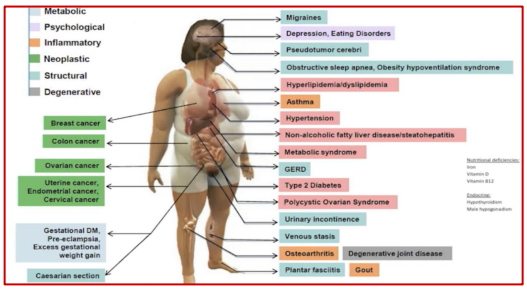
Health consequences of obesity

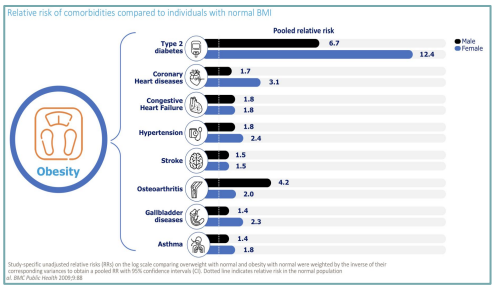
- **Excess adiposity leads to major risk factors and common chronic diseases**



CHD, coronary heart disease; CHF, coronary heart failure; CKD, chronic kidney disease; GERD, gastroesophageal reflux disease; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic stereohepatitis; OSA, obstructive sleep apnoea; T2D, type 2 diabetes. Heymsfield SB, Wadden TA. *NEJM* 2017;376:254–266







Metabolic syndrome

- Overweight/central obesity and insulin resistance, which causes glucose and lipid disturbances, seem to form the basis of many features of the metabolic syndrome.
- **There are two classification systems which are shown in Table 5.17. The differences are:**
  - A **large waist** is an absolute requirement for the International Diabetes Federation (IDF), but not in the ATP III NCEP.
  - The IDF criteria use **lower cut-off values for waist circumference** (close to values of people with a BMI of 25 kg/m2) and lower fasting blood glucose concentrations.
- This means that the **prevalence of metabolic syndrome will be higher using the IDF criteria** and the IDF criteria will identify at-risk patients at an earlier stage. This could lead to further investigations following on from the initial screening, and earlier institution of preventative as well as therapeutic measures.

Table 5.17 Classification systems for metabolic syndrome: ATP III of the National Cholesterol Education Programme (NCEP) and International Diabetes Federation (IDF)

Risk factor	ATP III NCEP (any 3 of the 5 features)	International Diabetes Federation (large waist + any other 2 features)
Waist circumference		
Men	>102 cm (40 in)	>94 cm (37 in)
Women	>88 cm (35 in)	>80 cm (35 in)
Triglycerides	>1.7 mmol/L (150 mg/dL)	1.7 mmol/L (150 mg/dL)
HDL cholesterol		
Men	<1.03 mmol/L (40 mg/dL)	<1.03 mmol/L (40 mg/dL)
Women	<1.29 mmol/L (50 mg/dL)	<1.29 mmol/L (50 mg/dL)
Blood pressure	>130/85 mmHg	>130/85 mmHg
Fasting glucose	>5.6 mmol/L (100 mg/dL)	>5.6 mmol/L (100 mg/dL)

ATP III, Adult Treatment Panel 3.

1-Obesity increases the risk of having a fatty liver disease that may progress to hepatocellular carcinoma and liver failure

2-Mechanical stress happens to those who have fat mainly in the abdomen that causes mechanical pressure

Complications of obesity

Complications of obesity can be classified into three categories:

1 Metabolic

Cardiovascular [1]

Obesity and overweight are linked to several factors that increase **risk for CVD (Coronary artery disease and stroke):**

- **High blood lipids**, especially high triglycerides, LDL cholesterol, and total cholesterol and low HDL cholesterol
- **High blood pressure:** can be challenging to accurately measure blood pressure in obese patient
- **Impaired glucose tolerance or type-2 diabetes**
- **Metabolic syndrome (Mets)**
- **Enlarged left ventricle (increased risk for heart failure)**

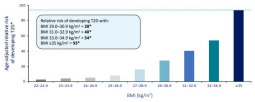
➔ AACE recommends **weight loss of 5% to 10% to reduce CVD risk**

Type 2 diabetes

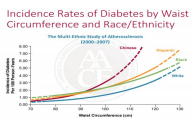
- Greater risk of developing T2D with higher BMI

Consequences of obesity in Diabetes :

- Increase risk of cardiovascular comorbidities:
  - Hypertension
  - Dyslipidemia
  - Atherosclerosis



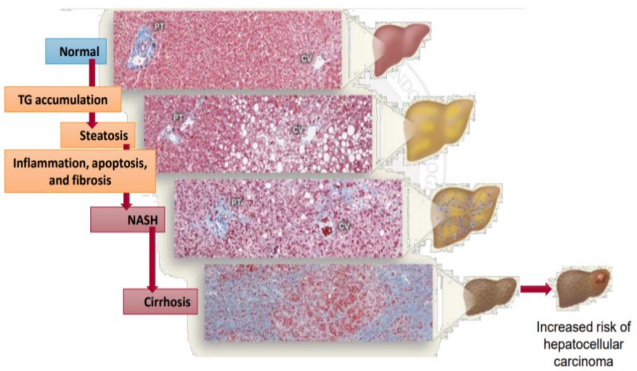
- May limit ability to engage in physical activity
- increase insulin resistance
  - Worse glucose tolerance
  - Necessitates higher exogenous insulin doses
- Change neuroendocrine signaling and metabolism
- Reduce quality of life



Goal: 5%-10% weight loss

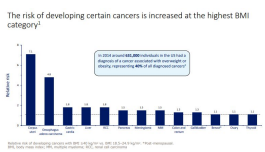
NAFLD

- **Progression of NAFLD**



Other complications

- **Cancers:** 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 and Kidney
  - Non-Hodgkin lymphoma
  - Multiple myeloma
- **Infertility [2]**
- **Gout**
- **Thrombosis**
- **Gallstones**



1-People with Obesity have the risk of PE

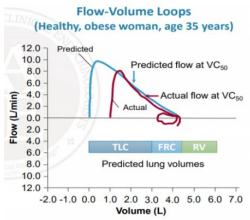
2-It affects sperm number in males and ovulation in females. Obese females are susceptible to having an irregular menstrual cycle which will become regular and increase fertility when they lose weight

Complications of obesity

2 Mechanical

Lung function

- **Stiffening** of total respiratory system
  - Reduced lung and chest wall compliance
  - Reduced tidal volume and short, rapid breathing pattern
- Reduced lung volume and vital capacity
- Increased risk of airway closure and ventilation distribution abnormalities leading to pulmonary hypertension

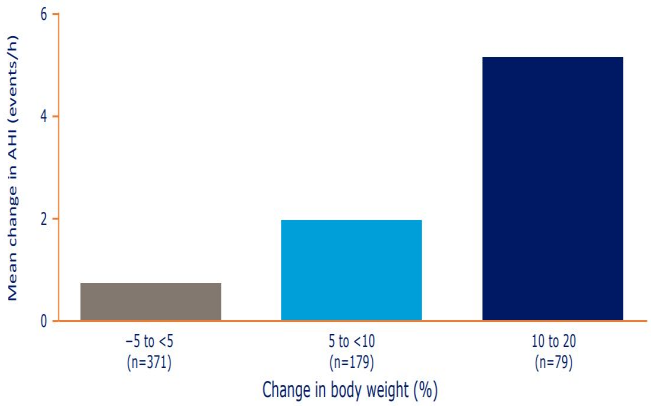


Digestive disorder (GERD)

- Obesity is associated with significant increased risk of Gastroesophageal reflux disease **(GERD**) symptoms and GERD-related due to increased intraabdominal pressure and fat
- **Complications:**
  - Barrett's esophagus
  - Erosive esophagitis
  - Esophageal adenocarcinoma
- Central\Abdominal obesity more closely related to GERD against BMI

Obstructive sleep apnea

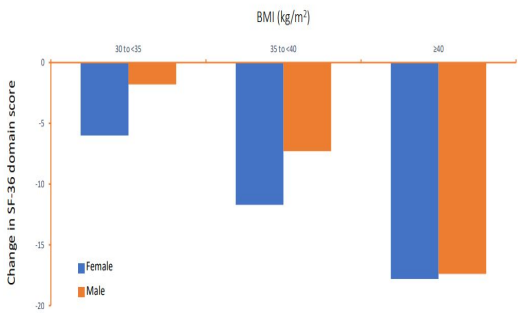
- **Weight gain increases severity of obstructive sleep apnoea**
- Longitudinal study data:



Sleep-disordered breathing includes a wide spectrum of sleep-related breathing abnormalities related to increased upper airway resistance include snoring, upper airway resistance syndrome (UARS), and obstructive sleep apnoea-hypopnoea. AHI, apnoea-hypopnoea index; CI, confidence interval

Physical function

- Obesity is associated with impaired physical function (When compared with normal weight (BMI 18.5–<25 kg/m2)
- They also have increased risk of infection due to decreased hygiene (they cannot take care of themselves)

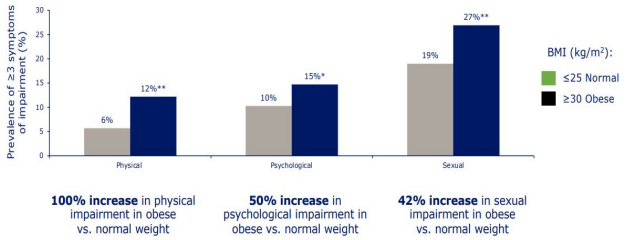


Complications of obesity

3 Mental

Psychological and psychiatric consequences

- Obesity negatively affects physical, psychological and sexual aspects of life
- Weight stigma also increase the risk of:
  - **Anxiety**
  - **Depression**: depressed individuals
    Tend to eat more = even more weight Gain
  - Suicidality
  - Low self-esteem
  - Avoidance of physical activity
  - Avoidance of health care services
  - Increased risk of weight gain

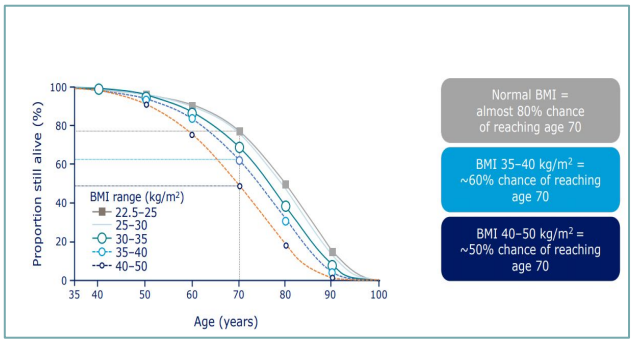


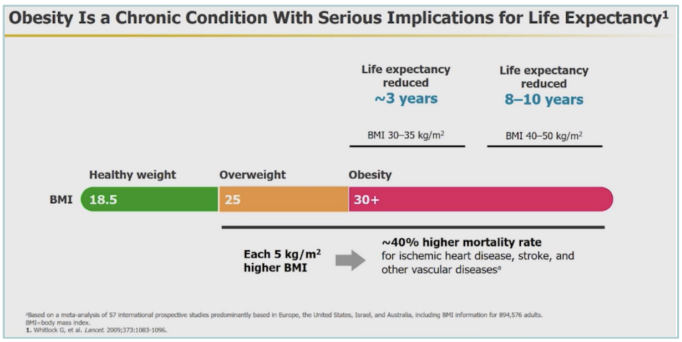
Social consequences

- Especially in females
- Public view obesity as a personal problem of bad choices
- The misconception about “fat shaming” shaming people with obesity about their weight, will help the individual lose weight, specially in school-age children
- Many symptoms are related to psychological problems or social pressures, such as the woman who cannot find fashionable clothes to wear.
- Weight discremntiantion usually manifests directly as testing, bullying, or being socially ignored
- **Weight stigma** - a negative response to someone based on their weight
- Is the fourth most common form of social discrimination amongst adults - after age, gender and race
- Is the only form of discrimination still widely deemed to be socially acceptable

◀ Obesity and mortality

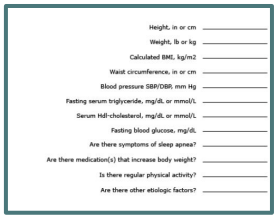
- **Life expectancy decreases as BMI increases.**
- Obese patients are at risk of early death, mainly from **diabetes**, **coronary heart disease (Major cause)** and **cerebrovascular disease**.
- Weight reduction **reduces this mortality** and therefore should be strongly encouraged
  - Bariatric’ surgery is by far the most effective long-term treatment for obesity and is the only anti-obesity intervention that has been associated with reduced mortality.





Assessment and screening

- First and most important thing is when the patient comes to your clinic for other causes rather than his obesity, and you notice that he is overweight; you have to take permission and make sure that the patient doesn't mind and is prepared to discuss about his overweight.
- After that go with the management systematically:



1 | BMI measurement (**Assess** the level of Obesity)

- 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**

2 | Waist circumference (Where is the fat located ?)

- Associated with increased risk of morbidity and mortality
- Measurement of central adiposity and 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 man

3 | Identify the aetiology (Rule out secondary causes of obesity)

- 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

4 | 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, GERD.
- Check for the **complications** of obesity (By history for e.g. knee pain, and by investigations e.g blood glucose, lipid level and blood pressure)
- **CVD risk factors that would affect mortality risk:**
  - **HTN, Smoking**
  - **DM2** (fasting blood glucose 110-125 mg/dl)
  - **Dyslipidemia** (low HDL < 35 or high LDL> 130)
  - **Family history of premature CAD**
  - **Physical inactivity**
- **Other risk factors:**
  - Age of onset of obesity

5 | Start the treatment (They should slowly lose their weight to avoid complications)

Management of obesity

◀ Treatment Goal

1) Prevention of further weight gain
2) Weight loss to achieve a realistic, target BMI
3) Long-term maintenance of a lower body-weight

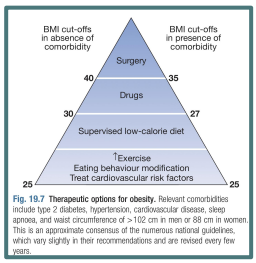


Fig. 19.7 Therapeutic options for obesity. Relevant comorbidities include type 2 diabetes, hypertension, cardiovascular disease, sleep apnoea, and waist circumference of >102 cm in men or 88 cm in women. This is an approximate consensus of the numerous national guidelines, which vary slightly in their recommendations and are revised every few years.

Treatment of Obesity

- **Lifestyle** (Diet,Exercise)
- **Pharmacotherapy**
- **Surgery**

1. Lifestyle

❖ **Most important recommendation:**
➢ Diet, Physical activity, Behavior change (decrease social gatherings)

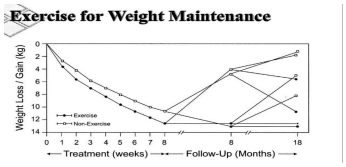
1 Lifestyle goals

- **Initial goal: 10% weight loss**
  - Significantly decreases risk factors
- **Rate of weight loss:**
  - 1-2 pounds (0.5-1kg) per week
  - Reduction of calories intake 500-1000 calories/day
  - importance of weight training and other exercises with diet induced loss to minimize risk of losing muscle strength.
- **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**
  - It is relatively easy for most people to lose the first few kilograms, but long-term success in moderate obesity is poor (no more than 10%). Weight loss will be greater initially owing to accompanying **protein and glycogen breakdown and consequent water loss**. After 3–4 weeks, further weight loss may be very small because **only adipose tissue is broken down** and there is less accompanying water 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**

Table 5.15 Potential benefits that may result from the loss of 10 kg in patients who are initially 100 kg and suffer from co-morbidities

Mortality	20–25% fall in total mortality 30–40% fall in diabetes-related deaths 40–50% fall in obesity-related cancer deaths
Blood pressure	Fall of about 10 mmHg (systolic and diastolic)
Diabetes	Reduces risk of developing diabetes by >50% 30–50% fall in fasting blood glucose 15% fall in HbA_{1c}
Serum lipids	10% fall in total cholesterol 15% fall in LDL cholesterol 30% fall in triglycerides 8% increase in HDL cholesterol

2 Physical Activity



- **Start slowly:**
  - Change of daily living activities , Avoid injury
- **Increase intensity and duration gradually**
- **Exercise by it self will not cause weight loss** unless it's heavy exercise, it is important for:
  - increase body fitness and **improve cardiopulmonary function**, **reduce stress**, also **maintain weight loss and prevent weight regain**
- **Long –term goal:** 30-45 min or more of physical activity daily, 5 or more days per week, Burn 1000+ calories per week

Management of obesity

1. Lifestyle *cont.*

3 Diet therapy/ Healthy eating

- **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
- **Atkins diet:**
  - This type of diet is good for the short term under the supervision of a physician, it's not perforable for long term. also don't forget to cover if with vit and other supplementation to avoid nutritional deficiency

6 months result (good)

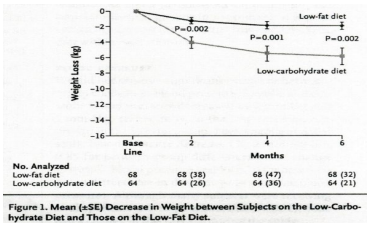
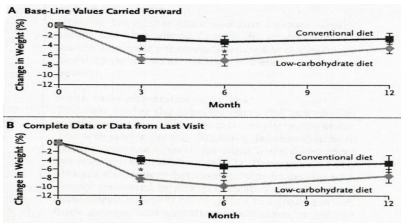


Figure 1. Mean (±SE) Decrease in Weight between Subjects on the Low-Carbohydrate Diet and Those on the Low-Fat Diet.

24 months result (Bad)



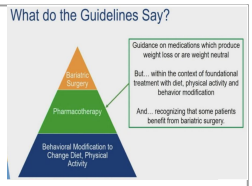
Dangers of atkins diet:

- **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

2. Pharmacotherapy

If the lifestyle modifications fail, start pharmacotherapy

Indications



- **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**
- Metformin is not approved for use in obesity

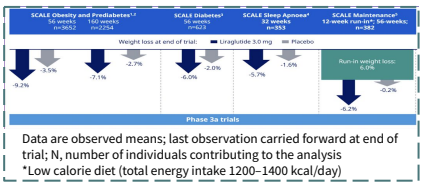
➔ **Note:** Drugs can be used in the short term (up to 3 months) as an adjunct to the dietary regimen, but they do not substitute for strict dieting.

Simaglutidec

- Long acting GLP-1 receptor agonist more effective than liraglutide, weight loss could reach up to 20-22%
- Taken once weekly 2.4mg

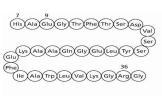
Liraglutide

- Liraglutide is a human GLP-1 analogue
- taken once-daily
- It will decrease food intake and help in long term weight maintenance,
  It can decrease body weight **15-18% maximum.**



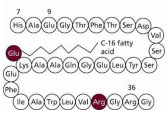
Data are observed means; last observation carried forward at end of trial; N, number of individuals contributing to the analysis
*Low calorie diet (total energy intake 1200–1400 kcal/day)

Human endogenous GLP-1



T½= ~2 mins

Liraglutide



Slow absorption from subcutis Long plasma half-life **(T½=13 h)**

97% amino acid homology to human GLP-1; improved PK: albumin binding through acylation; heptamer formation

Management of obesity

2. Pharmacotherapy *cont.*

Orlistat (meniscal)

- A lipase inhibitor, reduces the absorption of dietary fat
- Lowers Cholesterol (4-11%) & LDL (5-10%)
- Weight regain occurs after the drug is stopped.
- It's weaker than liraglutide as it decrease body weight **by 8-10% maximum** and most people will loss **only 5%, it has more side effects than liraglutide e.g. diarrhea**
- People do not continue on this drug because when they eat fat food they will have greasy stool and sometimes they can not control it
- **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

- Most of the medications have a lot of side effects ,mainly cardiac side effects, and little effect on losing weight (5Kg / year) except **liraglutide (saxenda)** & **semaglutide (ozempic)** both are GLP-1 receptor agonists and help to lose weight (around 5-15 kg /year) depending on the patient's lifestyle.

- Basically, They are DM medications taken in a high doses which cause decreased gastric emptying , decreased blood sugar and increased satiety & fullness .

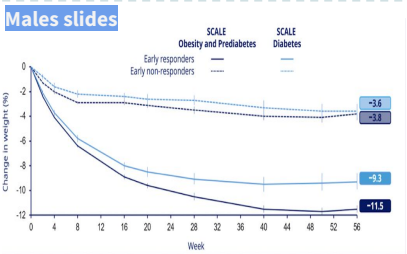
- **Ozempic** is only used for DM and isn't approved yet in KSA for obesity. However, it has shown weight loss in diabetic patients and is used in other countries

Agent	Action	Approval by US FDA	Scheduled Drug
Phentermine	• Sympathomimetic amine; norepinephrine release and to lesser extent releases other monoamines	Approved 1959	• YES
Orlistat	• Pancreatic lipase inhibitor; Blocks absorption of 30%of ingested dietary fat	Approved 1999 OTC Approved 2006	• NO
Lorcaserin	• 5-HT_{2C} serotonin agonist • Little affinity for other serotonergic receptors	Approved 2012	• YES
Phentermine/ Topiramate ER	• Sympathomimetic • Anticonvulsant (GABA receptor modulator carbonic anhydrase inhibitor, glutamate antagonist)	Approved 2012	• YES
Naltrexone ER/ Bupropion ER	• Opioid receptor antagonist • Dopamine/norepinephrine reuptake inhibitor	Approved 2014	• NO
Liraglutide 3.0 mg	• GLP-1 receptor agonist	Approved 2014	• NO

Agent	Common AE	Contraindication	Safety Consideration	Tolerability
Phentermine	**Insomnia** Dry mouth Agitation Constipation	**CVD, CHF, arrhythmias** Uncontrolled hypertension MAOI use Hyperthyroidism Glaucoma, Pregnancy	Primary pulmonary hypertension	Discontinuation (CNS): Phentermine – 17% Placebo – 3%
Orlistat	**GI complaints**	**Chronic malabsorption** **Gallbladder disease**	**May increase cyclosporine exposure; Liver failure** **Multivitamin administration**	Discontinuation: Orlistat – 8.8% Placebo – 5%
Phentermine/ topiramate ER	Dry mouth Paresthesias Headache Insomnia	Glaucoma Hyperthyroidism MAOI use Pregnancy	**Teratogenicity** Metabolic acidosis **Glaucoma**	Discontinuation: Top dose – 17% Low doses – 12% Placebo – 8%
Lorcaserin	**Headache** Dizziness Fatigue Dry mouth	MAOI use **Use with caution with serotonergic drugs** Pregnancy	Serotonin syndrome Valvular heart disease Depression Priapism	Discontinuation: Lorcaserin – 8.6% Placebo – 6.7%
Naltrexone SR/ Bupropion SR	**Nausea** GI complaints Headache Insomnia	Seizure disorder Uncontrolled hypertension **Chronic opioid use** MAOI use, Pregnancy	Suicidality in adolescents Elevated blood pressure, pulse Glaucoma Hepatotoxicity	Discontinuation: Naltrexone/bupropion – 24% Placebo – 12%
Liraglutide 3.0	**Nausea** GI complaints	**Personal/family history of medullary thyroid carcinoma or MEN2** **History of pancreatitis** Pregnancy	Thyroid c-cell tumors (rodents) **Acute pancreatitis** **Gallbladder disease** **Hypoglycemia,** Tachycardia Renal impairment, Suicidal behavior	Discontinuation: Liraglutide – 9.8% Placebo – 4.3%

All data from product labels

Males slides



Basically if the patient did not lose **5% or more of his weight after 3 months,** he is considered as a **non-responder** and there is **No benefit** from continuing the pharmacological treatment

Management of obesity

3. Bariatric surgery

- Most of the patients regain weight after bariatric surgery because of their lifestyles

i 19.9 Effectiveness and adverse effects of laparoscopic bariatric surgical procedures

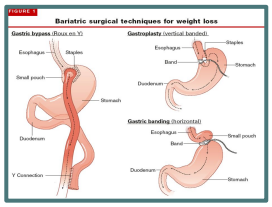
Procedure	Expected weight loss (% excess weight)	Adverse effects
Gastric banding	50–60%	Band slippage, erosion, stricture Port site infection Mortality <0.2% in experienced centres
Sleeve gastrectomy	50–60%	Iron deficiency Vitamin B_{12} deficiency Mortality <0.2% in experienced centres
Roux-en-Y gastric bypass	70–80%	Internal hernia Stomal ulcer Dumping syndrome Hypoglycaemia Iron deficiency Vitamin B_{12} deficiency Vitamin D deficiency Mortality 0.5%
Duodenal switch	Up to 100%	Steatorrhoea Protein-calorie malnutrition Iron deficiency Vitamin B_{12} deficiency Calcium, zinc, copper deficiency Mortality 1%

Indications:

- Well-informed and motivated patients, and no psychological illnesses.
- Acceptable risk of surgery
- Failed previous non-surgical method
- **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
- Psychologically stable
- The number of bariatric surgeries is increasing worldwide and it's because the obesity is also increasing and it has become more safe for the patient to do the surgery, it's considered the most effective way in treating patients with obesity if done properly and patient have proper follow up because weight regain is possible.
- Surgery is not always considered as the last option, it can be first, second.. it depends, **It can be used as a first-line option for individuals with a BMI >50 kg/m^2.**

Types:

1 Restrictive-type of surgery



➔ **Which restrict the ability to eat, for example:**
- Adjustable gastric banding
- Vertical banded gastroplasty
- **Sleeve gastroplasty**
  - gastric bypass causes more weight loss than sleeve gastrectomy, but sleeve gastrectomy is faster to do and with less malabsorption complications

2 Malabsorptive and restrictive

➔ **Which reduce the ability to absorb nutrients, for example:**
- **Roux-en-Y gastric bypass**
- Biliopancreatic diversion

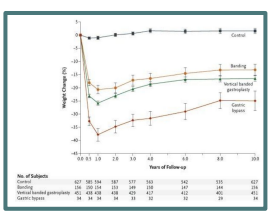
➔ The malabsorptive procedures cause nutrient deficiencies, malnutrition and in some cases, anastomotic leaks and the dumping syndrome (e.g. with the duodenal switch).

3 Restrictive plus malabsorptive procedures

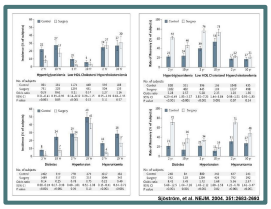
- e.g. Duodenal switch, Intragastric balloon

Follow up:

- **Follow up is crucial, It's important to have at least 1 year follow up in this critical period.**



- Classical figure of most of bariatric surgery, **the initial year is the golden year** where they lose weight and after that they start to regain weight but they should stop weight regain, if they don't they will go back to their usual weight which is a very bad outcome
- Make sure to support the patient in the beginning with **dietary supplementation** and make sure they don't have any dietary deficiencies. **most importantly** is **iron** after that **vit D** and **B12 come**



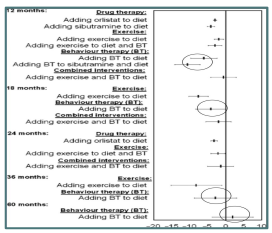
- After that you should support them by telling them this is the usual physiology, the weight will increase a little bit but keep exercising and good dietary habit.
- In the end you should tell them to keep a healthy lifestyle and they shouldn't be back to their baseline
- If done properly and follow up properly, surgery could reverse complications, people could be cured from diabetes, HTN, hyperuricemia.

Management of obesity

◀ Issues to consider in postoperatively care Males slides

Multidisciplinary post-operative follow up	Post-operative **nutritional and behavioral advice** make sure that patient does not consume high dense diet, like milk shake
Micro and Macronutrients **supplementation** (**iron**, vit D, B12)	Weight loss and **weight regain post-surgery**
Short and long-term complications	**Physical activity** (important to prevent weight regain)
Management of comorbidities	**Psychological aspects** a lot of Psychological issue patient go through after the surgery e.g depression

◀ What interventions should we add to weight reducing diets in adults with obesity?



- A systematic review of randomized controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions

◀ For those who don't lose weight, what should be done?

Reassess:

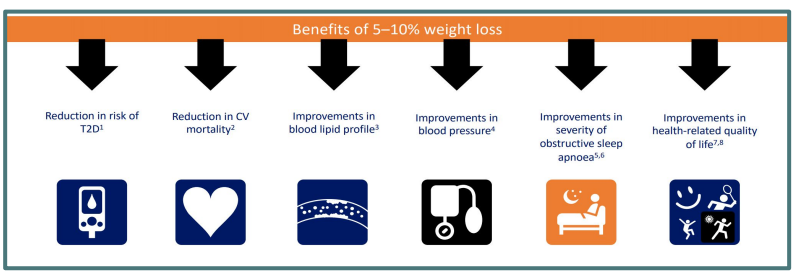
- Understanding and compliance with diet, physical activity, and drug regimen
- Accuracy of weight recordings, Possible Fluid retention (salt intake, etc)
- Changes in medical condition , Motivation for change, Social and personal stress
- Also setting goals and objectives is very important
- Is the provider of health care the root of the problem ?

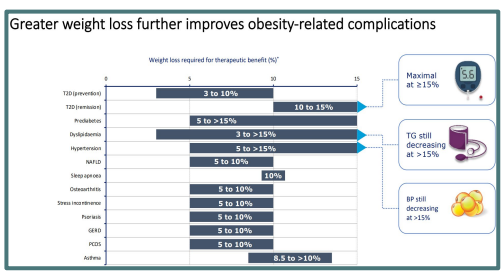
◀ For Those Who Don't Lose Weight and There is no Cause Except Noncompliance with Diet & Exercise, what should be done?

- Consider changing medication
- Consider referral to:
  - Dietitian, Behavioral counselor, Exercise professional, psychologist.
- Reconsider goal: i.e. simple maintenance or a rest from weight loss efforts
- Discuss surgical options if medically or psychologically indicated

◀ Metabolic benefits of weight loss

1. **Decreased insulin resistance**
2. **Decreased blood glucose**
3. **Decreased cholesterol**
4. **Decrease in fatty liver**





Summary

- **Obesity is a chronic relapsing progressive disease defined by abnormal or excessive adiposity that may impair health.**
- **Improved ability to engage in activities of daily living such as improved mobility and reduction in symptoms of joint pain, bladder incontinence and obstructive sleep apnea.**
- **Several metabolic benefits of weight loss including decreased insulin resistance, blood glucose, cholesterol and fatty liver.**

Etiological classification	1- Neuroendocrine 2- Drug-induced 3- Dietary obesity 4- Reduced energy expenditure 5- Genetic factor
Risk factors	1. Lifestyle 2. Sleep deprivation → less than 7 hours → ↓ leptin, ↑↑ Ghrelin → ↑ appetite 3. Cessation of smoking → due to nicotine withdrawal 4. Social influence 5. Diet
complications	● Gallbladder disease ● Sex-hormone related disorders ○ Polycystic ovary disease, female infertility and male hypogonadism ● Pulmonary disorder: ○ Obstructive sleep apnea ○ Asthma/reactive airway disease ● Biomechanical disorder ○ Osteoarthritis ○ Urinary stress incontinence ○ GERD ● Weight loss ameliorated all of these conditions
Screening	1. BMI measurement 2. Waist circumference 3. Evaluation of overall medical risks
Management	**1. Lifestyle intervention:** - Diet, exercise - Initial goal 10% weight loss - Slow weight loss is preferred **2. Pharmacotherapy:** - Indication: BMI above 30, BMI 27-30 with comorbidities. - Types: Sympathomimetics (sibutramine), Pancreatic lipase inhibitor (Orlistat), antidepressants, antiepileptic, diabetic drugs (metformin) **3. Surgical intervention:** - Indication: BMI above 40, BMI above 35 with comorbidities. - Types: - Restrictive (via a small stomach reservoir): Vertical banded-gastroplasty, and gastric banding. - Malabsorptive and restrictive (via decreasing small bowel length:Roux-en-Y gastric bypass (most common procedure), -Biliopancreatic diversion

Lecture Quiz

Q1: 42-year-old man sees you because of obesity. He played football in high school and at age 18 weighed 250 lb. He has gradually gained weight since. Many previous attempts at dieting have resulted in transient weight loss of 10 to 15 lb, which he then rapidly regains. He has been attending weight watchers for the past 3 months and has successfully lost 4 lb. Recent attempts at exercise have been limited because of bilateral knee pain and swelling. On examination height is 6 ft 0 in, weight 340 lb, BMI 46. Blood pressure with a large cuff is 150/95. Baseline laboratory studies including CBC, biochemical profile, thyroid-stimulating hormone, and lipids are normal with the exception of fasting serum glucose, which is 145 mg/dL. What is the best next step?

A- Discuss bariatric surgery with the patient
B- Refer to a commercial weight-loss program
C- Recommend a 1000-calorie per day diet
D- Recommend a low-fat diet

Q2: A 54-year-old male with type 2 diabetes mellitus reports 3 months of exertional chest pain. His physical examination is notable for obesity with a body mass index (BMI) of 32 kg/m2, blood pressure of 150/90, an S4, no cardiac murmurs, and no peripheral edema. Fasting glucose is 130 mg/dL, and serum triglycerides are 200 mg/ dL. Which of the following is most likely in this patient?

A- Elevated high-density lipoprotein (HDL) cholesterol
B- Insulin resistance
C- Larger than normal LDL particles
D- Reduced serum endothelin level

Q3: A 27 year old woman presents to clinic for the first time. She has no known medical history and takes no medications, but complains of lethargy and fatigue. She weighs 97 kg and has a body mass index (BMI) of 32 kg/m^2 . She states that her weight has been climbing over the past few years, more rapidly over the past few months. On examination, her temperature is 36.8°C, pulse is 70beats/min, and blood pressure is 128/78 mmHg. She has no conjunctival pallor, sclera are anicteric, examination of her neck is normal, there is no lymphadenopathy, and no cardiac murmurs are heard. Her abdomen is obese without ascites and there is no peripheral oedema. Which of the following is the best next step in management?

A- Check serum thyroid-stimulating hormone (TSH)
B- Measure triceps skinfold thickness
C- Prescribe orlistat
D- Recommend a very-low-calorie diet

Q4: A 34 year old woman with obstructive sleep apnoea and diabetes is referred to general surgery for a Roux-en-Y gastric bypass procedure. Her BMI is 41 kg/m and she has been unsuccessful in achieving weight loss with multiple attempts at lifestyle modification and pharmacological therapy. Which of the following statements would be most appropriate in counselling this patient?

A- It will likely take years to see improvement in diabetes control
B- She is at low risk for post-surgical complications such as wound infection
C- She should wait at least 2 years before considering pregnancy
D- She will likely experience amenorrhoea post-operatively

Answers: Q1:A | Q2:B | Q3:A | Q4:C

Answers Explanation File!

GOOD LUCK !

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