

ADDITIONS TO PREVIOUS LECTURE (INSOMNIA, NV)

- ▶ Withdrawal of benzodiazepine(BZ):The 1st half of the(BZ) taper (50% of the original dose) is generally easier and can processed more quickly than the last half of the taper.
- ▶ Withdrawal steps of short acting BZ is more severe than the long acting BZ, therefore a long acting a long acting can be substituted at an equivalent dose and then tapered.

DOMPERIDONE

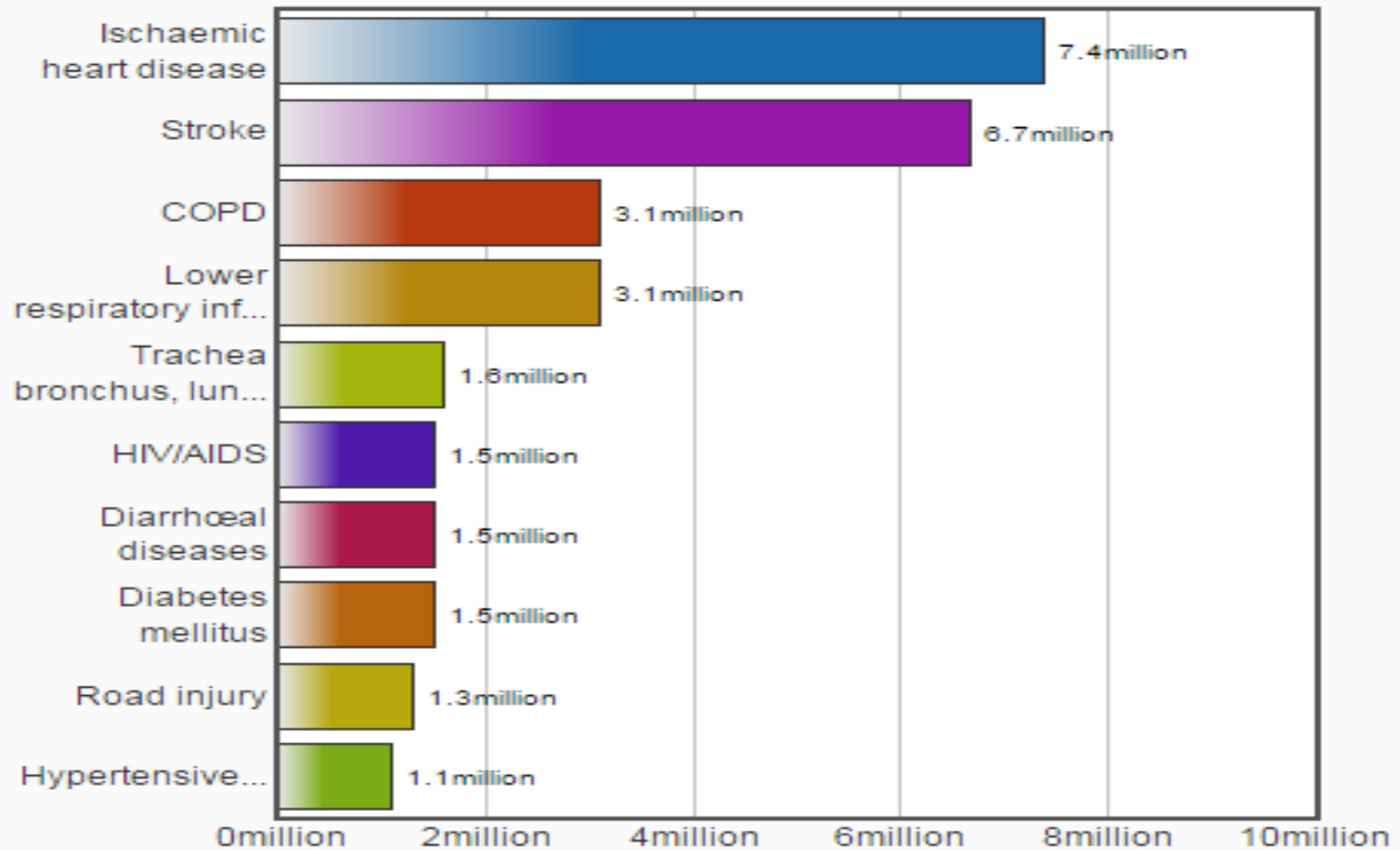
- ▶ Domperidone is available [over-the-counter](#) to treat gastroesophageal reflux and functional dyspepsia in many countries, such as [Netherlands](#), Italy, [South Africa](#), Mexico. Domperidone is not approved for use in the US, but is prescribable and limitedly available in this country for use in people with treatment-refractory gastrointestinal symptoms.
- ▶ In 2014, research was published which found domperidone, was associated with a small increased risk of heart rhythm problems and it should be restricted to prescription-only.

قال الرسول الكريم محمد صلى الله عليه وسلم:

(بحسب ابن ادم لقيمات يقمن صلبه فان كان ولا بد فثلث لطعامه
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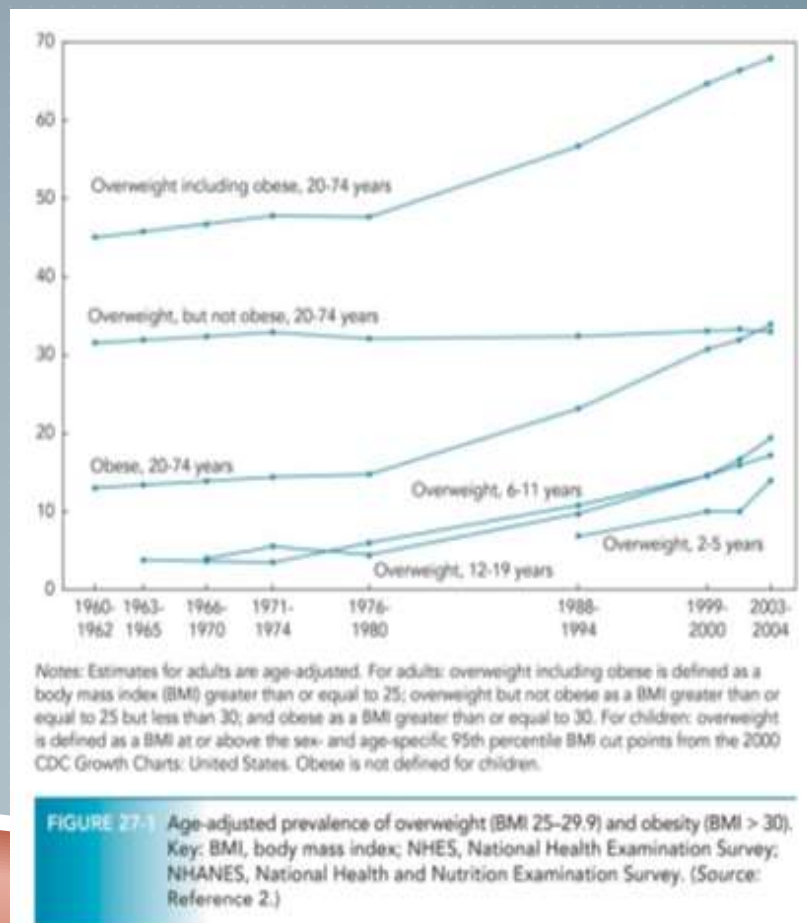
(نحن قوم لا نأكل حتى نجوع وإذا اكلنا لا نشبع)

The 10 leading causes of death in the world 2012



OVERWEIGHT AND OBESITY

- The incidence of obesity is increasing in men and women in all age groups



DETERMINATION OF OVERWEIGHT AND OBESITY

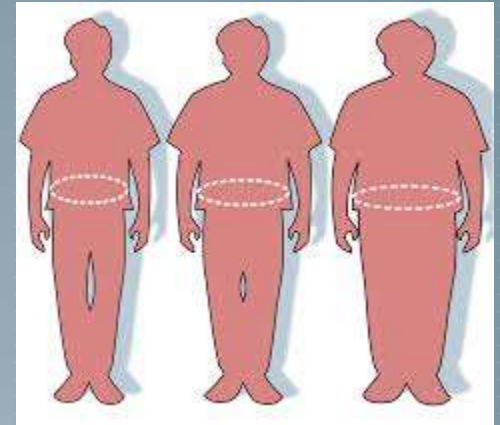
- ▶ According to BMI(body mass index) and waist circumference.

$BMI = \text{weight kg} / (\text{height m})^2$

Normal BMI=18-25

Overwt: BMI > 25 and WtC=94cm. or more for men and 80 cm. or more for women.

Obesity: BMI > 30 and WtC=102cm. or more for men and 88 cm. or more for women.



BMI classification	
Underweight	<18.5
Normal range	18.5 – 24.9
Overweight:	>=25.0
<i>Preobese</i>	<i>25.0 – 29.9</i>
Obese:	>=30.0
<i>Obese class I</i>	<i>30.0 – 34.9</i>
<i>Obese class II</i>	<i>35.0 – 39.9</i>
<i>Obese class III</i>	<i>>=40.0</i>

METABOLIC SYNDROME

Is a syndrome associated with increased risk of coronary artery disease and DM.

Patients with metabolic syndrome benefit from wt loss since they demonstrate insulin resistance.

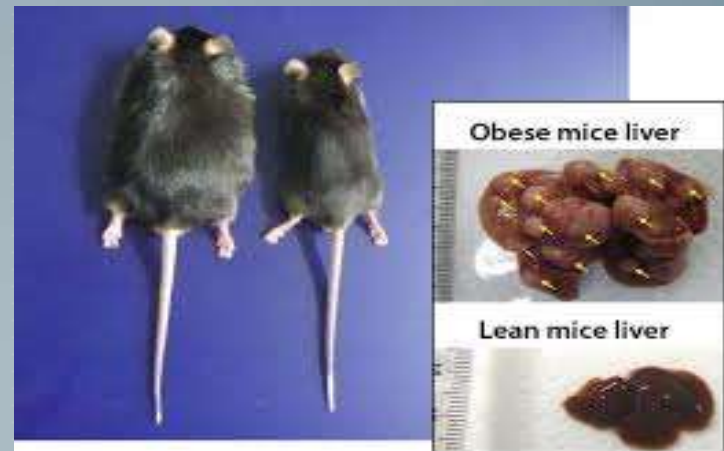
Patients with 3 or more of the followings are said to have metabolic syndrome:

- 1- WtC > 40 inches in men and 35 inches in women.
- 2- s. triglyceride 150mg/dl or greater.
- 3- HDL cholesterol < 40mg/dl in men or less than 50mg/dl in women.
- 4- BP 130/85 or higher.
- 5- FSG 100mg/dl or greater.

PATHOPHYSIOLOGY

- Genetic and environmental factors.
- Leptin resistance: leptin is a hormone released from the adipocytes that signals the hypothalamus regarding the amount of energy reserve in the body.

although administration of leptin to mice led to dramatic wt loss, most humans are leptin resistant.



- Increased Ghrelin(hunger hormone) levels following diet induced wt loss (this explains the difficulty in trying to keep from regaining wt).

Ghrelin is released from the stomach when it is empty.

- Sleep duration: high BMI value with shorter duration of sleep.

because of decreased leptin and increased ghrelin values with short sleep.

- Gut flora: obese persons have lower bacteroidetes bacteria and more firmicutes bacteria. (probiotics and antibiotics may be used for wt maintenance and wt loss???)

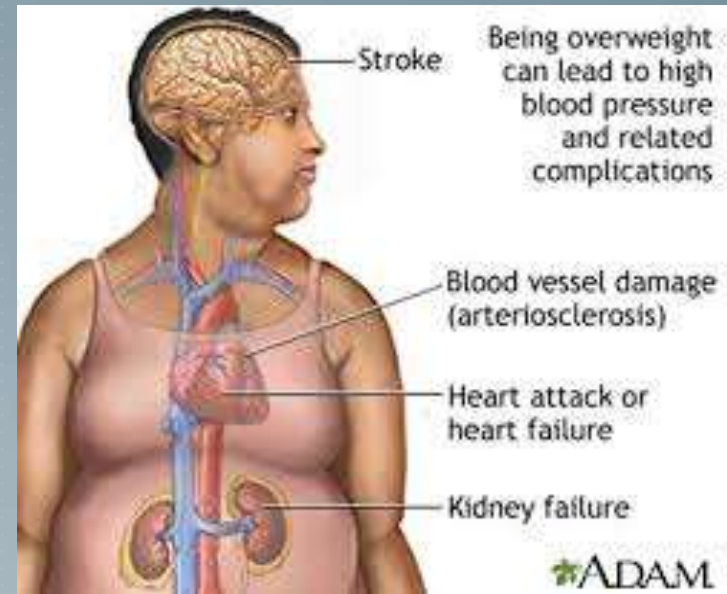
DRUGS WHICH CAUSES OBESITY

- ▶ CS.
- ▶ Hormonal contraceptives.
- ▶ Old antidepressants (TCAD) and MAOIs.
- ▶ Insulin, sulphonylurease, thiazolidindiones.
- ▶ Antipsychotics (clonazepin, olanzapin, risperidone)



COMPLICATIONS OF OBESITY

- ✓ Coronary heart disease: HT, dyslipidemia, arrhythmia, stroke....etc
- ✓ Type 2 DM.
- ✓ Psychopathy especially in children.
- ✓ Gall bladder disease.
- ✓ Osteoarthritis.
- ✓ Sleep apnea.
- ✓ Disorders of female reproductive system: polycystic ovary syndrome, infertility.
- ✓ End stage renal disease.
- ✓ Psoriasis.
- ✓ Gout.
- ✓ Cancer with hormonal basis (breast, prostat)



ECONOMIC IMPACT

- ▶ US costs \$ 75 billion 2003, this does not include indirect costs (lost productivity, mortality), but include hospitalization, take more POM.
- ▶ In 2008 , these costs were estimated to be \$147 billion.



MANAGEMENT

- ▶ Dietary modification:
 - Caloric restriction
 - Altered proportion of food groups
- ▶ Physical activity.
- ▶ Pharmacologic therapy using POM and OTC drugs.
- ▶ Bariatric surgery.

DIETARY MODIFICATION:

- ▶ Pharmacotherapy, in addition to lifestyle modification, is reserved for patients with a BMI of 30 kg/m² or greater or a BMI of 27 kg/m² or greater with other obesity-related risk factors.

DIETARY MODIFICATION

The goal is to reduce body wt by 10% over 6 months this 10% carries most health benefit and easiest to attain.

CALORIC RESTRICTION:

The dietary intake for a 30 year old man (BMI=18.5-25)=2200-3000Kcal/d, for woman= 1800-2800.

These are lower for older person and higher for younger.

For any wt loss program the deficit between 300-1000Kcal/d. using:

- 1- low caloric diet (LCD) 800-1500Kcal/d. or
- 2- very low caloric diet (VLCD) fewer than 800.

LCD, VLCD

- ▶ LCD Wt loss 1-2 pound/week.
- ▶ VLCD should be under the supervision of a medical care provider.
- ▶ VLCD diet should contain 1g/kg protein, and patient should consume multi-vitamins/ multi-minerals if he was consuming < 1200 Kcal/day for prolonged period.
- ▶ Adverse effects of using VLCD:
 - ❖ Dry skin, hair loss.
 - ❖ Dizziness.
 - ❖ Diarrhea or constipation.
 - ❖ Irregular menses in females.
 - ❖ Gall stone and gall bladder diseases.
 - ❖ Total fasting may be proposed leading to ketosis and ketoacidosis.

ALTERED PROPORTION OF FOOD GROUPS

Carbohydrate restricted diet:
CHO restricted diet have more favorable effects than fat restricted diet because low CHO diet prevent elevated insulin levels that promote storage of body fat seen with higher CHO diet.

Effects of low CHO diet:

- 1- low insulin levels.
- 2- Causes ketosis which decreases appetite.
- 3- Decreases triglyceride and increases HDL.



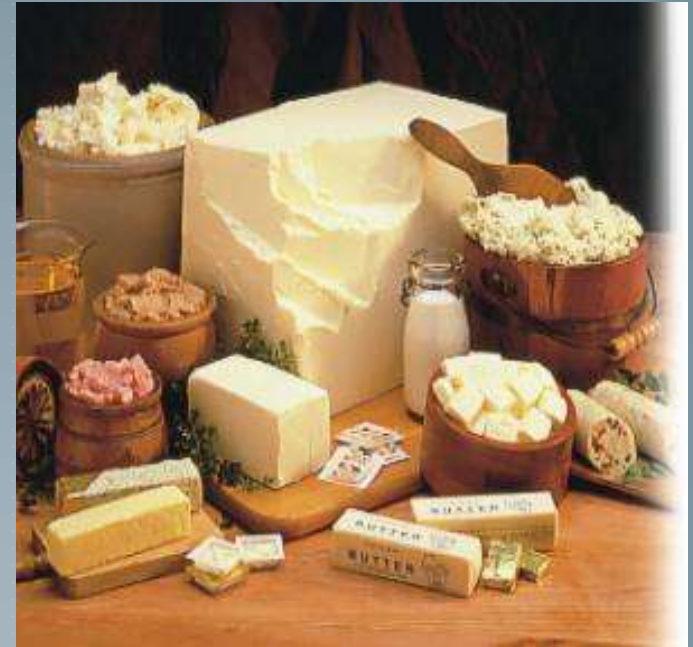
FAT RESTRICTION

Although results in regression of coronary atherosclerosis, very low fat vegetarian diet may cause:

- 1- essential fatty acids deficiency.
- 2- deficiency of fat soluble vitamins.
- 3- increased triglycerides and lower HDL because of ???

Triglyceride and HDL are affected more with low CHO diet whereas low fat diet have more favorable effects on LDL and total cholesterol).

- 4- lack of essential nutrients (Pot., Ca., Mg.) important for BP control.



PROTEINS

High protein diet have bad effects on human health:

- 1- proteins are rich in purine which inc. uric acid.
- 2- high animal proteins inc. Ca excretion in urine and affect bone health.
- 3- high protein causes dehydration, hyperfiltration by kidney causing kidney damage.



FRUIT,VEGETABLES AND FRUITS



Their restriction increase incidence of cancer by depleting essential vitamins, minerals and fibers.

USE OF FOOD ADDITIVES

- ▶ **Saccharin, aspartam...etc.**



Meal replacement therapy

Replacing 2 meals with liquid drink: commercial products cause early wt loss, due to sod. Content which causes water loss

PHYSICAL ACTIVITY



Although wt loss is lower with physical activity than dietary modification but it produces, fitness and increases muscle that has higher metabolic rate than fat.

Some patients may have a medical illness (angina), which makes some types of physical activity contraindicated.

BARIATRIC SURGERY



Only for patients with BMI=40 or more, or a BMI =35 + comorbid condition.

PHARMACOLOGIC THERAPY

► POM :

Many of these drugs (phenylpropanolamine containing products, ephedrine and related alkaloids) have been withdrawn because of their stimulant effect, however they are still marketed in dietary supplements :

Benzphetamine.

Methamphetamine.

Diethyl propion.

Orlistat.

► OTC:

Orlistat: used in conjugation with mildly hypocaloric diet.

POM (120mg tid) used >12 years.

Since 2007 and 2009 in US and European union respectively it was used as an OTC (60mg tid) used > 18 years.

In Canada it continues to be a POM

Mech of action:

↓ absorption of fat by inhibiting hydrolysis of triglyceride.

Inhibit gastric and pancreatic lipase.



Side effects:

Minimally absorbed so exhibit little SE:

1- decreased absorption of fat soluble vitamin so they should be supplemented and taken at bed time or 2hr after orlistat dose..

2- GI SE: flatulence, loose fatty stool, fecal urgency and incontinence.

These effects can be minimized by decreasing amount of ingested fat, and they usually resolve within few weeks of initiating therapy.

DI OF ORLISTAT

Because of limited absorption it has minimal DI

- Warfarin: since orlistat dec. amount of absorbed vit.K close monitoring of INR is recommended.
- Cyclosporine: orlistat should be avoided.

Contraindication to the use of orlistat:

1- malabsorption disorders.

2- hx. Of thyroid disorders, cholelithiasis, nephrolithiasis, and pancreatitis.

NOTE: if a meal is missed or contains no fat, the dose of orlistat should be omitted.

Duration of treatment: beyond 12 months.

ANORECTIC DRUGS

Benzocaine:

- ▶ Anesthetic effect on oral and GI mucosa.
- ▶ Alter food taste.

INAPPROPRIATE MEDICATIONS USED FOR WT LOSS

- ▶ Metformin.
- ▶ Diuretics.
- ▶ Laxatives.
- ▶ Chorionic gonadotrophin.

CHILDHOOD OBESITY

- ▶ Childhood obesity is one of the most serious public health challenges of the 21st century. The problem is global and is steadily affecting many low- and middle-income countries, particularly in urban settings. The prevalence has increased at an alarming rate. Globally, in 2013 the number of overweight children under the age of five, is estimated to be over 42 million. Close to 31 million of these are living in developing countries.
- ▶ Overweight and obese children are likely to stay obese into adulthood and more likely to develop noncommunicable diseases like diabetes(type 2) and cardiovascular diseases at a younger age. Overweight and obesity, as well as their related diseases, are largely preventable. Prevention of childhood obesity therefore needs high priority.

WORLD'S HEAVIEST LIVING WOMAN

BY GUINNESS WORLD RECORDS

THE 47-YEAR-OLD FROM CALIFORNIA HAS BEEN CONFIRMED AS WEIGHING 291.6 KG (643 LBS) BY GUINNESS WORLD RECORDS™.



An obese women (BMI =30) in her mid forties with metabolic syndrome (HDL=45mg/dl), serum triglyceride = 300 mg/dl. FSG = 200 mg/dl. If you know that she had a history cholilithiasis. Which is the best for her:

Select ONE correct answer:

- ▶ Carbohydrate restricted diet.
- ▶ Fat restricted diet.
- ▶ Orlistat 60 mg tid.
- ▶ Very low caloric diet (VLCD).
- ▶ Very low fat vegetarian diet

An obese, hypertensive woman, fail to control weight using dietary modification and physical activity. Orlistat was prescribed for her, but she complained from flatulence and fatty stool. Drug history: simvastatin 20mg, and Lisinopril 10mg daily. The pharmacist should advise her:

Select the correct answer(s):

- ▶ These are temporary side effects and will disappear after few days.
- ▶ Reduce fat intake will reduce severe GI side effects.
- ▶ The OTC dose of orlistat is half the strength of the POM dose.
- ▶ Drug interactions will occur between orlistat and the given drugs.

Patient: The problem is that obesity runs in our family.

Doctor: No, the problem is that no one runs in your family.