SHEET 37

METABOLISM

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* ملاحظة :: الشيت سهل جدًا

Mmmm who doesn't like chocolate?!

Here we can start our lecture **OBESITY**.

-It's defined as an disorder affecting body weight regulatory systems, **HOW?!**

Basically by the accumulation of excess body fat.

-The availability of food nowadays, our new lazy lifestyle and technology made obesity a **PANDIMIC** disease.

-Carbohydrates are the main source of our diet that causes obesity.

-The most dangerous and common disease we fear from as a risk from obesity is: Diabetes.

-Childhood obesity three folds increased in the last four decades.

-Obese people today are way more than malnourished people.

(Take a moment to think of it..)

-17% of those age **ARE** obese (2-19 years old).

-Approximately in Jordan 1/3 of the population **ARE** obese.

-You have a chance of 50% to become overweight and a chance of 25% to become obese.

-Many huge numbers and statistics show us how serious the problem is.

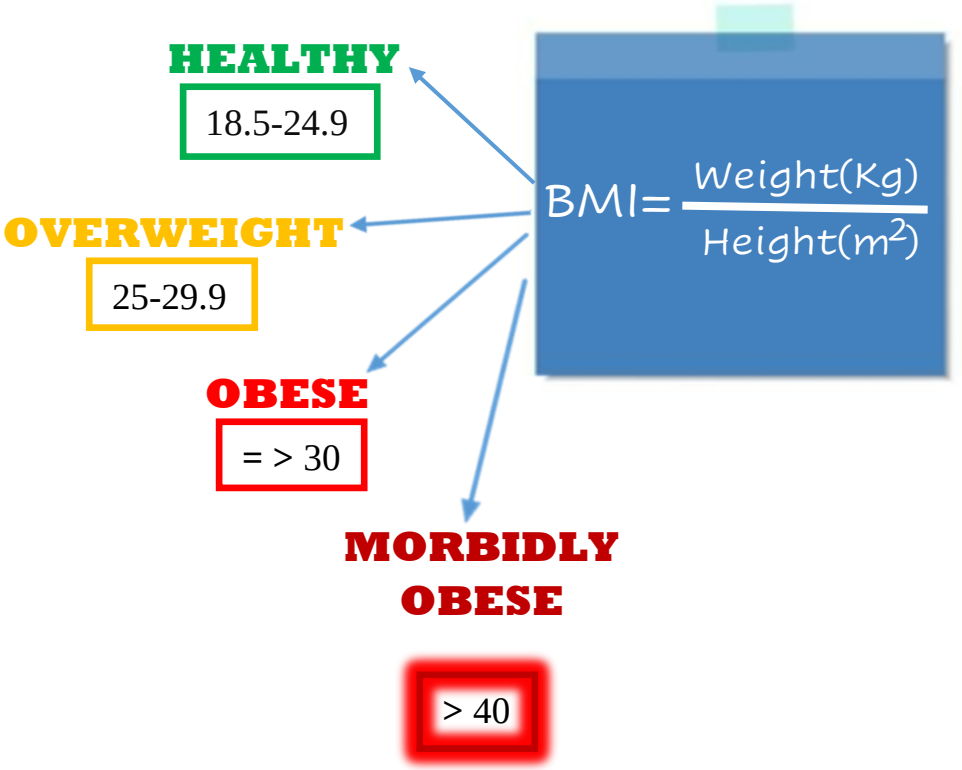
More associated diseases: (hypertension, cardiovascular disease).

How do we measure/define obesity?!

1. BMI (Body Mass Index):

-The best indicator for obesity.

-It's how much weight do you have divided by your squared height.



-Morbidly obese leads to surgical and medical intervention, because at this stage obesity **IS** a disease.

2. Waist circumference:

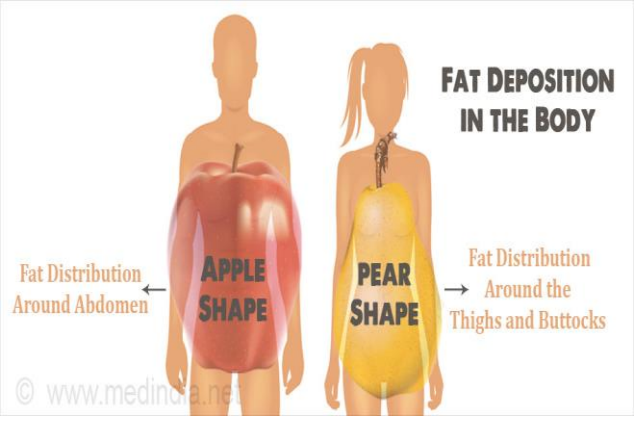
- ≥40 in (2.54cm) (men) / ≥35 in (women) they considered obese which is a risk factor for other diseases.

3. Waist to hip ratio:

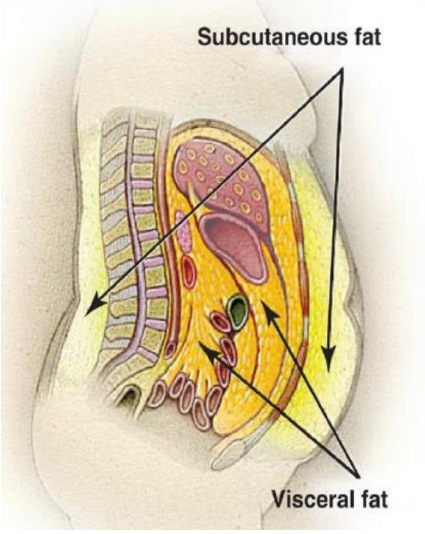
-People are different in fat deposition (males/females) and their body shape between each gender.

-It is strongly connected to the BMI, so it does give you a specific measure for obesity.

- >0.8 for women & > 1.0 for men then it may become a risk factor, below this ratio it doesn't make any problem otherwise, it tells you that the hip has more accumulation of fats than the abdominal.



Biochemical differences in regional fat depots:



Different between abdominal fats and gluteal fats:

Note :

2 types of abdominal fats : (subcutaneous fat and visceral fat) .

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Abdominal fat .	Gluteal fat .
Large cells.	Small cells.
Higher rate of fat turnover	
Activity of the enzymes on them is much easier. (visceral fats is also easier than subcutaneous fats).	In other words, mobilization of (FFA) from the TAG in the gluteal region is much harder to occur.
Worsley impact the health. Because it is very close to the liver So FFA go direct to the liver through portal vein and combine them to TAG again. converting them to the VLDL . VLDL is a risk factor for many diseases such as cardiovascular diseases .	FFA from the hip area enter the general circulation, so it decreases the amount of FFA that is converted to VLDL.

Depending on the previous info. it has been noticed that men can lose weight faster then women.

نتذكر بس توزيع الدهون بكلا الجنسين، في الذكور تتمركز حول منطقة البطن وفي الاناث عند الارداف، فالذكور يخسرون وزن اسرع لسهولة خسران دهون البطن (: مو لانه احسن منا :)

4- Number of fat cells :

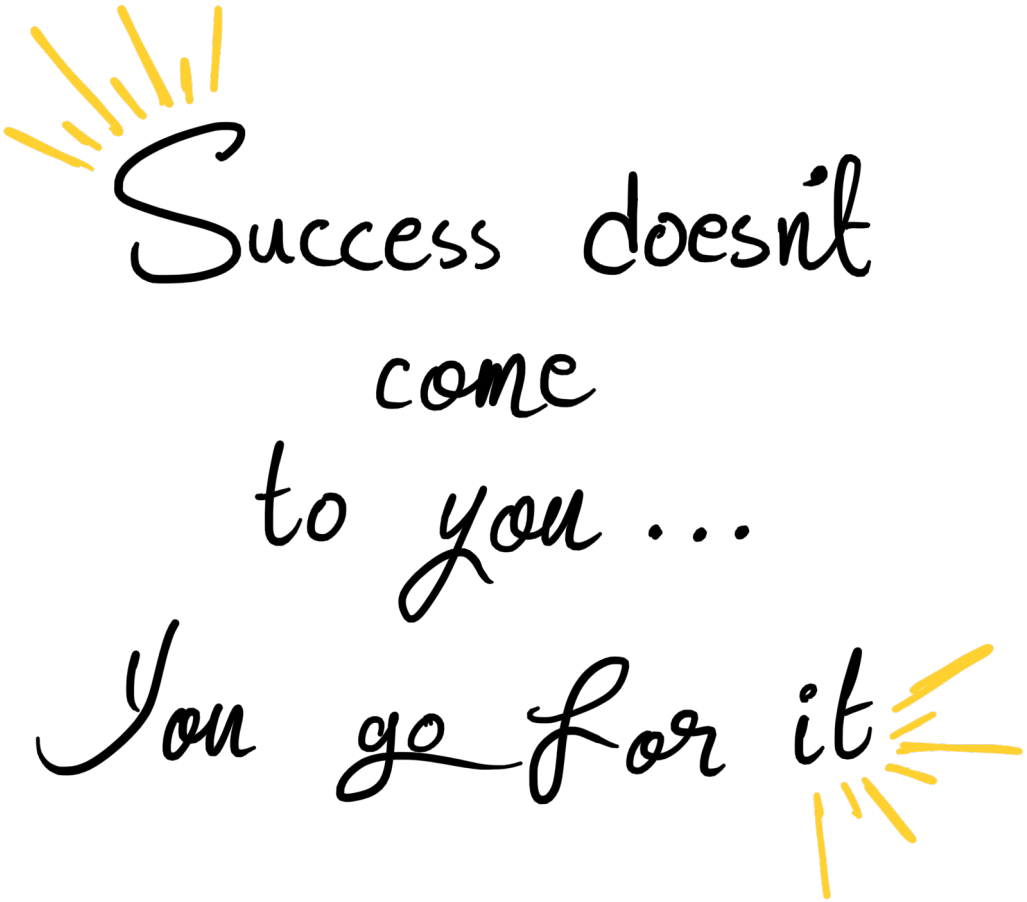
You must take care of your self since you were a child because Fat cells, once gained, may lose them **BUT** they have a very long cell cycle which can last up to **10 years**).

When you over eat, fat cells will expand (hypertrophy) 2 to 3 times of their original size, after this if you have an excess fat your body will store them as a new adipocytes (Hyperplasia).

-New adipocytes are formed from a preadipocytes which can NOT divide.

-you can not play with the number of cells because their remodeling takes several years, you can just decrease their size.

لهيك عادة الي بعاني من سمنة في طفولته صعب يخسر وزن عند كبره بسبب تكون الخلايا الدهنية .

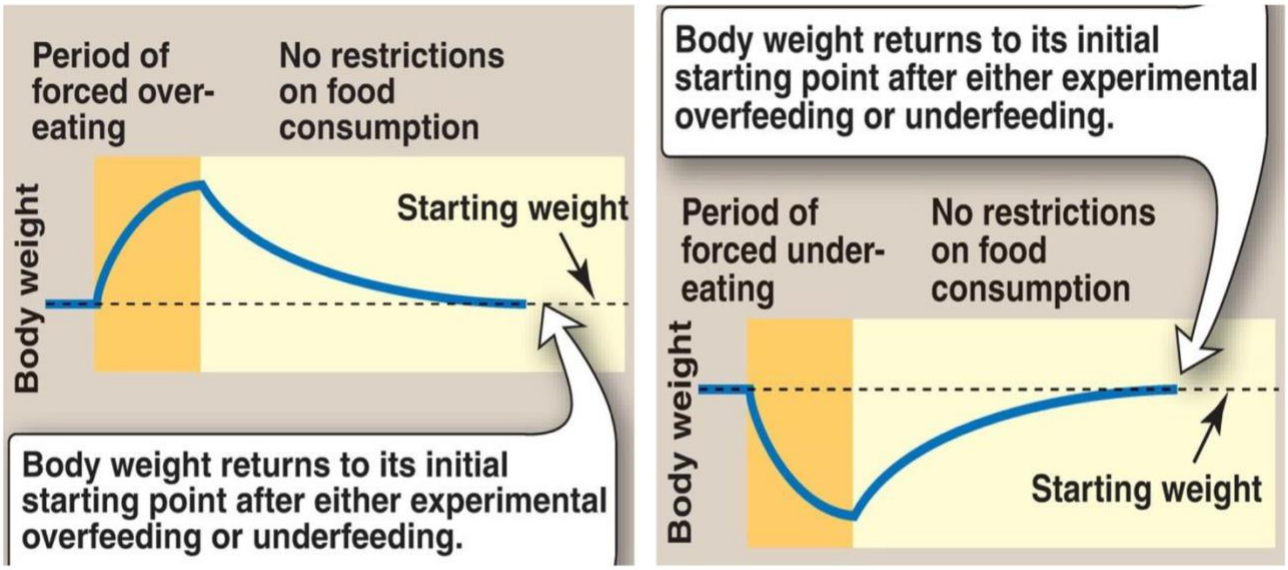


Body weight regulation

Body weight is stable as long as the behavioral & environmental factors that influence energy balance are constant.

Set point :

Every one has a set point of his weight and it can't be changed !!
even though this information may hurt a lot of you BUT unfortunately this is the ugly truth.



A - Genetic contributions to obesity :

Genetic factors have a role in obesity , obesity run in the family.
Ex :
Identical twins with similar or different behaviours/lifestyle have the same BMI.
Adopted children usually correlates with biologic parents.

Uncontrolled, greedy eating behaviour .
Often observed clustered in families

This concept (set point) explain some of the issues but it doesn't explain the whole issue of obesity

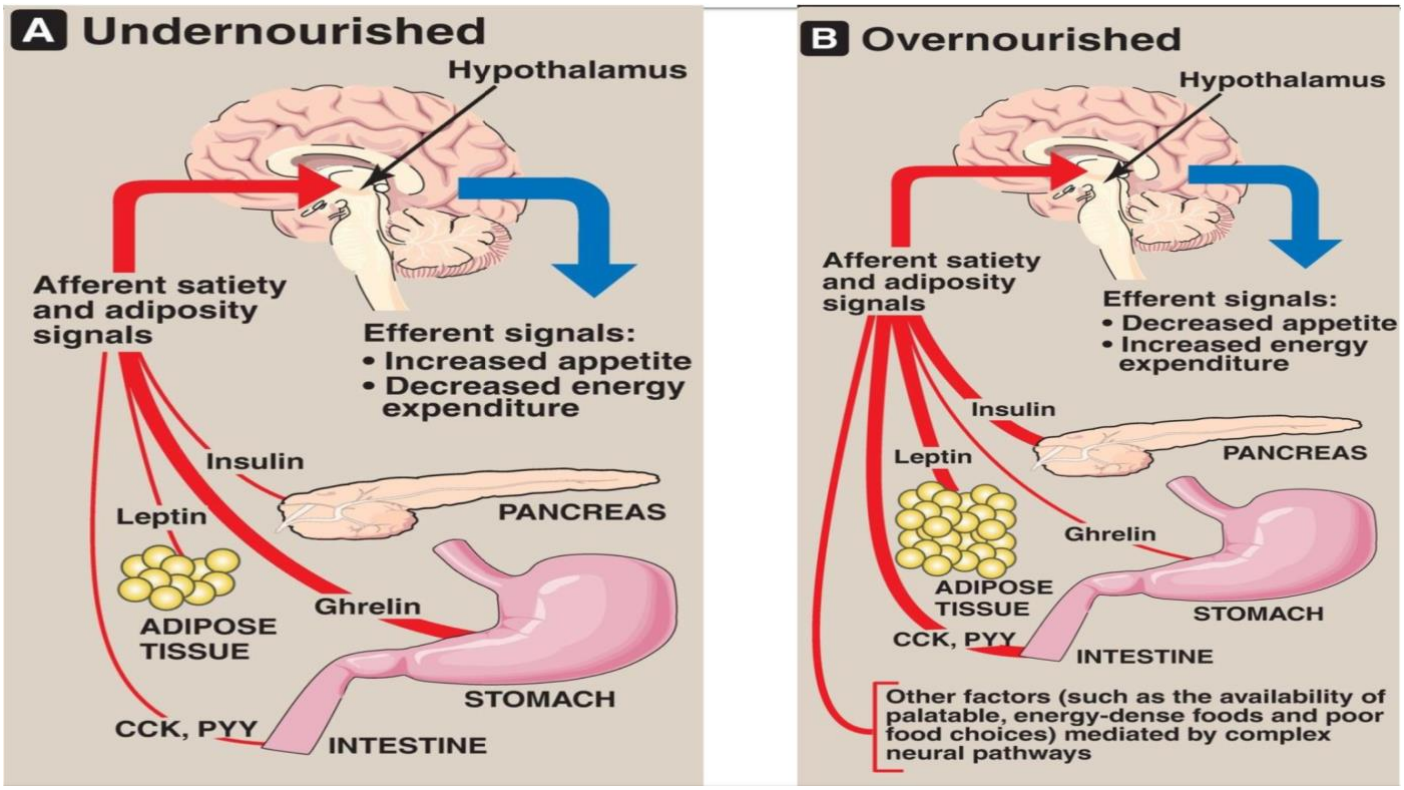
B – Environmental & behavioral contributions:

- Ready available food.
- Energy-dense food.
- Sedentary lifestyles: TV, cars, computer (energy-sparing).
- Eating behaviors: snacking, portion size, number of people.

Ex : Men in Japan (aged 46–49 years) are lean (BMI = 20),
But those are living in California (BMI = 24) .

C – Molecular influence :

Can be long term or short term .



Controlling the obesity is very complicated ,so the brain(hypothalamus), pancreas and GI system are the ones who takes the lead.

Molecules from these organs control your appetite and energy expenditures by something called (GOT – BRAIN ACCESS)

Adipose tissue is a hormonal organ produce many hormones called ADIPOCHINES such as ((leptin))

IN UNDERNOURISHED:

Insulin	low
Ghrelin (Hungry hormone)	High
Leptin	low
CCK ,PYY	low

CCK is Produced to activate trypsine secretion

Over nourished :

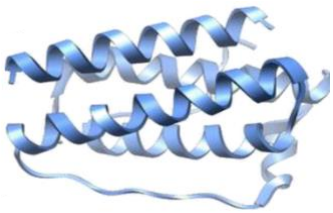
Insulin	High
Ghrelin (Hungry hormone)	Low
Leptin	High
CCK ,PYY	High

We stored all of our fats as TAG .

Long term signals :

1- LEPTIN: (only one that established scientifically)

Composed of alpha helices and product of OB gene (with reference to Obesity)



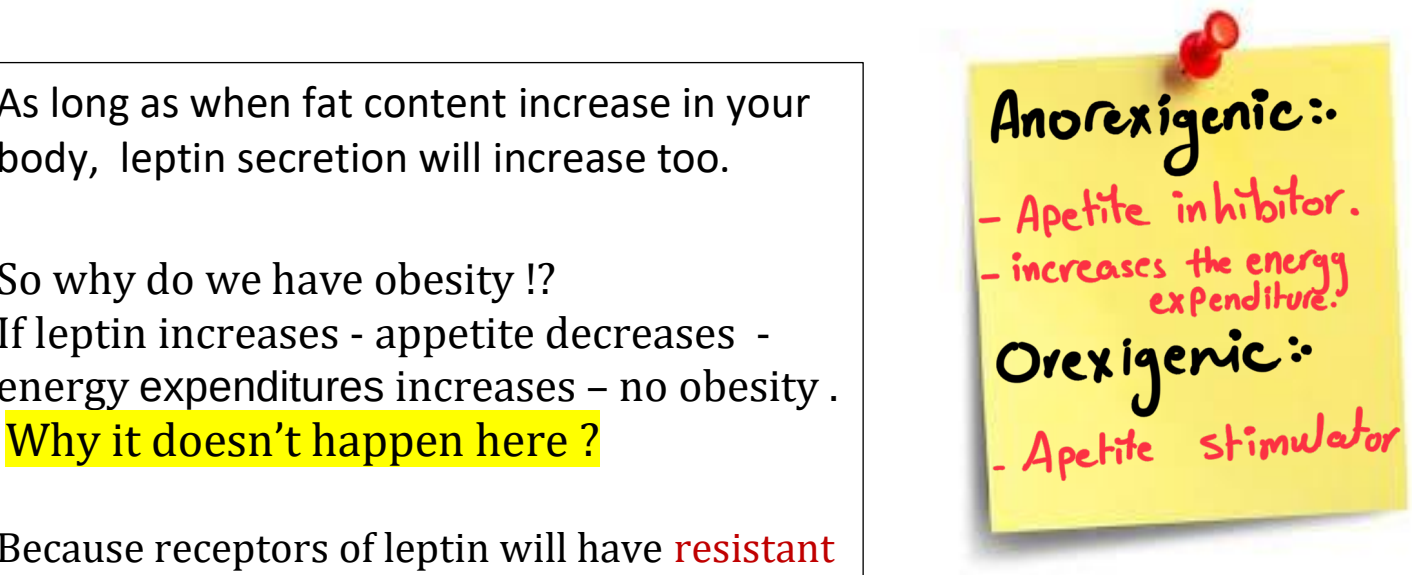
Produced proportionally to the adipose mass, Informs the brain of the fat store level .

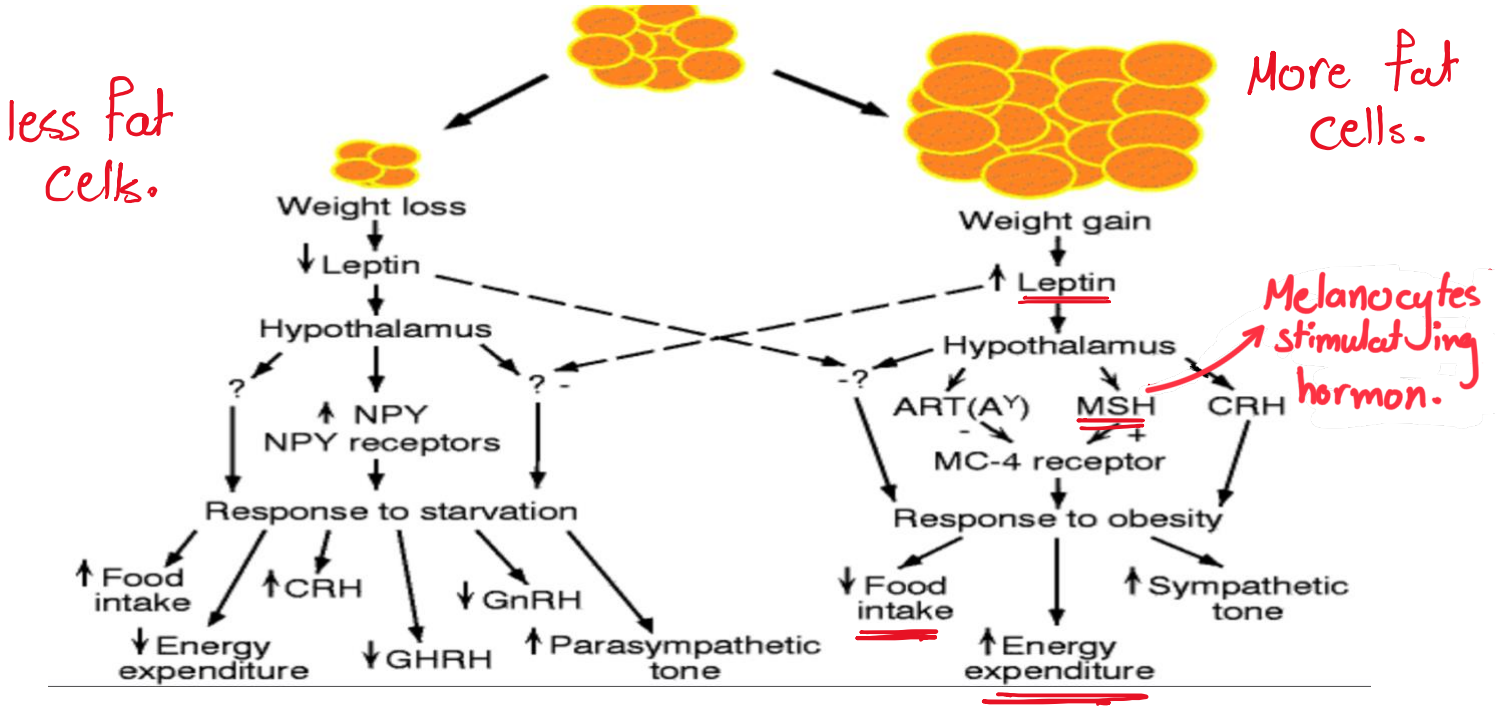
Function : Regulate body fat through the control of appetite & energy expenditure. (Anorexigenic effect)

As long as when fat content increase in your body, leptin secretion will increase too.

So why do we have obesity !?
If leptin increases - appetite decreases - energy expenditures increases – no obesity .
Why it doesn't happen here ?

Because receptors of leptin will have resistant against high concentration of leptin . (Same issue of DM with insulin)
Leptin is high but it isn't working (not functional because of resistance)





2- Insulin:

Obese individuals are also hyperinsulinemic (more concentration of insulin than normal people).

Like leptin : insulin acts on hypothalamic neurones to decrease appetite.
Obesity is associated with insulin resistance .

Short term signals:

control hunger and satiety.
Affect size (during eating) and number of meals(between the meals).

1- From the GI track : (CCK ,PYY, ghrelin)

In the absence of food intake (between meals)
Stomach produces ghrelin – orexigenic (appetite-stimulating)

As food is consumed
GI hormones (CCK and peptide YY) induce satiety (an anorexigenic effect) → terminating eating

2- From the hypothalamus:

neuropeptide Y [NPY] - orexigenic - .
α-MSH and neurotransmitters (serotonin and dopamine) – anorexigeni - .

Leptin increases secretion of α-MSH and decreases secretion of NPY

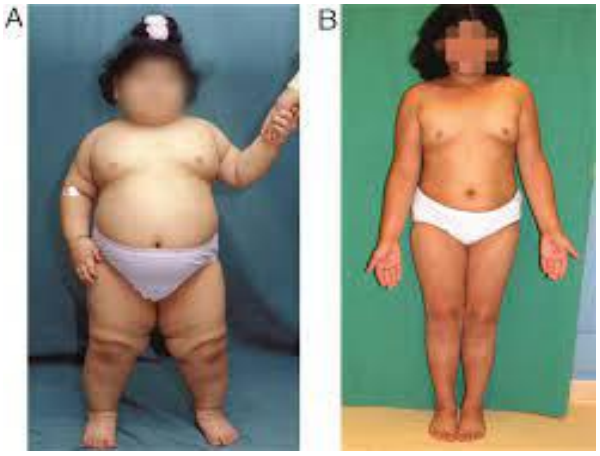
Long-term and short-term signals interact (in very complicated way) .

Mice treated with leptin lose a lot of weight, it can be used for human also (but still no single issue can solve the problem)

Note:

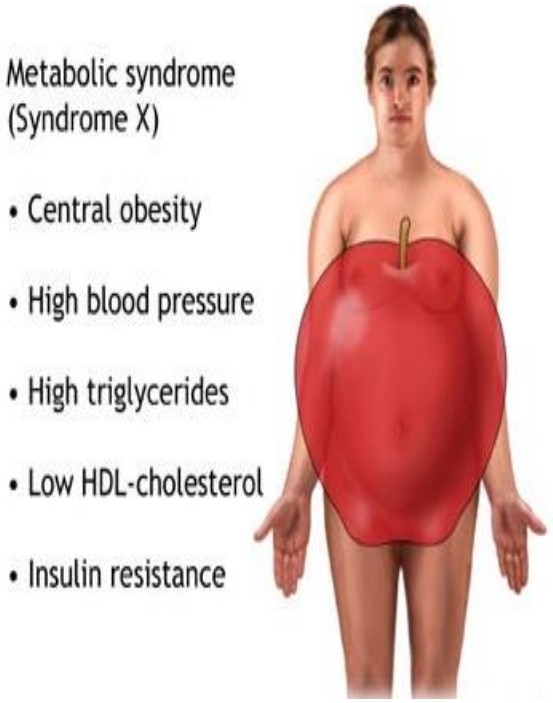
MC4 Receptors of α-MSH (proopiomelanocortin)-(very big protein)

Loss-of-function mutations to MC4R are associated with early-onset obesity



Metabolic changes observed in obesity .

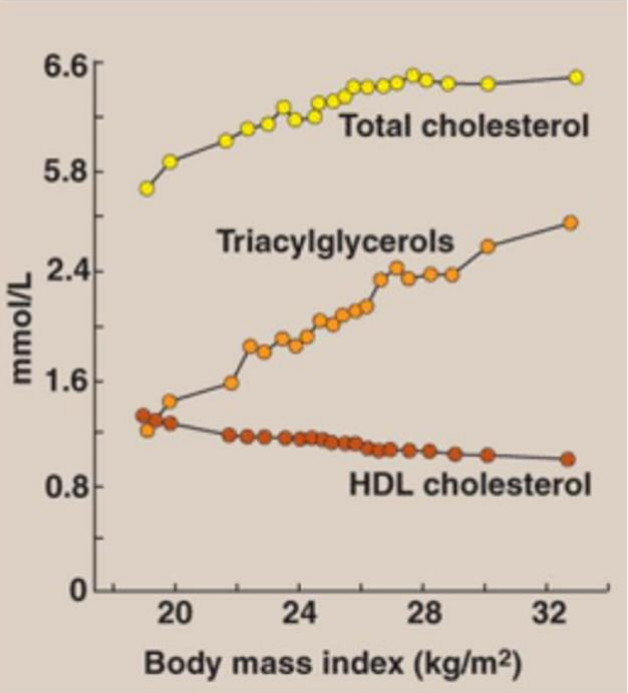
- It always associated with obesity.
- High B.P. (Hypertension) due to the increasing of the pressure on the vessels in the abdominal area .
- Increased risk for diabetes mellitus & cardiovascular disorders (men: 4 times higher mortality of (cardiovascular disease).
- Dyslipidemia.



Insulin resistance causes increased activity of hormone-sensitive lipase, resulting in increased levels of circulating fatty acids.

In liver converted to triacylglycerol & cholesterol.

Released as VLDL, resulting in elevated serum triacylglycerols (up to 3 folds) . Concomitantly, HDL (the best one of the lipoproteins) levels are decreased (when increasing the BMI)



Obesity and health:

Risk factor for:

Adult onset diabetes – Hypercholesterolemia- High plasma TAGs- Hypertension - Heart disease - Some cancers – Gallstones - Arthritis - Gout.

Correlated with increased risk of death :

1- The relationship is strong for <55 yrs.
2- The relationship is weak for >55 and < 74.
3- After age 74, there is no association between increased BMI & mortality.

Weight reduction:

1- Physical activity: عالفاضي

Create an energy deficit , cut the relation between the input and output of energy (making the output more than input) (And this is unacceptable) .

2-Caloric restriction : كمان عالفاضي

The most common approach .

1 pound (454 gm) of adipose tissue corresponds to approximately 3,500 kcal .

Ineffective over the long term for many individuals.

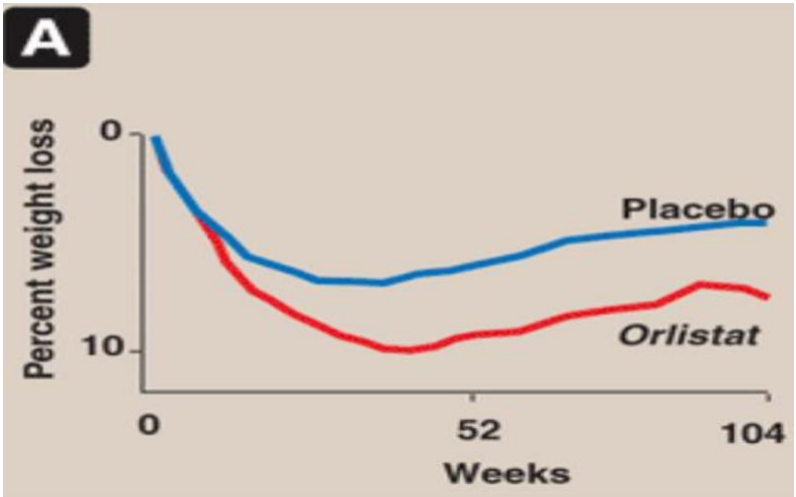
3-Pharmacologic (by drugs)

Some of them decrease the appetite and some of them acts on lipids .

Two medications (BMI ≥ 30):

Sibutramine : appetite suppressant that inhibits the re uptake of both serotonin and norepinephrine (an anorexigenic effect).

Orlistat: lipase inhibitor that inhibits gastric and pancreatic lipases .



Also the drugs not effective that much because our problem comes mainly from carbs digestion not from fat digestion

Again , you must take this drug for 104 weeks to lose just 10% of your weight.

انها لحياة طويلة..

4- Surgical procedures : (BMI > 40)

Are an option for the severely obese patients .

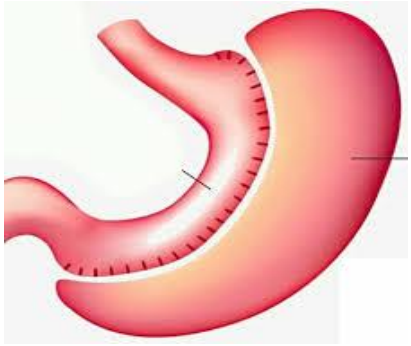
the whole idea is to reduce the size of the stomach and gives the best outcomes (lose 35% from their weight) but not the best lifestyle .

Risk factors :

1- The Stomach is a muscular tissue could be expanded again and every thing back to its normal.
2- Undigested food due to loosing the stomach function .
3- Hormonal increase (Ghrelin mainly) are produced from the stomach which effect the brain .

لهيك الأشخاص الي عاملين عمليات قص معدة دائمًا بكونوا جوعانين .

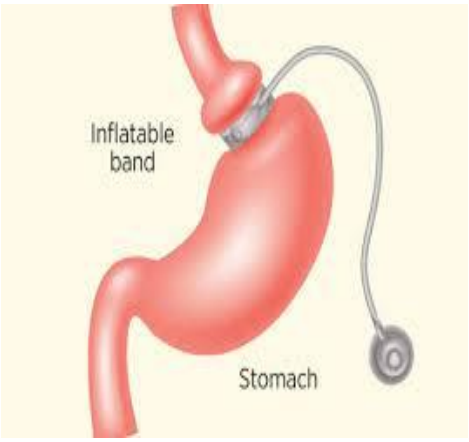
And this depends on the site of removal and how much cells are dead.



Another surgical interventions:

1- **gastric band** to decrease the amount of food that get inside the stomach. (Hormonal secretion and digestion don't change) .

2-**gastric bypass** surgeons link the jejunum to the stomach, so the food doesn't pass by the stomach it passes through the jejunum also, they link the jejunum to the duodenum to receive the pancreatic enzymes.



اعذرونا على التقصير والخطأ...
تحياتي على عجال.

وبس كده يا مؤمن