بسم الله الرحمن الرحیم
The most common nutritional problem in developed countries
Worldwide obesity has more than doubled since 1980.

65% of the world's population live in countries where overweight and obesity kills more people than underweight.

Obesity is an International Epidemic
Obesity: Is an ancient health problem

Has been evident in the human record for over 20,000 years and affected numerous aspects of human life and society.

Stone relief from the tomb of the Mereruka at Saqqara, Egypt (c. 2350 B.C), showing Mereruka in a boat, being fed by one of his servants.
Obesity rates could double in 30 years

% of population BMI >30

Year

USA
England
Australia
Mauritius
Brazil

Worldwide prevalences of obesity and overweight
شیوع اضافه وزن و چاقی در ایران (20 سال)

<table>
<thead>
<tr>
<th>شهروند</th>
<th>اضافه وزن (BMI 25-29.9 kg/m2)</th>
<th>چاقی (BMI ≥30 kg/m2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>رستا</td>
<td>35%</td>
<td>15%</td>
</tr>
<tr>
<td>شهر</td>
<td>40%</td>
<td>21%</td>
</tr>
</tbody>
</table>
TLGS : Phase 1
Prevalence of overweight and obesity

N = 8647 (aged 20-70 years)

TLGS : Phase 1
Prevalence of overweight and obesity by sex

N = 8647 ( 3622 men and 5025 female aged 20-70 years )

Prevalence of overweight and obesity among Tehranian males between 1999 and 2002

Prevalence of overweight and obesity among Tehranian females between 1999 and 2002

4402 adults, aged 20 years, participated in 3 phases of TLGS (1999-2008).

Men: 41.6%, Women: 58.4%

Median follow-up of 6.6 years
The prevalence of Over weight, Obesity and Abdominal obesity in 3 phases of TLGS. (1999-2008)

<table>
<thead>
<tr>
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<th>1</th>
<th>2</th>
<th>3</th>
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<th>3</th>
<th>1</th>
<th>2</th>
<th>3</th>
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</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td>n=1835</td>
<td></td>
<td></td>
<td><strong>Women</strong></td>
<td>n=2567</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight %</td>
<td>60.6</td>
<td>66.9</td>
<td>70.1</td>
<td>15.8</td>
<td>18.6</td>
<td>21*</td>
<td>36.5</td>
<td>57.2</td>
<td>63.3*</td>
</tr>
<tr>
<td>Obesity %</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>Abdominal obesity %</td>
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</tbody>
</table>

20 – 29 Y. = 23.8%  
20 – 29 Y. = 88.3%

* P<0.001
Defining Obesity

The word "obesity" (from the Latin obesitas) 
**Obesitas** is the condition of the **obesus**:

\[
\text{Ob} = \text{over}, \quad \text{Esus} = \text{to eat}
\]
Defining Obesity

“The excess accumulation of fat (adipose tissue) throughout the body”

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12-18%</td>
<td>20 – 30%</td>
</tr>
<tr>
<td></td>
<td>, &gt; 22%</td>
<td>, &gt; 32%</td>
</tr>
</tbody>
</table>
The main role of fat cells is to store energy and release it when needed.

Fat tissue acts as an endocrine organ, releasing hormones related to appetite and metabolism.

In adults, the upper limits of the total of normal fat cells: $40 \times 10^9$ to $60 \times 10^9$

The number of fat cells increases most rapidly during late childhood and puberty, but may increase even in adult life.
Excess body fat accumulates:

when people
Consistently take in more food energy than they spend.
Why they do this?
Is it:
- Genetic?
- Environmental?
- Cultural?
- Behavioral?
- Socioeconomic?
- Psychological?
- Metabolic?
- All of these?
Aetiology of Obesity:
Numerous Complex and Interrelated Factors

- Genetic
- Neurologic and Physiologic
- Biochemical
- Environmental
- Cultural and Psychosocial
Behavioral Determinants

Energy intake
- Diets with a high energy density
- High consumption of carbonated beverages
- Large portion size
- Eating pattern

Energy expenditure
Sedentary Behavior

- TV Viewing: A key behavior
- Computers and Video games

Walking the dog
Energy Expenditure

- Resting energy expenditure
- Thermo genesis
- Physical activity

Physical activity is the behavioral component that can be modified.
Components of energy expenditure contributing to voluntary and involuntary control of energy expenditure

SPA, spontaneous physical activity;
NEAT, nonexercise activity thermogenesis.
Etiology of Obesity

- Energy Intake
  - High fat, high-calorie diet
- Genetic Predisposition
- Sedentary lifestyle
- Energy Expenditure
Obesogenic Compounds

- High calorie diet and lack of exercise are not the sole causes of obesity.

- Obesity is strongly linked with exposure to risk factors during fetal and infant development.

- Researchers are gathering convincing evidence of chemical "obesogens":

  Dietary, Pharmaceutical, and Industrial compounds (alter metabolic processes and predispose some people to gain weight)

- There are 15 to 20 chemicals that have been shown to cause weight gain.
Known and Suspected Obesogens

- **Diet**:
  - Fructose
  - Genistein
  - Monosodium Glutamate

- **Pharmaceuticals**:
  - Diethylstilbestrol
  - Estradiol

- **Nicotin**

- **Organophosphate Pesticides**

- **Industrial Chemicals**
  - Bisphenol A
  - Organotins
  - Perfluorooctanoic Acid (PFOA)
  - Phthalates
  - Polychlorinated Biphenyl Ethers

- **Other Environmental Pollutant**
  - Bebzopyrine
  - Fine Particulate Matter
  - Leed
Different obesogenic compounds may have different mechanisms of action, affecting:

- The number of fat cells,
- The size of fat cells,
- The hormones that affect appetite, satiety, food preferences, and energy metabolism.
Medical evaluation of the Overweight or obese patient

- Measuring Body Composition
- Measuring the degree of obesity:
  - BMI and Waist Circumference
- Assessing risk: Beyond BMI and WC
  - Family Hx. of DM, CAD, HTN
  - Age
  - Physical inactivity
- Screening for other diseases
  - DM, HTN, Hyperlipidemia, Hypothyroidism, Cushing
Methods for Measuring Body Composition

Direct methods:

- Underwater weighing (Hydrodensitometry)
- Magnetic resonance imaging (MRI)
- Computerized tomography (CT)
- Dual-energy X-ray absorptiometry (DEXA)
- Bioelectrical impedance analysis (BIA)
- Air-displacement plethysmography
Magnetic resonance imaging (MRI)

MRI whole-body scans and fat maps of young adult women (24–30 y), each of whom has a BMI around 25 kg/m2. Total body fat is subdivided in subcutaneous fat (green) and visceral fat (yellow).
CT images of the abdomen of a man with central obesity

Visceral fat

(Subcutaneous fat)

(Fat highlighted in yellow)
Dual energy X-ray absorptiometry (DEXA), widely used to measure bone mineral, can also be used to measure fat and fat-free components.

<table>
<thead>
<tr>
<th>Body Part</th>
<th>BMD (g/cm²)</th>
<th>BMC (g)</th>
<th>Lean mass (g)</th>
<th>Fat mass (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>2.65</td>
<td>616</td>
<td>2,766</td>
<td>6,668</td>
</tr>
<tr>
<td>Trunk</td>
<td>0.97</td>
<td>897</td>
<td>15,651</td>
<td>9,533</td>
</tr>
<tr>
<td>Abdomen</td>
<td>1.10</td>
<td>380</td>
<td>7,554</td>
<td>4,181</td>
</tr>
<tr>
<td>Arms</td>
<td>0.86</td>
<td>351</td>
<td>4,249</td>
<td>3,888</td>
</tr>
<tr>
<td>Legs</td>
<td>1.01</td>
<td>882</td>
<td>12,446</td>
<td>7,272</td>
</tr>
<tr>
<td>Total</td>
<td>1.13</td>
<td>2,746</td>
<td>35,113</td>
<td>21,361</td>
</tr>
</tbody>
</table>

Whole-body DEXA scan, of a woman with a BMI of 22 kg/m².
The electrical resistance of the body, measured using a weak current delivered through the foot plate, is used to derive total body water and fat-free mass.
Subject seated in an air displacement plethysmograph for measuring body density. By applying standard equations, body fat mass and composition can be estimated from the density.
Methods for Measuring the degree of obesity and distribution of body fat

- Body mass index (BMI)
- Waist circumference and WHR
- Skin-fold thickness
### Table 4.1  Methods of measuring body fat and fat distribution

<table>
<thead>
<tr>
<th>Methods</th>
<th>Accuracy</th>
<th>Practicality</th>
<th>Sensitivity to change</th>
<th>Cheapness</th>
<th>Fat distribution detection</th>
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<tbody>
<tr>
<td><strong>Laboratory: ‘standard’ methods</strong></td>
<td></td>
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<tr>
<td>Underwater weighing</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>−</td>
</tr>
<tr>
<td>Potassium-40 counting</td>
<td>+++</td>
<td>+ +</td>
<td>+</td>
<td>+++</td>
<td>−</td>
</tr>
<tr>
<td>Dual-energy X-ray absorptiometry</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Computerized tomography</td>
<td>+++</td>
<td>+ +</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Magnetic resonance imaging</td>
<td>+++</td>
<td>+ +</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Multi-compartment models</td>
<td>+ +</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Air displacement (BOD POD)</td>
<td>?</td>
<td>+ + + +</td>
<td>?</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td><strong>Field: anthropometric methods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skinfold thickness</td>
<td>+++</td>
<td>+ + + +</td>
<td>+++</td>
<td>+++</td>
<td>−</td>
</tr>
<tr>
<td>Circumference</td>
<td>+++</td>
<td>+ + + +</td>
<td>+++</td>
<td>+++</td>
<td>+++ + + +</td>
</tr>
<tr>
<td>Body mass index</td>
<td>+++</td>
<td>+ + + +</td>
<td>+++ + + +</td>
<td>+++</td>
<td>−</td>
</tr>
</tbody>
</table>
Adolphe Quételet (1796–1874) was one of the early leaders in developing and validating mathematical measures of obesity. Quételet was responsible for the concept of the ‘average man’ and suggested that the ratio of the subject’s weight divided by the square of the height could be used as a measure of fatness that corrected for differences in height. This unit, the Body Mass Index (BMI), is still known as the ‘Quételet Index’ (QI) in some European countries.
BMI = body mass index

Is a simple method which is now generally used.

\[ \text{BMI} = \frac{\text{weight in kilograms}}{\text{(height in meters)}^2} \]
Body Mass Index

NIH, National Heart Lung and Blood Institute 1998
BMI cut-off curves defining overweight and obesity for (a) boys and (b) girls
BMI for assessing risk

American Cancer Society Study of 750,000 Men and Women

Mortality Ratio

BMI

Digestive and Pulmonary Disease
Cardiovascular and Gallbladder Disease
Diabetes Mellitus

Moderate Very Low Low Moderate High Very High

Men Women

0 1.0 1.5 2.0 2.5
WAIST CIRCUMFERENCE

- Measures distribution of body fat
- Should be measured along with BMI

Anatomical landmarks for measuring waist circumference: the mid-point between the iliac crest and the lower rib margin
Waist Circumference

- Men > 102 cm
- Women > 88 cm

NIH, National Heart, Lung, and Blood Institute, 1998

Iranian population (Adult > 30 years):

- Men and Women > 95 cm
Visceral Fat: The Critical Adipose Depot
Hypertrophic obesity

Enlarged fat cells are the pathologic sign of obesity. Enlarged fat cells tend to correlate with an android or truncal fat distribution, and are often associated with metabolic disorders such as: glucose intolerance, dyslipidemia, hypertension, and coronary artery disease.

Hypercellular obesity

An increase in the number of fat cells usually occurs when obesity develops in childhood. This type of obesity tends to be severe. Increased numbers of fat cells may also occur in adult life, and this is to be expected when BMI is >40 kg/m².
Android and Gynoid types of obesity with preferential accumulation of adipose tissue in the abdominal and gluteofemoral region, respectively.

The android pattern of adipose tissue distribution is more closely associated with the metabolic complications of obesity.
Skin Fold Thickness
Caliper
## The Burden Of Being Obese

<table>
<thead>
<tr>
<th><strong>PERSONAL ISSUES</strong></th>
<th><strong>MEDICAL ISSUES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Social isolation</td>
<td>Stroke</td>
</tr>
<tr>
<td>Reduced job prospects</td>
<td>Sleep apnoea</td>
</tr>
<tr>
<td>Low self esteem</td>
<td>Reflux Oesophagitis</td>
</tr>
<tr>
<td>Social pressure to conform</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Sweating</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>Snoring</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Poor quality of life</td>
<td>Gout</td>
</tr>
<tr>
<td><strong>The Contribution Of Obesity To Different Diseases</strong></td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td>T2DM, Dyslipidemia, Gout</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>Hypertension, Cardiac failure, Arrhythmias, CAD, Stroke, PVD</td>
</tr>
<tr>
<td><strong>Malignancies</strong></td>
<td>Endometrial, Colorectal, Hepatocellular, Breast, Lymphoma</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td>Fatty liver, Cirrhosis, Gall-bladder disease, Reflux esophagitis</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>Sleep apnea, Hypoventilation syndrome</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>Glomerulopathy, CRF</td>
</tr>
<tr>
<td><strong>Endocrine</strong></td>
<td>PCOS, Infertility</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td><strong>Psychiatric</strong></td>
<td>Depression</td>
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</tbody>
</table>
Obesity is the Prime Risk Factor for Type 2 Diabetes
Obesity And Cardiovascular Disease

Relative Risk of Nonfatal MI and Fatal CHD vs BMI, in Women

<table>
<thead>
<tr>
<th>BMI</th>
<th>Relative Risk</th>
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</thead>
<tbody>
<tr>
<td>&lt;21</td>
<td>1</td>
</tr>
<tr>
<td>21-22.9</td>
<td>2</td>
</tr>
<tr>
<td>23-24.9</td>
<td>3</td>
</tr>
<tr>
<td>25-28.9</td>
<td>4</td>
</tr>
<tr>
<td>&gt;29</td>
<td></td>
</tr>
</tbody>
</table>
Obesity And Infertility

Relative Risks by BMI at Age 18

Menstrual Cycle Irregularity

Relative Risk

Reference

Infertility

Relative Risk

Reference
Classification of obesity

1. Hypothalamic

2. **Hormonal disturbances:**
   - Cushing’s Syndrome
   - Hypothyroidism
   - PCOS
   - Pituitary disorders: pan-hypo., GH deficiency

3. **Drugs**

4. **Hereditary**
Hypothalamic obesity

Causes:
- Tumors
- Inflammation
- Trauma

Clinical features:
- Amenorrhea / impotence
- Impaired growth
- Diabetes insipidus
- Thyroid / adrenal insufficiency
- Papilledema
- Vomiting
- Somnolence
Drug induced obesity

<table>
<thead>
<tr>
<th>Class and drug</th>
<th>Increased appetite</th>
<th>Decreased energy expenditure</th>
<th>Other obesogenic effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gluocorticoids</strong></td>
<td>++</td>
<td>+</td>
<td>• ↑ Adipocyte differentiation</td>
</tr>
<tr>
<td><strong>Antidiabetic drugs</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>• Insulin</td>
<td>±</td>
<td>−</td>
<td>• Anabolic effects</td>
</tr>
<tr>
<td>• Sulphonylureas</td>
<td>±</td>
<td>−</td>
<td>• Abolish glycosuria</td>
</tr>
<tr>
<td>• Thiazolidinediones</td>
<td>−</td>
<td>−</td>
<td>• ↑ Adipocyte differentiation</td>
</tr>
<tr>
<td><strong>Antipsychotic drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ‘Atypical’ e.g. clozapine</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>• Classical e.g. haloperidol</td>
<td>++</td>
<td>+</td>
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<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
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</tr>
<tr>
<td>• Tricyclics</td>
<td>++</td>
<td>+</td>
<td>−</td>
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<td><strong>Antiepileptic drugs</strong></td>
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<tr>
<td>• Carbamazepine</td>
<td>++</td>
<td>−</td>
<td>−</td>
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<tr>
<td>• Gabapentin</td>
<td>++</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td><strong>β-blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Propranolol</td>
<td>−</td>
<td>++</td>
<td>−</td>
</tr>
<tr>
<td><strong>Endocrine drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Progestagens</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>• Tamoxifen</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
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<tr>
<td>• Antihistamines</td>
<td>++</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>• Cyproheptadine</td>
<td>++</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>• Pizotifen</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>• Flunarizine</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>• Cyclophosphamide</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>• 5-Fluorouracil</td>
<td></td>
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Hereditary Obesity

- Monogenic
- Polygenic
- Syndromic
## Monogenic Obesity

<table>
<thead>
<tr>
<th>Gene</th>
<th>Inheritance</th>
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<tbody>
<tr>
<td>Leptin</td>
<td>recessive</td>
</tr>
<tr>
<td>Leptin receptor</td>
<td>recessive</td>
</tr>
<tr>
<td>PC-1 (prohormone convertase-1)</td>
<td>recessive</td>
</tr>
<tr>
<td>POMC (Proopiomelanocortin)</td>
<td>recessive</td>
</tr>
<tr>
<td>MCR (Melanocortin-3, 4 receptor)</td>
<td>dominant</td>
</tr>
</tbody>
</table>
Regulation of Food Intake and Energy

The brain plays a critical role in the regulation of energy homeostasis through at least three physiological actions:

- Control of hunger and satiety
- Influence of the rate of energy expenditure
- Regulation of the secretion of special hormones
Hunger / satiety

Cerebral cortex

Hypothalamus

Adipose Tissue

Energy absorbed

GI tract

Energy ingested

Food intake

Leptin

Nutrient

Insulin

GI hormones

Neural signals

(Feed back mechanisms for control of energy intake)
Leptin and leptin receptor deficiency

- Sever hyperphagia
- Sever early onset obesity
- Hyperinsulinemia
- Advanced bone-age
- Abnormality in T-cell number and function
- High rate of childhood infection
Response to Leptin Therapy in a Child with Leptin Deficiency

3 years old 42 kg
7 years old 32 kg
Response to Leptin Therapy

Change in ad libitum food intake with leptin therapy in congenital leptin deficiency

Body weight curve in a child with a leptin mutation, showing early-onset morbid obesity. Body weight and fat fell rapidly during treatment with recombinant human leptin.
POMC Deficiency

- Initial presentation: adrenal crisis
- Pale skin and red hair
- Hyperphagia and early-onset obesity
- No specific treatment
- Selective MC4R agonists are being developed
MC4R Deficiency

- 0.5 – 1.0 % of obese adult to 6% in subjects with severe obesity starting in childhood
- Hyperphagia and obesity often start in the first year of life
- Increase Fat & Lean body mass & BMD
- Accelerated linear growth as a consequence of early hyperinsulinemia
**Syndromic Obesity**

- 20-30 mendelian disorders with:
  * Obesity
  * Mental retardation
  * Dysmorphic features
  * Organ specific developmental abnormalities
Syndromic Obesity

( Autosomal or X-linked )

- Prader – Willi syndrome
- Bardet - Biedl syndrome
- Albright's hereditary osteodystrophia
- Alstrom syndrome
Prader-Willi Syndrome

- The most common syndromal cause of obesity (1 / 25,000 birth)
- Deletion of the paternal critical segment or loss of the entire paternal chromosome 15
- Diminished fetal activity, hypotonia, mental retardation, short stature, hypogonadotropic hypogonadism
- Ghrelin: mediator of the obesity phenotype
Prader-Willi Syndrome
Bardet-Biedl Syndrome

A rare autosomal recessive (1/100000)

- Central obesity
- Mental retardation
- Dysphormic extremities
- Retinal dystrophy or pigmentary retinopathy
- Hypogonadism
- Renal abnormalities
Bardet-Biedle syndrome
Albright hereditary osteodystrophy
Pseudohypoparathyroidism

• **PTH resistance**
  Typically presents in early childhood
  Short stature
  Round facies
  Cataracts
  Short 4th metacarpal bone

**Hypocalcemia**
**Hyperphosphatemia**
**Increased PTH**
**Alström syndrome** is a rare and severe autosomal recessive disorder with:

- Atypical retinal pigmentary degeneration
- Sensorineural hearing loss
- Obesity
- Type II diabetes mellitus
- Normal mentation

(A) Truncal obesity and scoliosis  
(B) Short distal phalanges  
(C) Flat, wide, and thick feet

Physical features in a 13-year-old girl with Alström syndrome
Strategies for treatment of obesity

- Diet
- Exercise
- Behavior therapy
- Medications
- Surgery
Treatment Goals

- Prevent further weight gain (minimum goal)
- Reduce body weight.
- Maintain lower body weight in the long term
Goals of therapy

- The ideal outcome is a return to normal body weight, but this is unrealistic.
- **Effective therapy:**
  - Weight loss > 2 kg during the 1\(^{st}\) month
  - Weight loss > 5% below baseline by 3 to 6 months
  - Remain at this level
- Weight loss of 10 – 15 %: very good response
- Weight loss > 15%: Excellent response
Practical Solution is: 5-10% weight reduction
Indications for pharmacotherapy in obesity

- Clinically significant obesity:
  - BMI 30 kg/m², or
  - BMI 25 kg/m² with 1 obesity-related co-morbidity

- Failure of adequate trial (3–6 months) of lifestyle and dietary modifications
  - Weight loss <1 kg/month, No specific contradictions
For weight loss, the obese patient must go into negative energy balance.

**Medications**

**Energy intake**

**Energy expenditure**
Medications

1. Those that act primarily on the CNS to reduce food intake

2. Those that act primarily outside the brain
Many anti-obesity drugs have been withdrawn because of poor efficacy and/or severe side effects:

- **Amphetamines**: high risk of dependence
- **Fenfluramine**: in 1997 risk of pulmonary hypertension and valvular heart disease
- **β3 adrenergic agonists**: poor efficacy and sympathetic side effects
- **Thyroxine**: adverse effects including cardiac arrhythmias.
- **Rimonabant**: in 2008, risk of depression, psychosis
- **Sibutramine**: in 2010 due to cardiovascular safety concerns
**Orlistat**: is a semi-synthetic inhibitor of gut lipases, which decreases the absorption of dietary fat by up to 30%.
Dosage: 120 mg thrice daily.
Side effects: steatorrhea and (potentially) deficiencies of fat-soluble vitamins.

**Sibutramine**: acts centrally to inhibit the reuptake of both serotonin and noradrenaline, thus enhancing the action of both these appetite-suppressing monoamines.
Dosage: 10 or 15 mg once daily.
Problems: sympathomimetic effects such as tachycardia and dry mouth and occasionally hypertension.

**Rimonabant**: is a centrally-acting antagonist at the cannabinoid CB1 receptor, which mediates the appetite-stimulating action of endocannabinoids released in the brain.
Dosage: 20 mg once daily.
Side effects: severe psychiatric problems (depression and anxiety), nausea and dizziness.
Licensing approval for *Rimonabant* was withdrawn in Europe in late 2008.
After market withdrawal of sibutramine in 2010 due to cardiovascular safety concerns, clinicians are left with only one prescription drug, Orlistat, for the long-term treatment of obesity.

Two investigational drug treatments, other than phentermine plus topiramate, have been investigated in phase 3 trials, and are being reviewed by the US Food and Drug Administration.

- **Lorcaserin** is a new drug that is thought to reduce food intake through the activation of serotonin 5-HT2C receptors.

- **Cetilistat**, a pancreatic lipase inhibitor with fewer GI adverse events
The evolution of surgical technique

The initial phase (1950 – 1970): small bowel bypass

Surgical management of obesity began with the introduction of the jejunoileal bypass (JIB) in the 1950s by Payne and DeWind. In this procedure the proximal jejunum was diverted to the distal part of the gut, leaving a long segment of excluded small intestine and a marked reduction in absorptive capacity.
The evolution of surgical technique

The middle phase (1970 – 1990): stomach stapling

The Roux-en-Y gastric bypass (RYGB) operation was introduced by Edward Mason in 1980. In this procedure the stomach was completely partitioned into a small upper gastric pouch, draining into a Roux-en-Y limb of proximal jejunum of variable length from 40 to 150 cm, and a distal excluded stomach.

Edward E. Mason (born 1912)
American bariatric surgeon
An inflatable band, which can be tightened by injecting saline into a subcutaneously-implanted reservoir, is placed around the proximal stomach to create a tiny gastric pouch. The operation is usually performed laparoscopically (LAGB).
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RISK FACTORS: DM, HTN, CAD, Dyslipidemia, OSA
خداپايين صدم، ذوق دادي جوبروان، دل مرشوق دادي

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