


Obesity and nutritional disorders

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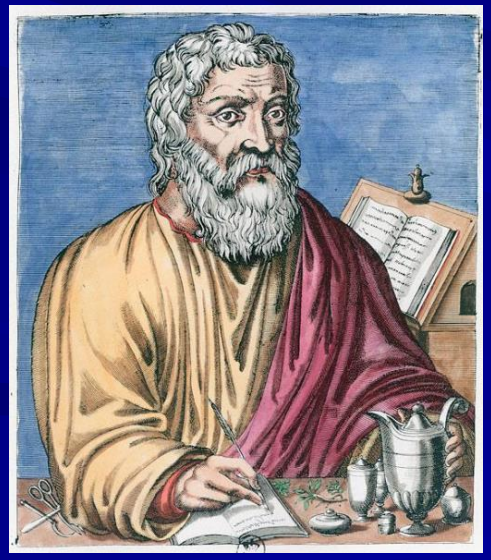
"Nature has given us all the pieces required to achieve exceptional wellness and health. But has left it to us to put these pieces together."

~ Diane McLaren

"Let food be thy medicine, and let thy medicine be food"

~ Hippokrates



Nutrition

- includes the intake and utilization of food in the body (digestion, transport, absorption, storage, metabolism, and excretion)
- is the result of deciding what, how much, when, how, and where a person consumes

Nutrition

- energy supply in the form of chemical energy (1 kcal = 4.186 kJ)
- supply of organic and inorganic substances for the construction and maintenance of the body:
  - proteins 17.2 kJ/g
  - lipids 38.9 kJ/g
  - saccharides 17.2 kJ/g
  - vitamins, macrominerals - Na, K, Ca, Cl, Mg, P;
    trace elements - Fe, Zn, Cr, Cu;
    fiber, water

Healthy (rational) nutrition

- a biologically complete diet
- contains the necessary and appropriate amount of nutrients:
  - proteins, fats, carbohydrates (so-called macronutrients)
  - minerals and vitamins (so-called micronutrients)

- *healthy nutrition – part of a modified lifestyle → prevention of obesity, diabetes, cardiovascular diseases*
- *improper nutrition – part of an unhealthy lifestyle and unhealthy diet*

Nutritional recommendations

a) general recommendations

b) nutritional standards

c) recommendations based on food groups

Nutritional recommendations

a) general recommendations

- achieve optimal body weight
- limit fat and sugar intake
- limit salt consumption (max. 5 g/day; 2400 mg Na/day)
- increase consumption of fruits and vegetables, legumes, whole grains and nuts

→ reduce morbidity and mortality

Nutritional recommendations
b) nutritional standards

- amount of nutrients per day that should cover the normal need in healthy people:
  - 15% protein (0.8 g protein/kg weight)
  - 30% fat (1 g fat/kg weight)
  - 55% carbohydrates (5-6 g carbohydrates/kg weight)

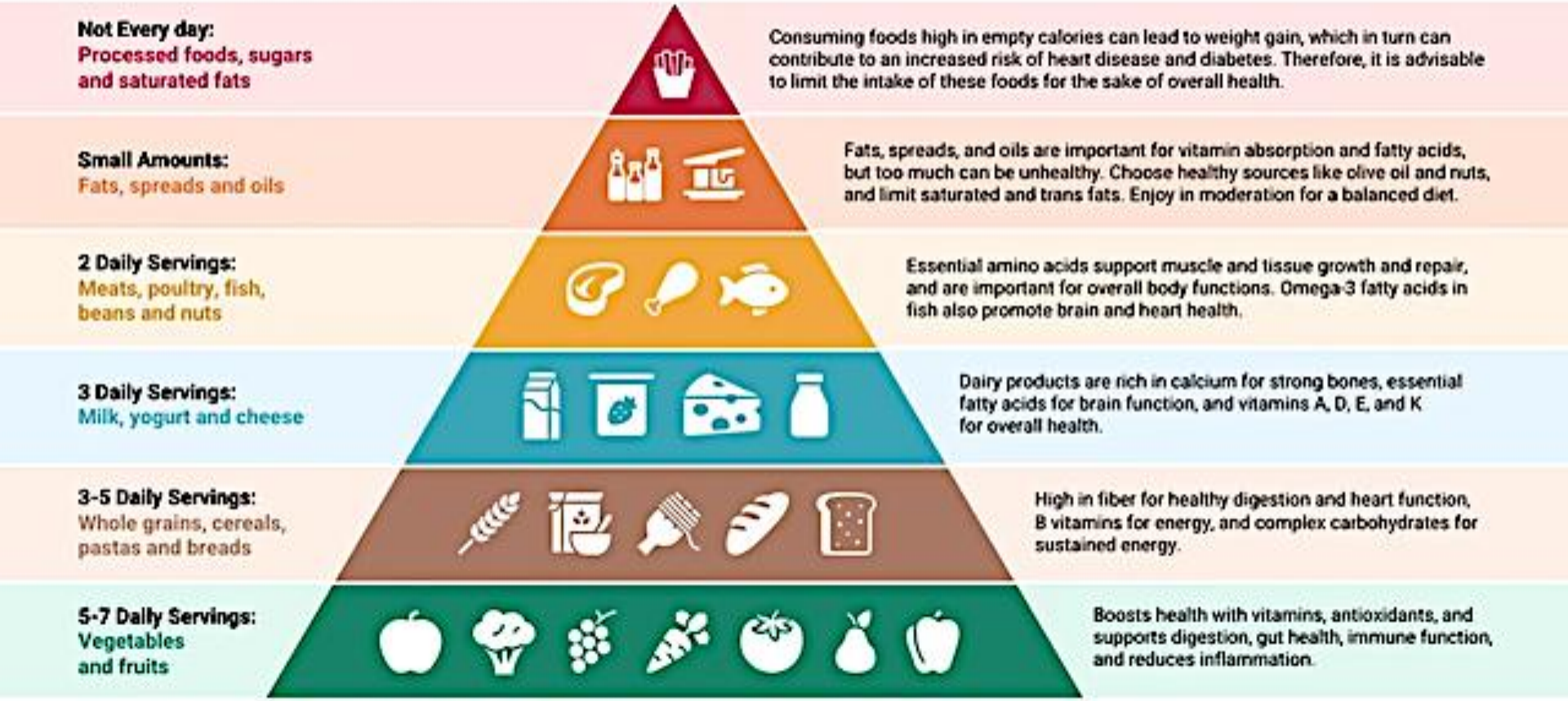
Nutritional recommendations

c) recommendations based on food groups

- recommendation of specific foods and their quantity in portions in the form of a food pyramid

Nutritional Daily Food Servings Guidelines

WELLNESS CO.
Nutrition & Dietetics



https://venngage.com/templates/infographics/nutritional-food-pyramid-infographic-template-fc56cab0-8938-43d4-b4a7-caa420a61045


Yogurt

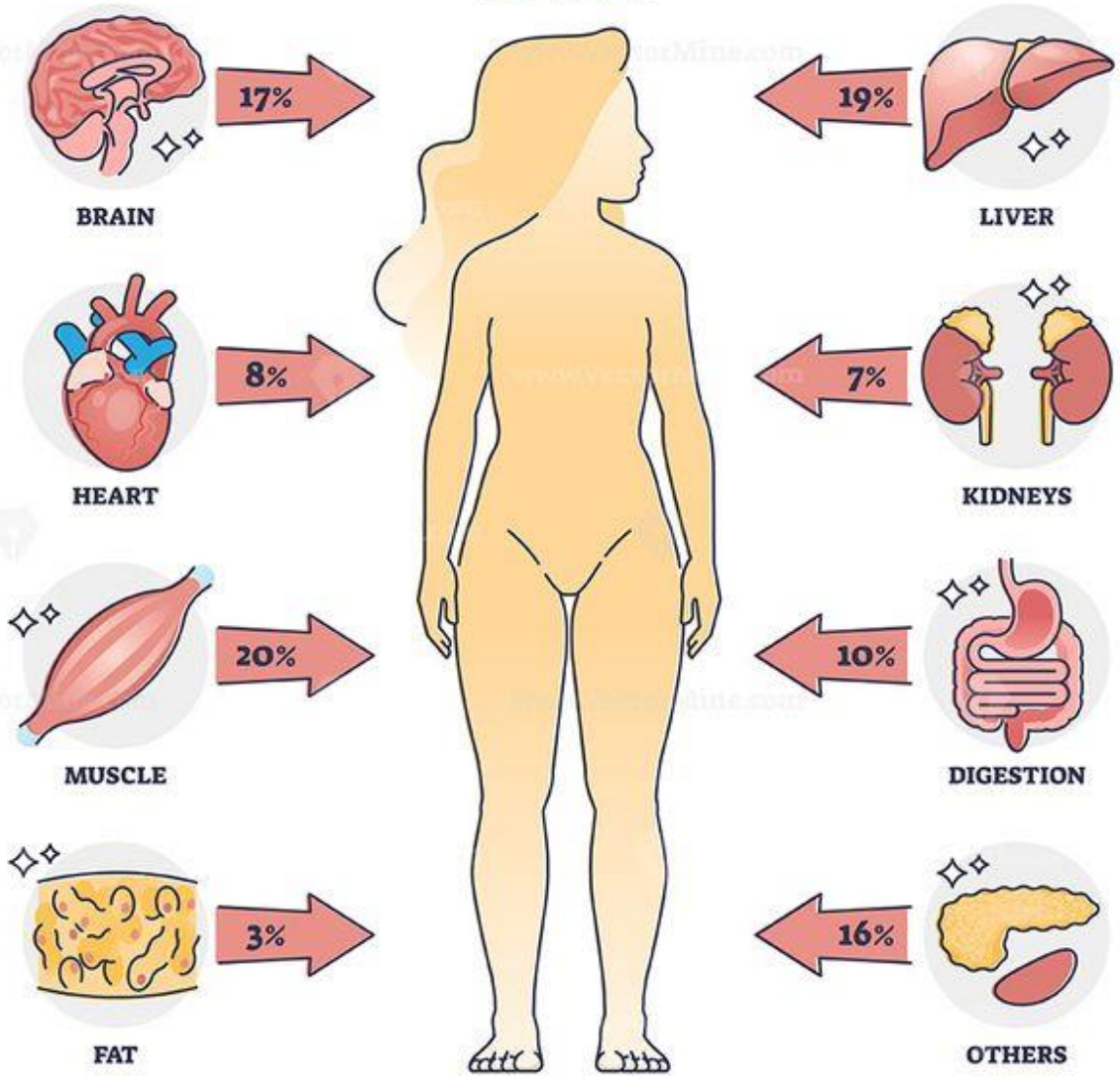
Energy expenditure

- Basal metabolism – basic metabolic turnover – energy consumption at complete rest (transport mechanisms, biosynthesis, heat production, heart, intestine work...): 5,900 – 8,400 kJ/day

- Working metabolism – energy consumption during exercise

BASAL METABOLIC RATE

BMR



PHYSICAL ACTIVITY **Light intensity activities**	**<3**
Sleeping	0.9
Watching television	1.0
Writing, desk work, typing	1.8
Walking, 1.7 mph (2.7 km/h), level ground, strolling, very slow	2.3
Walking, 2.5 mph (4 km/h)	2.9
Moderate intensity activities	**3 to 5.9**
Bicycling, stationary, 50 watts*, very light effort	3.0
Walking, 3.0 mph (4.8 km/h)	3.3
Calisthenics, home exercise, light or moderate effort	3.5
Walking, 3.4 mph (5.5 km/h)	3.6
Bicycling, <10 mph (16 km/h), leisure, to work or for pleasure	4.0
Bicycling, stationary, 100 watts, light effort	5.5
Vigorous intensity activities	**≥6**
Singles tennis	6.5
Jogging (5 mph)	7.5
Squash racquets	8.5
Running (6 mph)	10.0

*Note: 1 watt ~6 kg•m•min^{-1}; Adapted from Ref. [42].

ENERGY REQUIRED (METs) FOR LIGHT TO MODERATE EXERCISE

from the Compendium of Physical Activities

Light gardening	2.3
General cleaning & straightening up	2.5
Washing dishes, clearing the table	2.5
Putting away groceries	2.5
Walking 2.0 mph	2.8
Walking 3.0 mph	3.3
Scrubbing the floor	3.8
Gardening, weeding	4.0
Multiple household tasks at once with vigorous effort	4.3
Salsa or swing dancing	4.5
Softball	5.0
Walking 4.0 mph*	5.0
Walking with a light (15 lb) load	5.0
Walking 3.0 mph at 3-5% grade (uphill)	5.3
Golf: walking and pulling clubs	5.3
Mowing the lawn	5.5
Moving furniture and carrying boxes	5.8
Biking 9-10 mph	5.8

**Energy ratings are based on METs (metabolic equivalent). Light exercise is less than 3.0 METs. Moderate exercise is 3.0-5.9 METs. Vigorous exercise is 6.0 METs and above.*

Intensity levels in sports and activities vary from person to person. Visit https://sites.google.com/site/compendiumofphysicalactivities/home for a more complete list of activities.

whyiexercise.com

EXERCISE INTENSITY (METs) FOR CARDIO WORKOUTS

from the Compendium of Physical Activities

 Walking 3.0 mph at 3-5% grade (uphill)	5.3
 Biking 9-10 mph	5.8
 Stationary bike 100 watts	6.8
 Climbing stairs	8.0
 Circuit training / body weight exercises	8.0

 Biking 13 mph	8.0
 Swimming 50 yd / min	8.3
 Rowing 150w or 8.6 mph	8.5
 Running 6 mph or 10:00/mile	9.8
 Rollerblading 11 mph	9.8

 Biking 15 mph	10.0
 Swimming 75 yd / min Breaststroke	10.0
 Jumping rope	11.0

**Energy ratings are based on METs (metabolic equivalent). Light exercise is less than 3.0 METs. Moderate exercise is 3.0-5.9 METs. Vigorous exercise is 6.0 METs and above.*

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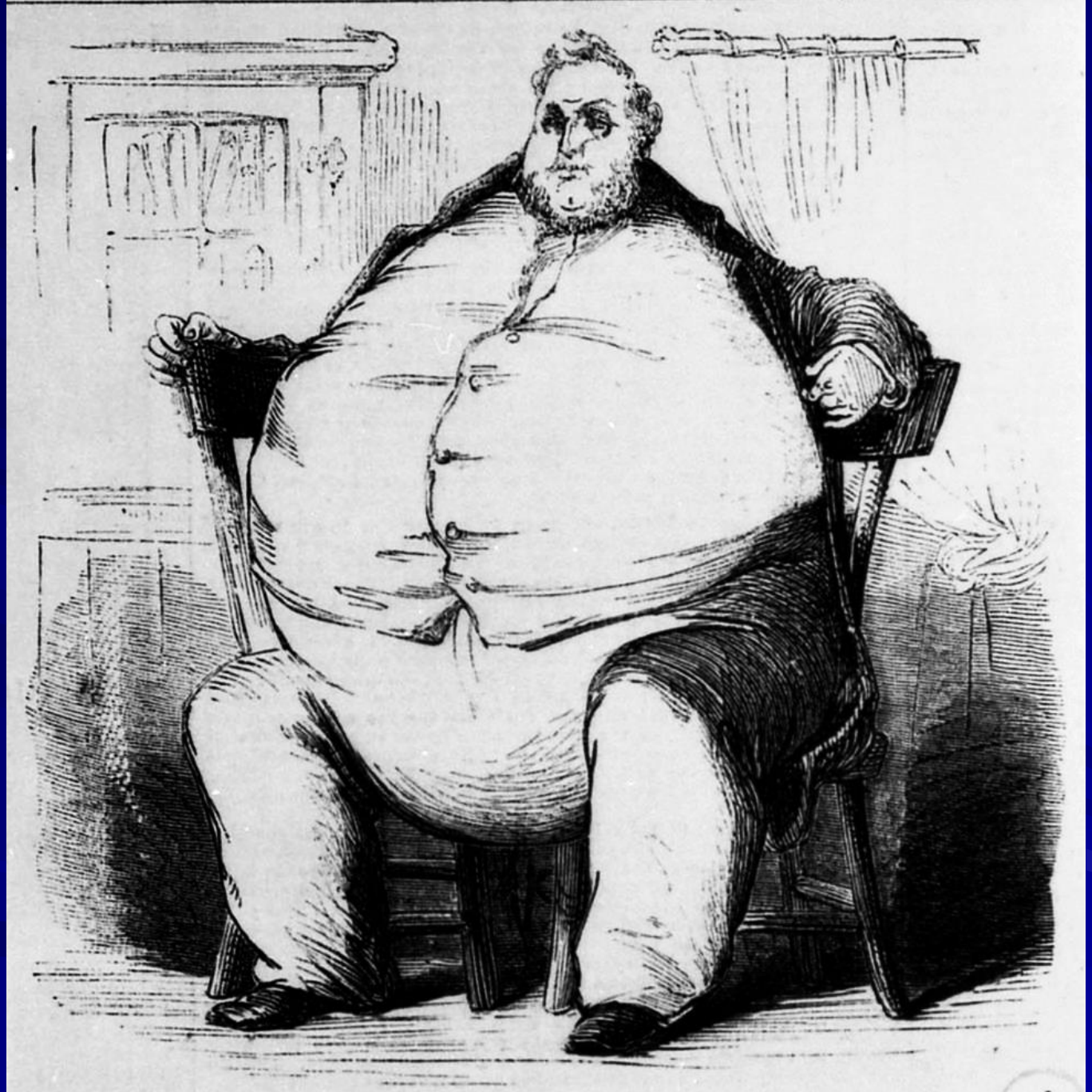
Nutritional disorders

- Overnutrition
  - obesity (adiposity)
  - hypervitaminosis
- Insufficient nutrition
  - quantitative
    - starvation
    - chronic malnutrition
  - qualitative
    - kwashiorkor
    - hypo-, avitaminosis
    - deficiency of trace elements

(Pre)obesity



DR. E BROWN, THE LARGEST MAN IN AMERICA.—FROM A PORTRAIT BY MR. J. R. DIX.

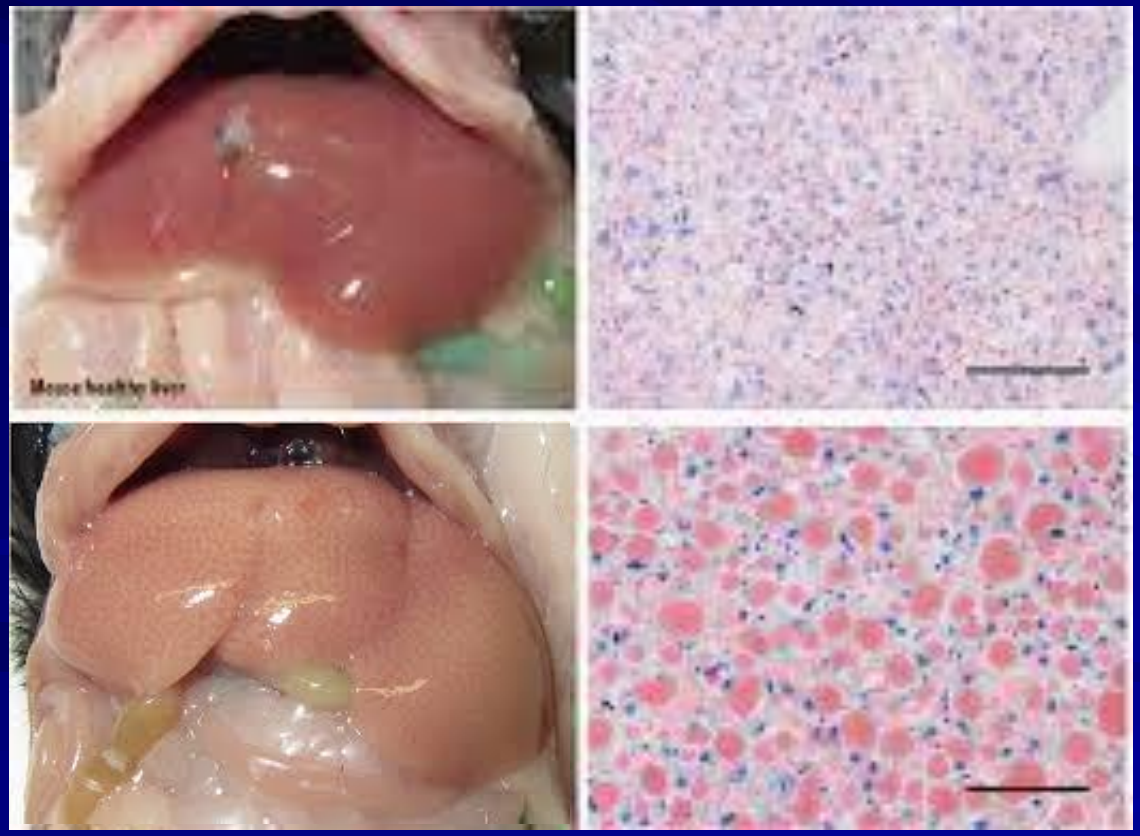
(Pre)obesity

- frequent, severe, complex, chronic, progressive and relapsing systemic metabolic disease with its etiology, signs and symptoms
- characterized by increased fat accumulation and its insufficient mobilization from tissues with simultaneous weight gain due to multifactorial causes
- increased proportion of body fat in body weight (>25% in men and >30% in women)
- disturbed distribution and functionality of adipose tissue

(Pre)obesity

- fat deposition in non-adipose tissues, which are mechanically and functionally altered, which subsequently results in impaired regulation of metabolic and cardiovascular homeostasis at the systemic and local levels, multi-organ IR associated with a pro-inflammatory and pro-atherogenic state
- structural and functional changes culminate in multiple organ-specific pathological complications (metabolic, structural, inflammatory, neoplastic, degenerative, etc.)

(Pre)obesity - MAFLD



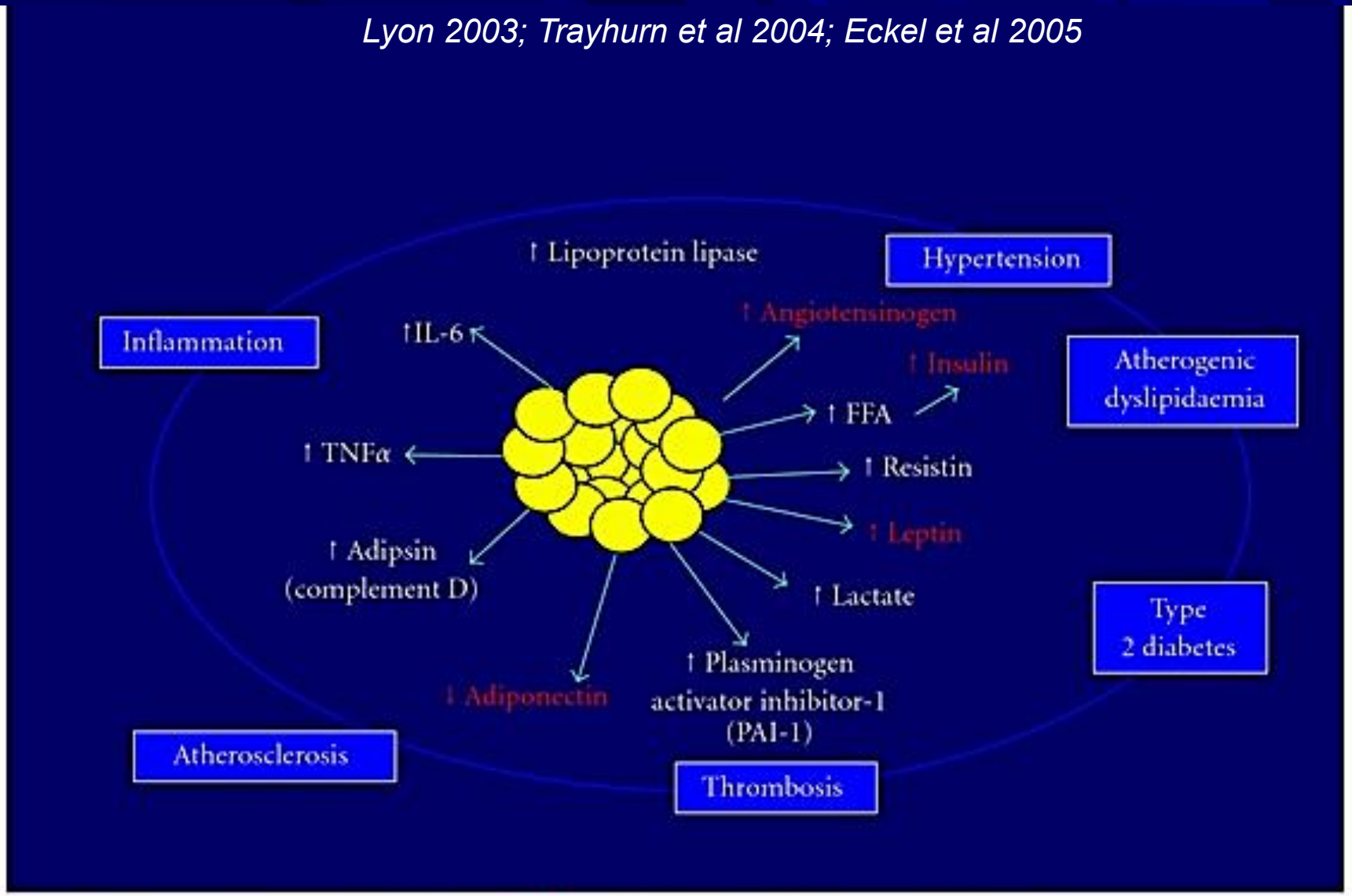
MAFLD - Metabolically Associated Fatty Liver Disease, a new term for liver disease associated with metabolic disorders. The diagnosis of MAFLD involves the presence of fat in the liver, associated with one of the following: overweight/obesity, DM2, or other signs of metabolic dysfunction. The goal of changing the name from the original NAFLD (non-alcoholic fatty liver disease) is to better reflect the nature of the disease and stratify patients at risk.

(Pre)obesity

(pre)obezita je ochorenie	
chronické	vyvíja sa dlhodobo a vyžaduje chronický – celoživotný manažment
komplexné	metabolické, somatické, psychobehaviorálne, psychiatrické a sociálne dôsledky
progredujúce	**na začiatku** ochorenia pacienti s (pre)obezitou nemusia mať žiadne príznaky, symptómy alebo patologické hodnoty v laboratórnych vyšetreniach, avšak v porovnaní s osobami s normálnou hmotnosťou majú vyššie riziko vzniku ďalších chronických ochorení asociovaných s obezitou **v priebehu** času sa u jedinca s (pre)obezitou vyvíjajú rôzne ďalšie chronické, preventabilné ochorenia – vznik, priebeh a závažnosť týchto ochorení býva variabilná, závisí od genetickej predispozície (väčšinou podmienená polygénovo), od pôsobenia obezitogénneho prostredia a v nemalej miere aj od správania sa jedinca s (pre)obezitou
relapsujúce	bez ohľadu na spôsob komplexnej liečby (pre)obezity (zmena životného štýlu, KBT, farmakoterapia alebo BMO, prípadne kombinácia BOM a farmakoterapie antiobezitikami) je dlhodobé udržanie zredukovanej hmotnosti náročné (v dôsledku metabolickej adaptácie – fyziologického procesu charakterizovaného zmenami v hladinách regulujúcich hormónov chuti do jedla a poklesom energetického výdaja) a vyžaduje si celoživotnú kontrolu, často prírastok hmotnosti býva vyšší ako dosiahnutá redukcia hmotnosti („jo-jo“ efekt)

Fábryová a spol., Klinická obezitológia 2023

Lyon 2003; Trayhurn et al 2004; Eckel et al 2005



Visceral fat accumulation is characterized by a dysregulation in adypokines production with decreased levels of protective adiponectin and increased levels of proinflammatory/proatherogenic adipokines. This dysregulation is involved in the pathophysiology of all the components of MetS (hypertension, diabetes, and dyslipidemia) and in the occurrence of inflammation, thrombosis, and atherosclerosis. IL-6: interleukine-6; TNF α: tumor necrosis factor α ; FFA: free fatty acids.

Physiology: Central Pathways

Anorexigenic

- Leptin
- α-MSH
- CART
- GLP-1
- C-NTF
- CRH/Urocortin
- Neuromedin U
- Serotonin
- CCK
- Insulin
- Bombesin
- Calcitonin
- Enterostatin
- TRH
- IL-1B
- Neurotensin
- Oxytocin
- Vasopressin

Orexigenic

- Neuropeptide Y
- MCH
- AGRP
- Orexin A, B (Hypocretin 1,3)
- Galanin
- Dynomorphin
- Norepinephrine
- B-endorphin

Important to know that complex regulation exists. Identify Leptin as important.

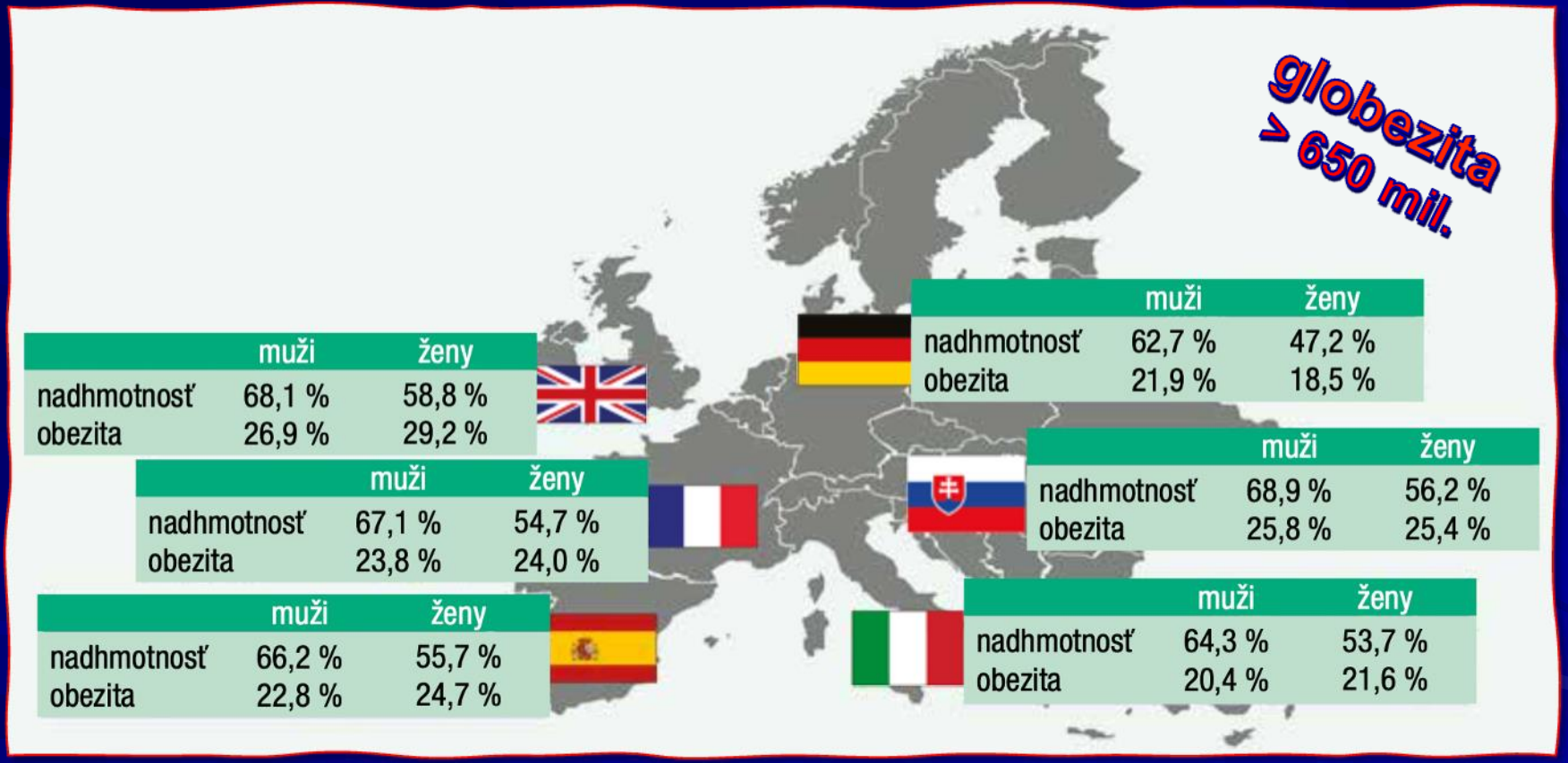
Obesity

- ↓ quality of life and life expectancy (Abdelaal et al., 2017)
- requires a long-term controlled individualized comprehensive preventive, diagnostic, therapeutic approach
- 236 comorbidities (Kahan, 2016; Fábryová, 2023)
- ↑ morbidity and mortality from metabolic and CV diseases

Facts – obesity and overweight

- In 2022, one in eight people in the world lived with obesity. Global adult obesity has more than doubled since 1990, and adolescent obesity has quadrupled.
- In 2022, 2.5 billion adults (aged 18 and over) were overweight. Of these, 890 million were living with obesity. In 2022, 43% of adults aged 18 and over were overweight, and 16% were living with obesity.
- In 2024, 35 million children under 5 years of age were overweight. In 2022, more than 390 million children and adolescents aged 5–19 were overweight, including 160 million who were living with obesity.

Obesity prevalence



- a global epidemic with widespread health and socio-economic consequences

NCD-RisC: Lancet 2017; 390(10113): 2627–2642

Obesity prevalence

- The prevalence of overweight varies by region, from 31% in the Southeast Asia and African regions to 67% in the Americas.
- https://ourworldindata.org/grapher/obesity-prevalence-adults-who-gho

Obesity

- a chronic complex disease defined by excessive fat storage that can impair health
- BMI 30 or more kg/m2

Preobesity / Overweight

- state of excessive fat storage
- BMI 25-29.9 kg/m2

Children under 5 years old

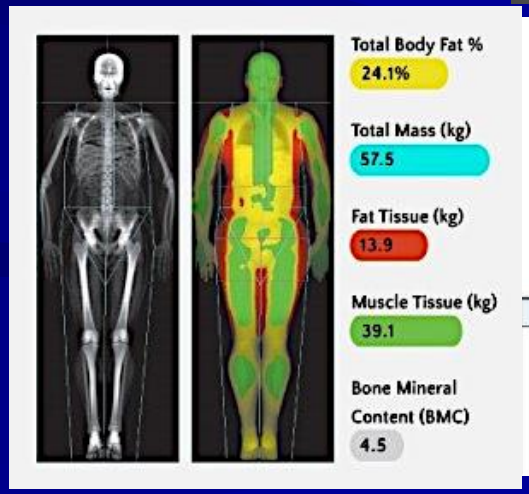
- overweight is a weight-for-height ratio greater than 2 standard deviations above the median of the WHO child growth standards;
- obesity is a weight-for-height ratio greater than 3 standard deviations above the median of the WHO child growth standards

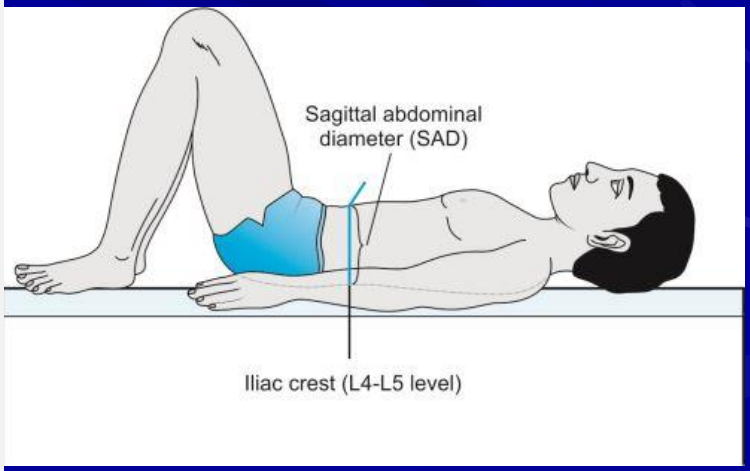
Children from 5 yrs to 19 years

- overweight is a BMI for age greater than 1 SD above the median of the WHO reference height;
- obesity is greater than 2 standard deviations above the median of the WHO reference height.

Assessment of the amount of adipose tissue

- BMI (Quetelet index)
- SAD (sagito-abdominal diameter)
- air-displacement plethysmography
- bioelectrical impedance measurement
- Dual-energy X-ray absorptiometry (DEXA scan)
- CT, MR, 3D scan
- callipometry
- hydrometry
- underwater weighing





https://www.cosmed.com/en/products/body-composition/bod-pod-gs-x

https://www.youtube.com/watch?v=SGHf_mze1RA

Body mass indices

- BMI (Quetelet index):

Imperial English BMI Formula

$$\text{weight (lbs)} \times 703 \div \text{height (in}^2\text{)}$$

Metric BMI Formula

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

- Broca index:

Normal body weight = height in cm – 100
Ideal body weight = (height in cm – 100) – 10-15%

https://www.topendsports.com/testing/tests/broca-index.htm

Classification of (pre)obesity

WHO CLASSIFICATION OF WEIGHT STATUS	
WEIGHT STATUS	**BODY MASS INDEX (BMI), kg/m^2**
Underweight	<18.5
Normal range	18.5 – 24.9
Overweight	25.0 – 29.9
Obese	≥ 30
Obese class I	30.0 – 34.9
Obese class II	35.0 – 39.9
Obese class III	≥ 40

Body fat distribution

Waist Girth and Health Risk

	Men	Women
Normal	78–94cm	64–80cm
Overweight (Elevated Risk)	94–102cm	80–88cm
Obese (High Risk)	>102cm	>88cm

- waist to height ratio, waist to hip ratio
- calipometry – skinfold thickness over the biceps, triceps, subscapular, suprailiac

Adipose tissue

- Connective tissue type

Structure:

- Adipocytes, endothelial cells, fibroblasts, adipocyte precursors, leukocytes, macrophages

Location:

- Subcutaneous – 80% (abdominal, gluteo-femoral)
- Between muscle fibers
- Visceral – peri-digestive organs (mesenteric and omental) and retroperitoneal depot (kidneys)
- Bone marrow

Adipose tissue

Types of adipose tissue:

- White adipose tissue
- Brown adipose tissue
- Beige adipose tissue

Function:

- Energy storage
- Insulation
- Thermoregulation
- Endocrine function – production of adipokines and cytokines
- Insulin resistance and diabetes mellitus
- Metabolic syndrome
- Chronic inflammation
- Tumors

Types of adipose tissue

a) White adipose tissue:

Function:

- Fat storage
- Increases body weight
- Reduces energy expenditure
- Reduces tissue sensitivity to insulin

Location:

- Subcutaneous
- Visceral

Types of adipose tissue

b) Brown adipose tissue:

Function:

- Thermogenesis
- Improves energy metabolism and glucose homeostasis
- Increases energy expenditure
- Reduces body weight
- Increases tissue sensitivity to insulin

Localization:

- Newborns - interscapular, perirenal region
- Adults - cervical, subclavicular, axillary, paravertebral, suprarenal region

Types of adipose tissue

c) Beige adipose tissue:

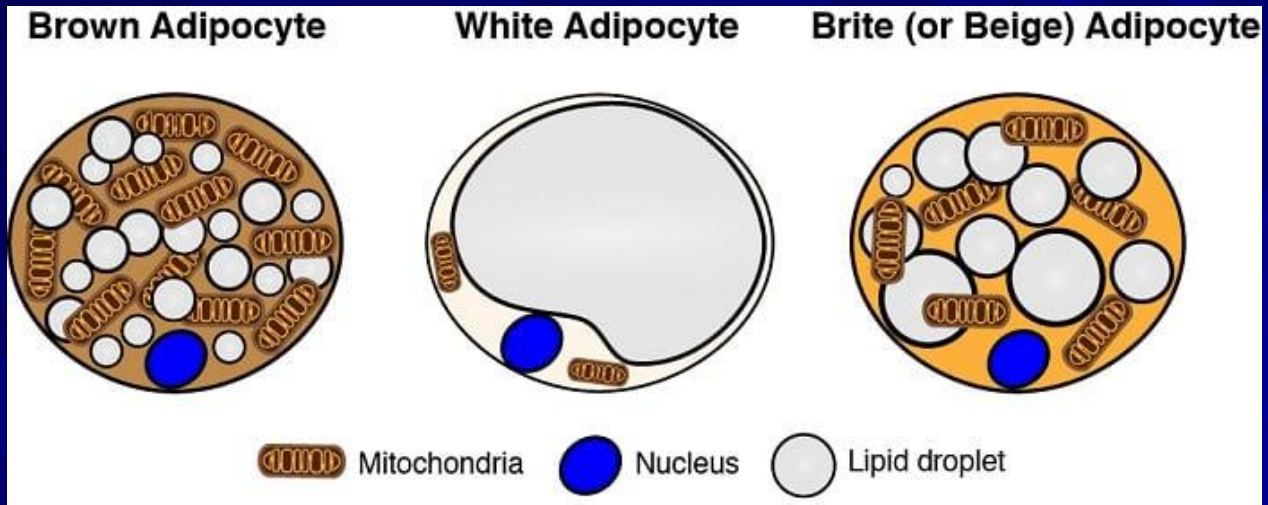
Function:

- Like brown adipose tissue

Location

- In subcutaneous white adipose tissue

Types of adipose tissue



	Brown	*White*	*Brite/beige*
UCP1 Expression	Positive	Negative	Positive
Mitochondrial Density	High	Low	Medium
LD Morphology	Multi-locular	Uni-locular	Multi-locular
Primary Function	Thermogenesis Endocrine	Energy storage Endocrine	Thermogenesis? Endocrine?

Adipose tissue growth

- hypertrophy, hyperplasia

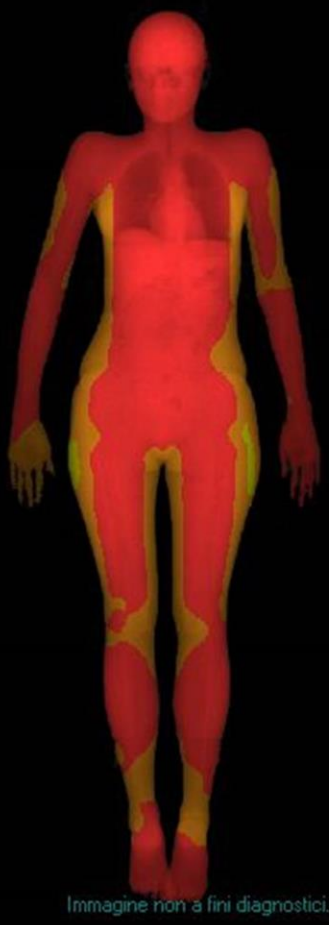
Factors:

- Chronic overnutrition
- Genetic predisposition
- Hormonal factors:
  - Insulin – insulin resistance promotes proliferation and differentiation of preadipocytes into mature fat cells.
  - Cortisol – increases fat storage
  - Estrogen – higher tendency to hyperplasia during puberty, pregnancy and especially in postmenopausal women
- Dietary composition
- Hypoxia
- Inflammation – persistent “low-grade inflammation”.

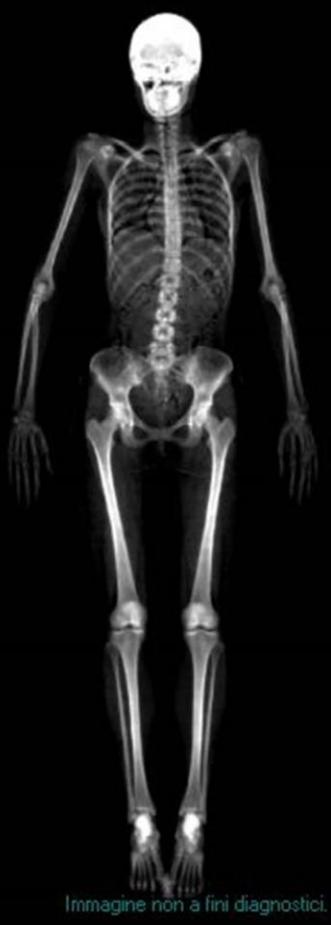
Localization of adipose tissue

- gynoid obesity (gluteofemoral, pear-shaped) with accumulation of adipose tissue in the thighs and hips, less cardiometabolically risky
- android obesity (central, abdominal, visceral, apple-shaped) with accumulation of visceral adipose tissue (in the abdominal area), cardiometabolically risky

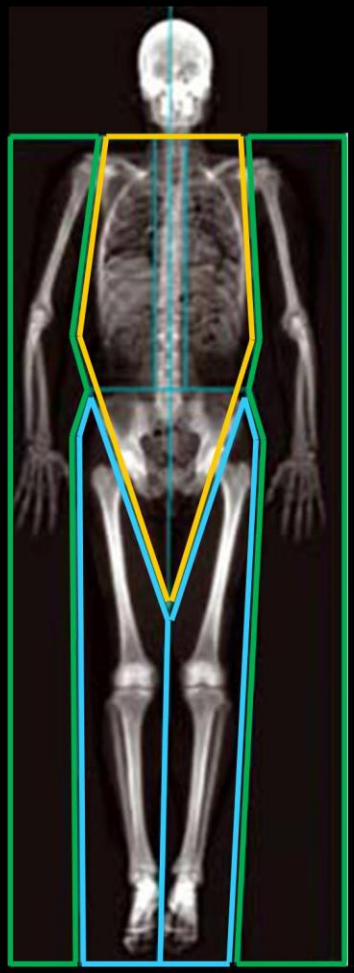
Fat Mass
(FM)



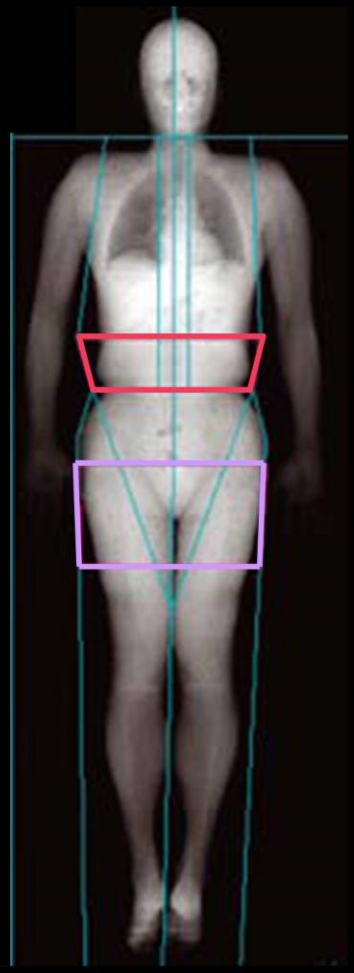
Lean Mass
(LM)



Bone Mineral
Content (BMC)



Superior arms
Inferior arms
Trunk

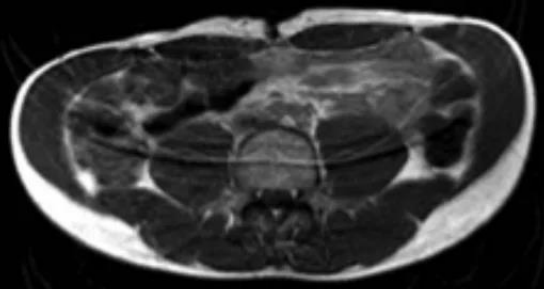


Android
Gynoid

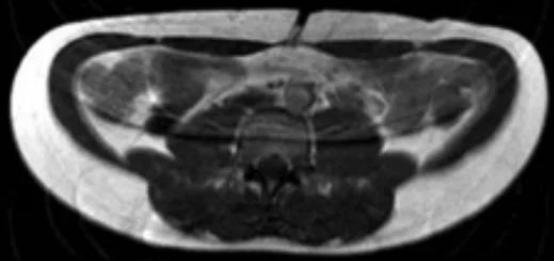
Visceral fat

- Intra-abdominal adipose tissue
- The amount of visceral fat and the ratio of subcutaneous to visceral fat depends mainly on:
- Genetic predisposition
- Sex
  - Men of any age (testosterone)
  - Postmenopausal women
- Age
  - Older age
- Total body fat – Energy intake

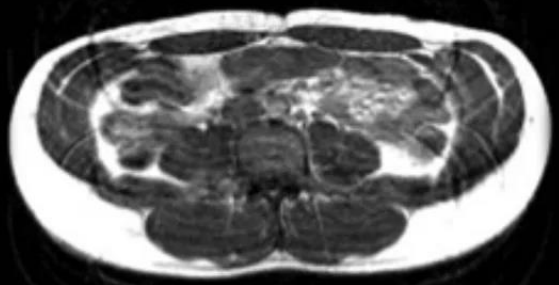
Variation in visceral fat content in men with the same waist circumference.



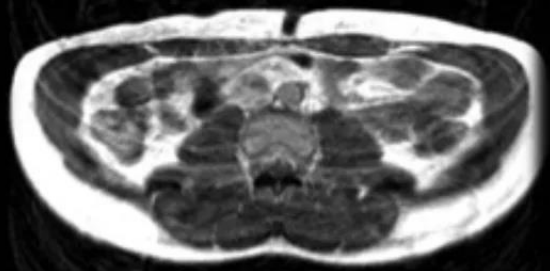
Visceral fat = 0.5 L



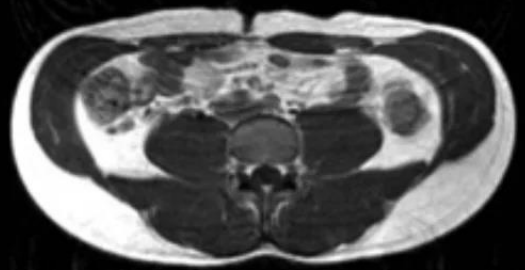
Visceral fat = 1.1 L



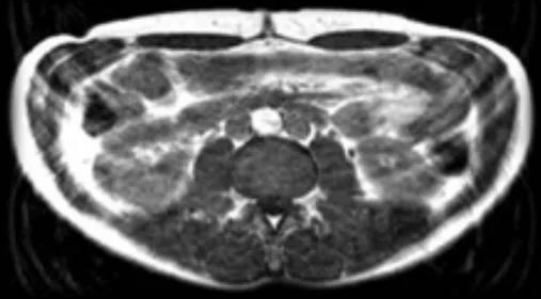
Visceral fat = 1.2 L



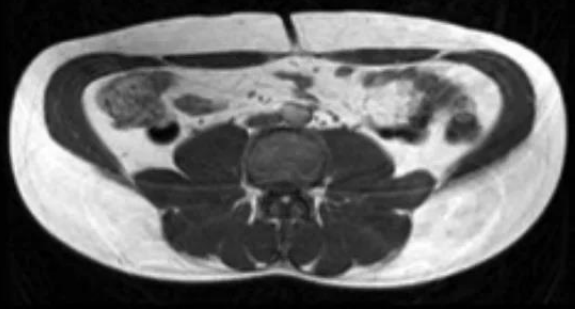
Visceral fat = 1.3L



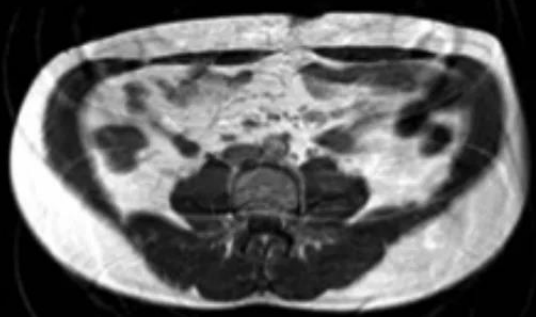
Visceral fat = 1.7 L



Visceral fat = 1.8 L



Visceral fat = 4.2 L

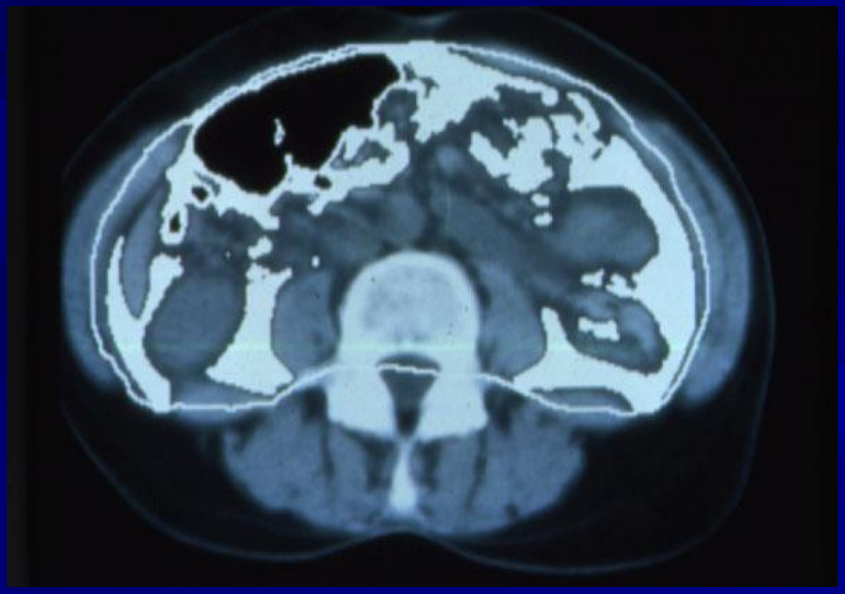


Visceral fat = 4.3 L

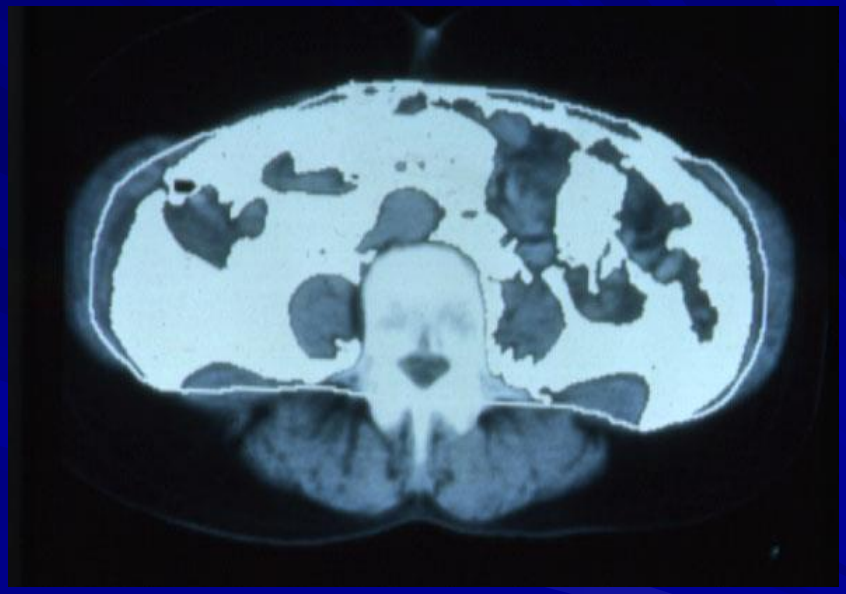
Visceral fat

- It has increased lipolytic activity – causes hyperlipidemia
- Causes hyperinsulinemia and insulin resistance
- Produces hormones and cytokines – causes permanent low-grade inflammation
- Therefore, it is a risk factor for the development of
  - Cardiovascular diseases
  - Type 2 diabetes mellitus
  - Some cancers – endometrial tumors, colorectal cancer, breast, pancreatic, ovarian, prostate cancers...

Body fat distribution



normal

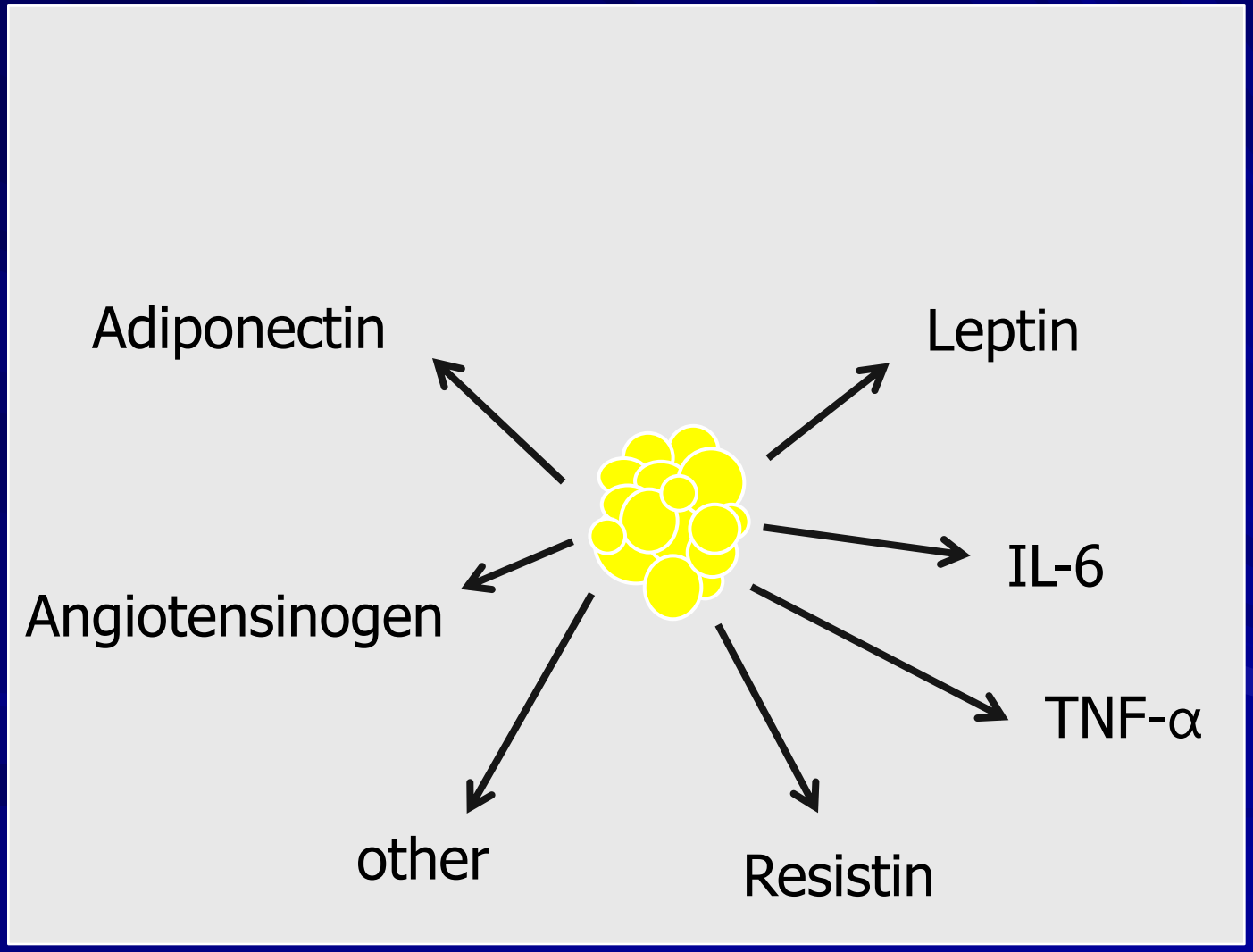


Type 2 diabetes

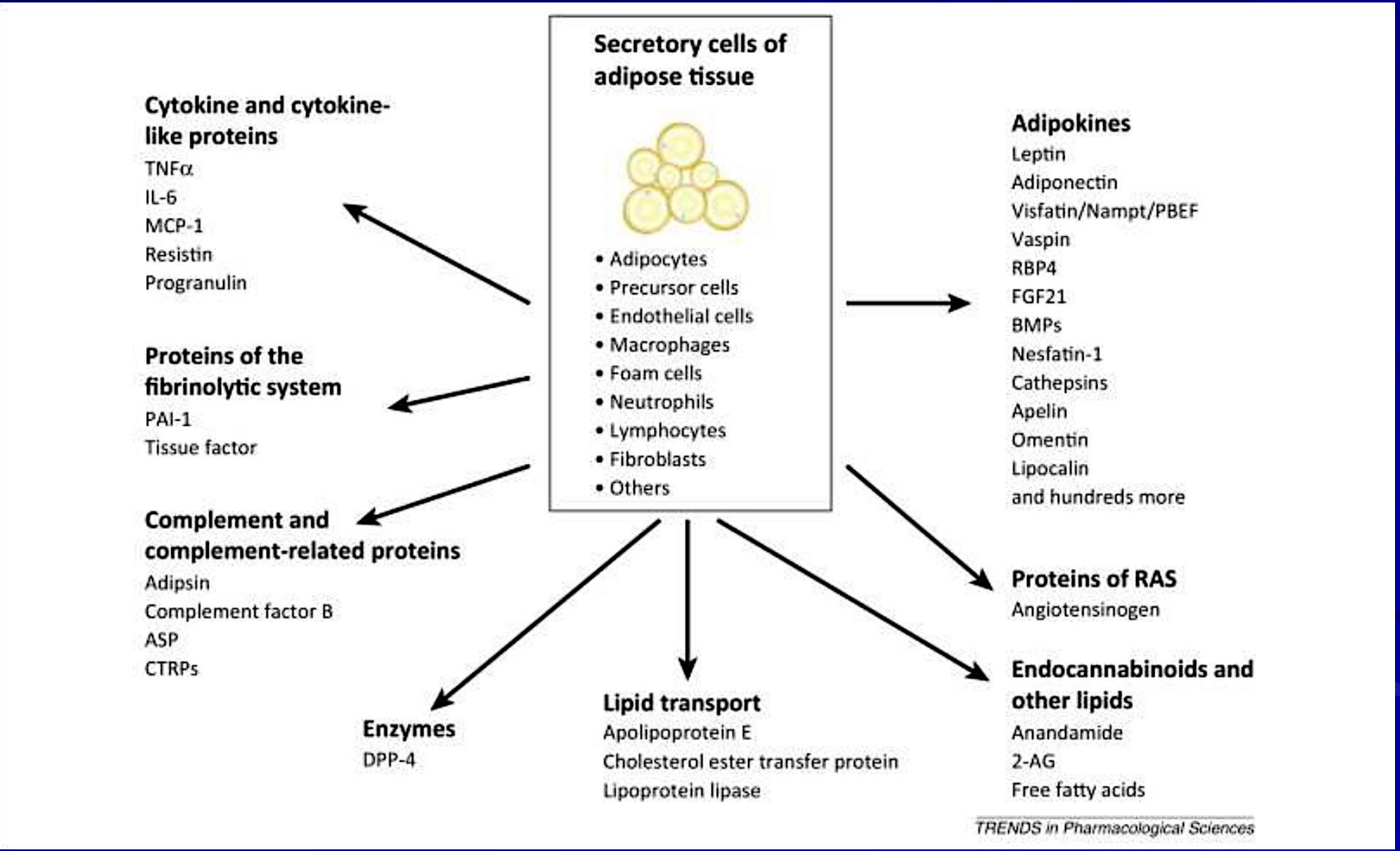
Ectopic adipose tissue

- local obesity of organs
- in liver, skeletal muscle, pancreas, perivascular, intra/extramyocellular, pericardial and epicardial (USG)
- potentiation of chronic subclinical inflammation with all its consequences

Adipose Tissue: An Endocrine Organ



Secretory cells of adipose tissue



https://www.sciencedirect.com/science/article/pii/S0165614715000905

Phenotypic classification of obesity

- metabolically unhealthy normal weight (MUNW)
- metabolically healthy (pre)obesity (MHO)
- metabolically unhealthy (pre)obesity (MUO)
- sarcopenic obesity (SO)

Phenotypic classification of obesity

- **Metabolically Healthy Normal Weight (MHNW):** Normal weight with good metabolic health.
- **Metabolically Unhealthy Normal Weight (MUNW):** Normal weight but with metabolic dysfunction, also known as Normal Weight Obesity (NWO) or Metabolically Obese Normal Weight (MONW).
- **Metabolically Healthy Obesity (MHO):** Obese but with preserved metabolic health.
- **Metabolically Unhealthy Obesity (MUO):** Obesity accompanied by metabolic complications like metabolic syndrome.
- **Sarcopenic Obesity (SO):** Low muscle mass in addition to excess fat.
- **Lipodystrophic Phenotype (LP):** Abnormal fat distribution

Gut-Brain Axis Phenotypes

- This classification describes different patterns of eating behavior influenced by the gut-brain axis.
- **Hungry Brain:** Difficulty recognizing satiety signals, leading to increased calorie consumption.
- **Hungry Gut:** Experience of hunger shortly after a meal due to faster gastric emptying.
- **Emotional Hunger:** Eating driven by emotional triggers rather than physiological hunger.
- **Slow Burn:** A slower-than-average metabolic rate, making it harder to burn calories.

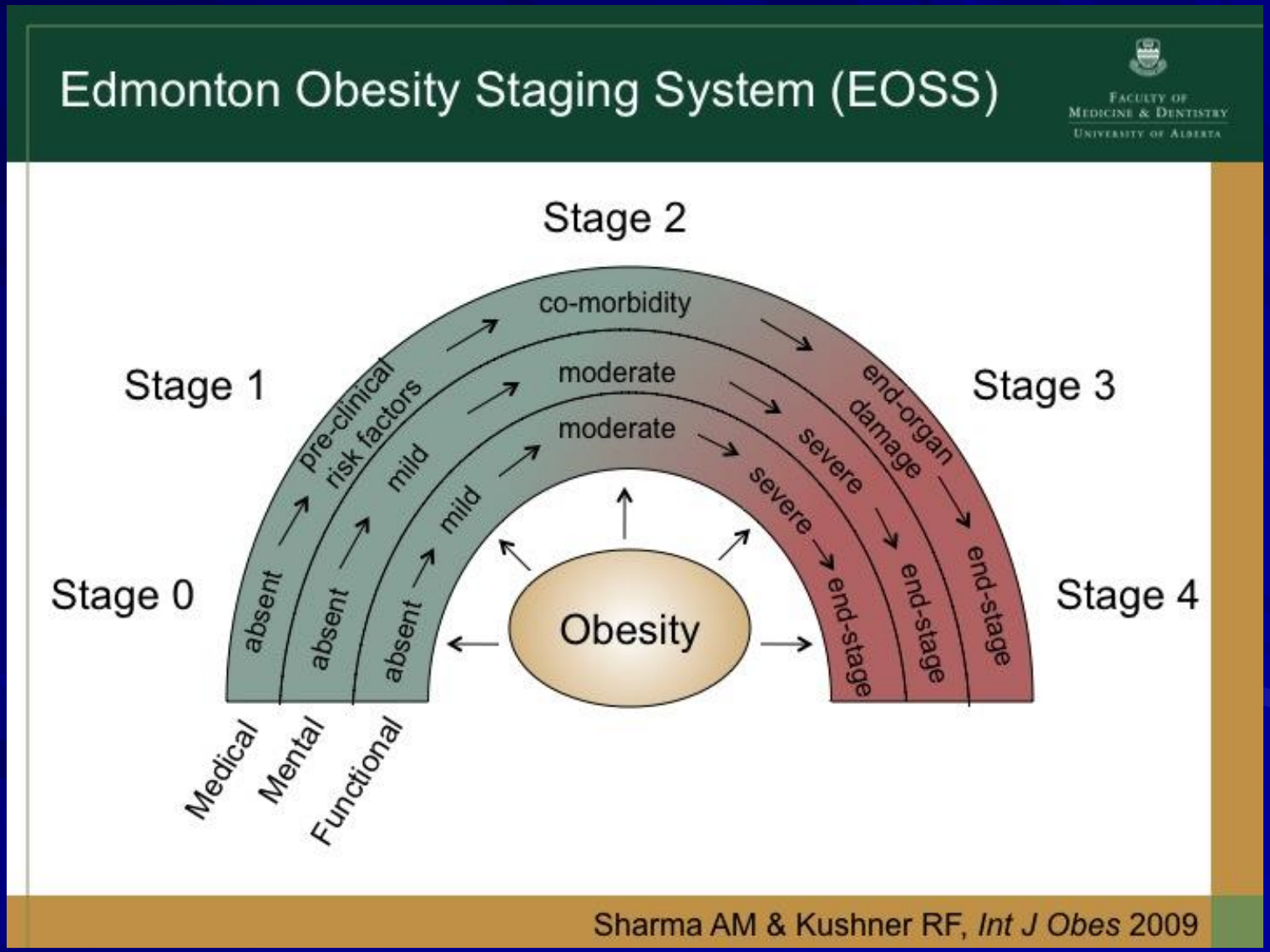
Adiposity-Based Chronic Disease (ABCD)

- a new diagnostic term for obesity, refers to the precise pathophysiological basis and avoids the stigma associated with the different uses of the multiple meanings of the term "obesity"
- based on 3 dimensions: etiology, degree of adiposity and health risks related to (pre)obesity

Edmonton Obesity Staging System

- stratifies the presence and severity of obesity-related health impairments
- a five-stage system of obesity classification that considers the metabolic, physical, and psychological parameters in order to determine the optimal obesity treatment
- EOSS has been reported to be a better predictor of mortality than BMI or metabolic syndrome.

Edmonton Obesity Staging System



Edmonton Obesity Staging System

Stage 0	No risk factors No physical or psychological symptoms No limitations	Lifestyle interventions, Prevention, Counseling & Regular medical control
Stage 1	Existing risk factors OR Light physical complaints OR Light psychological complaints / constricted well-being	
Stage 2	Pronounced risk factors requiring medical care OR Moderate psychological complaints OR Moderate functional limitations in daily routine	Lifestyle interventions & Consider metabolic surgery
Stage 3	Significant end organ damage OR Considerable psychological complaints OR Severe functional limitations OR Severe deterioration of well-being	Lifestyle interventions & Metabolic surgery
Stage 4	Chronic disease caused by overweight OR Grave psychological symptoms OR Grave functional limitations	

Etiopathogenesis of (pre)obesity

- in up to 90% of cases, (pre)obesity is a complex multifactorial disease
- only in a very low percentage of individuals with obesity are we able to identify the exact cause of the development of (pre)obesity (monogene-related obesity, obesity caused by endocrinopathy, pharmacotherapy associated with weight gain, etc.)

Etiopathogenesis of (pre)obesity

- genetically determined factors:
- body weight, resting and postprandial energy expenditure, spontaneous physical activity, postprandial thermogenesis, taste preference for fats and carbohydrates, appetite regulation, ability to metabolize nutrients, body composition and fat distribution, behavior, eating and exercise habits of the individual

- non-genetic factors:
- "obesitogenic" environment - excessive energy intake and insufficient energy expenditure, increased consumption of ultra-processed foods, composition of the gut microbiome - decrease in phylogenetic diversity of the gut microbiome, psychological and emotional factors, chronic stress and inadequate sleep, social, economic, educational and cultural factors, environmental factors (persistent organic pollutants)

Etiology of obesity

- Monogenic causes of obesity
- Polygenic causes of obesity
- Causes responsible for excessive food intake

Types of obesity from a genetic perspective

- polygenic (common) type of obesity
- syndromic obesity
- monogenic obesity

Polygenic obesity

- there are changes in several genes (currently more than 1000 loci are known), which in interaction with the obesogenic environment help develop the resulting phenotype of (pre)obesity
- the gene for melanocortin receptor 4 (MC4R) is associated with increased hunger, reduced satiety and increased total protein and fat intake
- the genes for adipokine and adipokine receptor, the gene encoding dopamine, serotonin and cannabinoid receptors

Polygenic obesity

- FTO gene (fat mass and obesity associated) is associated with obesity, IR, DM2, lipids and blood pressure
- FTO gene variants lead to increased total food intake as well as higher intake of fatty foods and reduced satiety and increased hunger
- SH2B1, KCTD15, MTCH2, BDNF, Mrap2 genes

Syndromic obesity

- diseases with Mendelian inheritance
- often mental retardation, dysmorphic features, and organ-specific developmental abnormalities
- more than 20 syndromes associated with obesity
- Prader-Willi syndrome, Bardet-Biedl syndrome, Albright hereditary osteodystrophy

Obesity syndromes

Zo zdrojov na internete

Bardet–Biedl syndrome	Prader–Willi syndrome	Albright's hereditary osteodystrophy
Alström syndrome	Cohen syndrome	WAGR syndrome
Down syndrome	Fragile X syndrome	Kallmann syndrome
Leptin	Smith–Magenis syndrome	Börjeson–Forssman–Lehmann syndrome
PCSK1 deficiency	MC4R deficiency	Melanocortin 4 receptor
Myt1l-variants Syndrome	POMC deficiency	Pseudohypoparathyroidism
SH2B1 deficiency		

Syndromes associated with obesity

ochorenie	prevalencia	dedičnosť	gén/lokus
achondroplázia	1–9 : 100 000	AD	*FGFR3*
Albrightova hereditárna osteodystrofia (Pseudohypoparatyreóza 1a)	3–7 : 1000 000 (Japonsko)	AD, 2 : 1 (ženy : muži)	*GNAS1*
Alstromov syndróm	< 50 rodín	AR	*ALMS1/2p13*
Bannayanov-Rileyov-Ruvalcabov syndróm	neznáma	AD	*PTEN/10q23*
Beckwithov-Wiedemannov syndróm	1–5 : 10 000	multifaktoriálne	*11p15.5.*
Bardetov-Biedlov syndróm	1 : 13 000 (1 : 17 000 východné pobrežie Kanady), 1 : 160 000 (Európa)	AR	geneticky heterogénne
Borjesonov-Forssmanov-Lehmannov syndróm	5 publikovaných rodín	X-viazané	*PHF6/Xq26.3*
Carpenterov syndróm	140 opísaných prípadov	AR	*RAB23/6p11*
Cohenov syndróm	100 opísaných prípadov	AR	*COH1/8q22-q23*
syndróm fragilného X	1–5:10 000	X-viazané dominantne	*FMR1/Xq27.3*
MEHMO	niekoľko opísaných prípadov na svete	X-viazané recesívne, mitochondriálna dedičnosť	*21.1–22.13p*
Praderov-Williho syndróm	1 : 10 000–15 000	imprinting	*SNRPN, Necdin/15q12, 15q11-q13*
Simpsonov-Golabiov-Behmelov syndróm	< 100 opísaných prípadov	X viazané recesívne	*GPC3/ Xq26*
Smithov-Magenisov syndróm	1–9 : 100 000	sporadická	*RAI1/17p11.2*
Sotosov syndróm	1–9 : 100 000	AD sporadická	*NSD1/5q35*
Wilsonov-Turnerov syndróm	14 opísaných prípadov (muži)	X viazané recesívne/ dominantne	*p21.1-q22*
Ulnarov-Mammaryov Schnitzelov syndróm	< 1 : 1000 000	AD	*TBX3/12q*
Weaverov syndróm	7 opísaných prípadov	AD	*NSD1* u troch opísaných prípadov

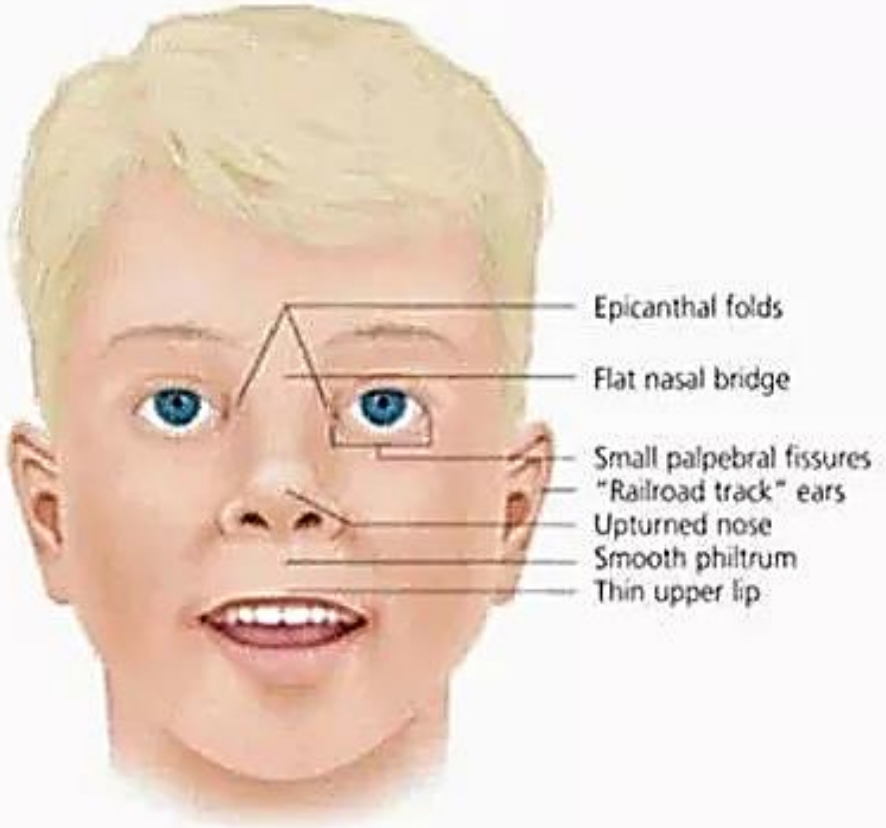
Prader-Willi syndrome

- *Prader-Labhart-Willi syndrome, Willi-Prader syndrome, Prader-Willi-Fanconi syndrome*
- incidence 1:25,000 live births
- imprinting mutations, translocation, paternal deletion 15q11q13 or maternal uniparental disomy at this locus
- in the first year of life it is manifested by hypotonia, hypogonadism and failure to thrive
- in the subsequent period constant non-selective hyperphagia and development of morbid obesity
- facial dysmorphia (almond-shaped eyes, narrow upper lip, high forehead), mental retardation, growth hormone deficiency (shorter height)

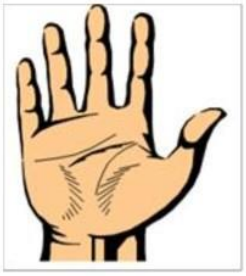
PRADER WILLI FEATURES

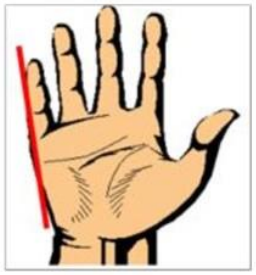
Mnemonic : H30

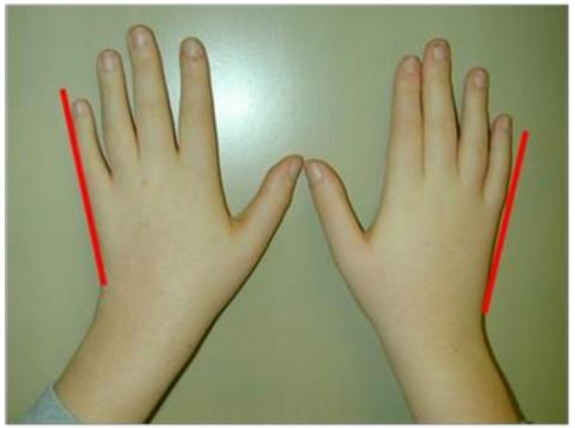
- **Hyperphagia**
- **Hypotonia**
- **Hypopigmentation**
- **Obesity**

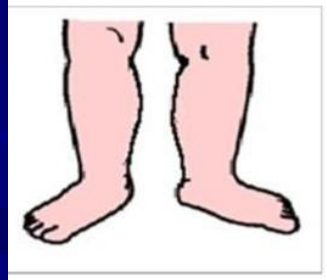


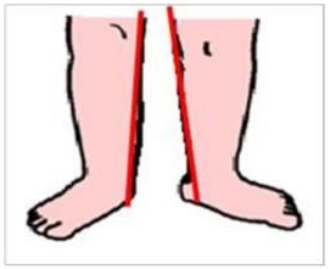
Prader-Willi syndrome

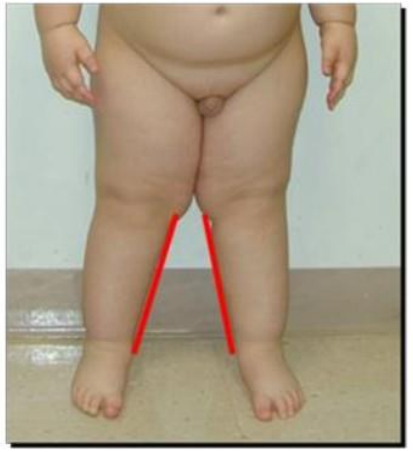












Prader Willi Syndrome

Chr 15

A **rare genetic disorder** caused by a **methylation defect** on **chromosome 15**, leading to the loss or silencing of **paternal genes**, typically due to a **deletion**, **imprinting defect**, or **uniparental disomy** *(where the child inherits both copies of chromosome 15 from the mother)*. This disrupts the function of the hypothalamus, which regulates hunger, hormones, and mood. It usually results from **a sporadic mutation** and is **not inherited**, though genetic counseling can help identify the cause.

Imprinting disorder

Imprinting is a genetic process where the expression of certain genes depends on whether they are inherited from the mother or father, with some genes being activated or silenced accordingly.

CLINICAL FEATURES

Symptoms in infancy

- **Hypotonia**
- **Failure to thrive**
- Lethargy
- Weak cry
- **Difficulty feeding/poor suck**

Symptoms in childhood

- **Behavioural concerns**
  - Compulsive
  - Stubborn
  - Manipulative
- **Obesity**
- **Hyperphagia**

Facial:

- **Almond-shaped eyes**
- Narrow bitemporal diameter
- Up-slanting palpebral fissures
- Thin upper lip
- Small-appearing mouth
  - Down-turned corners of mouth
  - "Triangular mouth"

Hand findings:

- Short fingers
- Partial syndactyly
- Thumb hypoplasia

Neurologic:

- **Global developmental delay**
- **Mild to moderate intellectual disability (ID)**

Genitourinary:

- **Hypoplastic genitals**

Endocrine

- **Short stature**
- **Delayed puberty**
- Osteoporosis
- Hypothyroidism
- Small hands and feet

DIAGNOSIS

- **DNA methylation studies**
- **Chromosomal microarray** to confirm microdeletions/ duplications, or paternal uniparental disomy

OBESITY-RELATED COMPLICATIONS

- Type 2 diabetes
- Heart disease
- High blood pressure
- Obstructive sleep apnea (OSA)
- Gallstones
- Liver disease

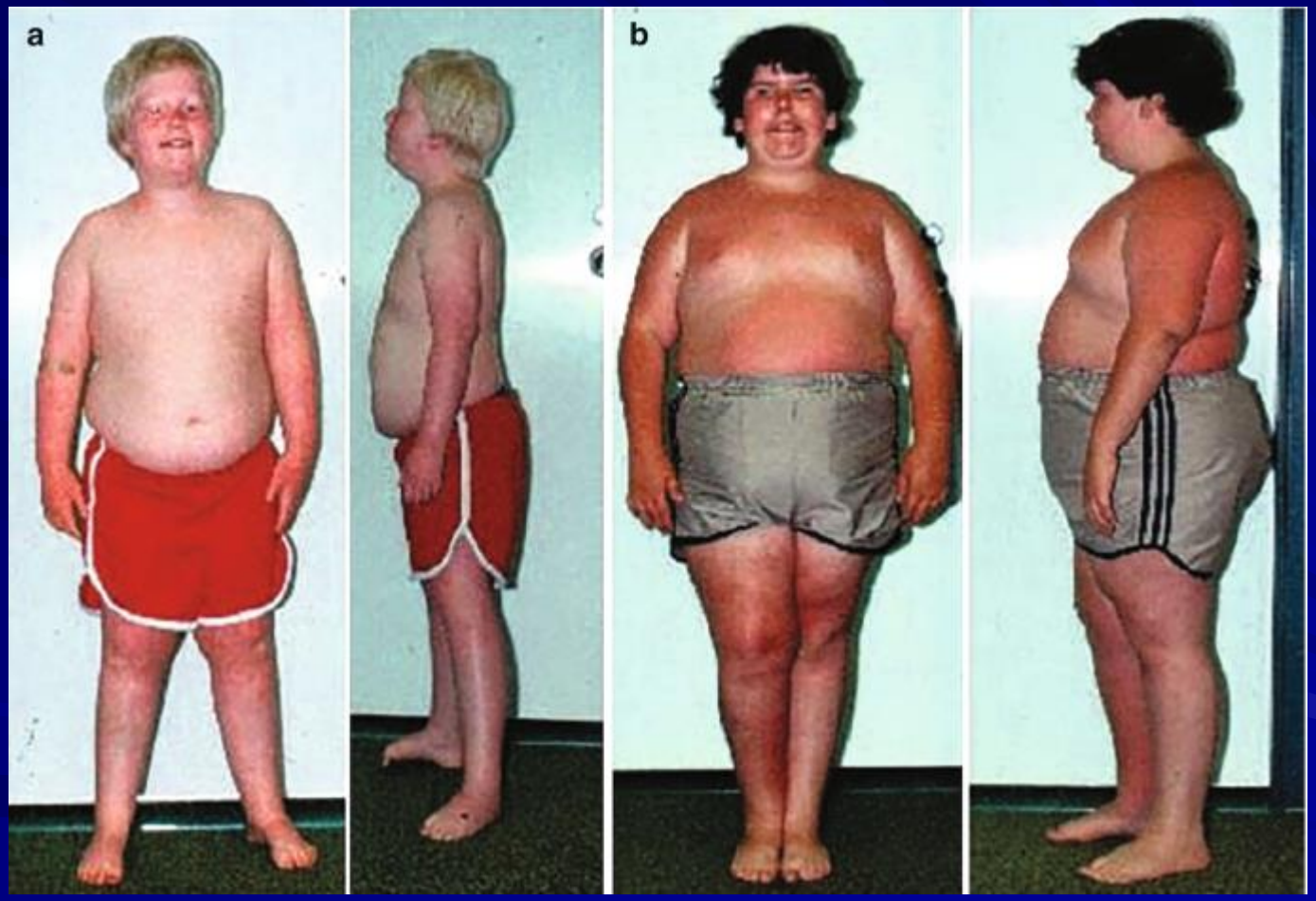
MANAGEMENT

- **Nutrition in infancy**: hypercaloric formula to promote weight gain.
- **Therapy**: physical, speech, occupational, and developmental therapies for movement, communication, and life skills.
- **Mental health care**: support for obsessive behaviors, mood disorders, and psychological issues.
- **Sleep treatment**: address sleep apnea to improve behavior and daytime functioning.
- **Weight management**: reduced-calorie diet, increased physical activity, and supervision of meals during childhood.
- **Growth hormone**: improves growth, muscle tone, and reduces body fat.
- **Sex hormone replacement therapy**: for delayed puberty.

February 2025

Dr. Katharine V. Jensen (Pediatric Resident, University of Alberta) and Dr. Karen Forbes (Professor of Pediatrics, University of Alberta) for www.pedscases.com

Prader-Willi syndrome

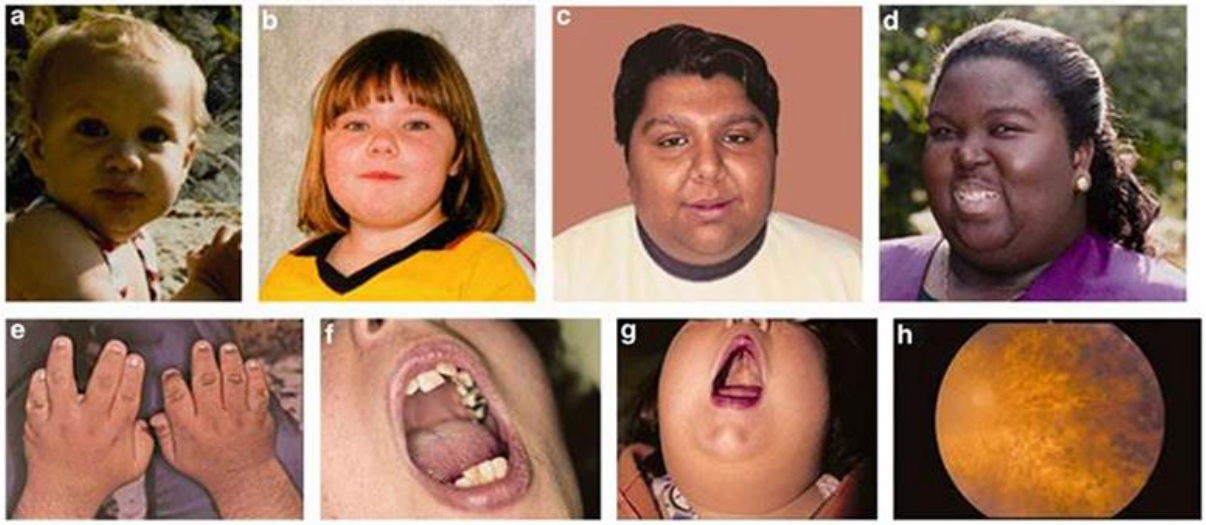


Bardet-Biedl syndrome

- 1: 125 000 – 1: 175 000
- Ar, mutations in 21 different genes (BBS1-BBS12) → ciliary anomalies in organs (kidneys and eyes)
- childhood obesity, pigmentary retinopathy, postaxial polydactyly, kidney disease (polycystic kidney disease), hypogenitalism and learning and behavioral disorders, mental deficit
- common DM2, AH, congenital cardiomyopathy, Hirsprung's disease, risk of kidney failure, development of blindness

Bardet-Biedl syndrome

i. Clinical features of Bardet-Biedl syndrome



ii. Diagnostic features

Primary features	*Frequency*
Rod-cone dystrophy	93%
Polydactyly	63–81%
All four limbs:	21%
Upper limbs only:	9%
Lower limbs only:	21%
Obesity	72–92%
Genital anomalies	59–98%
Renal anomalies	53%
Learning difficulties	61%
Secondary features	
Speech delay	54–81%
Developmental delay	50–91%
Diabetes mellitus	6–48%
Dental anomalies	51%
Congenital heart disease	7%
Brachydactyly/ syndactyly	46–100%/8–95%
Ataxia/ poor coordination	40–86%
Anosmia/hyposmia	60%

- Dental anomalies - malocclusion, anterior crowding, micrognathia, deep palate, hypodontia, small tooth roots, enamel hypoplasia and microdontia
- A disease characterized by dystrophy of rods and cones of the retina (retinitis pigmentosa). 4 primary or 3 primary and 2 secondary criteria are required to make the diagnosis.

Albright's hereditary osteodystrophy

- 3-7:1,000,000 in Japan, with a 2:1 ratio of women to men
- AHO is an AD hereditary syndrome caused by a mutation in the GNAS1 gene, which encodes the alpha subunit of the stimulatory G-protein
- short stature, obesity, round face, short neck, brachydactyly, pseudohypoparathyroidism and ectopic calcifications, resistance to parathyroid hormone (pseudohypoparathyroidism type A1 or PHP1a) and to other hormones (especially TSH).
- AHO is characterized by manifestations of hypoparathyroidism (hypocalcemia, hyperphosphatemia) and elevated parathyroid hormone levels.

Albright's hereditary osteodystrophy

Albright's hereditary osteodystrophy

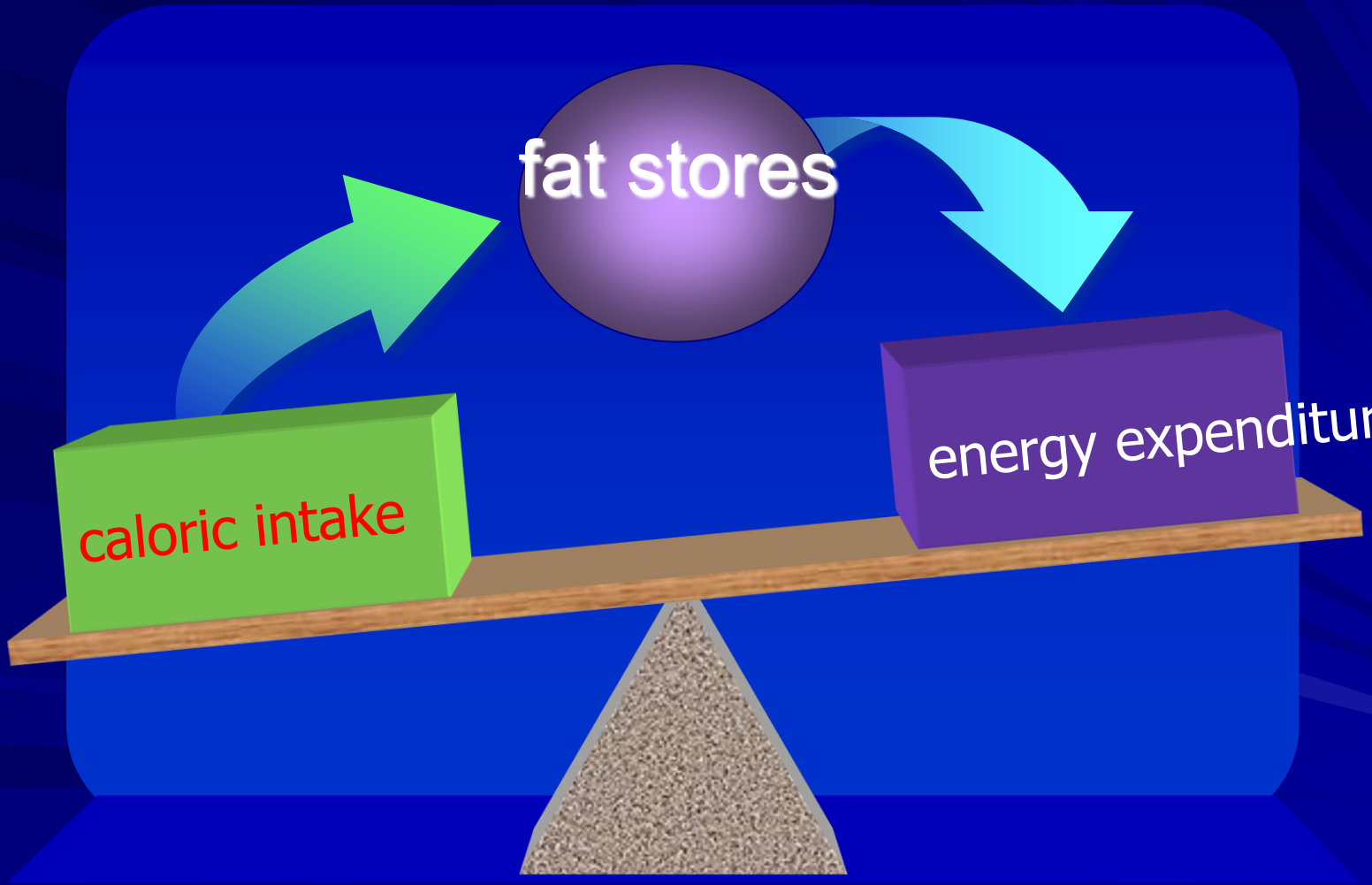
Causes responsible for excessive food intake

- positive energy balance
- increased caloric intake
- low energy expenditure
- combinations
- genetic predisposition to (pre)obesity

Causes responsible for excessive food intake

- genetic predisposition to (over)obesity - mostly polygenic (up to 600 genes are associated with an increased risk of obesity)
- the resulting phenotype is caused by the cumulative effect of variants in multiple genes, but mainly by the action of epigenetic and environmental factors

Obesity caused by long-term positive energy balance



Obesity is caused by long-term positive energy balance

- Obesity is caused by ingesting more energy than is expended over a long period of time. The excess calories that are consumed lead to an accumulation of body fat either by being stored as fat or preventing the mobilization and oxidation of endogenous fat.
- In general, ingesting 3500 kcal more (or less) than expended will lead to a gain (or loss) of approximately 1 lb of fat. Genetic factors may influence the amount of weight gained with overfeeding.
- In one study, weight gain varied greatly among 12 monozygotic twin pairs who were chronically overfed 1000 kcal/d. However, weight gains were very similar within each member of a twin pair. In another study, body fat gain after 8 weeks of overfeeding also varied among study subjects but was inversely related to changes in non-volitional energy expenditure, such as fidgeting, which may be determined genetically.

Genetic-metabolic mechanisms of (pre)obesity

- prenatal determinants of the development of (pre)obesity in childhood:
  - Maternal weight before conception
  - Increase in body weight during pregnancy
- Risk periods of life for the development of (pre)obesity: prenatal period, adolescence (especially in girls), in adulthood these are periods of significant changes in lifestyle, such as ending a sports career/active sports, university studies, pregnancy, changing jobs, starting a family, onset of menopause, retirement, quitting smoking and others

Genetic-metabolic mechanisms of (pre)obesity

- the importance of preconception influence of lifestyle or excessive nutrition of parents on reprogramming of imprinted traits during gametogenesis and early development
- acquired instability of imprinting can be transmitted to the next generation and increase the risk of chronic diseases in adulthood
- high birth weight is also an important factor predisposing to (pre)obesity

Genetic-metabolic mechanisms of (pre)obesity

- Macrosomic newborns (BW >4,000 g) will become (pre)obese children in 20% of cases, (pre)obese children will become obese teenagers in 55% of cases and become obese adults in 80% of cases
- nutrigenomics - provides genetic understanding of how common dietary components affect the balance between health and disease by changing the expression or structure of the individual's genetic makeup
- nutrigenetics - describes how the genetic profile influences the body's response to and bioactive components of food by influencing their absorption, metabolism, storage and site of action

Psychic and psychological factors of (pre)obesity

- stress, anxiety, depression, sleep deprivation, eating disor.
- 20% to 60% of obese individuals have a mental disorder
- 32.6% prevalence of metabolic syndrome in patients with severe mental disorders [Vancampfort et al. 2015]
- > 40% of patients taking AAP ↑BW [Mittal et al., 2017]

Metabolic effects of psychotropic drugs

antipsychotics, antidepressants, anticonvulsants/thymostabilizers

direct effects:

development of visceral adiposity

development of chronic inflammation

development of hyperlipidemia

increased hepatic gluconeogenesis

worsening insulin resistance

progression of glucose intolerance

fully-developed diabetes mellitus

indirect effects mediated by:

sedative effect

impact on sleep and its architecture

by potentiating imbalances in energy homeostasis

neuroendocrine increase in appetite

gut dysbiosis

negative impact on motivation, sexual activities and the reward system

risky behavior

other consequences of hypoactivity

Metabolic dysregulations in psychopharmacotherapy

Multifactorial influence of psychotropic drugs on:

i. neurotransmission, neurotransmitter-receptor interactions
ii. expression of hypothalamic orexigenic/anorexigenic neuropeptides, peptides, incretins, adipokines, pituitary hormones and others regulating appetite
iii. pro-inflammatory cytokines, intestinal microflora
iv. thermoregulation, energy balance

Metabolic solutions

Possibilities to influence phenotype

- *influence on the expression of an/orexigenic peptides, incretins, adipokines, pituitary hormones, receptors, ...*
- *increasing striatal density of dopamine D2 receptors*
- *by preference for low-fat and low-carbohydrate meals*
- *by reduction of increased body weight*
- *by lifestyle modifications*
- *by pharmacotherapy with anti-obesity drugs, including incretins*

Obesity → ↓ striatal D2 receptor density. Chronic consumption of high-fat and high-carbohydrate diet → ↓ DA receptor density = phenotype similar to chronic drug abuse with ↑ DA signaling [Val-Laillet et al. 2015]

Metabolic solutions

Possibilities to influence phenotype

- modulation of striatal prefrontal pathways → positive changes in reward expectation = alternative prevention mechanisms ↑BW
  - planned daily domain / social / social / relaxation non-addictive activities – reward system, dopamine "recharging"
  - partial DA agonists – DA stabilizers (aripiprazole, brexpiprazole, cariprazine)

Metabolic solutions

Possibilities to influence energy balance

- low-carbohydrate ketogenic diet (nutritional ketosis)
- restoration of disrupted circadian rhythms - a potential therapy for the treatment of comorbid psychiatric and metabolic disorders [Hühne-Landgraf et al. 2023]
- education and psychoeducation
- strengthening rational strategies for coping with stressful situations and the subsequent ability to make good choices

Metabolic solutions

Nutritional ketosis – ketogenic diet

Modified Ketogenic Diet

- *60-75% Fat*
- *5-7% Carbohydrates*
- *18-35% Protein*
- *6-8 weeks... 4 months*
- *target blood ketone levels 1-4 mmol/L*
- *mild ketosis: 0.5-1.0 mmol/L*
- *optimal ketosis 1-3 mmol/L*
- *high ketosis: 3-5 mmol/L*
- *target blood glucose: 4-7.8 mmol/L*

Metabolic solutions

Gut microbiome modulation

- modulation of the microbiome-gut-brain axis influences emotional behavior [Ke et al. 2023]
- The probiotic Lactobacillus rhamnosus reduced anxiodepressive behavior in male mice, accompanied by changes in dopamine gene expression in the nucleus accumbens [Schell et al. 2023]
- Probiotics may improve cognition and alleviate depressive symptoms in humans [meta-analysis He et al. 2023]

Endocrine Causes of Obesity

- Hypothalamic injury or tumor
- Cushing's syndrome
  - Hypothyroidism
  - Hypogonadism
  - Growth hormone deficiency
- Polycystic ovarian syndrome
  - Manifestation of obesity versus cause

Monogenic obesity

- caused by a mutation in a single gene
- 5% of all patients with obesity
- severe obesity in childhood, may/may not be associated with endocrinological abnormalities or behavioral disorders
- there is no mental retardation, dysmorphic features or developmental anomalies
- the pathophysiology of monogenic obesity lies in the disruption of the so-called leptin-melanocortin axis, which plays an important role in the neuronal control of satiety and hunger, i.e. in maintaining the energy homeostasis of the organism

Monogeneic obesity

- Leptin
  - A few families
- Leptin receptor
  - A single family
- MC4-Receptor
  - Most common defect

Monogenic obesity

Clinical features:

- obesity with hyperphagia starting in childhood (0-5 years), severe obesity in adults
- BMI > 30, in children > 97th percentile, or BMI > 2.5 SDS for a given age
- positive family history of obesity starting in childhood
- frequent association with endocrinopathies
- accessory features (short stature, red hair, hypogonadism, hypopituitarism)

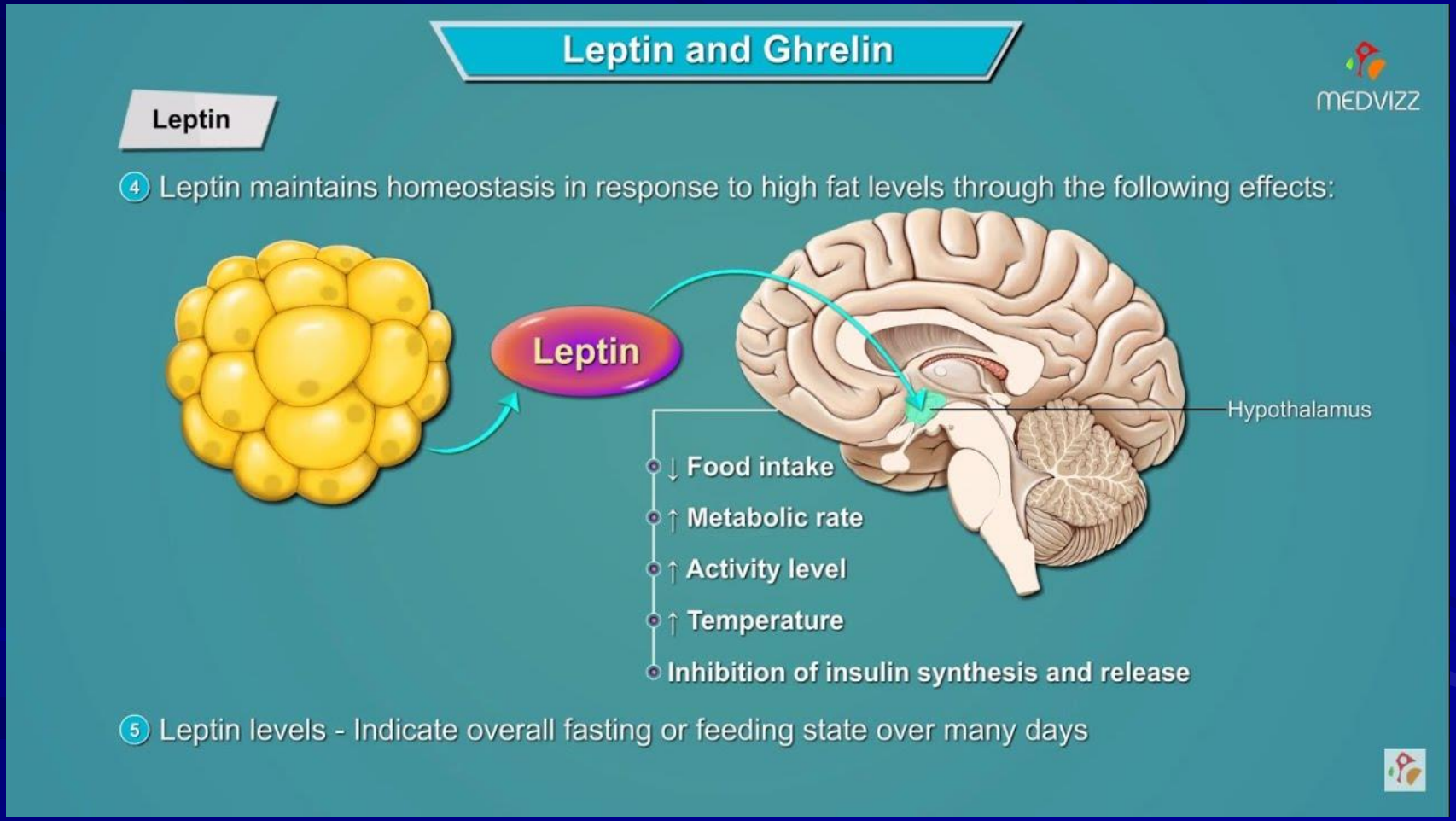
Leptin

- Leptin is a proteohormone secreted by adipocytes; its concentration correlates with the amount of body fat.
- Leptin acts mainly in the hypothalamus and activates several other pathways, including the expression of POMC in the arcuate nucleus of the hypothalamus.
- Activation of MC4R by peptides resulting from the cleavage of POMC (α-MSH) leads to a reduction in food intake and increased energy expenditure, which affects the maintenance of body weight. MC4R is inhibited by AGRP (agouti-related peptide), which is also produced in the hypothalamus.
- Genes whose mutations are involved in the development of monogenic obesity are located on autosomes. The inheritance of most of these diseases is autosomal recessive. The inheritance of MC4R mutations is autosomal codominant. Gene mutations are mostly point mutations (nucleotide substitutions, deletions, insertions).

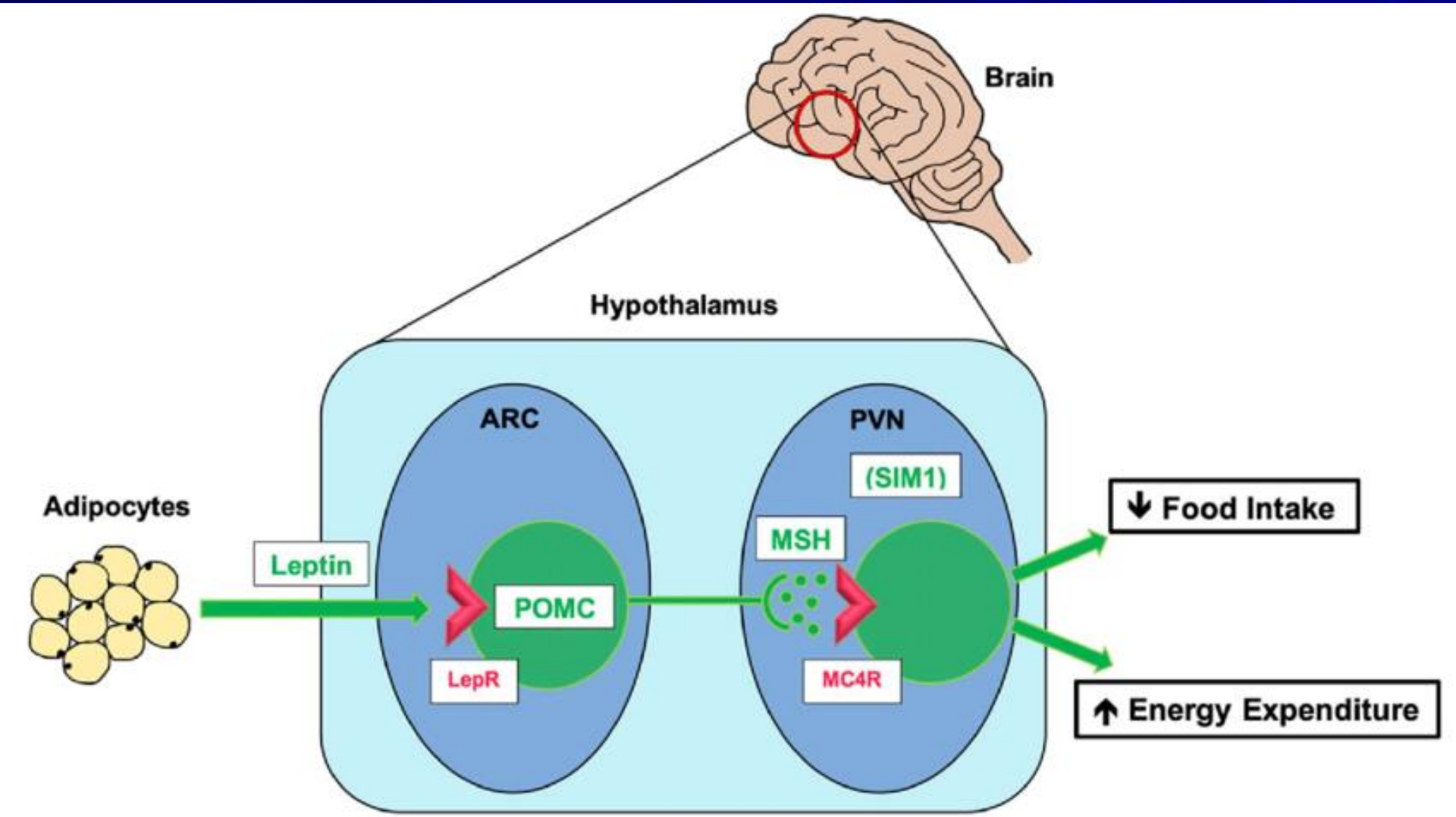
Leptin

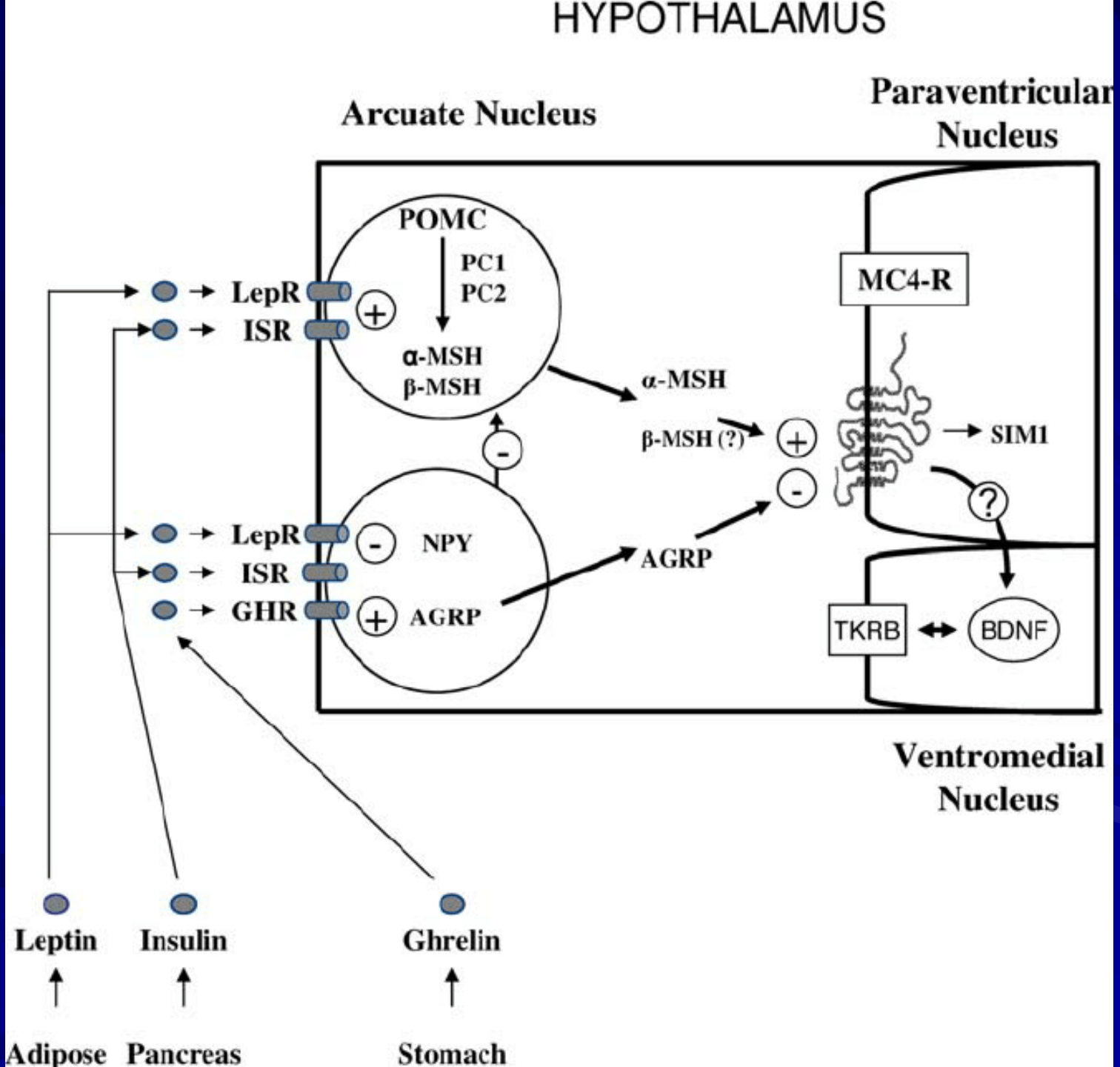
- Leptin's central actions :
  - Increase energy expenditure (via physical activity, sympathetic nervous system activity)
  - Decrease food intake
  - Decrease body weight
  - Increase insulin sensitivity
  - Help signal the onset of puberty
  - Regulate other pituitary hormone axes
- Leptin’s peripheral actions
  - Stimulate angiogenesis
  - Hematopoietic cell proliferation
  - T-cell immnunity

Leptin


Leptin and Ghrelin
MEDVIZZ
Leptin
4 Leptin maintains homeostasis in response to high fat levels through the following effects:
Leptin
Hypothalamus
↓ Food intake
↑ Metabolic rate
↑ Activity level
↑ Temperature
Inhibition of insulin synthesis and release
5 Leptin levels - Indicate overall fasting or feeding state over many days

The role of the leptin-melanocortin axis in body weight regulation

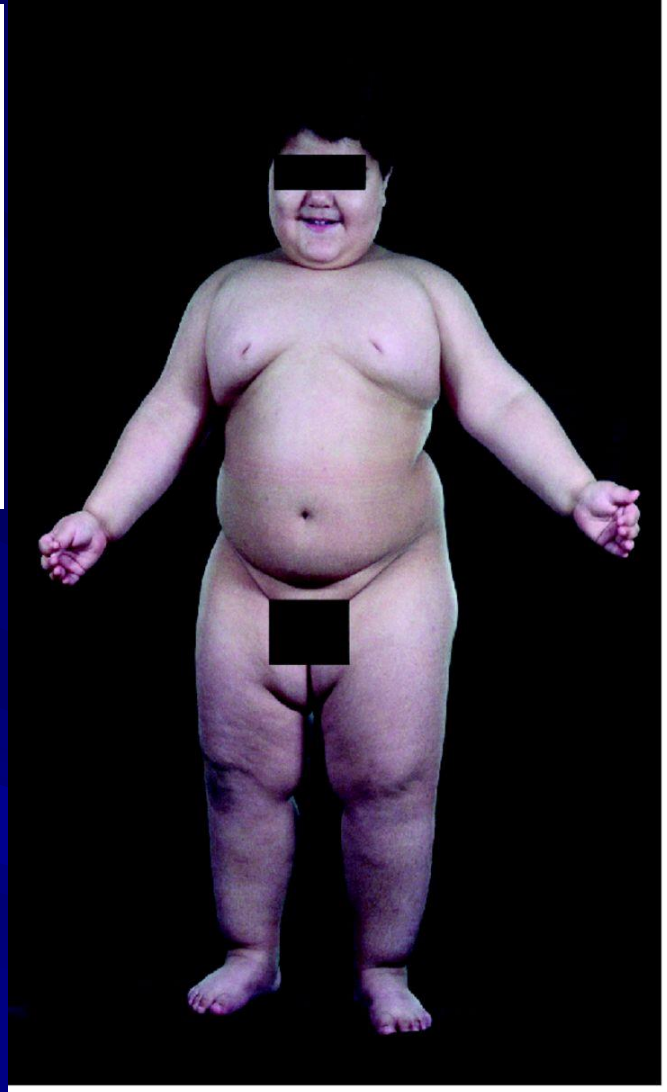



HYPOTHALAMUS
Arcuate Nucleus
Paraventricular Nucleus
POMC
PC1
PC2
α-MSH
β-MSH
LepR
ISR
LepR
ISR
GHR
NPY
AGRP
α-MSH
β-MSH (?)
AGRP
MC4-R
SIM1
?
TKRB
BDNF
Ventromedial Nucleus
Leptin
Insulin
Ghrelin
Adipose
Pancreas
Stomach

Monogenic causes of obesity

- mutation of the LEP gene for leptin
- mutation of the LEPR gene for leptin receptor
- mutation of the SH2B1 gene for SH2B1 adaptor protein
- mutation of the POMC gene for proopiomelanocortin
- mutation of the PCSK1 gene for prohormone convertase 1 (PC1)
- mutation of the CPE gene for carboxypeptidase E
- mutation of the MC4R gene for melanocortin receptor 4
- mutation of the SIM1 gene for single-minded homolog 1 (SIM1)
- mutation of the GNAS gene for guanine nucleotide binding protein
- mutation of the BDNF gene for hypothalamic neurotrophic factor (BDNF)
- mutation of the MC3R gene for melanocortin 3 receptor
- mutation of the GPR24 gene for G-protein coupled receptor 24
- mutation of other genes

ob/ob mouse

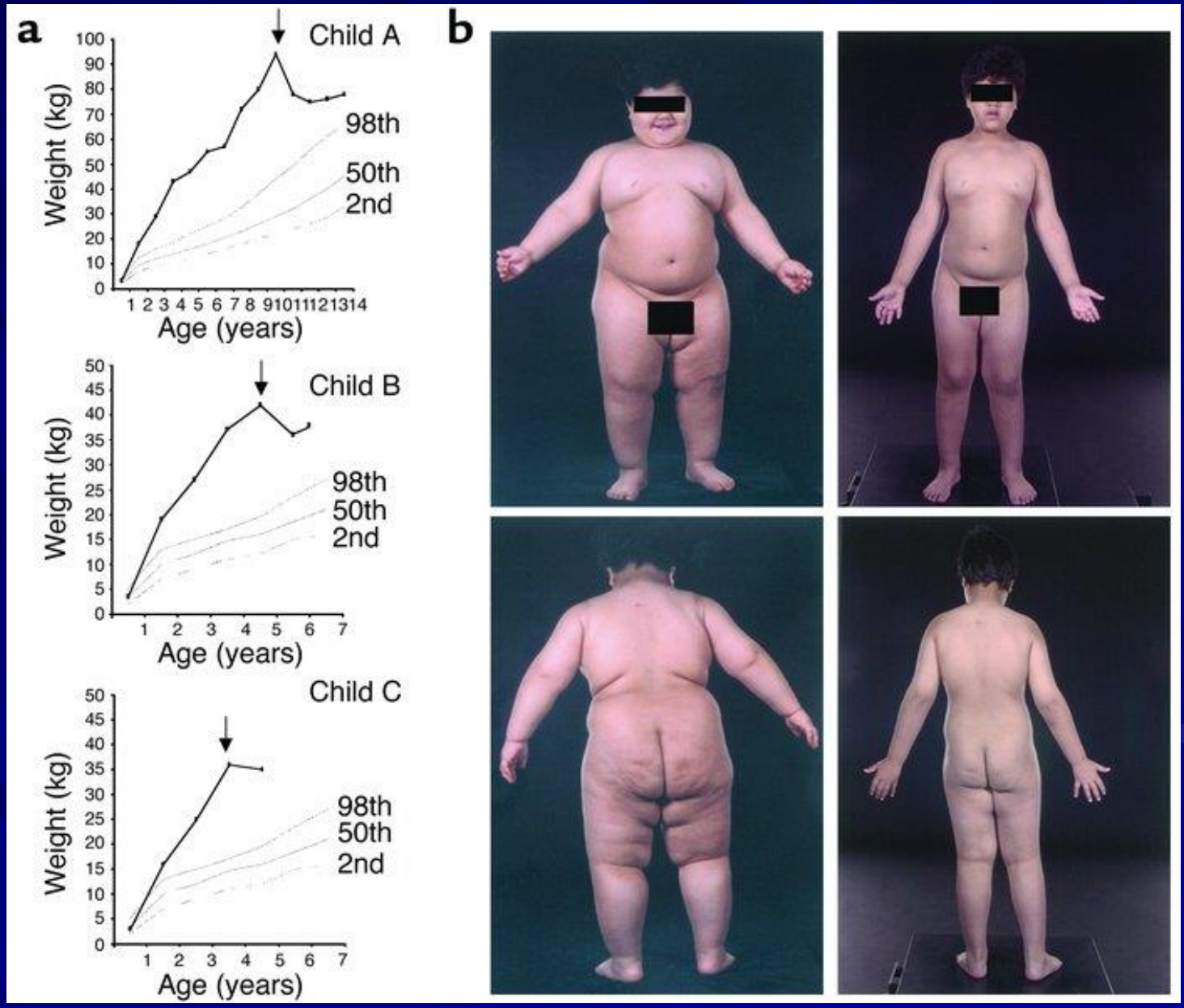


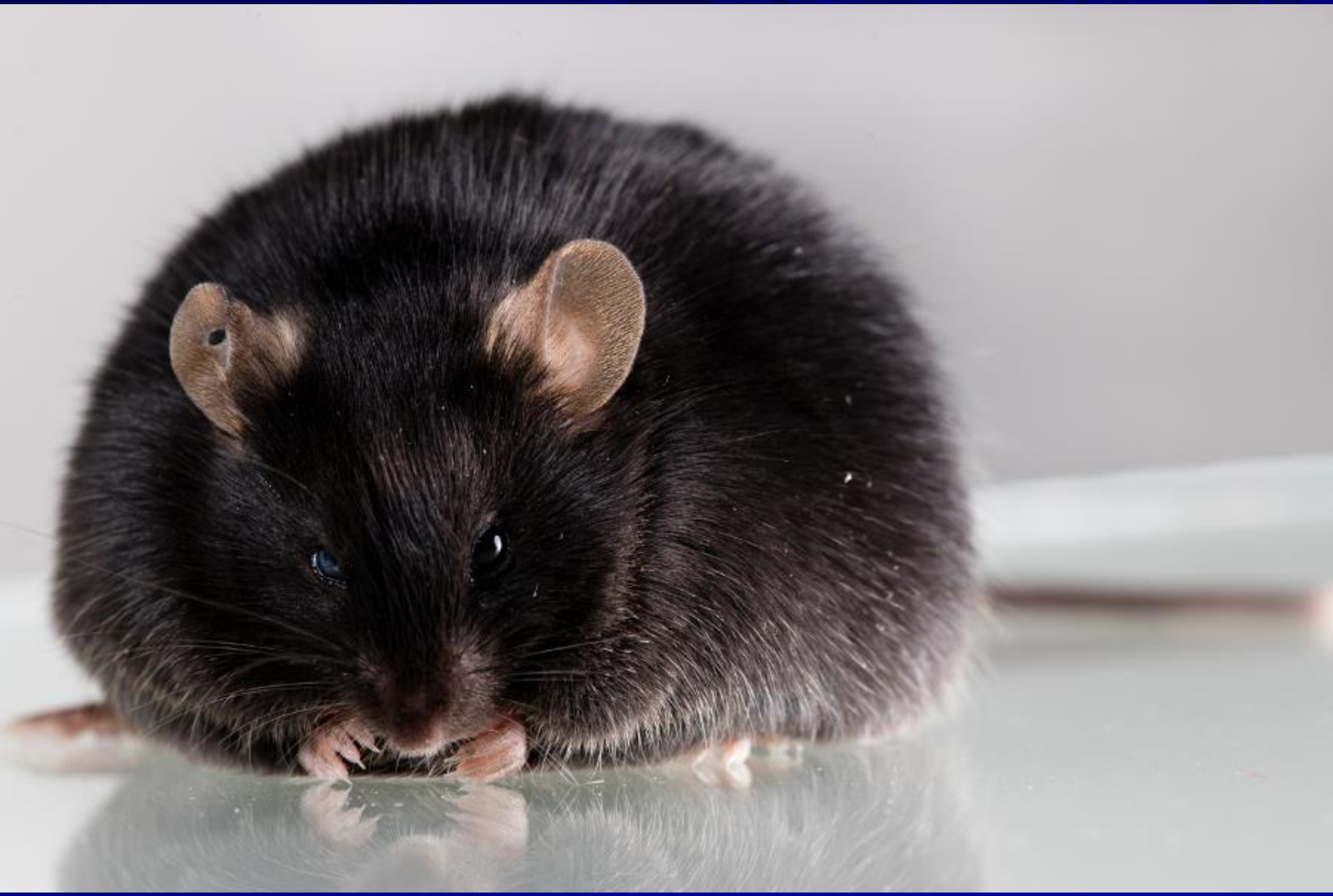
3yr old weighing 42 kg

7yr old weighing 32 kg

A 3-year-old boy with congenital leptin deficiency, weighing 42 kg before (left) and 32 kg after (right) 4 years of treatment with recombinant leptin therapy.

Child with congenital leptin deficiency - child B before (height = 107 cm) and 24 months after r-metHuLeptin therapy (height = 124 cm)





Metabolic syndrome

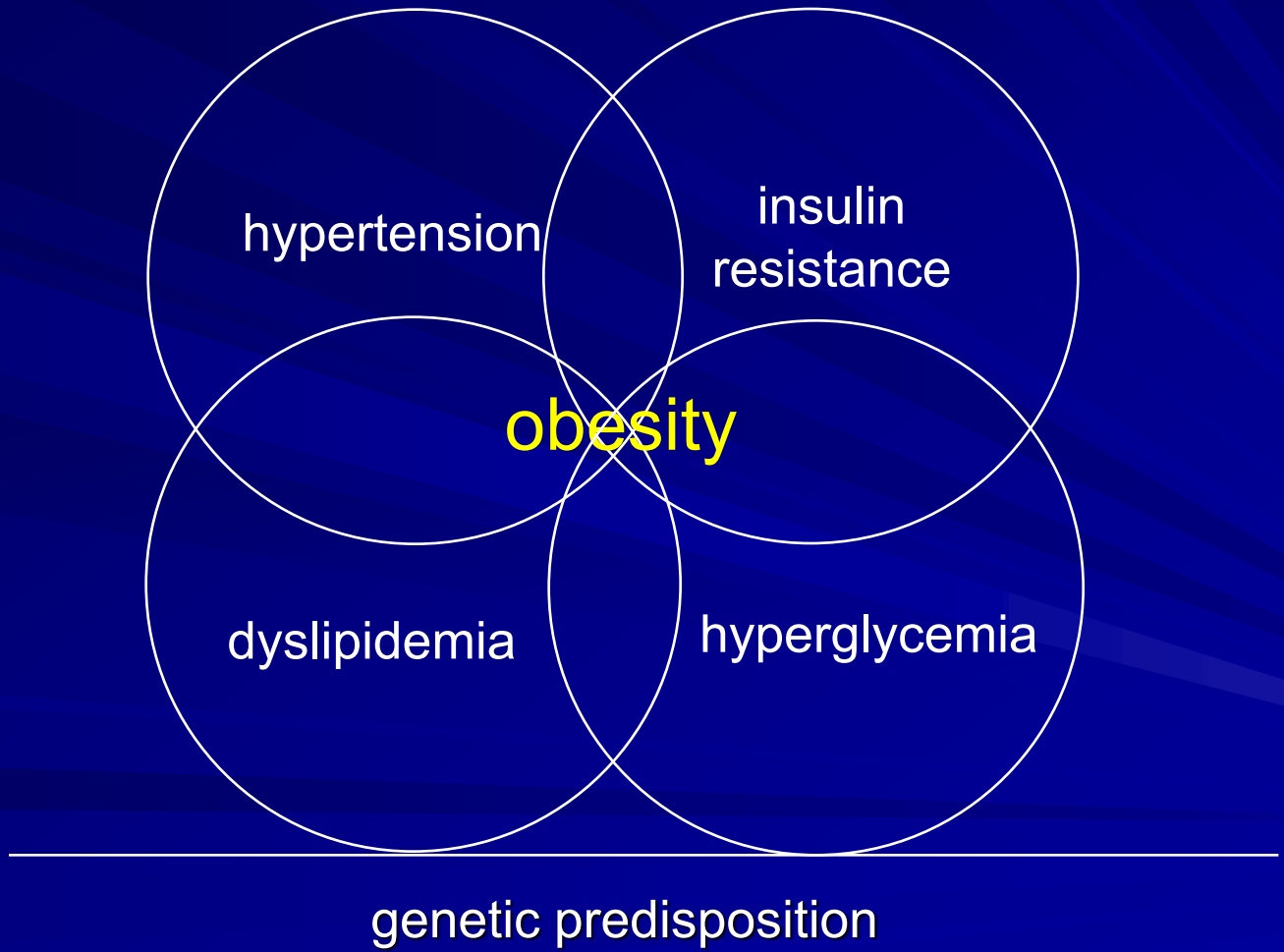
Metabolic syndrome

- syndrome X, Reaven syndrome, insulin resistance syndrome, deadly quartet
- leading cause of death in developed countries
- 1960s – syndrome X
- 1980 Kaplan: obesity + diabetes + hypertension + hyperlipoproteinemia = deadly quartet
- 1988 Reaven – metabolic syndrome X
  - insulin resistance
  - hyperglycemia or diabetes mellitus
  - hyperinsulinism
  - increased TAG
  - decreased HDL cholesterol
  - hypertension
  - ...

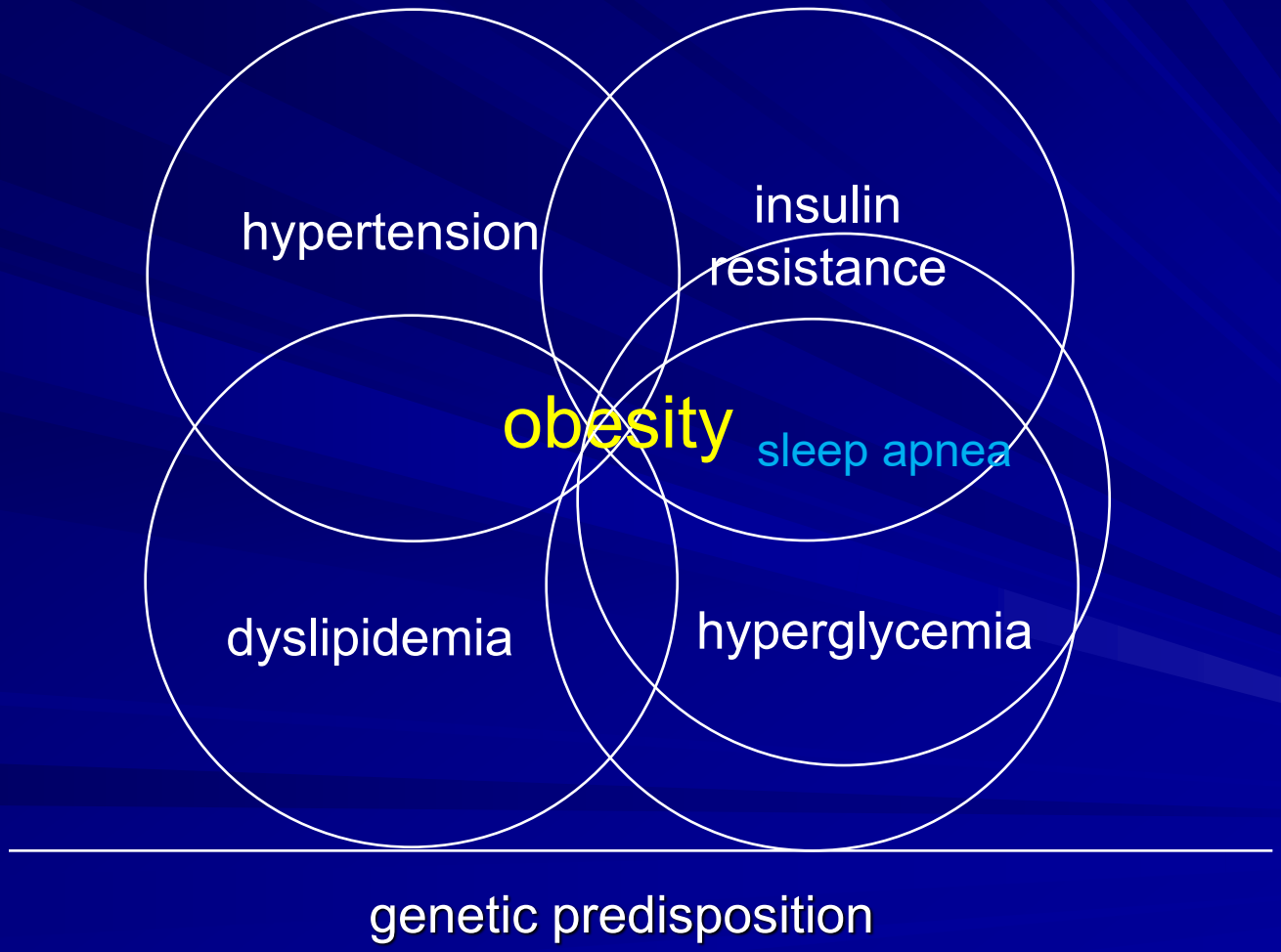
Criteria	MetS	WHO (1998)	EGIR (1999)	NCEP: ATP III (2001)	AACE (2003)	IDF (2005)	AHA/NHLBI (2009)
Central obesity	WC	-	≥94 cm (M) ≥80 cm (W)	>102 cm (M) >88 cm (W)	-	≥94 cm (M) ≥80 cm (W) *	≥94 cm (M) ≥80 cm (W) *
	BMI	>30 kg/m^2	-	-	-	>30 kg/m^2	-
	WTH	>0.90 (M) >0.85 (W)	-	-	-	-	-
Increased TG	TG	≥150 mg/dL #	>177 mg/dL or under Tx #	≥150 mg/dL	≥150 mg/dL	≥150 mg/dL or under Tx	≥150 mg/dL or under Tx
Reduced HDL	HDL	<35 mg/dL (M) <39 mg/dL (W) #	<39 mg/dL or under Tx #	<40 mg/dL (M) <50 mg/dL (W)	<40 mg/dL (M) <50 mg/dL (W)	<40 mg/dL (M), <50 mg/dL (W), or under Tx	<40 mg/dL (M), <50 mg/dL (W), or under Tx
Increased BP	BP	≥160/90 mmHg	≥140/90 mmHg or under Tx	≥130/85 mmHg	>130/85 mmHg	≥130/85 mmHg or under Tx	≥130/85 mmHg or under Tx
Increased glucose concentration	IFG	≥110 mg/dL	≥110 mg/dL (2 measures)	≥110 mg/dL	110–125 mg/dL	≥100 mg/dL or under Tx	≥100 mg/dL or under Tx
	IGT ¶	140–200 mg/dL	-	-	140–200 mg/dL	-	-
	IR	Yes †	Yes ‡	-	-	-	-
	DM	≥126 mg/dL	-	-	-	Yes	Yes
Other	MA	UAE ≥ 20 ug/min UACR ≥ 20 mg/g	-	-	-	-	-
Diagnosis		IGR §, DM, or IR + ≥2 other criteria	IGR § or IR + ≥2 other criteria	≥3 criteria	≥2 criteria	Central obesity + ≥2 other criteria	≥3 criteria

¶ Impaired glucose tolerance is defined as 2-h glucose levels of 140–200 mg/dL on the 75-g oral glucose tolerance test. † Insulin resistance refers to glucose uptake below lowest quartile for background population under investigation in euglycemic hyperinsulinemia conditions. ‡ Insulin resistance refers to top 25% of fasting insulin concentrations from non-diabetic population. § Impaired glucose regulation refers to impaired fasting glucose or impaired glucose tolerance. * Central obesity is defined as ethnicity-specific values of waist circumference: United States ≥ 102 cm (men) or ≥88 cm (women); Europids ≥ 94 cm (men) or ≥80 cm (women); and Asians ≥ 90 cm (men) or ≥80 cm (women). # Increased triglyceride and decreased high-density lipoprotein cholesterol are considered one criterion in WHO (1998) and EGIR (1999) definitions. Abbreviations: M = men; W = women; BMI = body mass index; BP = blood pressure; DM = diabetes mellitus; HDL = high-density lipoprotein cholesterol; TG = triglyceride; IGR = impaired glucose regulation; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; IR = insulin resistance; MA = microalbuminuria; Tx = treatment; UAE = urinary albumin excretion rate; UACR = urinary albumin-to-creatinine ratio; WC = waist circumference; WTH = waist-to-hip ratio; WHO = World Health Organization; EGIR = European Group for the Study of Insulin Resistance; NCEP: ATP III = National Cholesterol Education Program Adult Treatment Panel III; AACE = American Association of Clinical Endocrinology; IDF = International Diabetes Federation; AHA/NHLBI = American Heart Association/National Heart, Lung, and Blood Institute.

Syndrome X

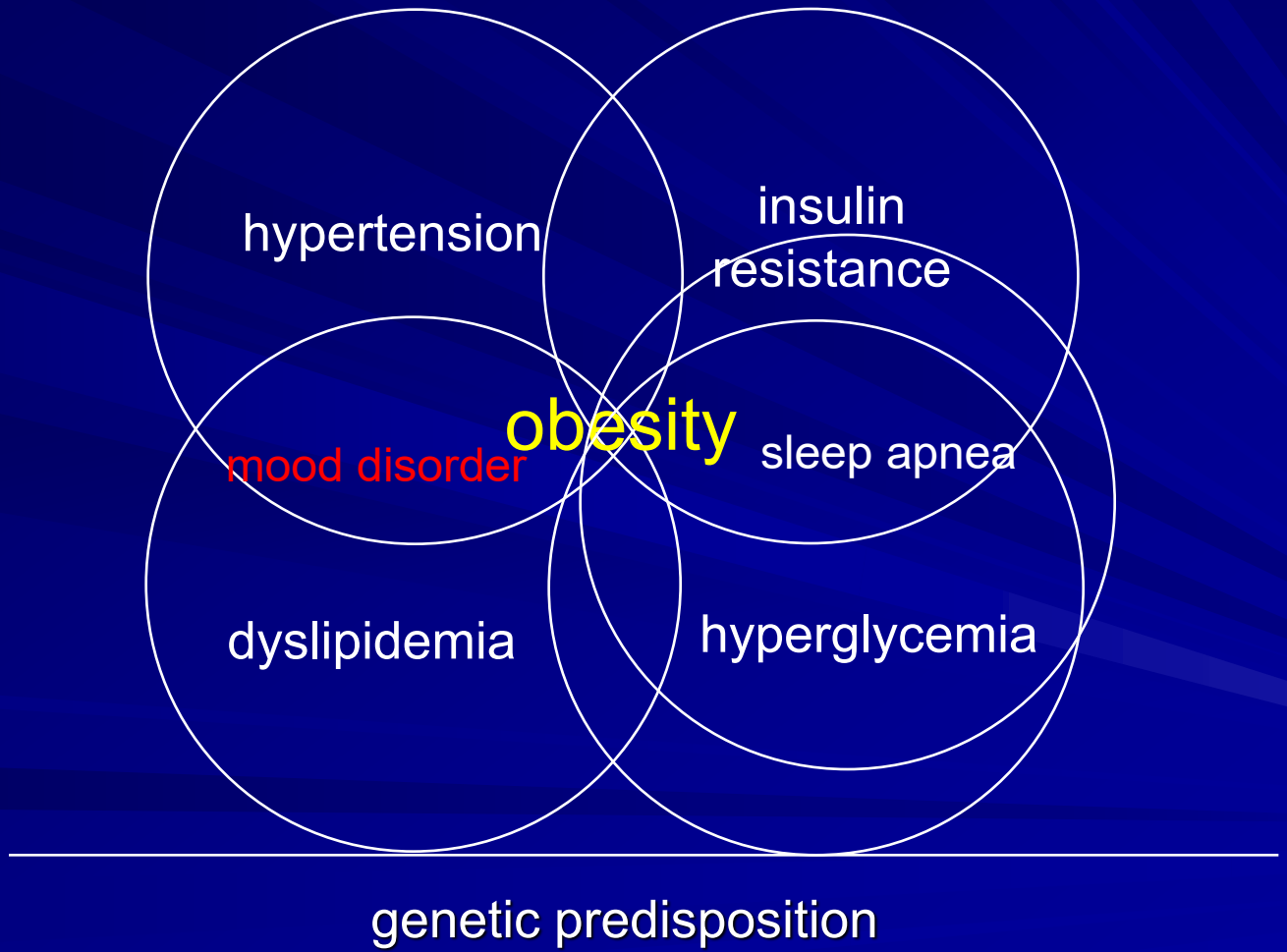

hypertension
insulin resistance
obesity
dyslipidemia
hyperglycemia
genetic predisposition

Syndrome Z

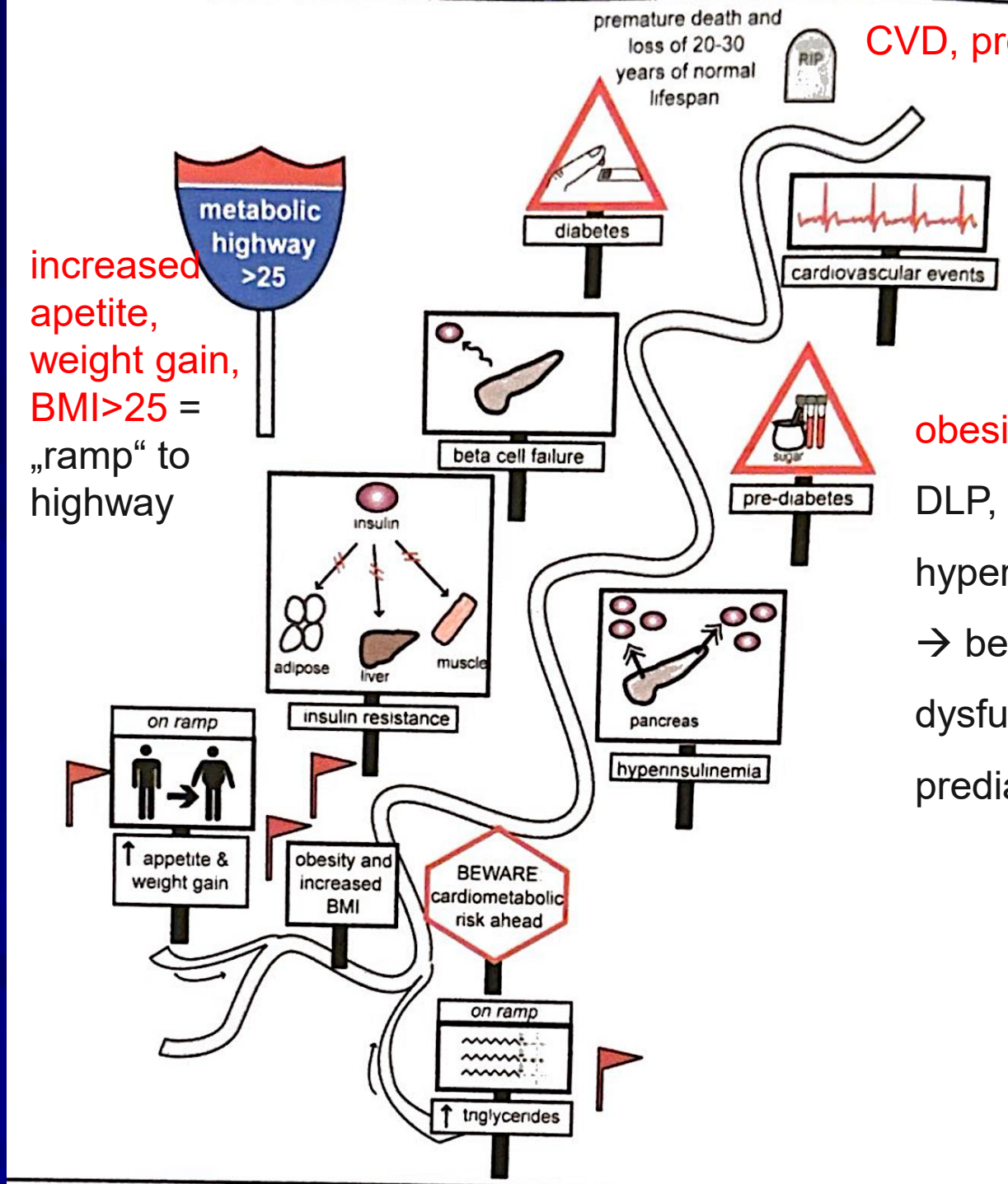


Wilcox et al. Thorax 1998; 53(Suppl 3): 25-28

Metabolic-mood syndrome



Metabolic highway



increased apetite, weight gain, BMI>25 = „ramp“ to highway

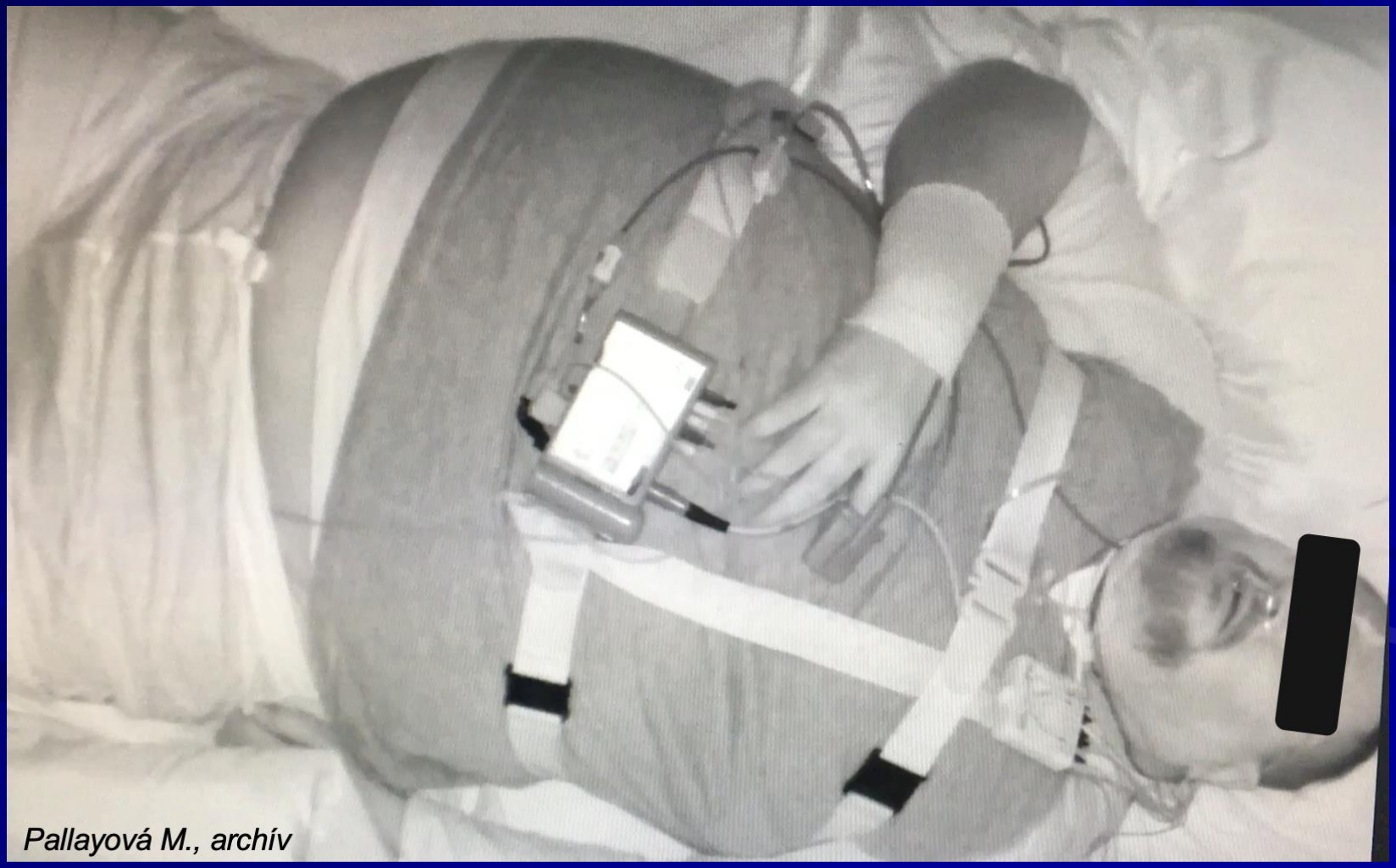
CVD, premature death

obesity → IR, DLP, TAG → hyperinsulinemia → beta-bb dysfunction → prediabetes → DM

Stahl, 2016

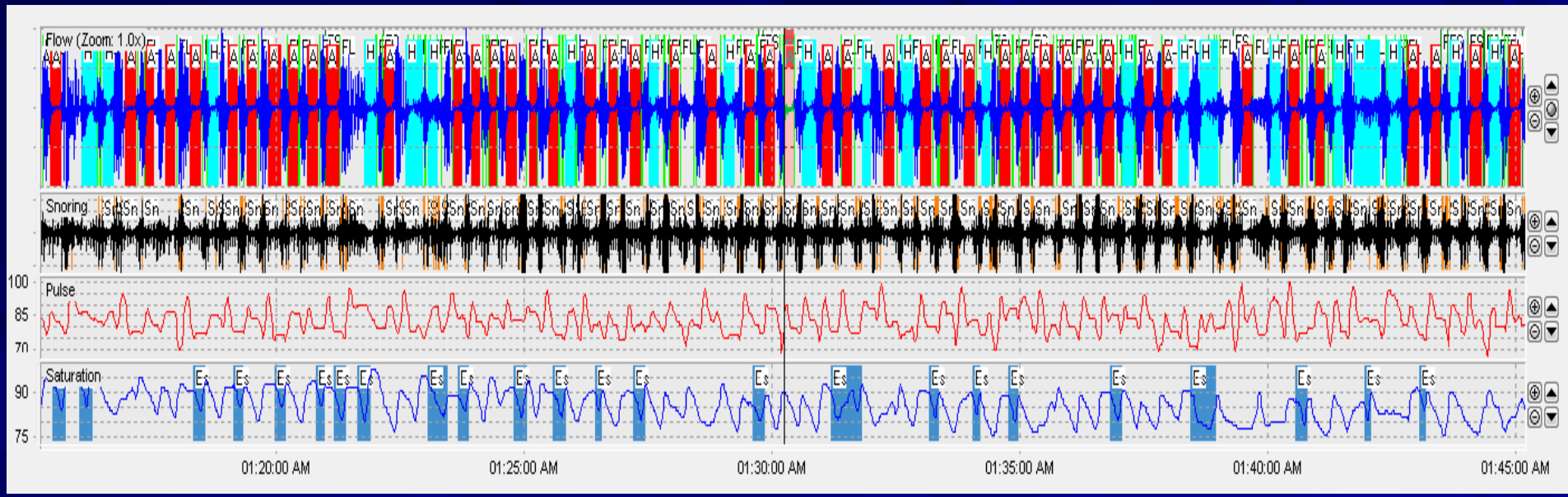
Syndrome Z

54-r. ♂, BMI 47 kg/m², AHI 100.3/h, ∅ $SatO_2$ 83%, Min$SatO_2$ 52%

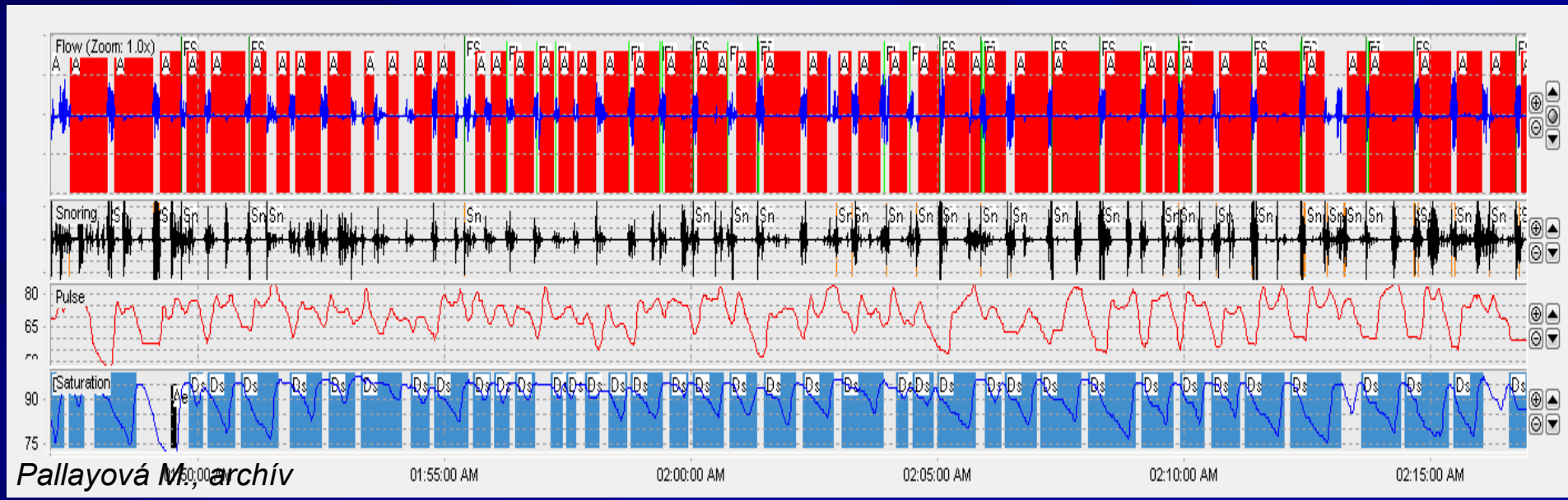


Pallayová M., archív

43-r. ♂ BMI 62.3, ESS 23/24, AHI 54/h, ODI 27/h, ∅ $SatO_2$ 91%, $MinSatO_2$ 78%



56-r. ♂ BMI 39.4, ESS 10/24, AHI 83/h, ODI 60/h, ∅ $SatO_2$ 85%, $MinSatO_2$ 70%



Pallayová M., archív

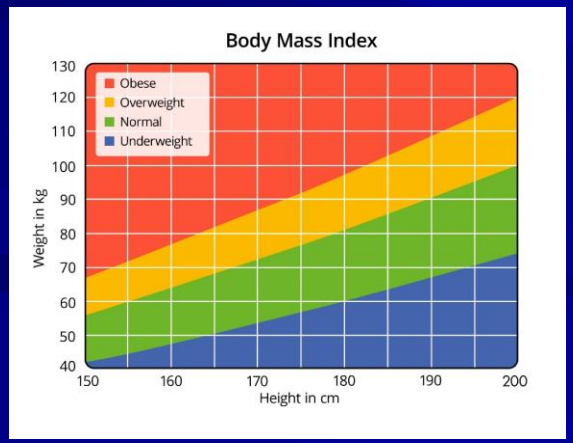
Pathophysiology of OSAS consequences in obesity

- intermittent hypoxemia
- sleep fragmentation
- sleep architecture disorders
- sleep deprivation

- reoxygenation and ischemic-reperfusion injury
- oxidative and nitrosyl stress (↑ generation of reactive oxygen and nitrogen species)
- DNA damage, activation of poly-ADP-ribose polymerase and suppression of glyceraldehyde-3-phosphate dehydrogenase
- activation of sympathetic NS
- dysfunction of the hypothalamic-pituitary-adrenal axis (↑catecholamines, ↑cortisol)
- systemic inflammation → endothelial dysfunction
- ↑ level of advanced glycation end products (AGE) → ↑ risk of DM
- ↑ secretion of hypoxic inducible factor-1, TNF-α, IL-6, NF-κB
- dysregulation of adipokines (↑ ghrelin ↑ leptin, ↓ adiponectin ↓ omentin)
- dysregulation of receptors, dopamine and leptin signaling, energy homeostasis, motivation and reward system, food intake, ...

Metabolic screening

- simple metabolic tool:
  - weight/BMI/waist circumference
  - fasting TAG
  - fasting glucose
  - BP

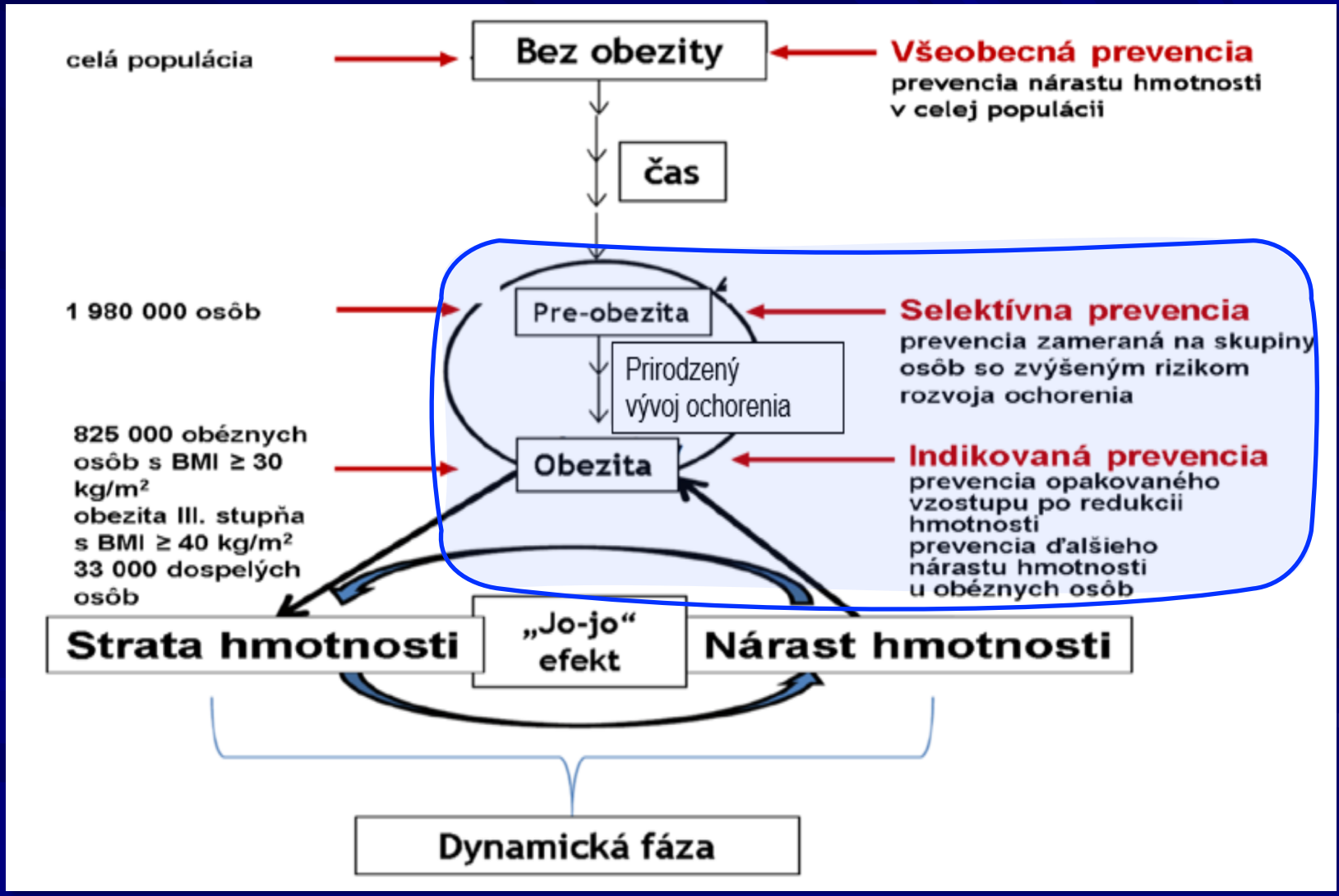


Prevention of obesity

- Comprehensive changes in regimen measures are key:
  - at the individual level:
    - healthy nutrition
    - reduction of sedentary lifestyle, increase in physical activity
    - elimination of stress
    - sufficient sleep
  - at the societal level (preconception):
    - general (primary) prevention
    - selective (secondary) prevention
    - indicated (tertiary) prevention

Durrer a kol., 2019; Martins a kol., 2019; Alber a kol., 2017

Prevention of obesity



Štandardný diag. a terapeutický postup na komplexný manažment nadhmotnosti/obezity v dospelom veku 2023

Recommendations for the treatment of (pre)obesity

Liečba	Kategória BMI (kg/m^2)				
	≥ 25 < 27	≥ 27 < 30	≥ 30 < 35	≥ 35 < 40	≥ 40
Diétne a režimové opatrenia	áno + komorbidity	áno + komorbidity	áno	áno	áno
Farmakoterapia		áno + komorbidity	áno	áno	áno
Bariatrická/ metabolická chirurgia			áno + DM2T (individuálne)	áno + komorbidity	áno
Reálny cieľ redukcie hmotnosti	5 – 10 %	5 – 10 %	5 – 15 %	> 20 %	> 20 %

https://easo.org/wp-content/uploads/2018/12/2015-OMTF-European-Guidelines-for-Obesity-Management.pdf

Yumuk et al. European Guidelines for Obesity Management in Adults. Obes Facts 2015;8: 402-424

Readiness for a “change” in the concept of (pre)obesity management

1) Pre-contemplation phase: the individual is not ready, does not intend to take steps to change their lifestyle in the foreseeable future.
2) Contemplation phase: the individual is considering a change, but is still not ready.
3) Readiness phase for change: the individual intends to take steps in the near future (usually within two weeks) towards changing or modifying their behavior.
4) Active change phase: the individual takes specific steps to modify problematic behavior, change their lifestyle, or acquire new, healthy behaviors.
5) Maintenance phase: the individual adheres to the newly acquired habits for at least six months and tries to prevent relapse.
6) The individual can leave the spiral of change at any stage and enter the unwanted sixth phase of relapse, i.e. returning to old patterns of behavior, starting to gain weight again. → restart of change

Undernutrition and malnutrition

Undernutrition

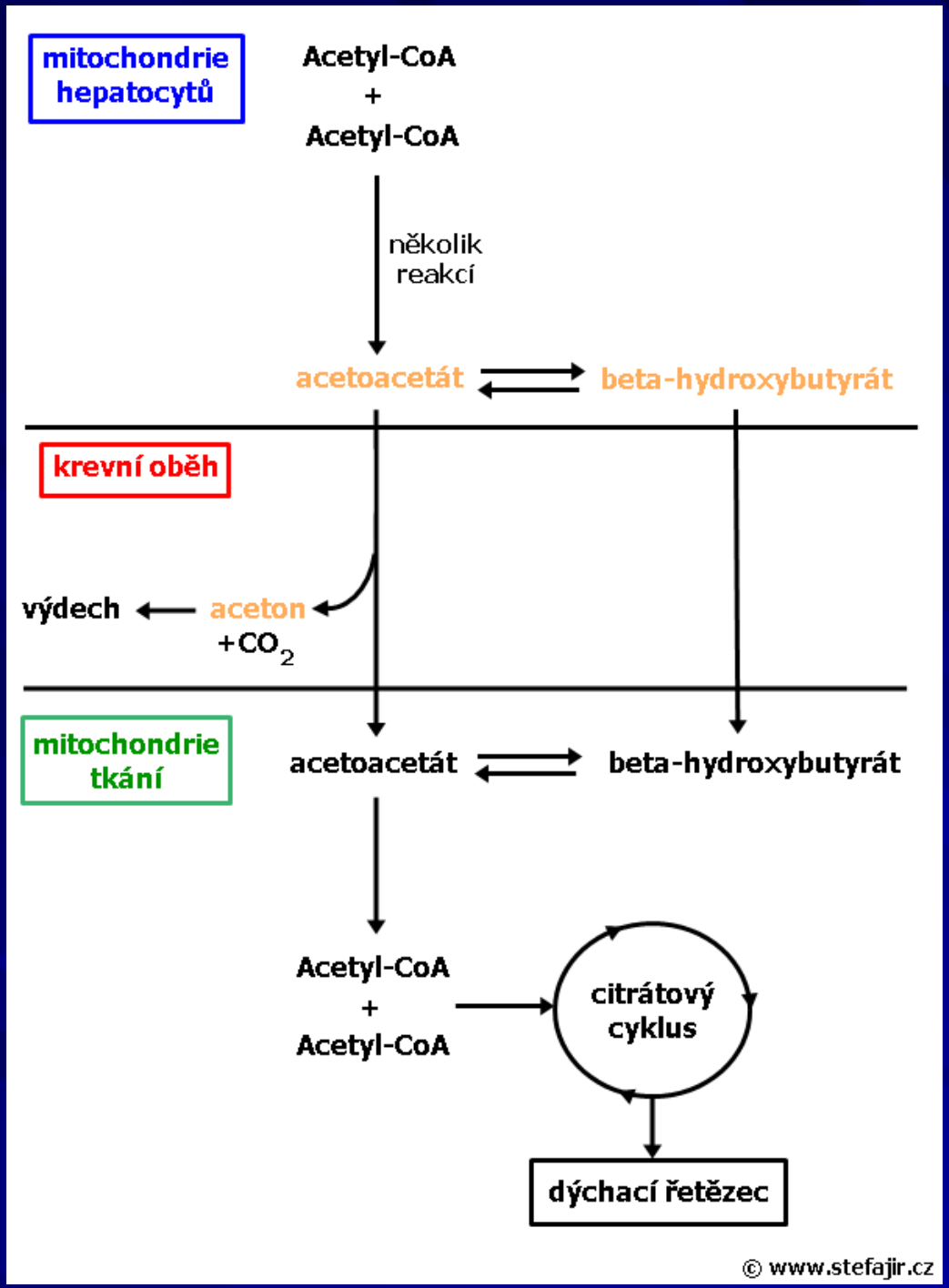
- Imbalance between the intake of a living organism and its needs
- hyponutrition - overall reduced nutrition
- malnutrition
  - poor composition of nutrition from a qualitative point of view
  - lack of one or more food components
- qualitative deficiency
  - lack of some nutrition or substances in food
- starvation
  - limited or completely stopped food intake

Causes of malnutrition

- exogenous
  - insufficient nutrient intake (starvation, loss of appetite, anorexia nervosa)
- endogenous
  - digestive disorders
  - absorption disorders
  - utilization disorders
  - increased nutritional demands (hyperthyroidism, pregnancy, breastfeeding, convalescence...)
  - loss of body fluids (bleeding)
  - loss of protein (nephrotic syndrome)

Secondary malnutrition

- arises as a consequence of other diseases and pathological conditions
- reduced nutrient intake
  - anorexia
  - GIT diseases with impaired nutrient absorption, Ca
- increased nutrient losses
  - diarrhea
  - vomiting
- increased requirements
  - fever
  - infection
  - surgical procedures



- Ketogenesis - especially in the mitochondria of hepatocytes, acetyl-CoA serves as a substrate.
- From the liver, ketone bodies are transported to tissues, including the brain, where they are converted back to acetyl-CoA, which is used in the citrate cycle connected to the respiratory chain to produce energy in the form of ATP.
- At the beginning of the formation of ketone bodies, 2 molecules of Acetyl-CoA are combined, subsequently acetoacetate is formed. → beta-hydroxybutyrate and acetone.
- Acetone not for energy production, is transported by the blood to the lungs, through which it is exhaled from the body.

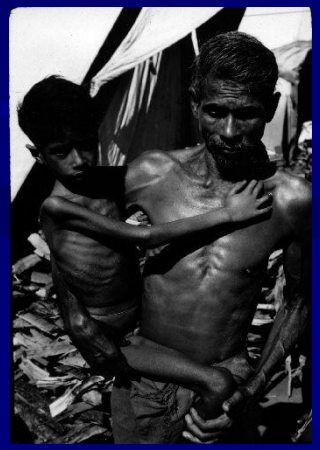
- Simple fasting - limited or completely interrupted food intake (not a concomitant manifestation of another disease)
  - changes in metabolism
  - economical use of available energy sources
- long-term fasting
  - negative changes in organ function due to lack of nutrients and energy, but also lack of vitamins and trace elements
- intermittent fasting
  - 16/8 method (eating window 8 hours during the day)
  - Eat-Stop-Eat method (fasting for 24 hours 1-2 times a week)
  - 5:2 method (two days of intake of 500 to 600 kcal)

Metabolic changes during fasting

- Glycogenolysis (stores last about 12-24 hours)
- Gluconeogenesis in the liver
- Insulin concentration decreases, glucagon increases
- lipolysis and beta-oxidation of fatty acids increase
- ketone body formation increases
- after fat stores are exhausted - protein breakdown

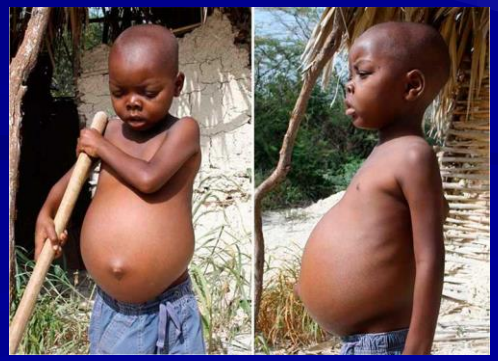
Marasmus

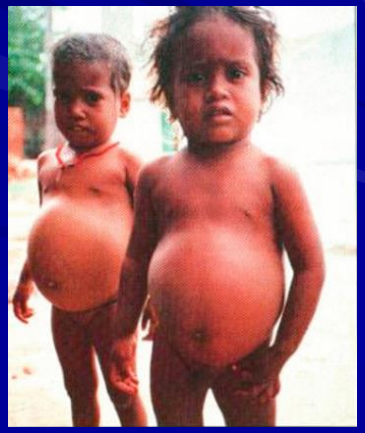
- Marasmus = insufficient supply of all nutrients, so-called balanced starvation
- Cause: poverty, mental disorder, starvation...
- Symptoms in children: shorter height, weight reduced to below 60% of the standard, muscle atrophy, increased susceptibility to infections, thin legs
- Symptoms in adults: cachexia



Kwashiorkor

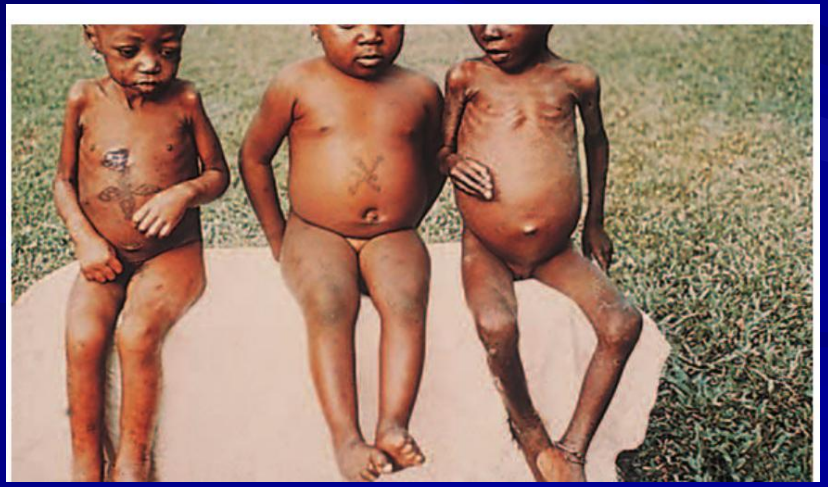
- protein malnutrition (sufficient / excessive carbohydrates)
- edematous malnutrition
- cause: poverty (mainly developing countries), cultural and social causes
- symptoms in children: edema, short stature, weight reduced to below 80% of the standard, sparse, thin depigmented hair and skin, diarrhea, anemia, apathy, delayed motor development, increased susceptibility to infections





Marasmic kwashiorkor

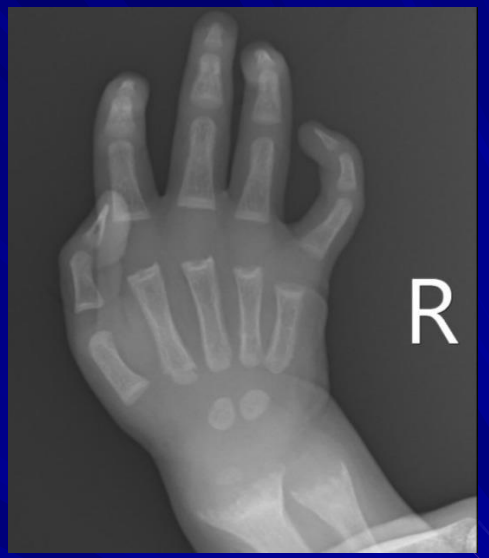
- most cases of protein-energy malnutrition
- lack of protein, energy, vitamins, trace elements + infections
- mainly developing countries
- cause: poverty + lack of knowledge about proper nutrition



Cachexia

- Wasting syndrome = a complex metabolic syndrome that involves unintentional loss of muscle mass and body fat, impaired food intake, and overall loss of strength.
- Causes:
  - Malnutrition (marasmus, anorexia...)
  - Tumors
  - AIDS
  - Other chronic diseases - COPD
  - Senile cachexia
- Mechanism:
  - Multifactorial etiopathogenesis
  - Changes in metabolism (cytokines e.g. TNF)
  - Changes in appetite regulation (leptin)

Qualitative malnutrition



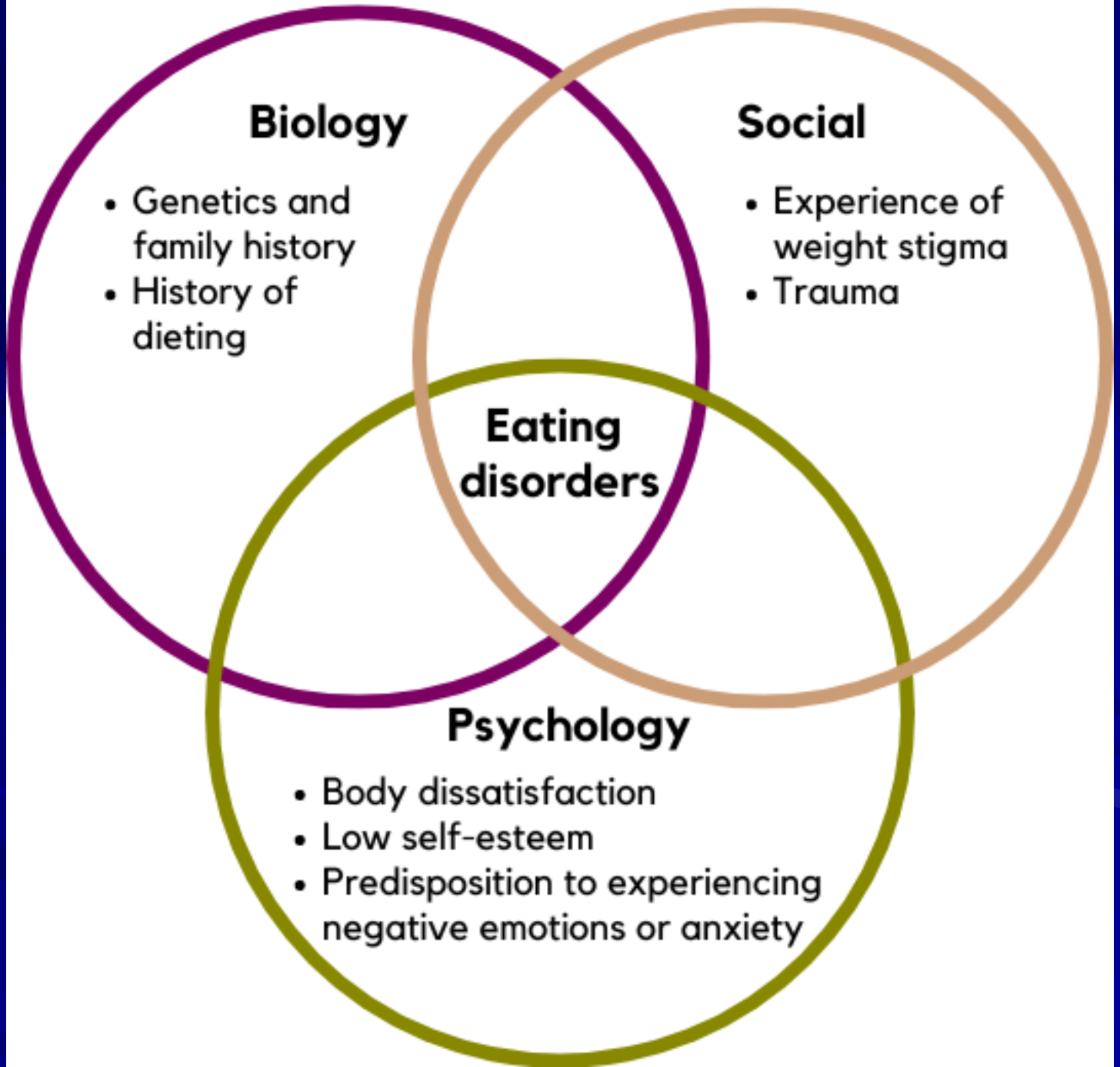
Qualitative malnutrition

- protein deficiency - kwashiorkor
- iodine deficiency - endemic goiter
- vitamin A deficiency - xerophthalmia
- Fe, folic acid, vitamin B12 deficiency - various types of anemia
- vitamin D, Ca, Mg, P deficiency - nutritional osteopathies (rickets, osteomalacia, osteoporosis)
- vit. B1 (thiamine) deficiency - beriberi
- vit. B2 (riboflavin) deficiency - inflammation
- nicotinic acid deficiency - pellagra
- vitamin C deficiency - scurvy

Eating disorders

- Anorexia nervosa
- Atypical anorexia nervosa
- Subclinical form of anorexia nervosa
- Bulimia nervosa
- Atypical bulimia nervosa
- Bingeing associated with other psychiatric disorders (e.g., sexual trauma)
- Vomiting associated with other psychiatric disorders (e.g., conversion disorder, hypochondriac disorder)
- Other eating disorders (e.g., pica)

→ bio-psycho-social-spiritual model of development


Biology
• Genetics and family history
• History of dieting
Social
• Experience of weight stigma
• Trauma
Eating disorders
Psychology
• Body dissatisfaction
• Low self-esteem
• Predisposition to experiencing negative emotions or anxiety

Mental anorexia

- anorexia = loss of appetite
- anorexia nervosa - a disorder characterized primarily by deliberate weight loss

Diagnostic criteria:

- active maintenance of abnormally low body weight (BMI 17.5 or less)
- specific psychopathology
- fear of obesity despite extremely low weight
- amenorrhoea in women

Mental anorexia

Anorexia nervosa
a) psychological symptoms

- increased irritability,
- loss of interest in surroundings with the exception of school performance,
- disorder of perception of one's own body (despite extreme weight loss, the patients feel that they are fat, are afraid of gaining weight), the feeling of hunger gradually disappears completely, in some girls/boys the feeling of hunger persists, preoccupation with food is noticeable, patients like to cook for others, collect recipes...,
- manipulation with food, hiding it, inducing vomiting,
- conflicts with parents who try to force the patient to eat

Anorexia nervosa
b) somatic symptoms:

- neuroendocrine: amenorrhea or irregular menstruation, abnormal glucose tolerance test with insulin resistance, hypothermia, increased levels of growth hormone and cortisol, sleep disorders,
- hair loss, noticeably dry skin, the skin is often covered with noticeably fine hair - "lanuga", increased brittle nails,
- GIT: abdominal pain, constipation, loss of tooth enamel, enlarged salivary glands, CVS: bradycardia, arrhythmia, hypotension,
- metabolic changes (resulting from nutritional deprivation, vomiting, abuse of laxatives, diuretics): hypokalemic alkalosis, hypochloremia, hypokalemia, which manifests itself in muscle weakness and can lead to cardiac arrhythmias up to cardiac arrest; dehydration, decreased vasopressin secretion,
- anemia, leukopenia, thrombocytopenia, low FW value,
- reduced levels of thyroid hormones due to decreased basal metabolism, hypercholesterolemia of unknown origin.

Bulimia nervosa

- a disorder characterized primarily by recurrent bouts of binge eating associated with excessive control of body weight

Diagnostic criteria:

- a strong and irresistible desire to overeat
- an attempt to prevent weight gain by vomiting, abuse of laxatives, diuretics, or episodes of fasting
- a morbid fear of being fat

Bulimia nervosa
a) psychological symptoms:

- attacks of huge hunger, when the patient is able to eat large amounts of food,
- desire for a slim figure, fear of being overweight,
- feelings of guilt,
- dominant thoughts about food, weight, slim figure,
- emotional lability, depressive experiences, risk of suicidal behavior,
- abuse of medications, alcohol, drugs,
- secondary devastation of relationships with loved ones, especially with parents,

Bulimia nervosa
b) somatic symptoms:

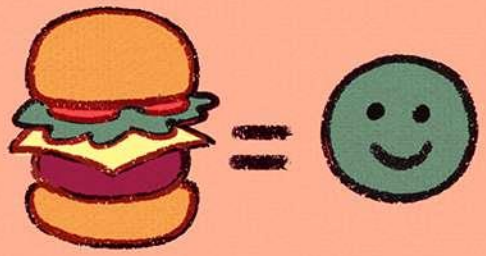
- vomiting leads to hypokalemic alkalosis with increased serum bicarbonate levels, hypochloremia, hypokalemia,
- laxative abuse leads to metabolic acidosis with decreased serum bicarbonate levels,
- hypokalemia can cause drowsiness, fatigue, cardiac arrhythmias,
- dehydration of the body,
- damage to tooth enamel and increased tooth decay,
- salivary gland enlargement, which is associated with increased serum amylase levels,
- rare complications – acute gastric dilatation, esophageal rupture.

Binge eating

- compulsive overeating
- unlike bulimia, there are no weight loss strategies
- Night binge eating – at night

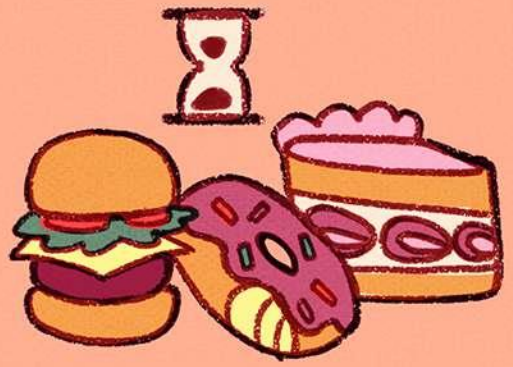
Signs of Binge Eating Disorder

Eating until uncomfortably full



Eating to ease stress and anxiety

Recording weight fluctuation



Consuming excessive amounts of food in short periods

Feeling desperate to control eating and lose weight

Self-disgust, guilt, and depression after binge eating

Vitamins: Main functions and deficiency syndromes

Vitamin	Functions	Deficiency Syndromes
Fat Soluble		
Vitamin A	A component of visual pigment	Night blindness, xerophthalmia, blindness
	Maintenance of specialized epithelia	Squamous metaplasia
	Maintenance of resistance to infection	Vulnerability to infection, particularly measles
Vitamin D	Facilitates intestinal absorption of calcium and phosphorus and mineralization of bone	Rickets in children Osteomalacia in adults
Vitamin E	Major antioxidant; scavenges free radicals	Spinocerebellar degeneration
Vitamin K	Cofactor in hepatic carboxylation of procoagulants—factors II (prothrombin), VII, IX, and X; and protein C and protein S	Bleeding diathesis
Water-Soluble		
Vitamin B_1 (thiamine)	As pyrophosphate, is coenzyme in decarboxylation reactions	Dry and wet beriberi, Wernicke syndrome, Korsakoff syndrome
Vitamin B_2 (riboflavin)	Converted to coenzymes flavin mononucleotide and flavin adenine dinucleotide, cofactors for many enzymes in intermediary metabolism	Ariboflavinosis, cheilosis, stomatitis, glossitis, dermatitis, corneal vascularization
Niacin	Incorporated into NAD and NAD phosphate; involved in a variety of redox reactions	Pellagra—"three D's": dementia, dermatitis, diarrhea
Vitamin B_6 (pyridoxine)	Derivatives serve as coenzymes in many intermediary reactions	Cheilosis, glossitis, dermatitis, peripheral neuropathy
Vitamin B_{12}	Required for normal folate metabolism and DNA synthesis	Megaloblastic pernicious anemia and degeneration of posterolateral spinal cord tracts
	Maintenance of myelinization of spinal cord tracts	
Vitamin C	Serves in many oxidation-reduction (redox) reactions and hydroxylation of collagen	Scurvy
Folate	Essential for transfer and use of 1-carbon units in DNA synthesis	Megaloblastic anemia, neural tube defects
Pantothenic acid	Incorporated in coenzyme A	No nonexperimental syndrome recognized
Biotin	Cofactor in carboxylation reactions	No clearly defined clinical syndrome

Selected trace elements and their deficiency syndromes

Element	Function	Basis of Deficiency	Clinical Features
Zinc	Component of enzymes, principally oxidases	Inadequate supplementation in artificial diets Interference with absorption by other dietary constituents Inborn error of metabolism	Rash around eyes, mouth, nose, and anus called acrodermatitis enteropathica Anorexia and diarrhea Growth retardation in children Depressed mental function Depressed wound healing and immune response Impaired night vision Infertility
Iron	Essential component of hemoglobin as well as a number of iron-containing metalloenzymes	Inadequate diet Chronic blood loss	Hypochromic microcytic anemia
Iodine	Component of thyroid hormone	Inadequate supply in food and water	Goiter and hypothyroidism
Copper	Component of cytochrome *c* oxidase, dopamine β-hydroxylase, tyrosinase, lysyl oxidase, and unknown enzymes involved in cross-linking collagen	Inadequate supplementation in artificial diet Interference with absorption	Muscle weakness Neurologic defects Abnormal collagen cross-linking
Fluoride	Mechanism unknown	Inadequate supply in soil and water Inadequate supplementation	Dental caries
Selenium	Component of glutathione peroxidase Antioxidant with vitamin E	Inadequate amounts in soil and water	Myopathy Cardiomyopathy (Keshan disease)