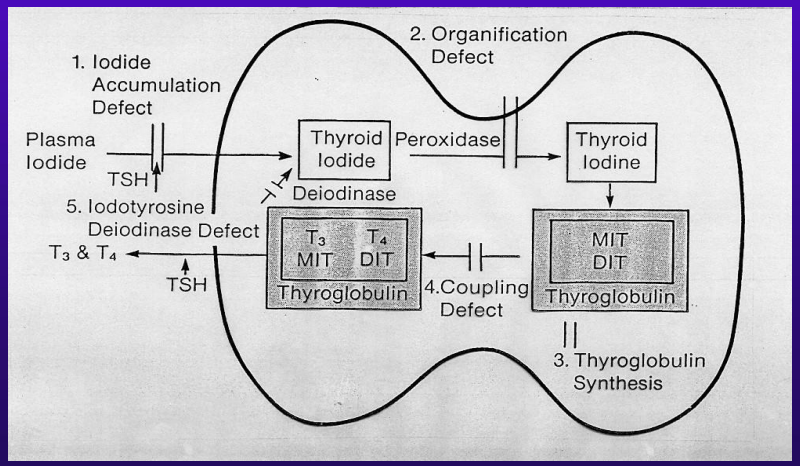
Pediatric endocrinology

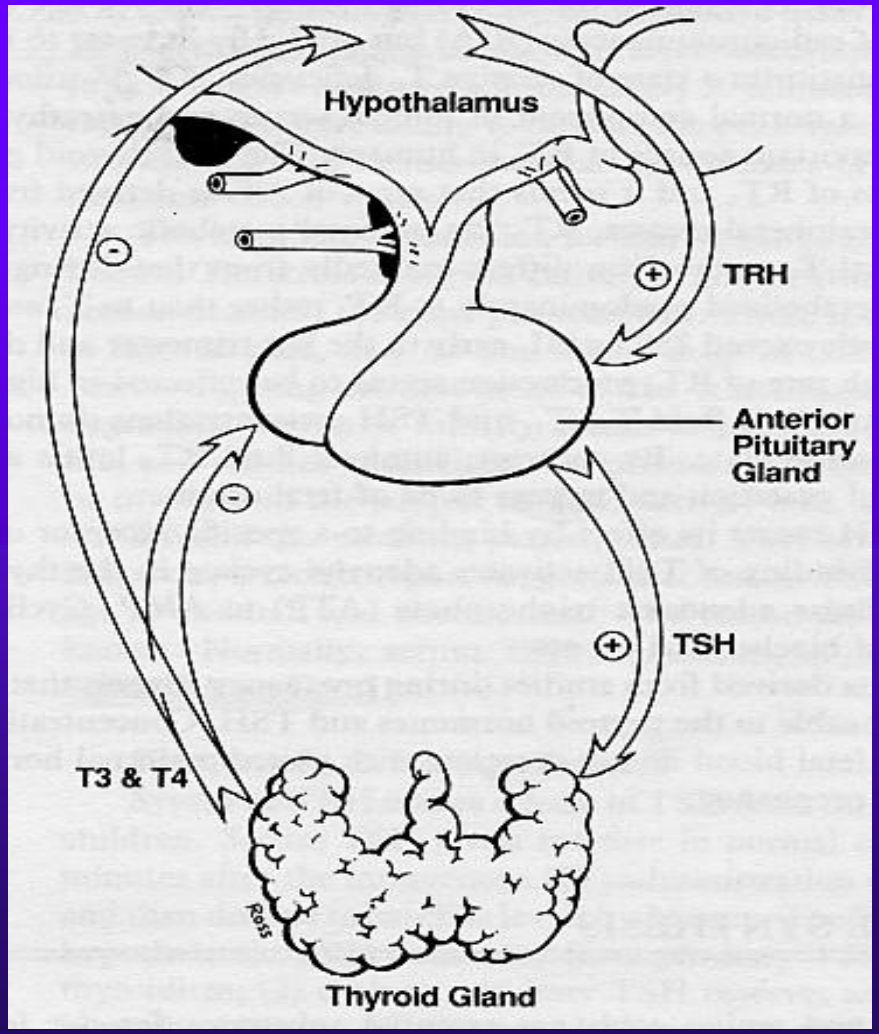
J. Kytnarová

Thyroid gland - hormone synthesis

- thyroxin (T4) 3,5,3´triiodothyronine (T3)
- substrates: iodine and amino acids
- iodine forms 59-65% of TG hormone molecules
- trapping in the follicular cells
- prohormone - thyreoglobulin
- T3 is the only functional thyroid hormone
- production of T4/T3 3:1 (T3 3-8x more efficient)



Regulation of hormone levels - negative feedback



Clinical manifestation of thyroid gland disease

- *History and physical examination*
- Goiter – thyroid enlargement
- Palpation
- The patient sitting or standing
- inspection of the neck from the front while the patient swallows
- Palpation - the size and consistency
- - local irregularities
- *Correlacion between estimates of thyroid size by palpation and ultrasonography is poor!!*

Physical examination

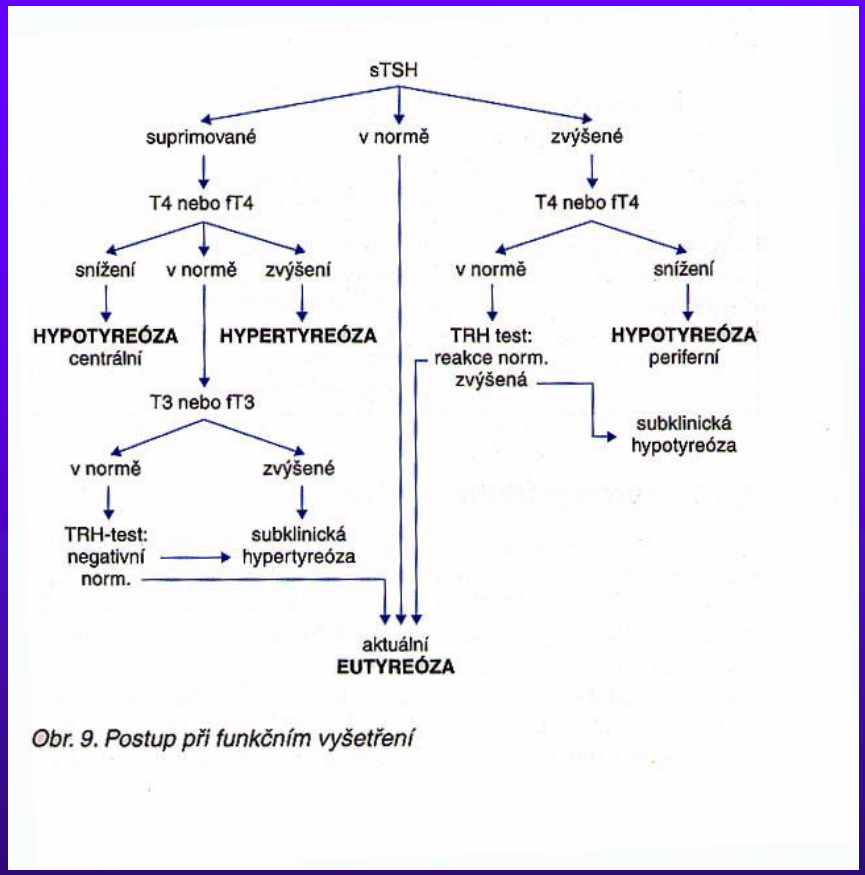
- *Signs of altered function of thyroid*
- Decreased function –hypothyreoidism
- Increased function –hyperthyreoidism

Sonography of Thyroid gland

Size - goiter

- difference palpation x ultrasound 25-29,7%
- **texture** - signs of autoimmune inflammation
- focal changes

Laboratory tests



Obr. 9. Postup při funkčním vyšetření

- **Antibodies**
- Against thyreoglobulin
CLT 70%, GBT30%
- against peroxidase
CLT 90%, GBT 86%
- TRAK - TSH-R-Ab (stim)
- GBT

Goiter - diferencial diagnosis

1. **Iodine deficiency**
2. **Chronic autoimmune inflammation of thyroid gland**
3. Congenital enzyme deficiencies
4. Thyreotoxikosis
5. Tumors

Iodine supply of organism

- Daily intake of iodine - 150 - 200 ug
- **Iodine deficiency**
- **intrauterine development:** abortions, congenital defects, cretenism, PMR
- **newborns:** goiter, hypothyreosis
- **children:** goiter, hypothyreosis, disorders of mental functions (prolongated reaction time), disorders of somatic development

Iodine supply of organism

- **Iodine excess**
- 350 - 500 ug
- „trigger" of autoimmune disease - iodination ↑antigenicity of TG
- **iodination of salt**
- more stabile iodate, 35 mg/kg
- iodination of food-processing salt and others foodstuffs
- **iodinaton of water supply, iodine oil injections**

Hypothyreosis

- **Congenital**

1. Dysgenesis of thyroid gland
2. Iodine deficiency-endemic kretenisms
3. Ectopic thyroid tissue
4. Defects of hormonogenesis
5. Disorders of hypothalamus-pituitary axis
6. Transplacental transfer of strumigens, rezistence of peripheral tissues to thyroid hormones

Congenital hypothyreosis clinical manifestation

- After delivery, during 2 months
- prolongated gestation
- ↑BW and BL, large posterior fontanel
- respiratory distress
- hypothermia, peripheral cyanosis
- low physical activity, feeding problems
- constipation, vomiting
- prolongated jauidnice
- myxedema - skin, eye lids, face
- makroglossy, broad and flat nose bridge
- growth impairement
- mental retardation

Endemic cretenisms

- **Neurologic form**
- spastic diplegia and mental retardation
- deaf-mutism, short stature, hypothyreosis
- goiter
- **Myxedematous form - central Afrika**
- insufficient production of hormones
- hypothyreosis, nanisms, epiphyseal dysgenesis, goiter

Congenital hypothyreosis

From Labhart A., Clinical Endocrinology, Springer-Verlag, 1974

Screening of congenital hypothyreosis

- Nonendemic cong. hypothyreosis - most common cause of *treatable* PMR
- (1 : 4000 births)
- **TSH** 4. day - dry drop (filter paper)
- *benefits*: cost
- *disadvantages*: lower detection of central hypothyreosis
- **TT4** -
- *advantages*: higher detection load of central hypothyreosis, TBG deficiencies
- *disadvantages*: higher number of re-screenings

Acquired hypothyreosis

- **Causes**
- **Chronic autoimmune thyreoiditis**
- Central hypothyreosis (TRH/TSH)
- Thyroidectomy…….
- **Patophysiology**
- **Genetic factors (predisposition)**
- **environmental factors („triggers“)**
- **Infections** - enterovirus - coxsackie B
- retrovirus - GBT
- **Drugs** - iodine (amiodaron, RTG contrast…)
- **psychotrophic drugs (**lithium)

Autoimmune thyreopathies classification

- ***Chronic autoimmune thyreoiditis (CLT)***
- Hashimoto thyreoiditis
- Focal thyreoiditis
- „Silent“ thyreoiditis
- lymphocytic thyreoiditis of children and adolescents
- chronic fibrotic thyreoiditis
- atrofic thyreoiditis
- postpartum thyreoiditis
- ***Graves-Basedow thyreotoxicosis (imunogennic thyreotoxicosis)***

Clinical manifestation

- ***Different manifestation in childhood***
- **Decreased growth velocity**
- Low final height
- **Delayed puberty and bone age**
- **Irreversible demage of CNS up to 2 years!!**

Clinical manifestation

- **Skin-** coarse, dry- myxedematous infiltration
- **Nose, voice, tongue**
- macroglossia - myxedematous infiltration
- deepening of the voice – myxedema of larynx
- **Gastrointestinal system** constipation
- **Cardiovascular system** bradykardia
- **central nervous system**
- less awareness of exteroceptive stimuli
- irreversible PMR (congenital hypothyreosis)
- **Eyes -** swelling around the eyes, loss of the lateral third of eyebrow

Hyperthyreosis -causes

- **Causes**
- **1. Autoimmune - Grave´s-disease**
- 2. Toxic nodular goiter
- 3. Independent adenoma ….

GT – clinical manifestation

- **K -** warm, moist skin, excessive sweating,
- heat intolerance,
- **L** - muscular weakness, myopathy
- **M -** weight loss, increased appetite, increased number of bowel movements, osteoporosis
- **N -** emotional lability, nervousness, irritability, tremor of the fingers, deterioration in school performance
- **O -** tachykardia, palpitations
- **P -** exophtalmos, retraction of the upper eyelid, protrusion

Diabetes mellitus - classification (ADA 1997, WHO 1998)

- **Type I** (juvenile, IDDM…)
- β cells destruction
- **Type II** (NIIDM, maturity onset)
- predominantly insulin resistance
- with relative insulin deficiency
- **Gestational diabetes mellitus**
- **Other specific types (**MODY, mitochondrial diabetes, drugs, infiltration of pancreas…..)

Etiology of DM I

- Immune - mediated disorder
- β cell autoimmunity - primarily T-cell mediated process, primary autoantigen is unknown
- Development of antibodies:
- ICA (islet cell antibodies)
- IAA (insulin autoantibodies)
- GAD (antiglutamic acid decarboxylase antibodies)
- IA2 (against islet protein tyrosine phosphatase)
- **Viruses -** Coxsackie B, enteroviral
- infection

Pathogenesis of DM

- ↓ secretion of insulin
  → catabolic state
- 1. →mobilisation of energy from muscle and fat (lipolysis and proteolysis)
- → AMK a FFA in liver →
  ↑ gluconeogenesis
- ↓ oxidation of FFA → ketones
- 2. ↓ratio ins/glukagon →
  ↑ ketones through direct effect on hepatocytes
- ↓ peripheral utilization of glucose and ketones
- FFA → ketones (β hydroxybutyrate, acetoacetate) → **metabolic acidosis**

Pathophysiology of DM

- **postprandial hyperglycemia**
- **fasting hyperglycemia** -late manifestation, excessive endogenous glucose production
- **glycosuria** - renal treshold (9,9 mmol/l)
- **osmotic diuresis → polyuria**, urinary losses of electrolytes, **dehydratation, compensatory polydypsia**
- **Metabolic acidosis → Kussmaul breathing**

Clinical manifestation ofDM

- Polyuria
- polydypsia
- **weight loss** (with ↑or N energy intake) – → catabolism and dehydratation
- Enuresis
- Kussmaul breathing,
- apathy, weakness
- pyogennic skin infections, candida vulvovaginitis
- Vomiting
- abdominal pains.. Cerebral edema, coma...
- **diabetic ketoacidosis - 25% first manifestation**

Diagnosis of DM

- **hyperglycemia** - fasting gly >7 mmol/l,
- OGTT -after 2 hours > 11,1 mmol/l
- ketoacidosis - above 16,5 mmol/l)
- Glykosuria > 55 mmol/l
- Ketonuria (often > 4 mmol/l)
- metabolic acidosis ,(pH < 7,3, bikarbonates < 15 mmol/l)

- *unclear diagnosis:*
- glykemic profile, HbA1C
- antibodies

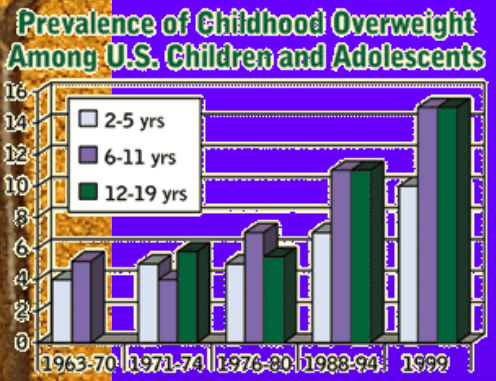
Therapy of ketoacidosis

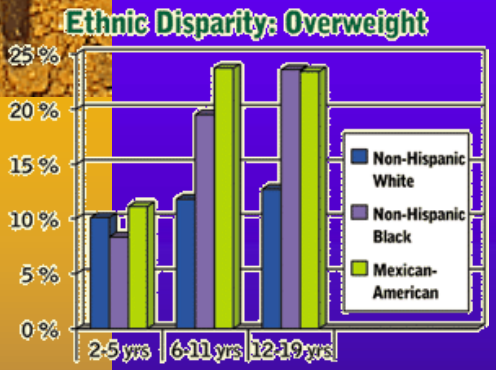
- **Expansion of intravascular volume**
- isotonic saline - ↓ gly to 16,5 mmol/l
- 5% dextrose with saline
- **correction of electrolyte depletion -** K, P…
- **correction of metabolic acidosis**
- bicarbonate if pH <7,2
- **Insulin therapy**
- After 1-2 hours of initial rehydratation
- constant infusion 0,05 -0,1 U/kg/h
- **s.c. insulin** 0,4 - 0,7 U/kg
- **Diet, self-monitoring**

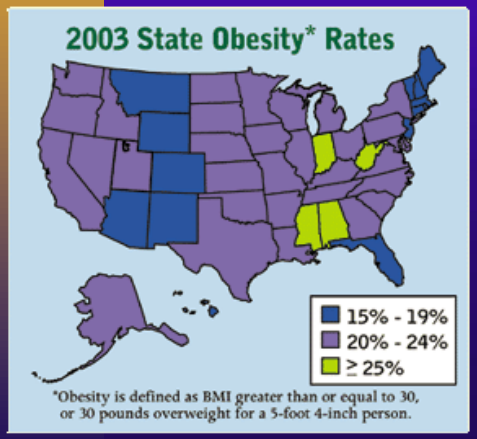
Childhood obesity

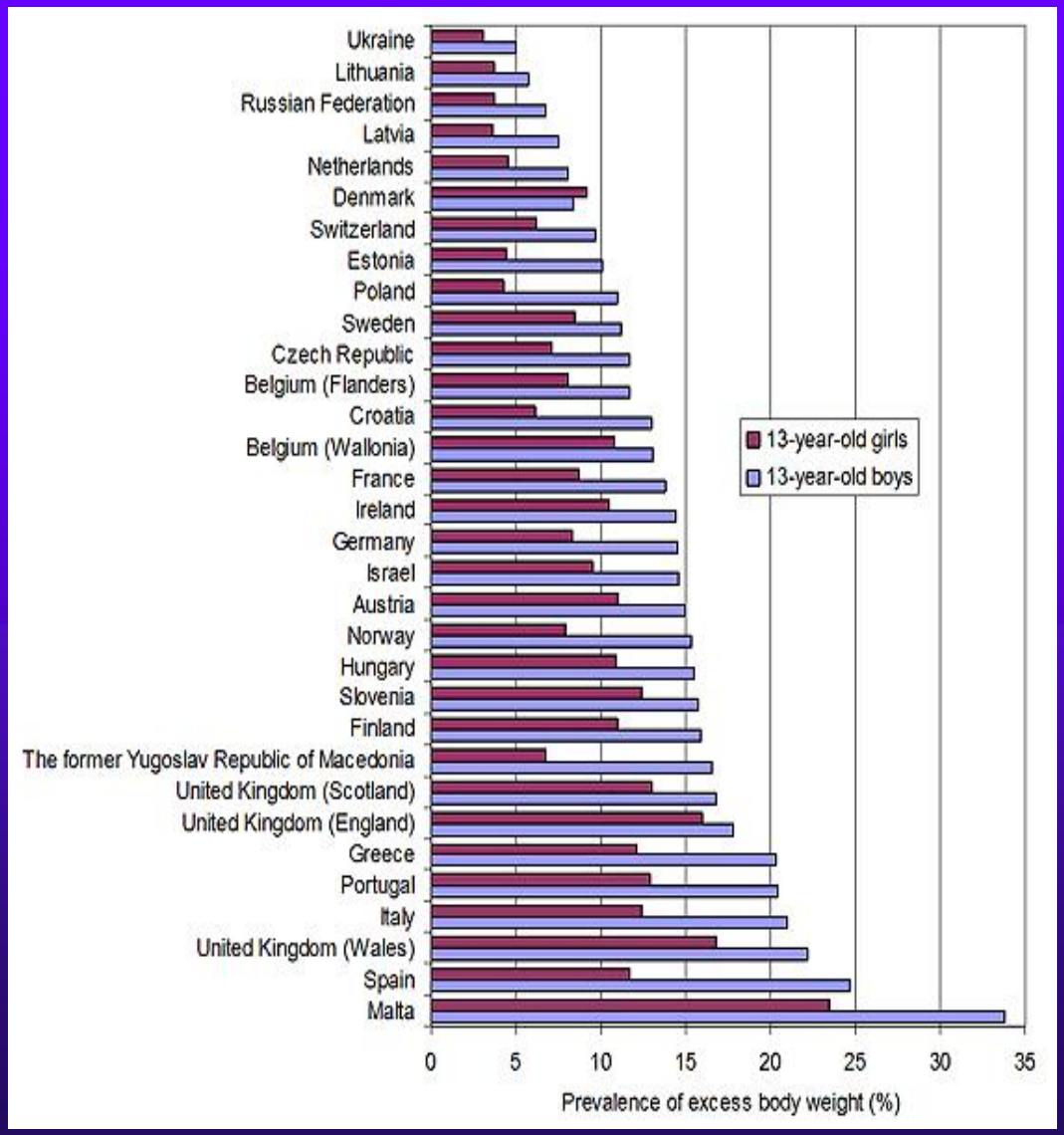
- **Prevalence of obesity**
- Between 1963 a 2004 - ↑ number of obese
- **Adolescents**
- More than three times (5% ⇒ 17%)
- **6-11 years**
- More than four times (4% ⇒ 19%)
- **2 – 5 years**
- More than twice (5% ⇒ 14%)
- *(Miller J.L., silverstein J.H., Nat Clin Pract Endocrinol Metab, 2007)*
- USA – 16 – 18% obese children, 21-24% overweight

World prevalence of obesity







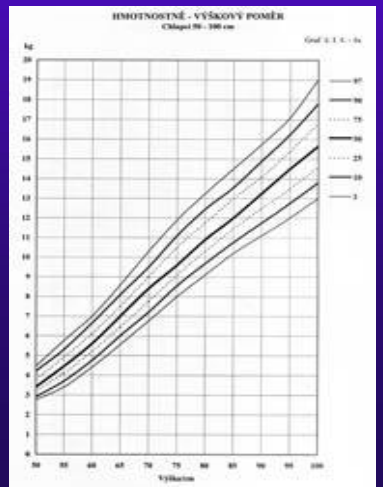


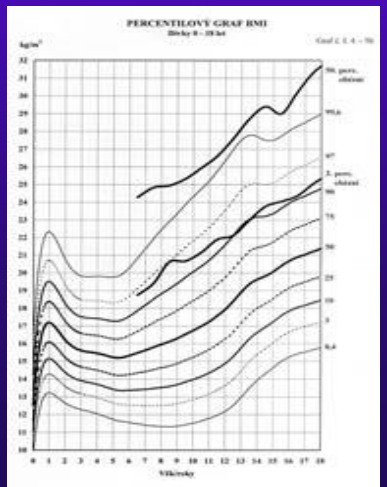
Children obesity prevalence in Czech republic

- Boys 6,6%, girls 5,6%. From 1991 increase of 3,6, resp. 2,6%
- (6th national anthropologic investigation 2001)

Definitions and diagnostics

- ***Definition***
- ↑ proportion of adipose tissue on total child bod weight
- ***Assesment of obesity***
- Weight/height ratio
- BMI (kg/m2, body mass index)
- Obesity – above 97. centile





Pathogenesis of obesity

- *Disproportion between energy intake and output*
- *Genetics* -25 - 40% (40 – 70%)
- Energy intake regulation
- Energy output regulation
- Substrate oxidation ability
- Hypothalamic regulation
- Monogennic types of obesity
- *Enviromental factors* – eating habits, physical activity, stress factors, medication...

Secondary types of obesity

- *Diseases*
  - Hypothyreosis
    - Decreased metabolism
    - Increased amounts of fluids in myxedaema
  - Overproduction of glukocorticoids
  - GH deficiency
    - Central fat distribution, rarely obesity
  - Hypogonadisms
  - Hypothalamic disorders
  - Hyperestrinisms
- Insulinoma (hyperinzulinemia of childhood)– 30%
- Polycystic ovary syndrom

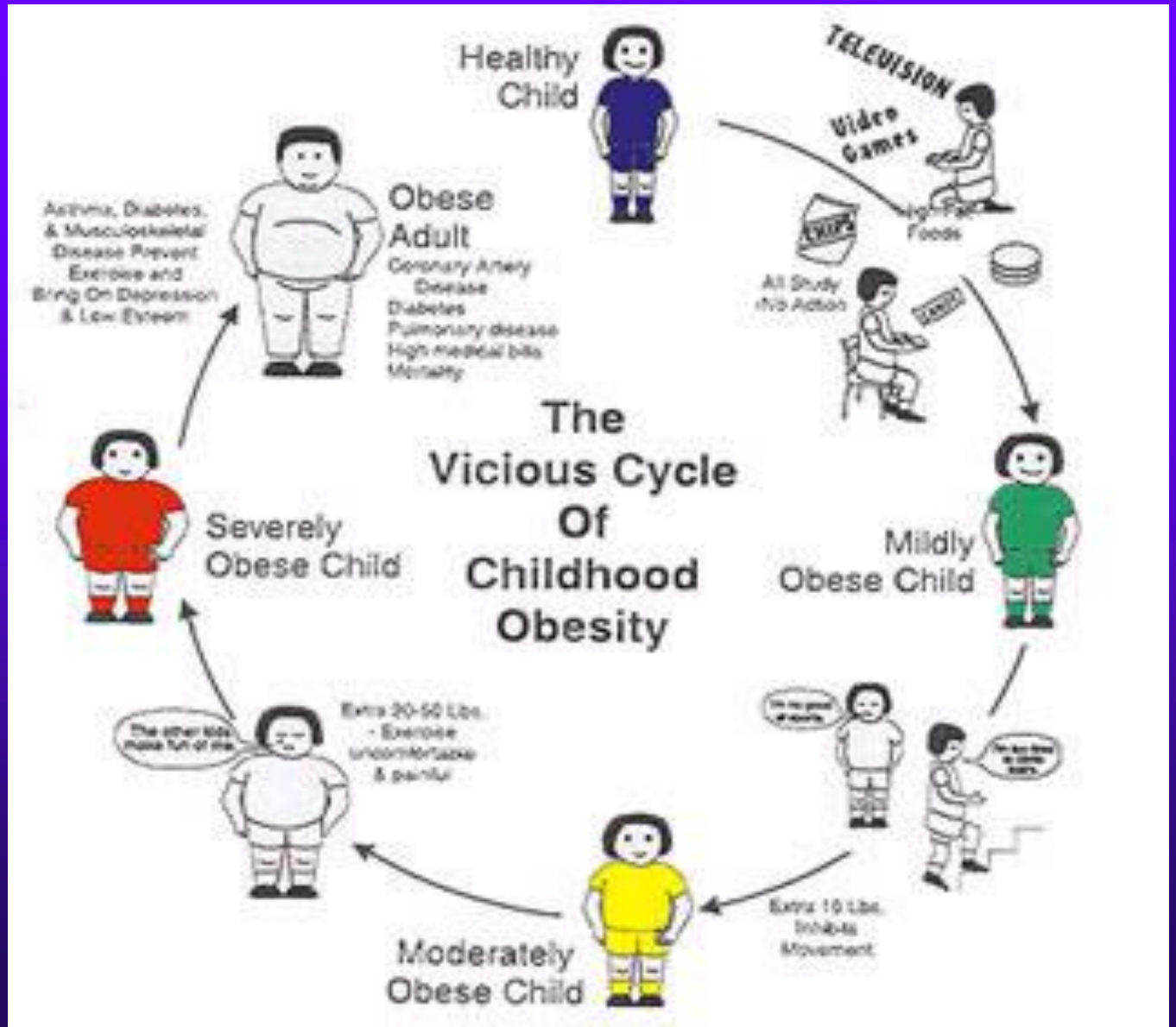
Secondary types of obesity – medications

- **Glukocorticoids**
- Dexamethason
- Prednison
- Hydrokortison ?
- **Antihistaminics** (loratidin – Flonidan x Claritine)
- **Antidepresive drugs -** tricyklic
- **Psychofarmacs** – clozapine, risperidone (Risperdal)
- **Antiepileptics** (valproate)
- **Neuroleptics** (Chlorpromazin)
- **Tyreostatics** (carbimazol, Propycil)
- **Hormonal contraceptive**

Genetic syndroms with obesity

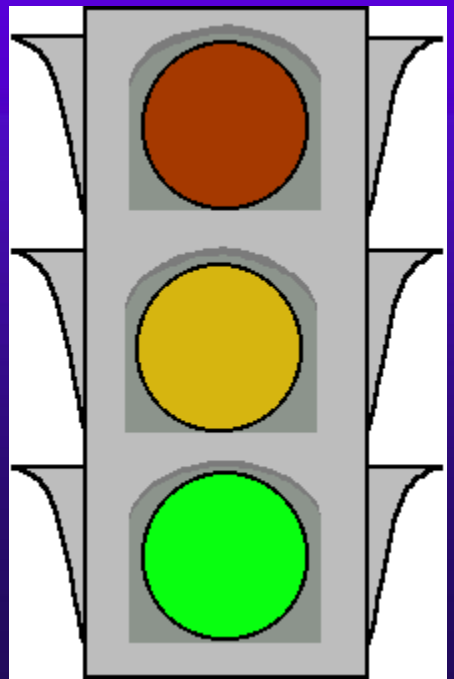
- **Prader-Willi syndrom**
- Výskyt 1:10 000 – 25 000
- **Beckwith-Wiedemann (EMG sy)**
- 1:12 000 – 15 000
- **Laurence-Moon-Biedl**
- <1:160 000, AR

Development of „simpe“ obesity in childhood



Therapy

- **<u>Energy restriction</u>**
- Calculation of energy intake
- „Exchange units“
- Pyramid
- „Traffic light method“
- *„red“ – stop*
- *„orange“ – be carefull*
- *„green“ - free! Go!*



Therapy

- **Physical activity**
- 30 – 60 min of aerobic activity at least daily
- Funny activities
- Changes in activities
- Restrict TV/PC/videogames –
- Below 2 hours daily
- **Cognitive – behavioral therapy**
- **Change of whole family lifestyle is necessary**

Prevention of obesity

- **Prevention – is better than therapy**
- *2003 – recommendation ofAmerican Academy of Pediatrics (AAP)*
- **Practical and family doctors**
- BMI – detection children in risk
- Propagation of breast feeding, healthy lifestyle habits
- **Education of parents**
- **National prevention programs against obesity**
- advertisements
- Automats (vendors) at school – soft - drinks
- school physical training
- Activities suitable for obese
- Legislative