DISORDERS OF WATER & ELECTROLYTE METABOLISM

LECUTRE FROM PATHOPHYSIOLOGY
DENTAL MEDICINE
2016/2017

EVA LOVÁSOVÁ & OLIVER RÁCZ

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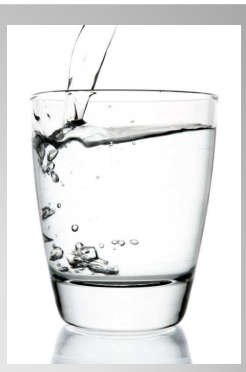

Water

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AGE DEPENDENCE OF FLUID HOMEOSTASIS

Age	Total water %	Daily exchange %
newborn[&]	79	
3-6 mo.	70	14-16
7-12 mo.	60	12-15
adult man	60	2-4
adult woman	51	2-4

[&] ECS > ICS, danger of dehydratation
In old age further ¯ & impaired adaptation, danger of dehydratation

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DISTRIBUTION OF WATER IN HUMAN BODY

Compartment	Volume litres	% of body mass	% of total water
ICS	28	40	67
ECS	14	20	33
ISF	11	15,7	26
IVF	3	4,3	7
SUMMA	42	60	100

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Water intake

- beverages 1,0 - 1,5 l/d
- water in food cca 1 l/d
- water from metabolism cca 0.3 l/d

oxidation of	100 g proteins	35 ml water
	100 g sugar	60 ml water
	100 g fat	107 ml water

- Total intake of water cca 2.0 – 2.5 l/d

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Water output

- Urine 1.0 – 1.5 l/d
- Perspiratio 0.3 – 0.6 l/d
  - Skin (sweating) 0.2 – 0.4 l/d
    (more – hot environment, physical activity, fever)
  - Lungs – respiration cca 0.2 l/d
- feces 0.1 – 0.2 l/d (more in diarhea)

- Increased output
  - vomiting
  - bleeding
  - redistribution of water - edema

- Total output of water cca 2.0 – 2.5 l/d

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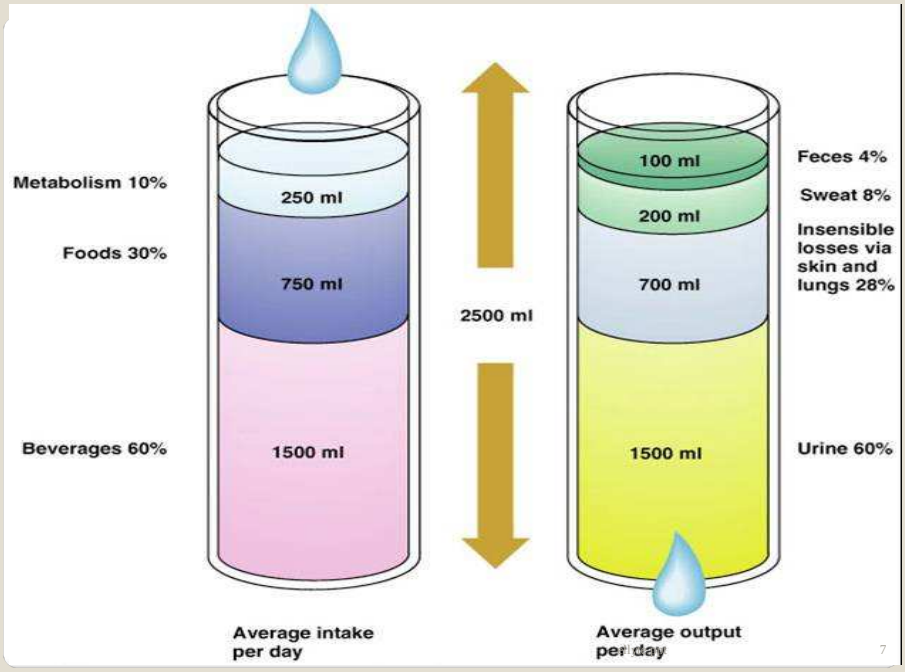
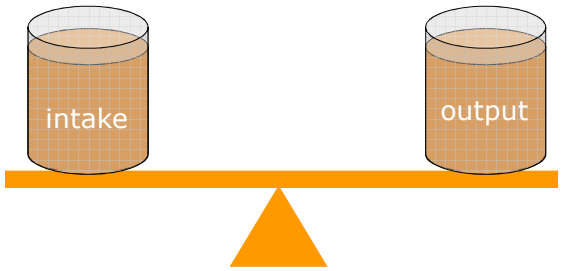
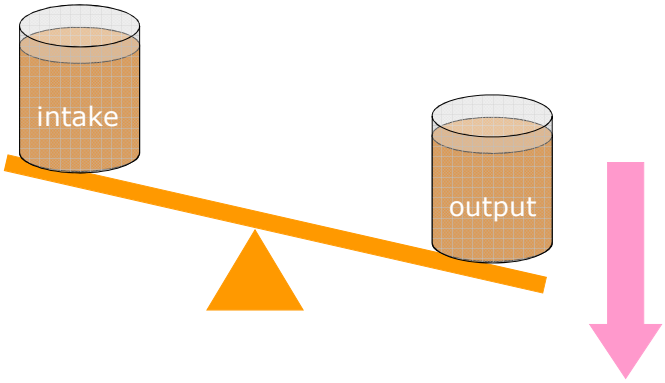


Water homeostasis

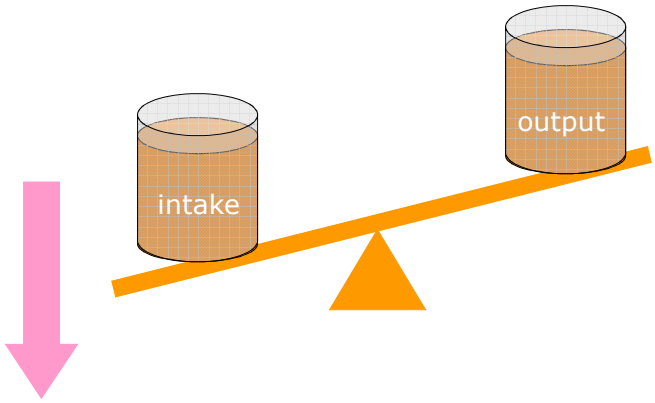
Water balance – equilibrium between intake and output of water



Water deficiency - ↑ thirst



Water excess - ↑ urination



Electrolytes

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Ion	Amount in body	Plasma mmol/l	Cells mmol/l
Sodium, Na^+	92 g 4 mol	141	10
Potassium, K^+	100-140 g 2,5-3,5 mol	4	155
Calcium, Ca^{2+}	1200 g 30 mol	2,5	< 0,001 (uneven in organelles)
Magnesium, Mg^{2+}	26,5 g 1,1 mol	1	15
Chloride, Cl^-	50 g 1,4 mol	103	8
Phosphate (as phosphorus)	775 g 25 mol	1	65

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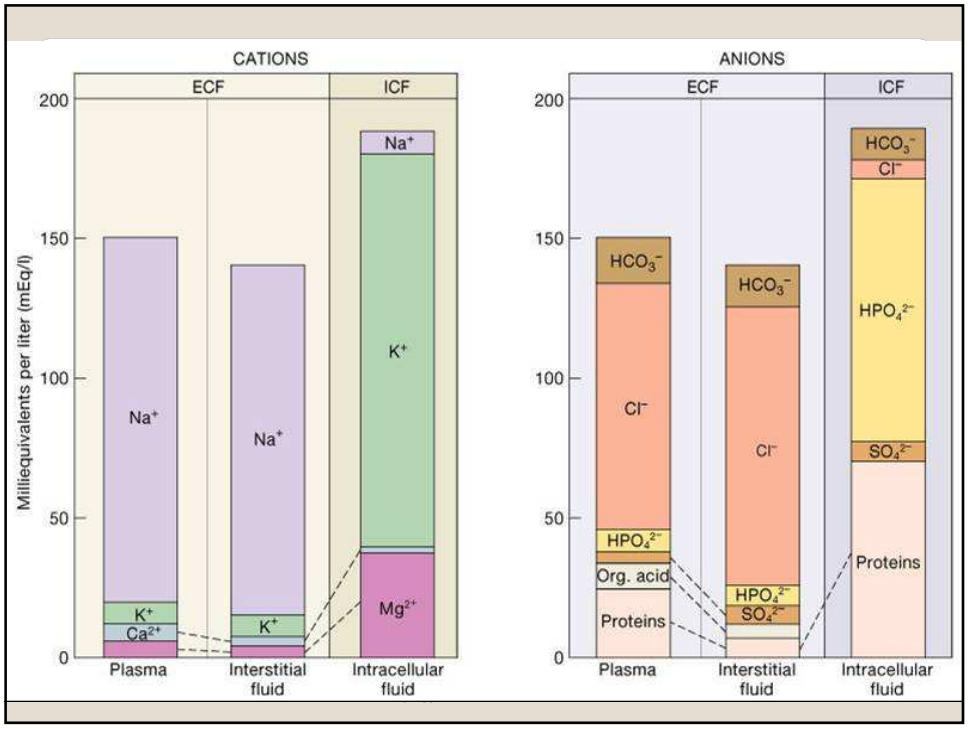

Osmolality of plasma

Osmolality - mmol/kg of solvent
Osmolarity - mmol/l of solvent

Osmolarity of plasma = 2*[Na] + [glucose] + [urea]

cca 290 ± 5 mmol/l
(kations 140 mmol/l + anions 140 mmol/l + glucose 5 mmol/l + urea 5 mmol/l)

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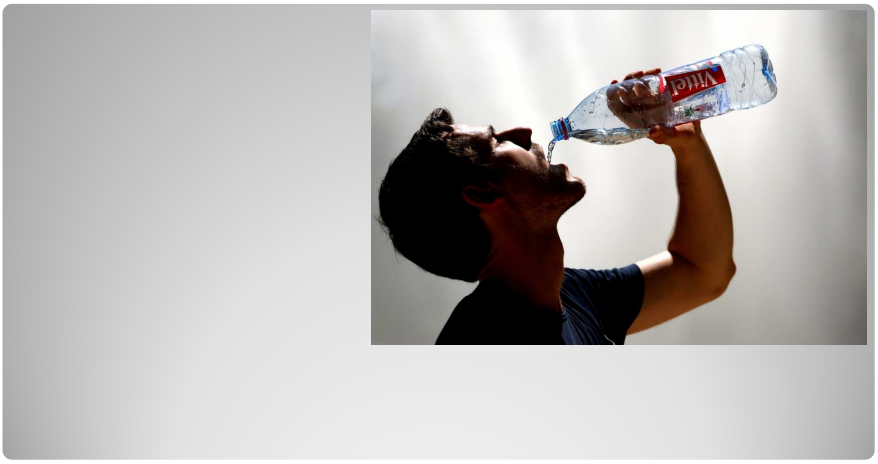

Regulation of water and sodium homeostasis

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Antidiuretic hormone

↓ plasma volume
↑ osmolality → drinking of water
dry mouth

↓

Hypothalamic osmoreceptors

↓

↑ antidiuretic hormone (arginine-vasopressin)

↓

↑ water reabsorption (aquaporins) and ↓ urination

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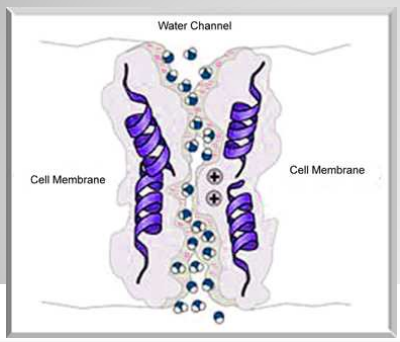
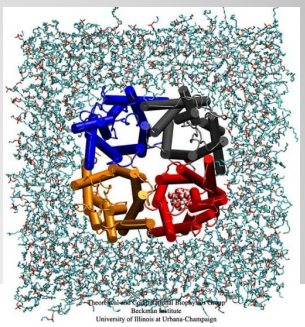
Aquaporins

- Water chanells
- Conduct water through cell membrane

- **2003 – Nobel price for chemistry**





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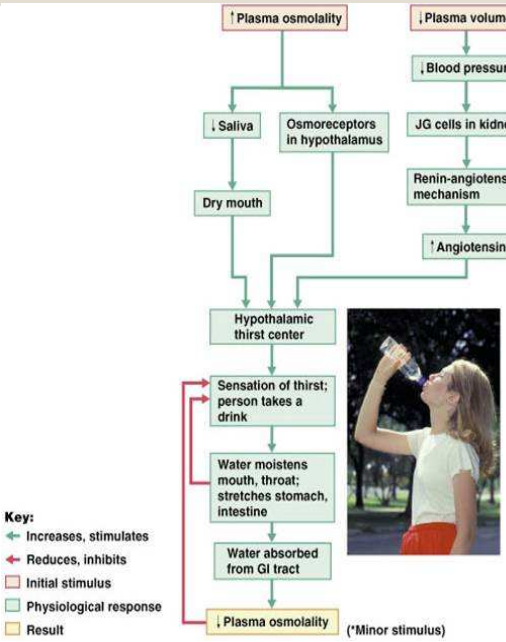

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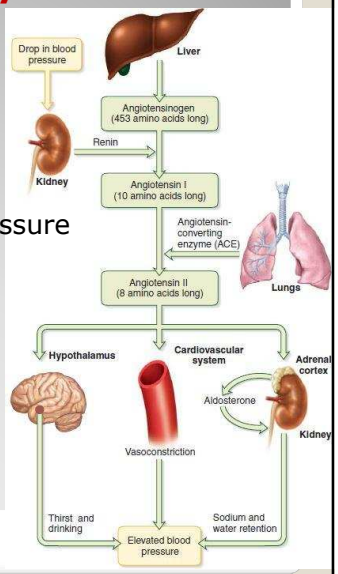
Renin-angiotensin-aldosteron system

- Angiotenzin II
  - Vasonconstriction – ↑ blood pressure
  - Antiinflamatory effect
- Aldosteron
  - Reabsorption of sodium
  - Secretion of potassium



Natriuretic peptides

- peptides which induce natriuresis

Types:

- Atrial natriuretic peptide (ANP) – produced in atria
- Brain natriuretic peptide (BNP) - ventricles in humans, brains in pigs
- C-type natriuretic peptide (CNP)
- Dendroaspis natriuretic peptide
- Urodilatin - kidneys

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Disorders of water and sodium homeostasis

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DISTURBANCES OF THE SYSTEM

- No pure forms – loss of water, salt...
- Immediate reaction of compensatory systems
- ECS is in contact both with external environment and with ICS
- ICS is in contact only with ECS
- Plasmatic concentrations are not amounts and does not inform on dynamics of compounds

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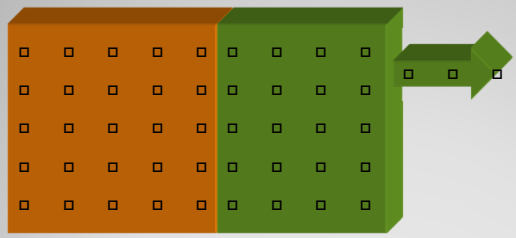
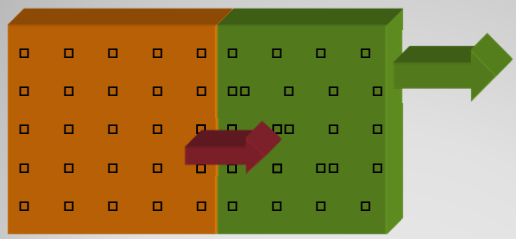
Loss of isotonic fluid



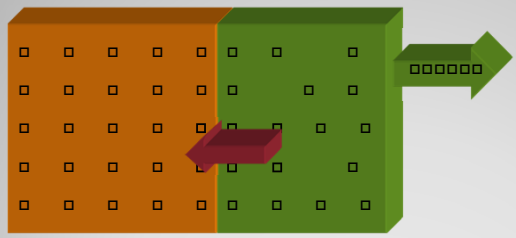
Reduction of ECS, thirst
no change of ICS
normal plasma sodium

Loss of hypotonic fluid



Reduction of ECS.
Hypernatremia compensated through water shift from ICS
Shrinkage of cells

Salt loss



Hyponatremia compensated through water shift from ECS into ICS,
Reduction of ECS, swelling (oedema) of cells

POSSIBLE CAUSES AND MECHANISMS

- ✓ Extreme deviations of external environment

  Dehydratation from insufficient water intake

- ✓ Disturbances caused by damaged function of effector systems (kidneys, GIT, etc.)

  Diarrhoea, vomitus, kidney diseases

- ✓ Disturbances caused by erroneous regulation (CNS, ADH, aldosterone)

  Diabetes insipidus, Conn sy., SIADH

  Heart failure & RAA activation

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WATER DEFICIENCY – REDUCTION OF ECS

Causes

- Insufficient fluid intake
- Inability to drink *(loss of consciousness)*
- Losses through GIT *(diarrhoe, vomitus)*
- Losses through kidneys
  (diuretics, osmotic diuresis, kideny diseases, m. Addison)
- Losses through skin *(increased sweating, burns)*
- Displacement into third place *(ileus, ascites)*
- Blood loss (?)

Symptoms: hypotension, tachycardia, dry skin, thirst, oliguria & decreased sodium excretion, increase of hematocrit

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Water deficiency signs in oral cavity

- Xerostomia
  - Decrased amount of saliva
  - Dry skin and mucous
  - Salivary gland swelled and painfull
  - Inflamatory changes – cheilosis, glosistis
  - ↑ risk of caries
  - ↑ risk of infection - candidiasis
- Dysphagia – problem with swallowing
- Dysfonia – loss of voice
- Dysgeusia – loss of taste

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WATER RETENTION – ECS EXPANSION

Causes

~~Increased fluid intake~~

- Increased intake & disturbed regulation – SIADH
- kidney failure
- nephrotic sy.
- heart failure
- liver cirrhosis

Symptoms: Oedema.

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Hypernatraemia >150 / 160 mmol/l

- Increased sodium intake
  - per os
  - parenteral
- Decreased eliminatin of sodium
  - Heart decompensation
  - Liver cirrhosis
  - Nefrotic syndrome
  - Renal insufficiency
  - Endocrine diseases – hyperaldosteronism (Conn syndrome)

Hypernatraemia

Low osmolality of urine – diabetes insipidus
Osmolality of urine & plasma – osmotic diuresis
(diabetes mellitus)
Osmolality of urine > plasma – dehydratation
diarrhoea, vomitus sweating
Conn syndrome (hyperaldosteronism)
→ hypernatremia, hypokalemia

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Hyponatraemia <130 / 120 mmol/l

- Extrarenal loss
  - GIT
  - Skin
  - Bleeding, burns
  - Sekvestration of Na^+
- Renal loss
  - diuretics
  - nephritis with loss of salts
  - Addison disease

Hyponatraemia

Plasma osmolality high → hyperglycemia ?!
Plasma osmolality low →
- Na in urine > 20 mmol/l & hypovolemia
  - *m. Addison, diuretics*
  - *salt losing nephritis*
- Na in urine < 20 mmol/l & hypovolemia
  - *diarrhoea, vomitus, sweating with inadequate fluid replacement*
- Na in urine < 20 mmol/l & oedema
  - *heart failure, cirrhosis, nephrotic sy.*
  - *SIADH*

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DISTURBANCES OF ADH SECRETION AND EFFECTS

Diabetes insipidus, neurogenic (AD)
- *AVP gene mutation*

Acquired forms – damage of hypothalamus
- *Complete & partial forms*

Diabetes insipidus, renal (X-related & AR)
- *Receptor (X) or water channel protein (AR) gene mutations*

Acquired – kidney diseases

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DISTURBANCES OF ADH SECRETION AND EFFECTS

SIADH – inadequate secretion of ADH

Expansion of ECS
hyponatremia, hypoosmolality
High urine osmolality & high Na in urine
Increased ANP
Renal & endocrine functions intact

Hereditary forms and stress ??!!

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Disorders of potassium homeostasis

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POTASSIUM HOMEOSTASIS

- Serum concentration: 3,8 – 5,5 mmol/l*
- Total amount depends on muscle mass (young > old; man > women) 37 – 52 mmol/kg body mass
- Intake: 2-6 g/d = 50-150 mmol/d
- Excretion through kidneys 10 – 20 mmol/d (0,4 – 0,8 g/d).
- Inverse association with Na excretion
- GIT excretion is important in kidney failure and in pathological conditions (diarrhoea)

*Depends on method. Preanalytic errors - hemolysis!

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FUNCTIONS OF POTASSIUM & INTERPRETATION OF RESULTS

Functions

- intracellular osmotic pressure
- resting & action potential
- enzyme activity, proteosynthesis

Problems:

1. assesment of cell homeostasis from extracellular concentration
2. pH changes: exchange H/K between ECF/ICF

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INTERNAL & EXTERNAL BALANCE

internal – ECF/ICF

- acidosis: H^+ enters the cells, K^+ out into ECF
- alkalosis: H^+ into ECF, K^+ enters the cells
- K^+ entry into cells: insulin (together with glucose), aldosterone, adrenaline
- rapid cellular proliferatiom (treatment of pernicious anaemia with B_{12} vitamin
- cell necrosis, hemolysis (crush sy, malignancies), K^+ into ECF

external – ECF/environment

- kidney or GIT retention/losses, parenteral intake
- dietary deficiency/excess as an additional factor

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HYPOKALAEMIA - CAUSES

Disorders of external balance

- GIT – diarrhoea, vomitus, tumors of colon, rectum, pancreas
- Kidneys - diuretics, polyuric stage of renal failure, hereditary tubulopathies,
- Primary & secondary hyperaldosteronism, abuse of liquorice, Cushing, ectopic ACTH production

Disorders of internal balance

- Treatment of diabetic hyperglycaemia with insulin (K^+ entry into cells together with glucose)
- Alkalosis
- Rapid cellular proliferation
- Familiar hypokalaemic periodic paralysis (hereditary)

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HYPOKALAEMIA - SYMPTOMS

- hypokalaemia < 4,0 mmol/l
- significant < 3,5 mmol/l
- dangerous < 3,0 mmol/l

- Membrane hyperpolarisation
- ✓ Weakness, constipation, ileus, hypotonia
- ✓ Depression, confusion
- ✓ Arrhytmia, potentiation of digitalis toxicity
- ✓ ADH resistance, polyuria, polydipsia
- ✓ ECG flat/inversed T, prolonged PR, ST depression, prominent U

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HYPERKALAEMIA - CAUSES

Disorders of external balance

- Decreased excretion. Under GFR 15 ml/min always.
  Anuria: K increase 1 mmol/l daily
  In mild impairment of kidney function only when other factors are present
- Increased intake (infusions, NaCl substitution) only in the case of impaired kidney function
- m. Addison, adrenogenital sy., inhibitors of angiotensin converting enzyme

Disorders of internal balance

- Acidosis
- Cell necrosis - rhabodmyolysis, burns, cytostatic treatment of malignanacies
- Digitalis overdosis
- Hyperkalaemic periodic paralysis (hereditary)
- Malignant hypertermia (hereditary)

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HYPERKALAEMIA - SYMPTOMS

- hyperkalaemia < 5,5 mmol/l
  - significant < 6,5 mmol/l
- dangerous < 7,5 mmol/l

- Low resting potential, short cardiac action potential, increased speed of repolarization ➔
- ✓ Can kill without warning
- ✓ Ventricular fibrillation and cardiac arrest may be the first signs! (if you do not check K & ECG)
- ✓ ECG: abnormal/absent P; broad QRS, peaked T, ST depression

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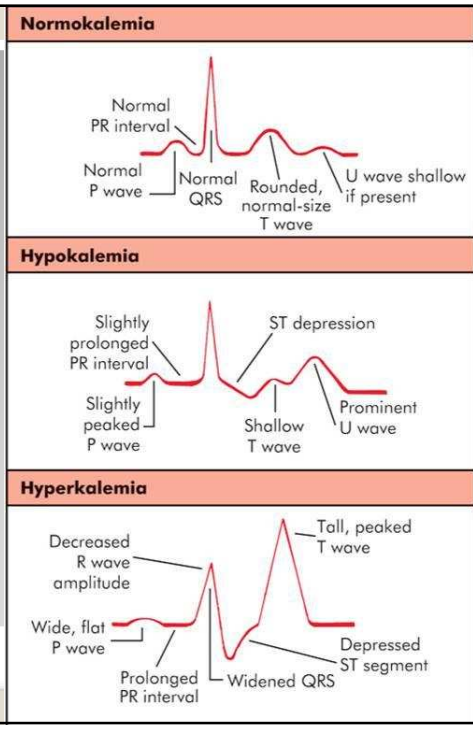

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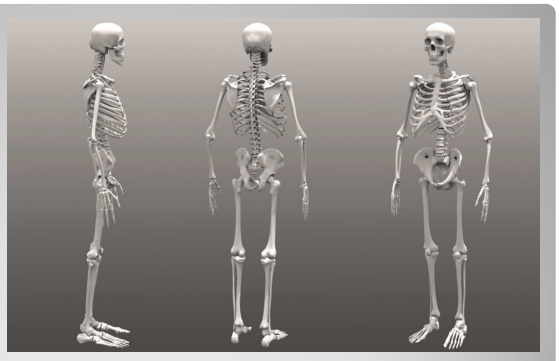

Disorders of calcium homeostasis

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CALCIUM

- Total body 1200 g 30 mol
- ECF 0,9 g 22,5 mmol
- Plasma 0,36 g 9,0 mmol
- Bone / ECF exchange 500 mmol/d
- Daily losses 25 mmol/d (1g)
  - urine 6 mmol (240 GF – 234 reabsorbtion)
  - faeces 19 mmol (+25 food, 12 in, + 6 secr.)
  - skin 0,3 mmol

Small changes in fluxes can have profound effect of plasma Ca

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FUNCTIONS OF CALCIUM

- Structural
- Neuromuscular

- Blood
- Signal systems

- Bone, teeth
- Control of excitability;
  Neurotransmitter release
  Muscle contraction
- Coagulation
- Messenger

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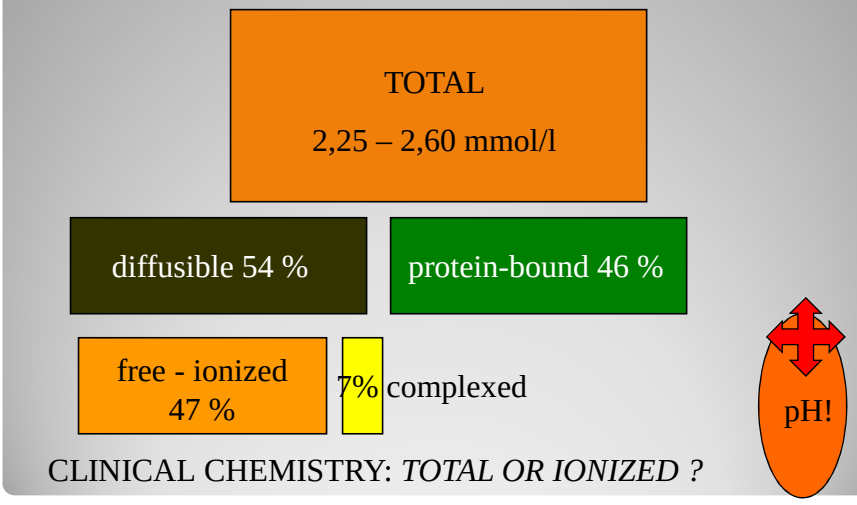
PLASMA CALCIUM



CLINICAL CHEMISTRY: *TOTAL OR IONIZED ?*

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CALCIUM REGULATING HORMONES

- **Parathormon**
- **Calcitriol**
- **Calcitonin**

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FUNCTIONS OF PARATHORMON

BONE

- Release of calcium ⇑ $[Ca^{2+}]$
- Osteoclastic resorption

KIDNEY

- Calcium reabsorbtion ⇑ $[Ca^{2+}]$
- 2nd hydroxylation of vit.D ⇑ Ca, P absorbtion
- Phosphaturia ⇓ $[PO_4]$
- Decrease of HCO_3^- reabsorbtion ⇓ pH

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HYPOCALCAEMIA - CAUSES

- Hypoparathyroidism
  - Congenital (with Di George sy.)
  - Acquired – autoimmune, surgery, hemochromatosis, tumors
- Pseudohypoparathyroidism
  - 2 hereditary disorders of PTH signaling pathway (cAMP dependent)
- Magnesium deficiency (pseudo ?)
- Deficiency of vitamin D (!)
- Disorders of vitamin D metabolism – end stage renal disease
- Acute pancreatitis, transfusions with citrate, neonatal

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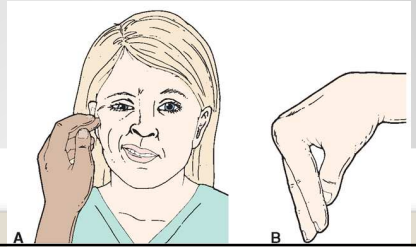
HYPOCALCAEMIA - SYMPTOMS

- Stupor, numbness, paraesthesia
- Muscle cramps and spasms „tetany"
- Laryngeal stridor
- Convulsions
- Chvostek+ Trousseau+, long QT on ECG
- Cataract in chronic hypocalcaemia
- Rickets (rachitis) in vitamin D deficiency



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HYPERCALCAEMIA - CAUSES

- COMMON (90% of all)
  - Primary hyperparathyroidism
  - Malignancies – bone metastasis (?), PTHrP and other humoral factors
- LESS COMMON
  - Thyreotoxicosis, sarcoidosis
- UNCOMMON
  - Lithium treatment, tbc, immobilisation, adrenal failure, renal failure, hereditary
- BUT ALSO HYPERPARATHYROIDISM WITHOT HYPERCALCAEMIA
  - Compensatory in vitamin D deficiency, renal disease

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HYPERCALCAEMIA - SYMPTOMS

- Weakness, tiredness, weight loss
- Imparied concentration, drowsiness (coma)
- Anorexia, nausea, vomiting, constipation
- Polyuria, dehydration
- Renal calculi, nephrocalcinosis
- short QT, arrhytmias

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Hyper- and hypocalcemia in oral cavity

- Hypercalcemia
  - Jaw bone demineralization
  - Loss of lamina dura
  - Osteitis fibrosa cystica – increased osteoclastic resorption, hemorrhage and cysts formation
- Hypocalcemia
  - Hypoplasia and discoloration of teeth
  - Possible teteany cramps

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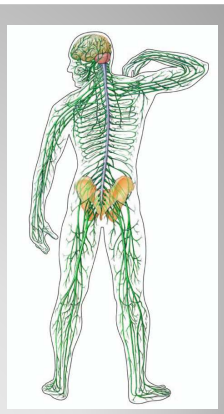

Disorders of magnesium and phosphates homeostasis

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MAGNESIUM

- 60 % in bones, higher in ICF than in ECF
- Only 0,3 % in blood, 30% protein bound
- Serum 0,7 – 1,0 mmol/l
- Regulator is not known! *adrenal medulla, insulin, parathormon ???*
- Regulated resorbtion from GIT ?
- 8 mmol/d is enough ? Is deficiency common ?
- Excretion through urine and stool

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MAGNESIUM

- Neuromuscular excitability (inhibition – mediated through decreased secretion of acetylcholine?)
- Bone structure
- Enzyme activity, energy production, transport mechanisms, ribosomes
- Regulation of haemocoagulation and membrane function
- Cardioprotective antiischemic, antihypoxic effects
- Sedative effect on NS
- Antihypertensive
- Antithrombotic

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MAGNESIUM

- Deficiency associated with soil and plant deficit Þ grass tetany of cattle
- Some drugs and stress can increase excretion
- Unhealthy diet (alcohol)
- High doses of calcium (!)

CONSEQUENCES

- ✓ Spasmophilia is more often a consequence of Mg deficiency as of Ca
- ✓ Tiredness, irritability, tremor
- ✓ Dysmenorea, preeklampsia
- ✓ arrythmias

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PHOSPHATE

- 85 % in bones
- in ICF and in ECF
- In plasma – phospholipids, phosphate esters and ionized phosphate
- Regulation – PTH, vit. D and calcitonin (together but opposite with calcium)

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Hypophosphatemia

- Causes
  - Intestinal malabsorption
    - Vit. D deficiency
    - Use of Mg- and Al-containing acids that bind phosphates
    - Alcohol abuse
    - Malabsorption abuse
  - Increased renal secretion
    - Hyperparathyroidism
- Signs and symptoms
  - Only in higher deficit
  - Disturbed energy metabolism – nerves and musles dysfunction
  - Erythrocyte, leukocyte and platelets dysfunction
  - ↑ risk of infection
  - Hemorhage

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Hyperphosphatemia

- Causes
  - Destruction of cells – tumors or anticancer therapy
  - Long term using of phosphate-containing drugs (laxatives)
  - Hypoparathyroidism
- Signs and symptoms
  - Symptoms of hypocalcemia – tetany
  - Calcification of tissues

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