

Nutrition

Attila Tóth, PhD

University of Debrecen
Division of Clinical Physiology

THE COST OF MALNUTRITION



Malnutrition costs \$3.5 trillion per year to the global economy



Undernutrition and micronutrient deficiencies cost up to \$2.1 trillion per year



The cost of obesity and overweight-related noncommunicable diseases was estimated at US\$1.4 trillion in 2010

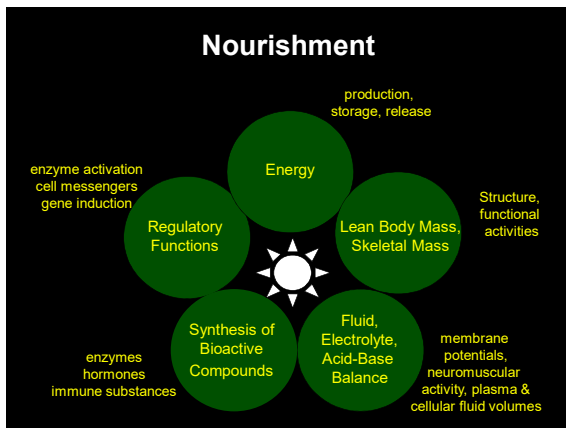


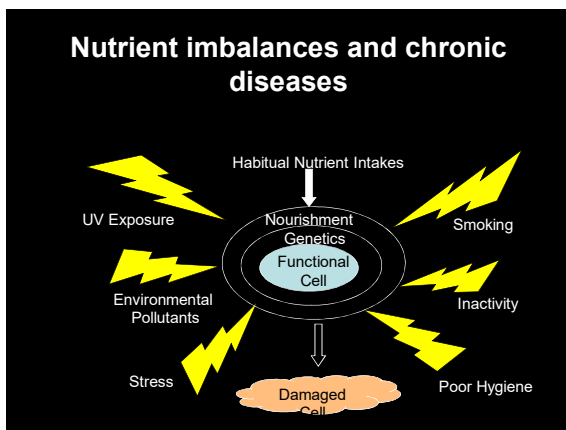
Child and maternal malnutrition is by far the largest nutrition-related health burden in the world

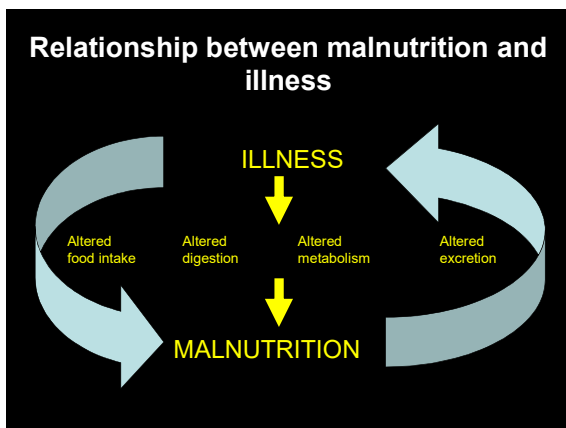
<http://www.fao.org/zhc/detail-events/en/c/238389/>

Malnutrition

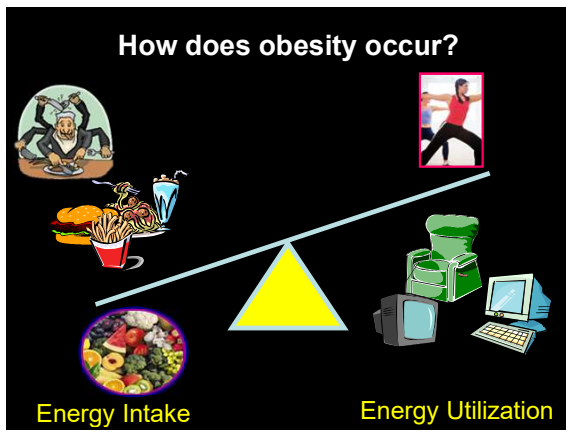
- **Over nutrition**
 - obesity
 - dietary induced dyslipidemia
- **Under nutrition**
 - protein energy nutrition
 - specific nutrient deficiency

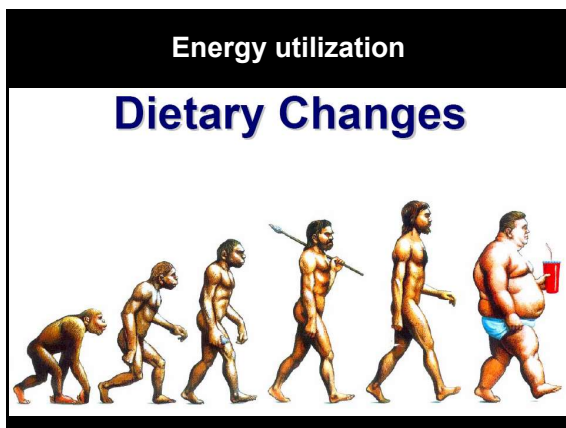


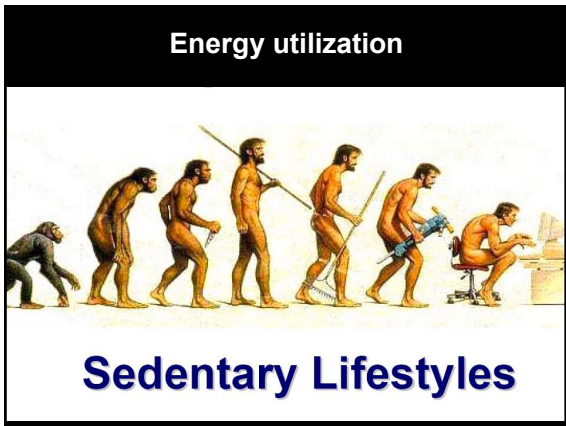


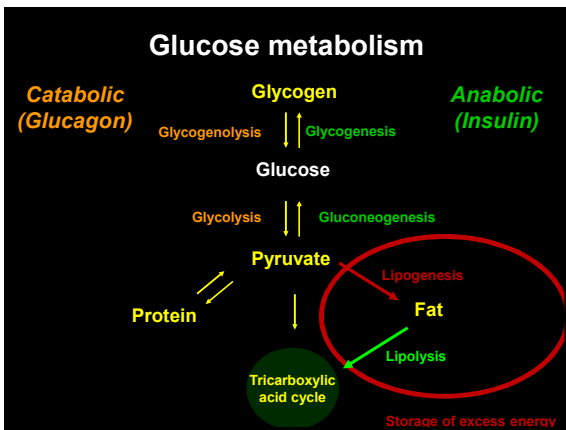


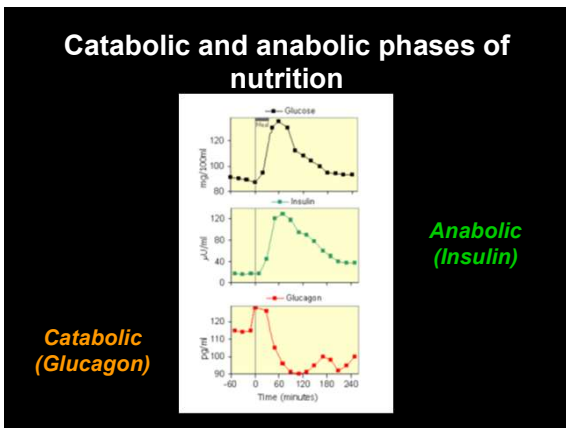
Over-nutrition

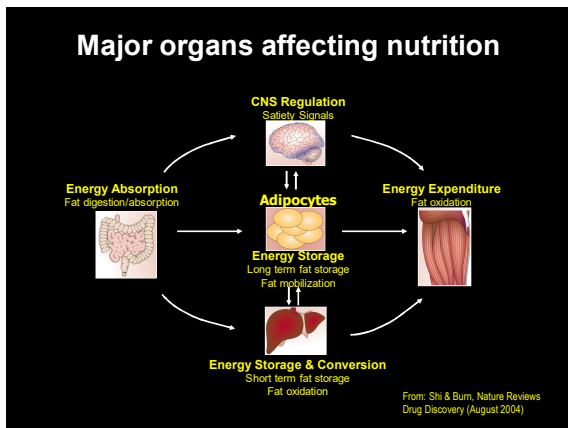


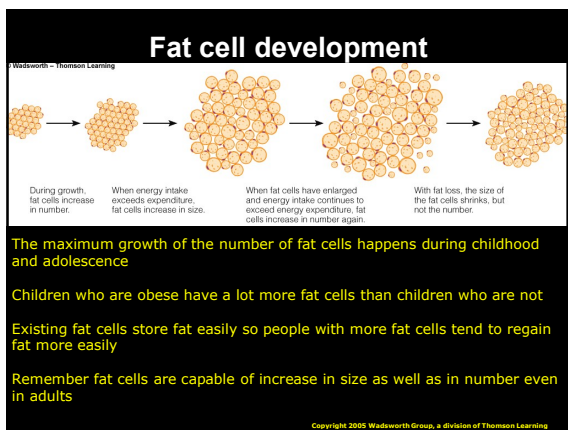


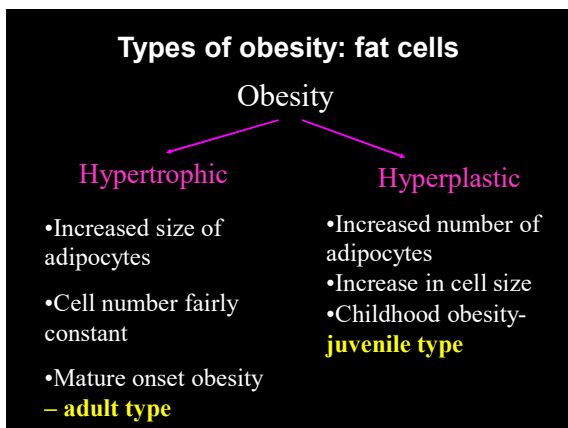




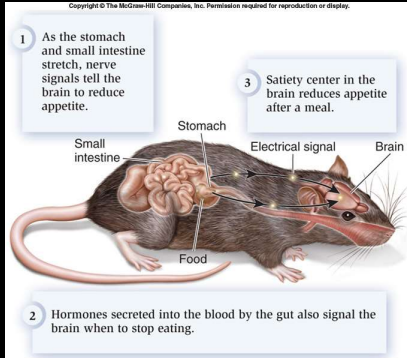




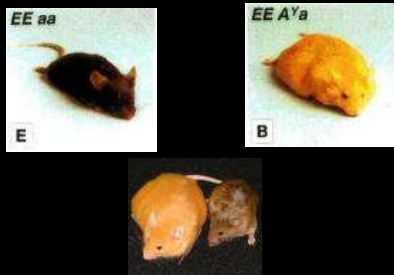




Hunger/satiety crosstalk



The Agouti A^y obese mouse



Maturity-onset obesity, yellow coat color, hyperphagia, hyperglycemia in males, hyperinsulinemia. Increased fat stores result from adipocyte hypertrophy.


The Agouti A^y obese mouse

- The agouti locus was positionally cloned in 1992.
- It encodes the secreted 131 residue agouti protein that normally antagonizes the melanocortin 1 receptor in peripheral hair follicles to control pigmentation.
- The obesity of A^y mice results from ectopic expression of agouti in the CNS, which antagonizes the melanocortin-4 receptor in the hypothalamus.
- Deletion of the MCR4 phenocopies A^y , Huszar *et al.*, *Cell* 88:131-40 (1997).
- Mutation of the MCR4 receptor is the most commonly occurring monogenic cause of inherited morbid obesity in human beings (~4% of the patient population).

ob/ob and db/db mice

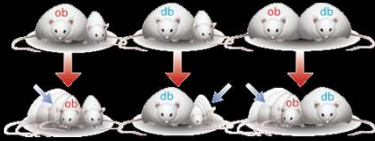
- ob/ob lacks functional leptin expression (adipose tissue)
- db/db lacks functional leptin receptor (hypothalamus)

ob/ob
db/db



wild type

Parabiosis



- ob/ob - +/+ mouse: ob/ob lost weight
- db/db- +/+ -db/db obese, +/+ stopped eating and lost weight
- ob/ob -db/db: ob/ob stopped eating and lost weight, whereas the db/db unaffected
- An additional experiment showed that when one of a pair of +/+ parabiotic mice was overfed, its "twin" lost weight.

Eat leptin and be thin: not for human

Percentage of people who are obese because they have a mutation in the gene for leptin = miniscule (only a few people in the world have this mutation)

Clinical trials failed to support the crucial role of leptin
 Giving daily leptin injections to obese patients only a third of the patients lost weight.
 some patients dropped out of the study finding the injections irritating
 some reported decreased appetite at first, and increased appetite after continued use (they developed leptin resistance).
 the people gained back the weight they had lost when the leptin injections ceased.

Obesity: definition

Obesity is defined as an excess accumulation of body fat

This excess accumulation is the result of a positive energy balance where caloric intake exceeds caloric expenditure



Body mass index (BMI)

Defined as weight in kilograms, divided by the square of the height in meters

What the Numbers Mean

BMI	Condition
Below 18.5	Underweight
18.5-24.9	Normal Weight
25-29.9	Overweight
Above 30	Obese

Types of obesity: body shape

Android – Apple type

Gynoid- Pear type

Male > Female

Female > Male

Upper body

Lower body

Waist > Hip

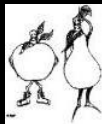
Hip > Waist

Central Obesity

Peripheral

Metabolic Complications

hyperlipidemia,
hypertension, cardiovascular,
diabetes, gallstones



CLASSIFICATION OF OVERWEIGHT AND OBESITY BY BMI, WAIST CIRCUMFERENCE AND ASSOCIATED DISEASE RISK*

	BMI (kg/m ²)	Obesity Class	Disease Risk* Relative to Normal Weight and Waist Circumference	
			Men ≤ 102 cm (≤ 40 in) Women ≤ 88 cm (≤ 35 in)	> 102 cm (> 40 in) > 88 cm (> 35 in)
Underweight	<18.5		—	—
Normal	18.5 – 24.9		—	—
Overweight	25.0 – 29.9		Increased	High
Obesity	30.0 – 34.9	I	High	Very High
	35.0 – 39.9	II	Very High	Very High
Extreme Obesity	≥40	III	Extremely High	Extremely High

Key facts about obesity

Worldwide obesity has nearly tripled since 1975.

In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 650 million were obese. 39% of adults aged 18 years and over were overweight in 2016, and 13% were obese.

38 million children under the age of 5 were overweight or obese in 2019.

Over 340 million children and adolescents aged 5-19 were overweight or obese in 2016.

Obesity is preventable.

<https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>

Obesity is a multifactorial disorder

Multifactorial disorders

Genetics:

polygenic, each gene having a small contribution in the presence of precipitating environmental factors

It has been long known that the tendency to gain weight runs in families. However, family members share not only genes but also diet and life style habits that may contribute to obesity.

Morbid obesity has a stronger genetic component than moderate level of excess overweight

Energy imbalance

Diet

obesity is associated with increased food consumption

Intake of excess dietary fat has been implicated as a major cause of obesity

Exercises

For a decades a strong link exists between physical inactivity and weight gain

Modifiable risk factors for obesity

Physical Activity

- Lack of regular exercise
- Sedentary Behavior
- High frequency of television viewing, computer usage

Socioeconomic Status

- Low family incomes and non-working parents

Eating Habits

- Over-consumption
- Some eating patterns that have been associated with this behavior are eating when not hungry, eating while watching TV

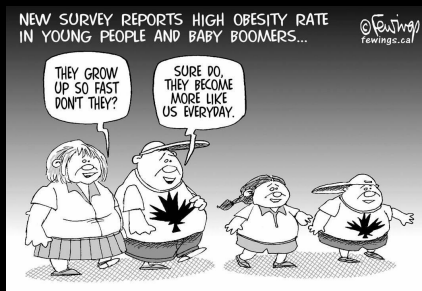
Environment

- Over-exposure to advertising
- Lack of recreational facilities

Unmodifiable risk factors for obesity

Genetics

- Greater risk of obesity has been found in children of obese and overweight parents



Diseases and drugs may also lead to obesity

Diseases

- Hypothyroidism, Cushing's syndrome, pancreatic insulinoma, growth hormone deficiency, and hypothalamic insufficiency
- A variety of psychosocial factors contribute to the development of **obesity** and to difficulty losing weight

Drugs

- antipsychotics** (phenothiazines, butyrophenones); **antidepressants** and **antiepileptics**, (tricyclic antidepressants, lithium, valproate, carbamazepine); and **insulin** and **some oral hypoglycemics**. Whereas most of these medications contribute modestly to **obesity**, the large doses of **steroids** sometimes used to treat autoimmune diseases can cause true **obesity**

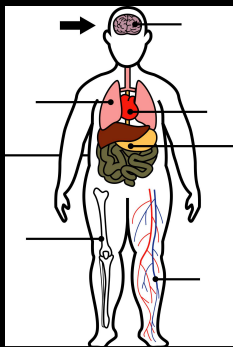
Why Does Overweight and Obesity Matter?



"What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?"

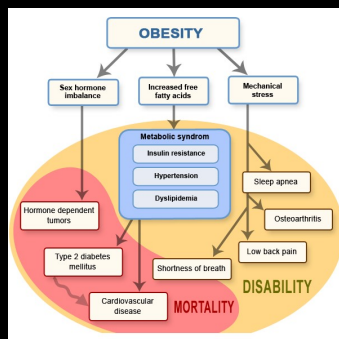
Obesity is a risk factor in many diseases

- Depression
- Poor self-esteem
- Eating disorders
- Sleep apnea
- Exercise intolerance
- Asthma
- High blood pressure
- Kidney problems
- Osteoarthritis
- Joint problems
- Flat feet



- Stroke
- Heart failure
- Heart disease
- High cholesterol
- Digestive problems
- Several cancers
- Insulin resistance
- Diabetes Type 2

Obesity related diseases



<https://dileepvenkat.files.wordpress.com/2011/02/obesity-model1.gif>

Drugs: there is no easy way

WEIGHT LOSS DRUGS*

Drug	Action	Adverse Effects
dexfenfluramine* fenfluramine*	serotonin reuptake inhibitor serotonin releaser	valvular heart disease primary pulmonary hypertension neurotoxicity
sibutramine	norepinephrine, dopamine, and serotonin reuptake inhibitor	increase in heart rate and blood pressure
orlistat	inhibits pancreatic lipase, decreases fat absorption	decrease in absorption of fat-soluble vitamins soft stools and anal leakage possible link to breast cancer

Under-nutrition

Simple starvation: marasmus



- decreased metabolic rate
- weight loss from both fat and muscle
- impaired wound healing and immune function
- Normal albumin level

Protein deprivation: **Kwashiorkor**

Kwashiorkor is the Ghanaian name for "the evil spirit that infects the first born child when the second child is born".

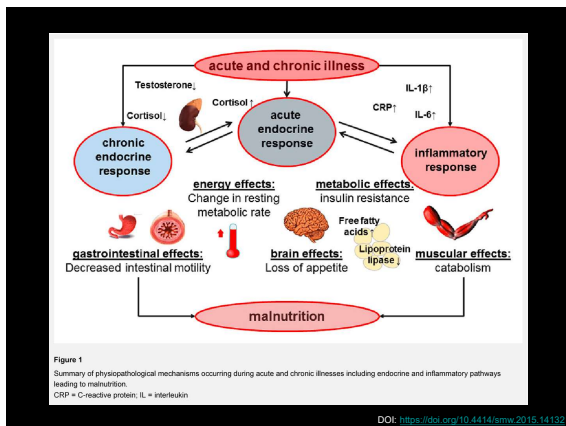
Kwashiorkor is a form of malnutrition **caused by inadequate protein intake** in the presence of fair to good energy (total calories) intake.



Characteristic	Marasmus	Kwashiorkor
Deficiency in nutrients	protein and energy	protein
Peripheral edema	No	Yes (abdominal and extremities)
Hair changes	No	Yes (sparsing and falling out)
Skin	Dry and wrinkled	Dermatosis, scaly skin
Appetite	Voracious	Poor
Subcutaneous fat	Absent	Reduced
Fatty liver	Uncommon	Common
Prognosis	Poor (but better than Kwashiorkor)	Poorest
Mood	Lethargic	Alert and irritable
Serum albumin levels	Normal or slightly lower	Low

In hospital malnutrition

- 30-60% malnourished, ~ 10 - 25% severe
- gets worse in hospital
- high morbidity, prolonged hospital stay
- higher mortality



Stress starvation

- Response to starvation and inflammation
- Days to weeks or months
- Depend on hormonal and cytokine control

<p>Cytokine response</p> <ul style="list-style-type: none"> • catabolic (IL-1, IL-6, TNF-α) <ul style="list-style-type: none"> - increased protein breakdown • vascular permeability 	<p>Hormonal response</p> <ul style="list-style-type: none"> • aldosterone/ADH <ul style="list-style-type: none"> - salt/ water retention • epinephrine, glucagon, cortisol <ul style="list-style-type: none"> - lipolysis - gluconeogenesis - severe protein catabolism
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Stress starvation

- **Change of body composition**
 - Extracellular fluid expansion / weight gain
 - body cell mass declines
- **Loss of body protein: functional change**
 - respiratory muscle
 - wound healing
 - immune response
- **Catabolic state cannot be reversed by nutrition alone: nutritional resistance**

Stress starvation



- **Kwashiorkor** or hypoalbuminemic malnutrition
- low albumin level/ edema
- Loss of body protein: functional change
 - respiratory muscle
 - wound healing
 - immune response
 - higher morbidity and mortality
