**DIABETES MELLITUS**

- **SACCHARIDS**
  - Utilization of gl. + glycogenolysis $\rightarrow$ hyperglycemia $\rightarrow$ glycosuria $\rightarrow$ osmotic diuresis.
  - Na, K $\rightarrow$ hemococoncentration (polydipsia)
  - Hypotension $\rightarrow$ anurie

- **Glykosylation of proteins**
  - Microangiopathy
  - Neuropathy, retinopathy, dg glycosylated Hb

- **Lipids**
  - Lipogenesis $\rightarrow$ lipolysis $\rightarrow$ lipemia $\rightarrow$ ketogenesis $\rightarrow$ acidosis (Kussmaul respiration)
  - $\rightarrow$ Na $\rightarrow$ dehydration

- **PROTEINS**
  - Catabolism $\rightarrow$ gluconeogenesis $\rightarrow$ loss of N in urine...
  - Cell dehydration

**Glucose transporters**

- Glut T1 – steady state – cerebral vessels
- Glut T2 – concentration dependent on glucose – intestine, β cells of pancreas
- Glut T3 – steady state – neurons
- Glut T4 – internalisation – migration – muscle + fett tissue

**Diabetes mellitus type I**

IDDM (insulin dependent)...
- Insulinopenia, juvenile
- Damage of β cells, genetic disposition, autoimmune, th. insulin

**Diabetes mellitus type II**

NIDDM (non insulindependent)...
- Insulinopeniathor, resistant to ln. – no response of cells (1 Glut T4)...
- Change in receptors for l...
- Disturbance of fusion of Glut T4 with membrane, β cells ? secretion till exhaustion

Disposition of 26% of population
**DIRECT ↑ OF THERMOGENESIS**

- **BROWN FAT** (some rodents, newborns; color by big amount of mitochondria with cytochrome enzymes) - expresses a mitochondrial **THERMOGENIN** (UCG uncoupling protein, that dissociates oxidative phosphorylation from ATP generation); ↑ β3 receptors take part in it;
- UCG is H+ channel, protons generated by electron transport system enter the mitochondria through thermogenin instead of taking part in ATP-synthesis → ↑ circulation of H+ → ↑ energy is not incorporated in ATP; free fatty acids open UCG channels because of activated lipolysis of triacylglycerol by adrenalin (also consuming energy for phosphorylation of protein kinase)

**CIRCULATORY AND RESPIRATORY RESPONSE TO ↑ METABOLISM**

- ↑ VENTILATION
- ↑ CARDIAC OUTPUT - TACHYCARDIA AND ↑ CONTRACTILITY (↑ pulse pressure),
- CUTANEOUS VASODILATION (thermoregulation) → ↓ PR
- → hypercirculation and hypotension

**VITAMINS**

- ↑ Formation of vit. A from carotene in liver
- ↑ consumption of vit., ↓ resorption of B 12

---

**GROWTH, DEVELOPMENT**

- CNS development of synapses, myelinisation → I thyroidal hormones - mental retardation, replacement therapy till 6 M (later irreversible changes)
- Bones - permissive effect for STH, hypothyreosis - dwarf
- Metamorphosis in amphibian tadpole-frog (axolotl, Laufberger)

---

**GOITER**

- Chronic treatment by TSH - hypertrophy - an enlargement
- ENDEMIC - decreased iodine intake in food
- EU...HYP... - HYPOTHYREOIDISM
- Low thyroid h. → I TSH
- Antithyroid substances
- Inhibition of accumulation of iodine as perchlorate, nitrate, thiocyanate
- Inhibition of iodination of thyrosin - thiouracil, excessive I I

---

**HYPOTHYREOIDISM**

- Etiology: congenital, iodine in water, autoimmune thyreoiditis - Hashimoto's goiter
- In children cretinism, bone growth delayed - dwarf
- In adults: ↑ BMR, cold intolerance - hypothermia, ↑ neuromuscular excitability, voice is husky and slow, sleepy, loss of memory, depression, weight increase, hyperlipidemia, hypercholesterolemia, ↓ CO and BP, deposit of mucopolysaccharides in skin - myxedema

---

**HYPERTHYREOIDISM**

- Etiology: thyroid-stimulating immunoglobulins (TSig thyreotoxicosis - Graves' disease
- Symptoms: ↑ BMR, hyperreflexia, tremor, muscular weakness, insomnia, anxiety, hyperphagia and weight loss, heat intolerance, ↑ HR and BP, ↓ and ↓ PR (cutaneous vasodilation), ↑ reaction time, exophthalmos - swelling of the eye muscle, accumulation of mucopolysaccharides
- High-output failure tachycardia and ↓ BP - ↑ CO
**PLASMATIC TRANSPORT of T3 and T4**

- *Bound to proteins <-> free*
  
  Dynamic balance
  
  **Tyrosin binding globulin (TBG)** (2/3)
  
  - prealbumin (TBPA)
  
  Serum albumin HSA (capacity, affinity)

**T4 in cells deionized to T3 - higher activity**

(Transformation 1 during starvation - 1 x T3 with low activity)

**Excretion -> liver** conjugated with sulfates, glucuronides

**EFFECT OF T3 a T4**

- Activation of thyroid hormone receptors in nucleus regulates transcription of genes

  - T3 is more effective than T4 (80% of effect): 50x more T4, but more bound to plasma proteins, deiodinated in cells, THR in nucleus have 10x 1 affinity to T3. (conversion of T4 to T3 1 during starvation, illnesses -> spare of E at unchanged level of TSH)

  - 1 Basal metabolism
  
  - 1 Cu consumption
  
  - 1 Heat production
  
  - Growth and development
  
  - Differentiation, metamorphosis
  
  - ↓ of reaction time

**SYNTHESIS OF Na-K PUMP**

- Muscle, kidney, liver

  - Incorporation of Na-K pump in membrane

  - Consumption of O2 for activity of pump

  - Activity of pump compensated by leak Na a K

  - Cycle of cations whereby energy is consumed without useful work

**SYNTHESIS OF ENZYMES**

- **Carbohydrates**: ↑glukoneogenesis, ↑glykogenolysis, glycemia buffered by ↑insulin, ↑resorption of glucose - postprandial hyperglycemia

- **Proteins**: ↑proteolysis in muscles together with ↑proteosynthesis, during hyperthyroidism neg.

- **N** bilance, uraturia, kaliuria, calciuria, creatinuria, weakness

- **Lipids**: ↑lipolysis, ↑number of receptors for LDL in liver → ↓cholesterolemia

**ADRENERGIC STIMULATION HEART**

- **Beta receptors** - synthesis in heart, muscle, fat tissue - tachycardia

**Therapy - Beta blockers**

- **Expression of gene for Alfa myosin heavy chain in myocardium**: ↑contractility and rapid fiber shortening