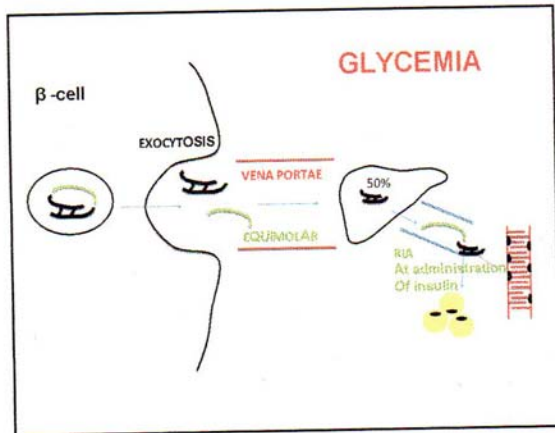
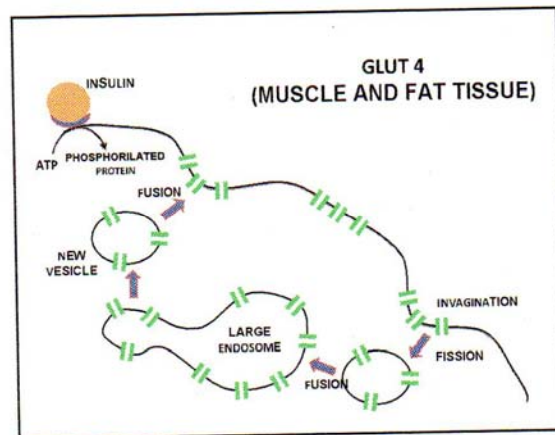
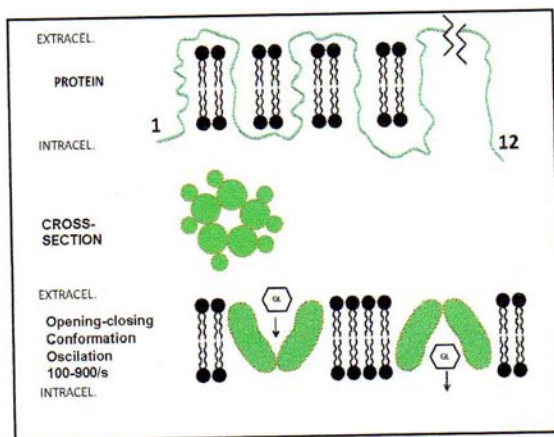


Endocrine sys. Disorders I



Glucose transporters

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



DIABETES MELLITUS

- **SACHARIDS** \downarrow utilization of gl. + \downarrow glycogenolysis \rightarrow hyperglycemia \rightarrow glycosuria \rightarrow osmotic diuresis..
Na, K \rightarrow hemoconcentration (polydipsie)
hypotension \rightarrow anurie
- **Glykosylation of proteins** microangiopatia
nephropatia, retinopatia, dg glycosylated Hb
- **Lipids** \downarrow lipogenesis, \uparrow lipolysis \rightarrow \uparrow lipemia \rightarrow ketogenesis \rightarrow acidosis (Kussmaul respiration)
 \rightarrow \downarrow Na ...dehydration
- **PROTEINS** \uparrow catabolism \rightarrow gluconeogenesis \rightarrow loss of N in urine....
- Cell dehydration

Diabetes mellitus type I

IDDM (insulindependent)...
insulinopenic, juvenil
damage of β cells, genetic disposition, autoimmune, th. insulin

Diabetes mellitus type II

NIDDM (non insulindependent)...
insulinoplethoric, resistant to In. – no response of cells (\downarrow Glut T4) Change in receptors for I.,
disturbance of fusion of Glut T4 with membrane,
 β cells \uparrow secretion till exhaustion

Disposition of 20% 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); ↑ beta3 receptors take part in it;
- UCG is H⁺ channel, protons generated by electron transport system enter the mitoch. 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 → ↓ thyroidal hormones – mental retardation, replacement therapy till 6M (later irreversible changes)
- **Bones** – permissive effect for STH, hypothyreosis - dwarf
- **Metamorphosis in amphibian tadpole** - frog (axoloti, Laufberger)

GOITER

- Chronic treatment by TSH - hypertrophy – an enlargement
- ENDEMIC – decreased iodine intake in food
- **EU ...HYPO.. – HYPETHYREOIDISM**
- Low thyroid h. → ↑ TSH
- **Anthithyroid substances**
Inhibition of accumulation of I⁻ anions as perchlorate, nitrate, thiocyanate
Inhibition of iodination of thyrosin – thiouracil, excessive ↑ I⁻

HYPOTHYREOIDISM

- **Etiology** congenital, ↓ iodine in water, autoimmune thyroiditis – Hashimoto' 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 mucopolysaccharids in skin - **myxedema**

HYPERTHYREOIDISM

- **Etiology** thyroid-stimulating immunoglobulins TSIG thyreotoxikosis – 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

Endocrine 179.

Disorders 2

PLASMATIC TRANSPORT of T3 and T4

- Bound to proteins \Leftrightarrow free

dynamic balance

Tyrosin binding globulin TBG (2/3)

" prealbumin TBPA

" Serum albumin HSA (1 capacity, ↓ affinity)

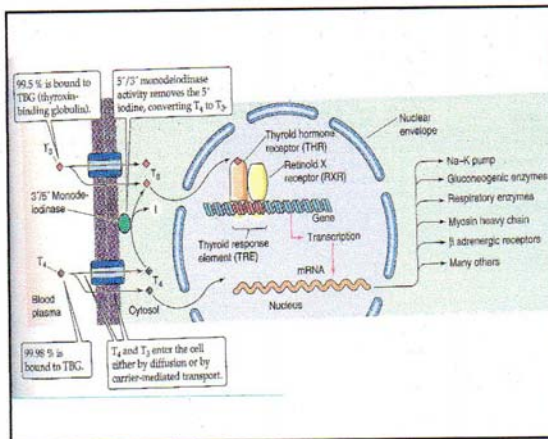
T4 in cells deionidated to T3 - higher activity
(transformation ↓ during starvation - ↑ rT3 with low activity)

Excretion - liver conjugated with sulfates, glukuronides

EFFECT OF T3 a T4

- ACTIVATION OF THYROID HORMONE RECEPTORS IN NUCLEUS REGULATES TRANSCRIPTION OF GENES - T3 is more effective than T4 (90% of effect) 50x more T4, but more bound to plasma proteins, deiodinated in cells, THR in nucleus have 10x ↑ affinity to T3, (conversion of T4 to T3 ↓ during starvation, illnesses → spare of E at unchanged level of TSH)

- ↑ BASAL METABOLISM
- ↑ O₂ CONSUMPTION
- ↑ 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 of 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 balance, uraturia, kaliuria, calciuria, creatinuria, weakness
- LIPIDS ↑lipolysis, ↑number of receptors for LDL in liver → ↓ cholesterolemia
- SYNTHESIS OF ENZYMES IN MITOCHONDRIA

ADRENERGIC STIMULATION HEART

- BETA RECEPTORS - synthesis in heart, muscle, fat tissue - tachycardia
Therapy - Beta blockers
- EXPRESSION OF GEN FOR ALFA MYOSIN HEAVY CHAIN IN MYOCARDIUM → ↑ contractility and rapid fiber shortening