Lectures for General medicine – 3rd year
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20th universary

PATHOPHYSIOLOGY
PATHOBIOCHEMISTRY

Ionic balance disturbances

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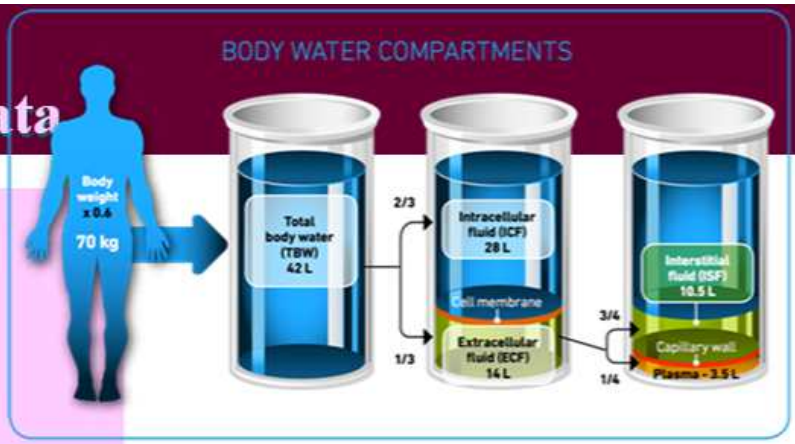
Water distribution - Data

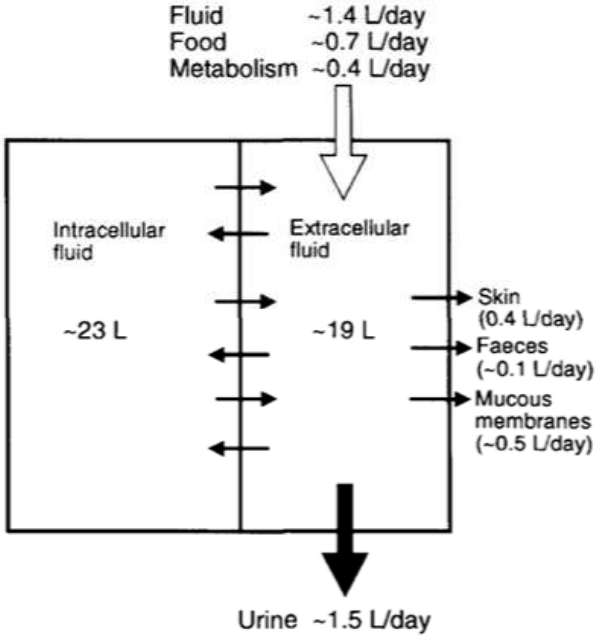


Total body water content according to sex and age % of body weight

- Infants 70
- Young males - 60
- Elderly males 50
- Young females - 55
- Elderly females - 45

Water distribution in a healthy young adult male. (%TBw, total body water content)

	litres	%TBw	%body weight
Total	42	100	-60
Intracellular	23	55	33
Extracellular	19	45	27
- Interstitial	16	38	23
- Plasma	3	7	4

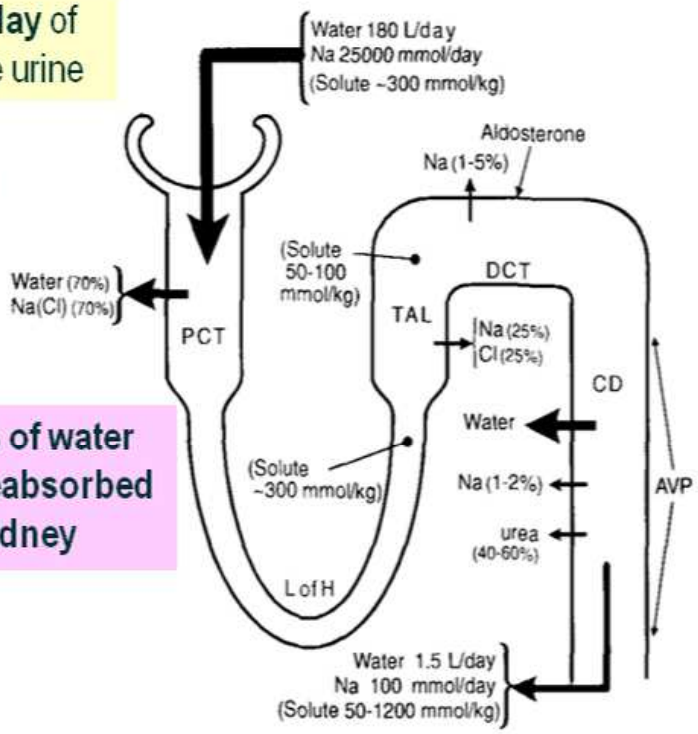


Water reabsorption – Data

Intake: of water: 2.5 l/ day;
Output of water 2,5 l /day; Urine (1,5 l/ d), Sweating, Lungs, Feces <100 ml /d,

~ **130-180 l/ day** of glomerular filtrate (primary urine)

1 - 2 l /day of definitive urine



- A) ~**70%** absorbed in the *proximal tubule* (vi sodium reabsorption), followed by osmosis
- B) **20-30%** absorbed in *thick segment of the ascending limb of the Henle loop* (the 'diluting segment')
- C) < **2%** collecting ducts (ADH)

99% of water is reabsorbed in kidney

- **Concentration and dilution**

- **dilute urine** (up to 20-30 L/day)
- concentrate the urine (0.5 L/day)
- **osmolality** ↓ to 50 - 100 mmol/kg.; fluid delivery --> 20 mL/min (-30 L/day)

Water turnover – Factors involved in H_2O homeostasis

a) Neural factors:

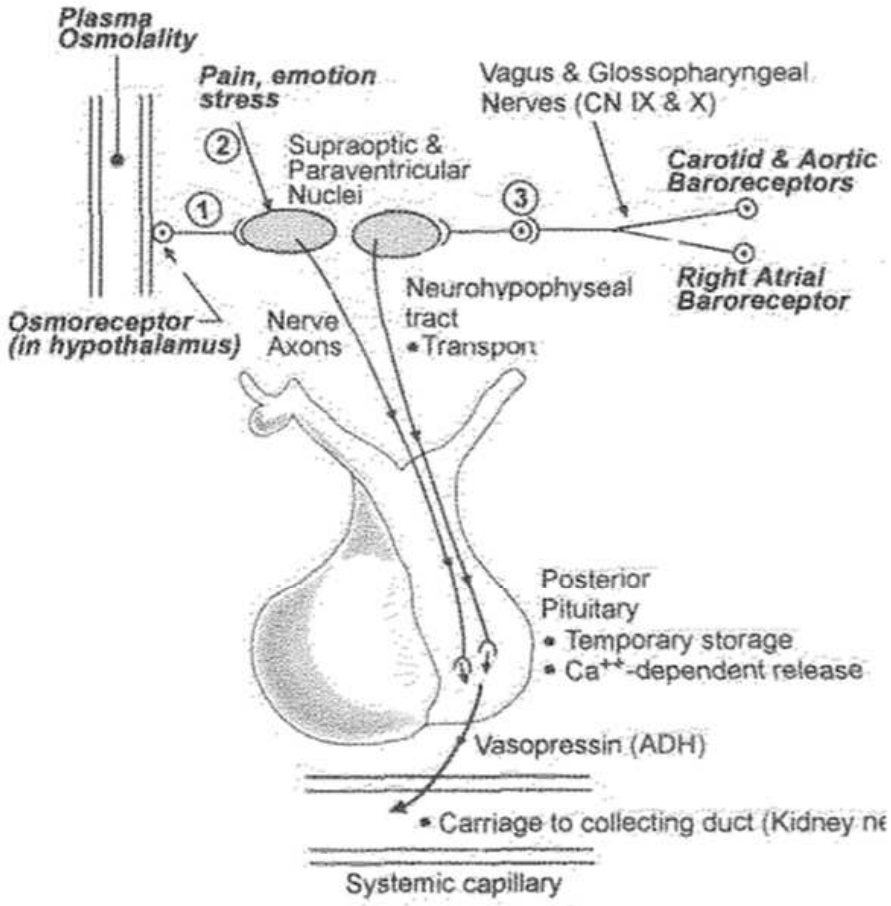
- **Thirst center** (cravling for water); trigger: ECF hypertonicity →↑ thirst; ↓ volume → thirst →↑ thirst ; pain +stress →↑ thirst
- **Sympathetic NS** → constriction in small muscular aa., precapillary sphincters

b) Renal factors: glomerular filtration rate, countercurrent multiplier, countercurrent exchange

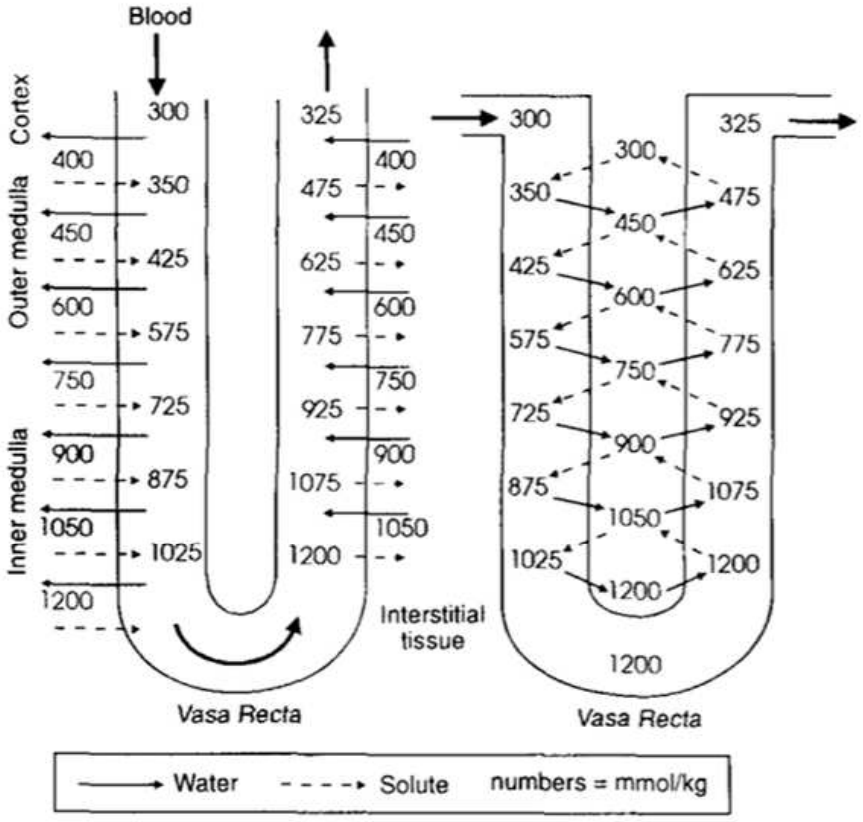
c) Circulating hormones:

- **Catecholamines** (vasoconstriction small musc. arteries, precapillary sphincter
- **ADH (vasopressin)** vasoconstriction in medium muscular arteries, reabsorption of pure water in collecting ducts
- **Atrial natriuretic factor** (ANF) (↓Na^+(S), H^+(S),):↑ Na excretion + GFR, ↓ renal vasoconstriction, ↓ renin secretion. antagonizes vasoconstriction relaxant effects on angiotensin II), ↓ blood pressure
- **Angiotensin II** (vasoconstriction) + **aldosterone** (↓K+, ↑Cl-,↑Na+, ↓H+)
- **Cortisol** (permissive effects) persmissive effect on catecholamines + mimick ALD

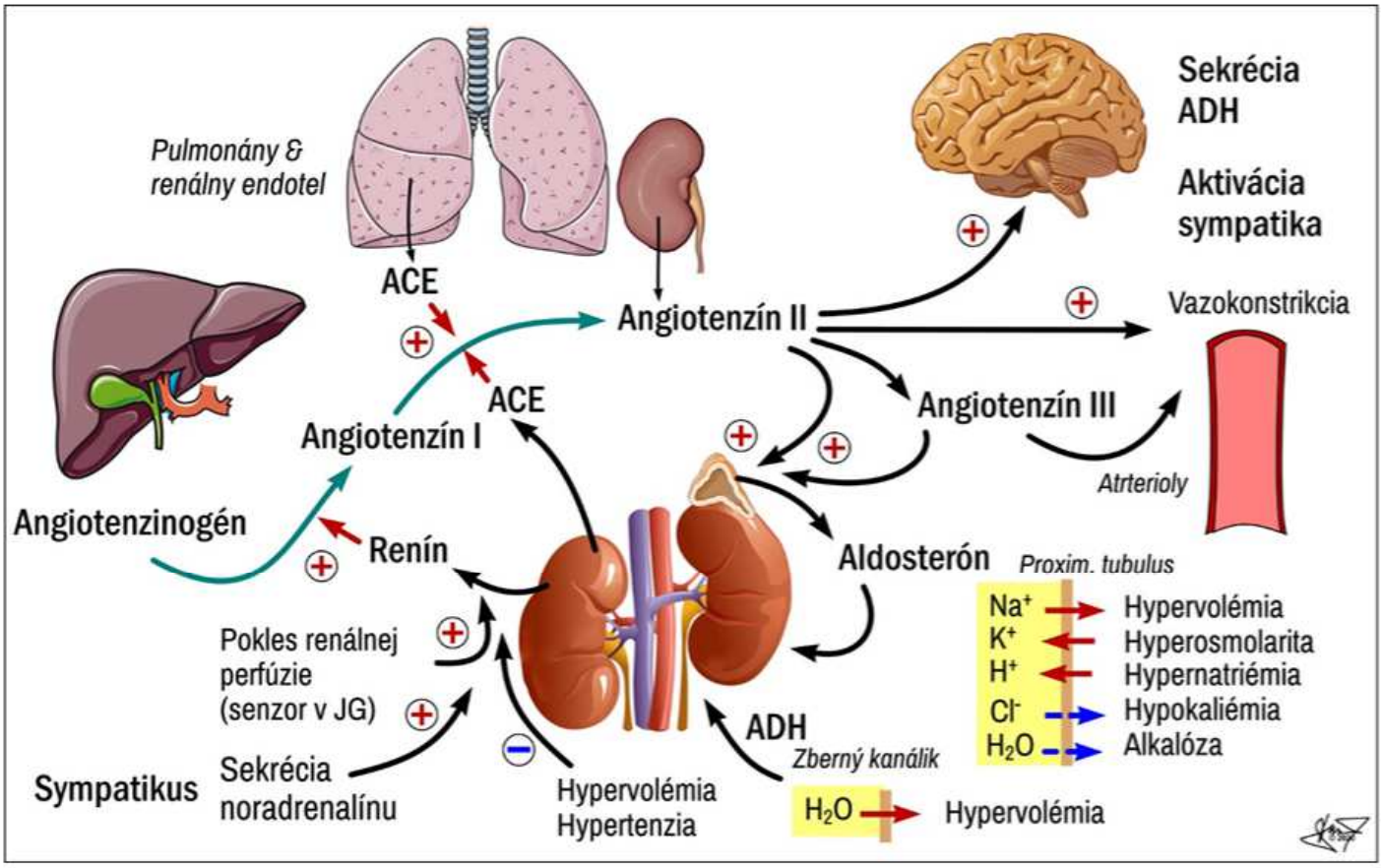
Vasopressin



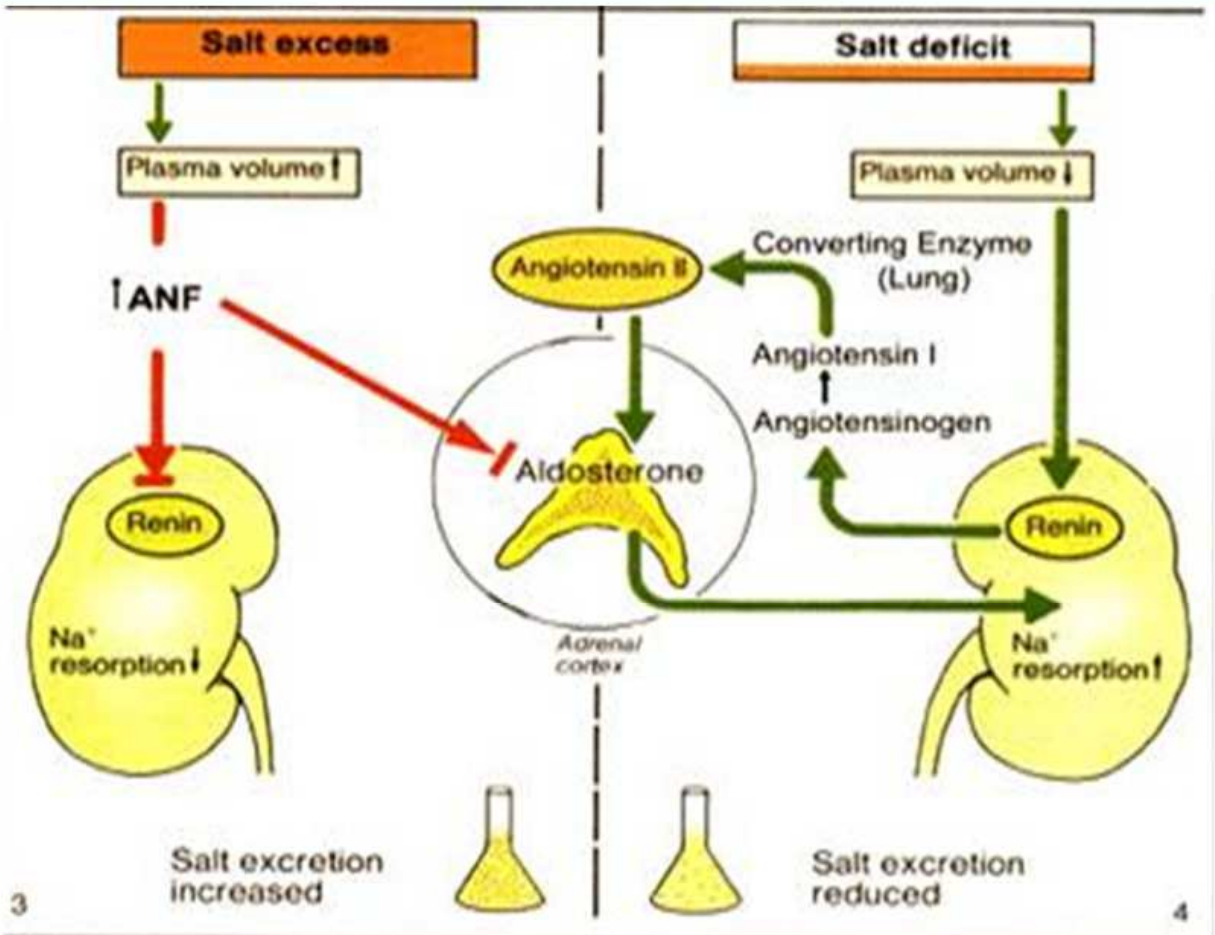
Coutercurrent mechanism



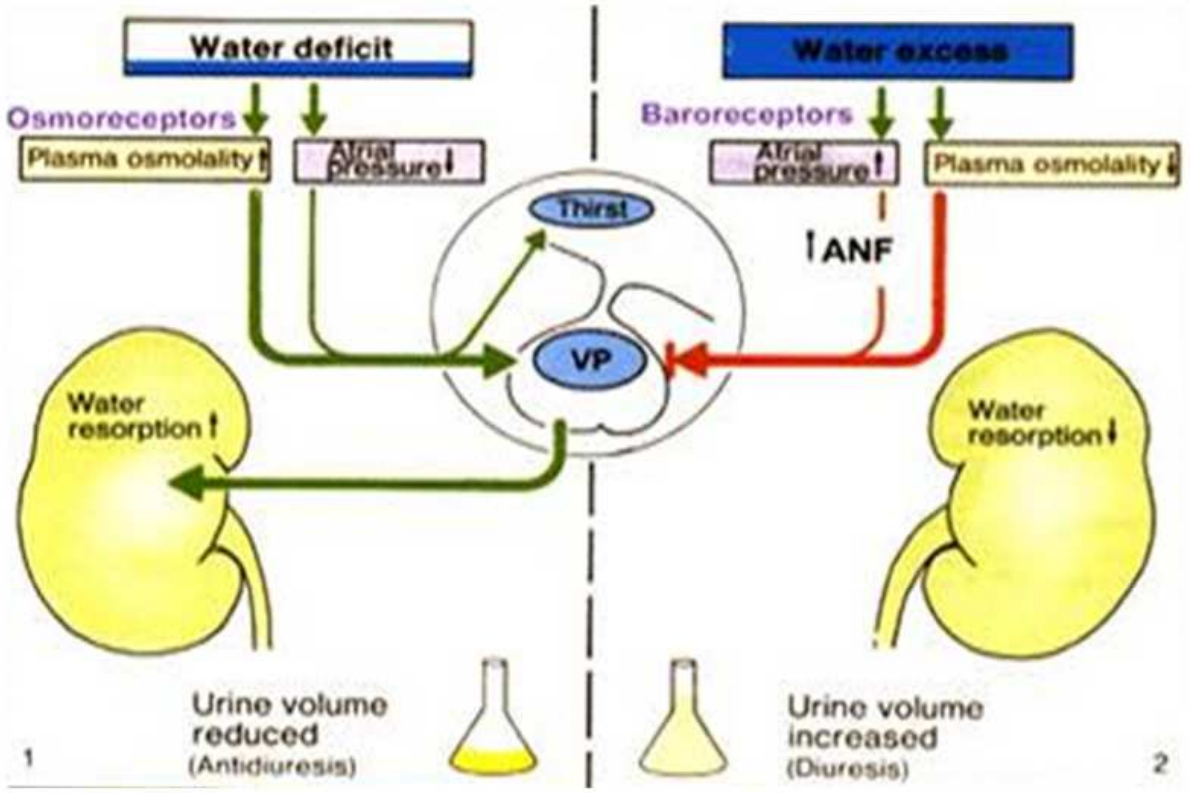
RAA - Renin Angiotensin Aldosteron



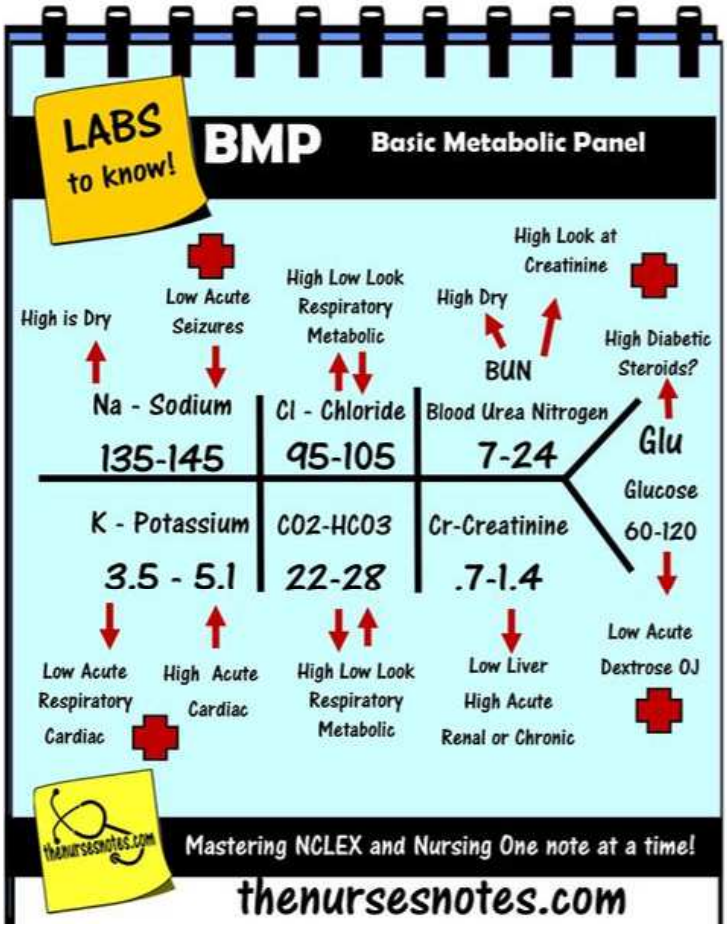
Salt excess and deficit

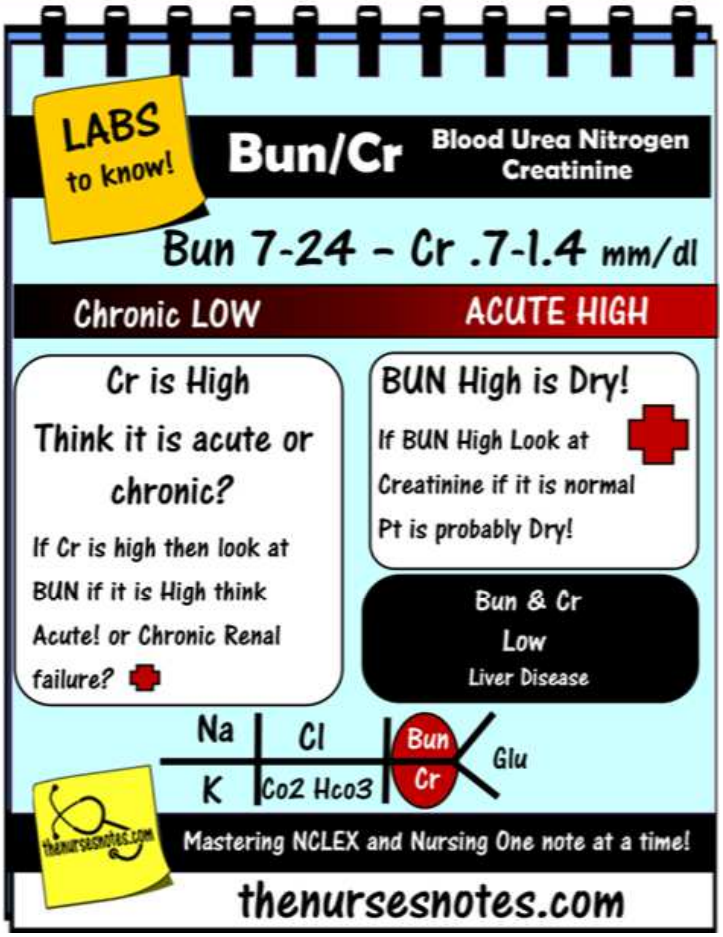


Water deficit and excess



Basic biochemical data.





Water and sodium

Dehydration – Causes

Excessive fluid loss

Excessive sweating
- High fever
- Hot climate
- Cystic fibrosis

Vomiting
- Pyloric stenosis
- Viral infections
- Gastroenteritis

Acute diarrhoea
- Viral gastroenteritis
- Bacterial gastroenteritis
  - *Shigella*
  - *E. coli*
  - *Salmonella*
  - *Campylobacter*
- Antibiotic-induced
- Food poisoning (toxins)
- Any acute infection

Fluid loss
- Burns
- Post surgery

Polyuria
- Diabetes mellitus, especially diabetic ketoacidosis

Inadequate intake

Inability to drink
- Herpes stomatitis
- Acute tonsillitis

Inadequate acces to water

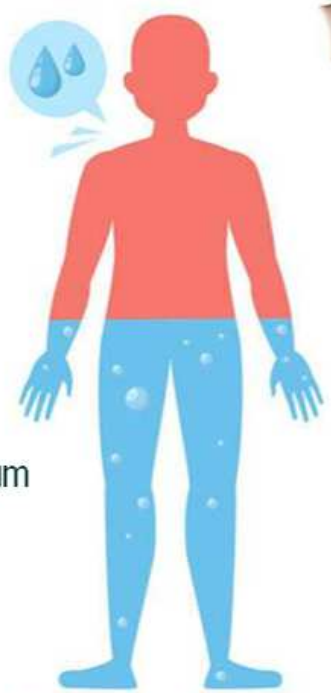
Hypohydrationjm – Causes

Hypotonic-Hypoosmolar	Normotonic – Isoosmolar	Hypertonic – Hyperosmolar
losses of water + electrolytes (ions > water)	losses of water + electrolytes (ions = water)	losses of water maily (ions << water)
▪ Excessive sweating (fever, on sun) ▪ Prolonged diarrhea ▪ Massive vomiting ▪ Addison's disease ▪ Polyuria - diabetes mellitus, diuretics	▪ initial stage of acute blood loss ▪ Extensive burns (loss of plasma) ▪ Diarrhoe: bacterial dysentery, cholera ▪ stenosis of pylorus (vomitng)	▪ low water intake ▪ drinking sea water in hypohydration ▪ hyperthermia, ▪ hyperpyretic fever. ▪ moistened gaseous mixture

Dehydration - Manifestations

Medium dehydration

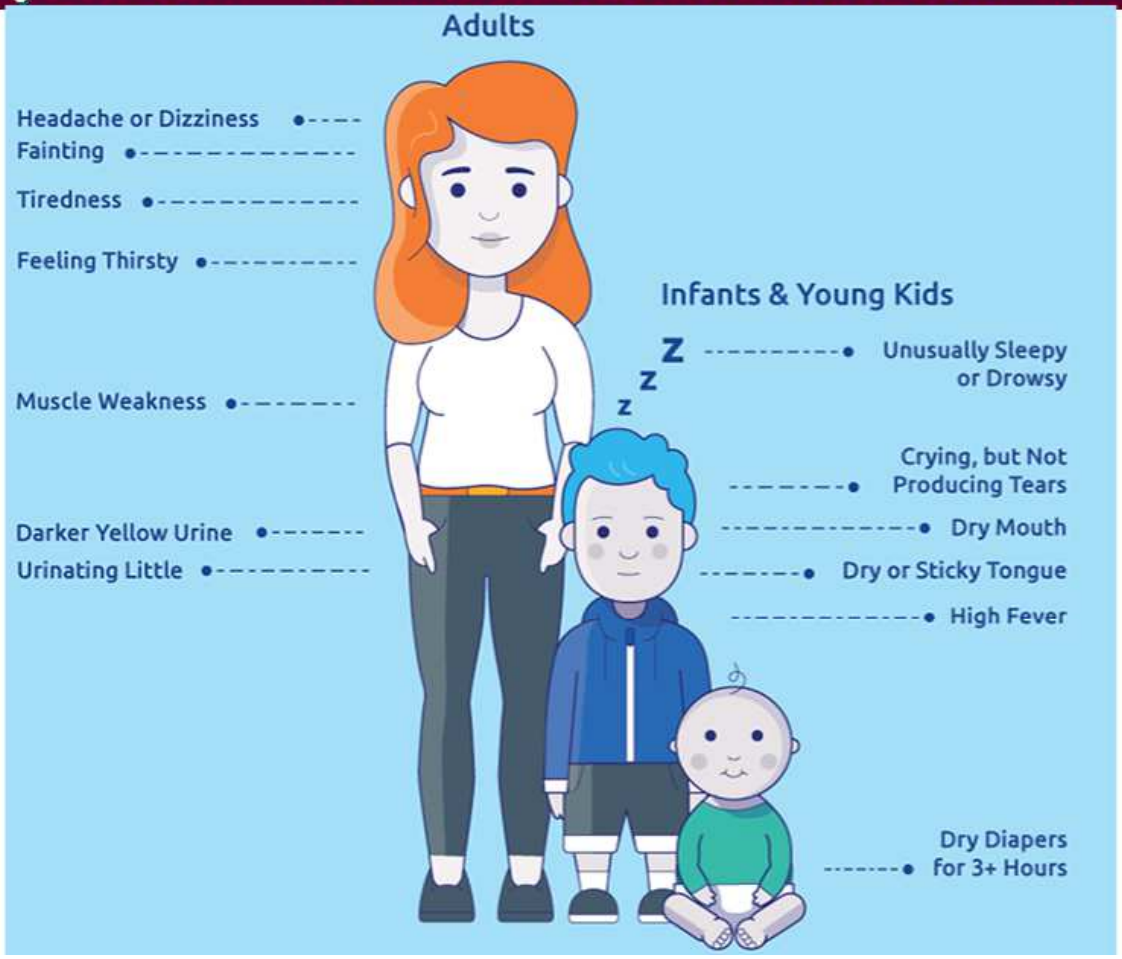
- Dizziness, Drowsy or fatigued, Lightheadedness, Headache
- Thirst, dry sticky mouth, dry skin
- Weight loss, constipation
- Darker, strong smelling urine



Strong dehydration

- Confusion, speachless, illusions, delirium
- Fever ! ! Extreme thirst, No tears,
- Dry skin, loss of turgor, cracked lips
- Dry mouth, mucous membranes
- Little or no urination (oliguria, anuria),
- Low blood pressure → comp. rapid heartbeat, rapid breathing, falls/difficulty walking
- Sunken eyes, Low eye ball tension + abnormal vision (fogging);
- ↑ of blood viscosity (hemoconcentration → stroke

Dehydration – Manifestations in adults and kids



Hypohydration - Manifestations

STATUS	No Dehydration	Some Dehydration	Severe Dehydration
CONDITION	Well, alert	Restless, Irritable*	Lethargic or unconscious; floppy*
EYES (Tears)	Normal (present)	Sunken (not present)	Very sunken and dry (not present)
MOUTH & TONGUE	Moist	Dry	Very dry
THIRST	Drinks normally, not thirsty	Thirsty, drinks eagerly*	Drinks poorly or not able to drink*
SKIN PINCH	Goes back quickly	Goes back slowly*	Goes back very slowly*
DECIDE	The child has no signs of dehydration	If the child has 2 or more signs, including at least 1 major sign, there is some dehydration	If the child has 2 or more signs, including at least 1 major sign, there is severe dehydration

Loss of 2- 15% body weight

- Dry or sticky mouth, strong thirst
- Lack of tears/ sweat, Poor skin turgor, Weight loss
- Lethargy, headache, Dizzines, Sunken eyes, abnormal vision, uconsciousness
- Confusion, inability to speak, illusions,
- Low or no urine input, Dark yellow urine
- Delayed capillary refill, high blood viscosity (hemoconcentration
- Rapid heart rate, Low blood pressure, low blood circulating volume,
- increased breathing, decrease in lungs perfusion (resp hypoxia),
- metabolic disturbances in organs (tissue hypoxia).
- Abnormal labs/electrolytes

Hyperhydration causes

hypoosmolar	isoosmolar	hyperosmolar
■ ↑water intake + ↓ function of the kidneys ■ treatment of hypohydration with pure water and low osmotic solutions ■ increase of ADH production	■ infusion of a great amount of isotonic solutions ■ congestive heart failure ■ hypoproteinemia ■ chronic lymphostasis	■ infusion of the hyperosmolar solutions ■ acute renal failure (↓ salt excretion) ■ forced intake of sea water ■ hyperaldosteronism

low normal high

concentration of electrolytes in blood plasma (osmotic pressure)

Hyperhydration - Manifestations

Overdrinking water

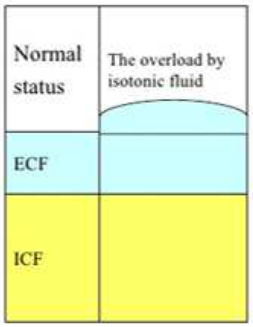
Light urine, frequent urination

Fatiguability, tiredness

- Brain edema (headache, inadequate behavior, disorders of consciousness, restlessness, tiredness, drowsiness|
- Crystal clear just like water,
- Muscle cramps
- Swollen lips, face, and leg
- High circulating volume → congestive heart disease; inotropy, tachycardiat, yachypne
- Increased Body Weight (water accumulation)
- Edemas (cardiac failure + relative hypoproteinemia, hyponatremia)
- Pulmonary edema → weak O2 exhamge → tissue hypoxia; + harsh lung sound or cracklws on auscultation
- Polyuria (in absence of kidney diseases)
- Nausea, vomiting (intracranial hypertension)
- Iatrogenic hypoponic infusions → hemolysis

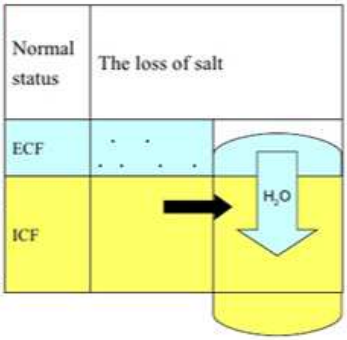
Causes

Isotonic hyperhydration



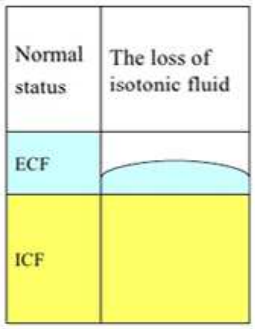
Typical situations
excessive infusions by isotonic saline
cardial insufficiency
renal diseases
(secondary hyperaldosteronism)
Consequences
expansion of ECF volume
ECF edema

Loss of hypertonic fluid (pure sodium)



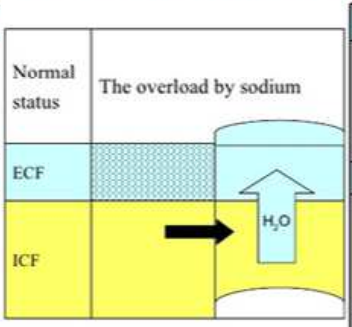
Typical situations
aldosterone deficit
diuretics
(also vomiting, sweating, diarrhea)
Consequences
ECF becomes hypotonic (hyponatremia)
water osmotically moves from ECF to ICF → hypovolemia + intracellular edemas
expansion of ICF → increase of intracranial pressure - imminent danger of cerebral edemas
ADH production ↓ (water excretion) + RAAS activation

Isotonic dehydration



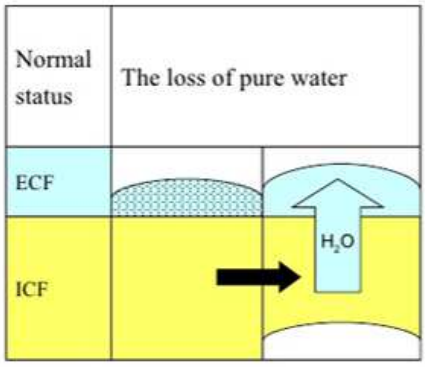
Typical situation
vomiting, diarrhea, bleeding, burns, (ascites)
Consequence
↓ ECF volume (hypovolemia)
activation of RAAS

Overload by hypertonic fluid (pure



Typical situations
excessive intake of salt / mineral waters
drinking sea water (ship wreck)
excessive infusions of Na-salts (ATB ...)
aldosterone hyperproduction
Consequences
ECF becomes hypertonic (hypernatremia) → hypervolemia
water moves osmotically from ICF to ECF
ECF (pulmonary) edemas + cellular dehydration
↑ ADH (to retain water)
↑ ANP / urodilatin (to excrete sodium)
RAAS inhibited

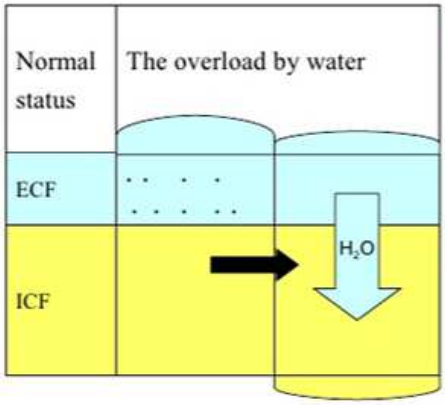
Hypertonic dehydration = loss of pure solute free water hypotonic fluid



Typical situations
hyperventilation
no drinking (older people)
osmotic diuresis
ADH deficit (diabetes insipidus)
Consequences
hypovolemia
ECF becomes hypertonic (hypernatremia)
water osmotically moves from ICF to ECF
cellular dehydration (cells shrink)*
ADH production ↑ (water retention)

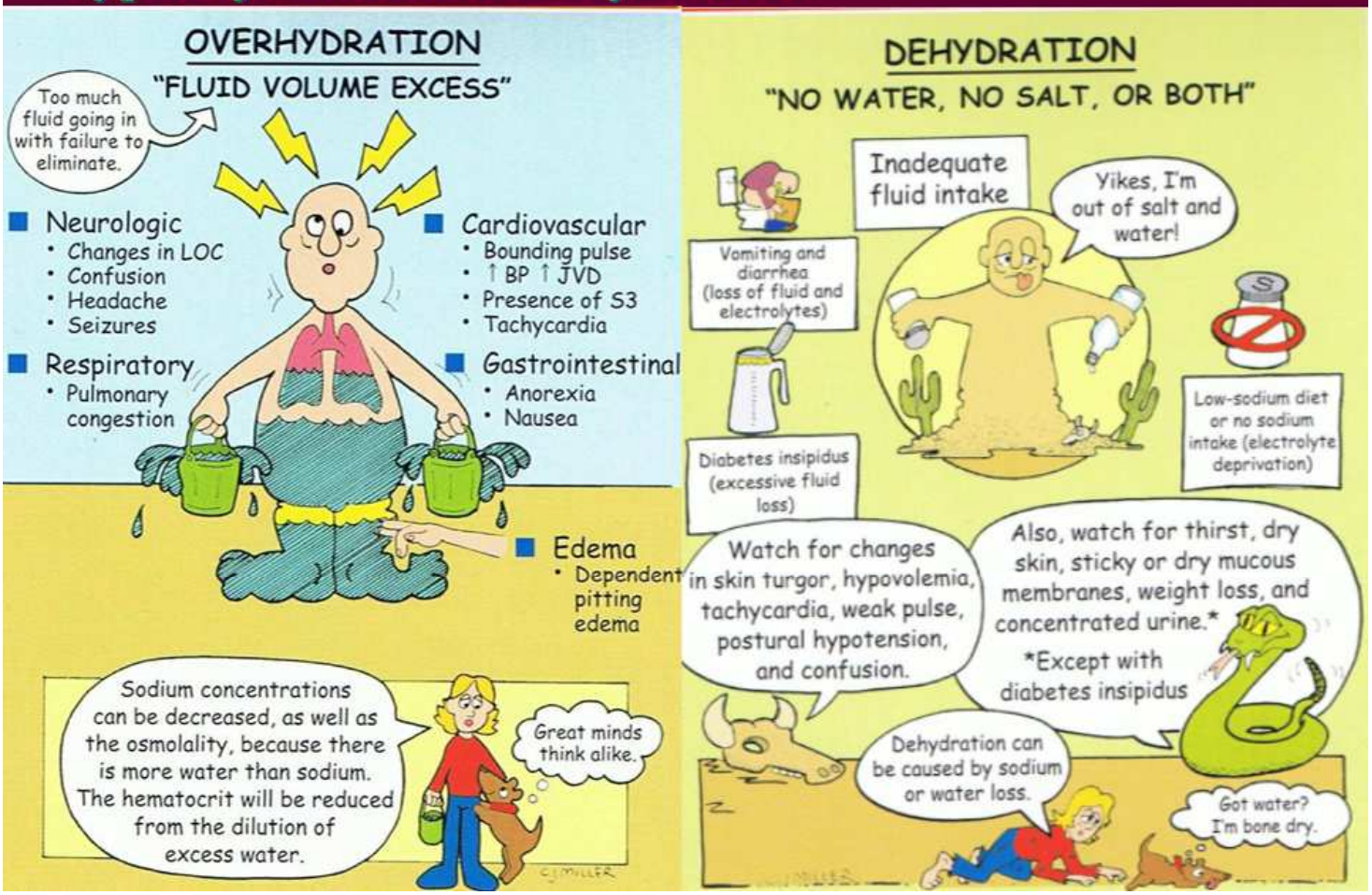
Hypotonic hyperhydration (water intoxication)

= Overload by pure solute free water/ hypotonic fluid



Typical situations
excessive drinking simple water
SIADH*, also stress, trauma, infections
gastric lavage
excessive infusion of glucose solution
Consequences
ECF volume expansion
ECF becomes hypotonic (hyponatremia)
water moves osmotically to ICF
ICF + ECF edemas
ADH production ↓ (water diuresis)

Hyperhydration vs dehydration



Natraemia

Sodium

Total body sodium content 3000 to 3500 millimoles; 90% located in the ECF

- **Intake:** 150 - 250 mmol/day;

Kidney: Each day 25000 mmol of Na is procesed

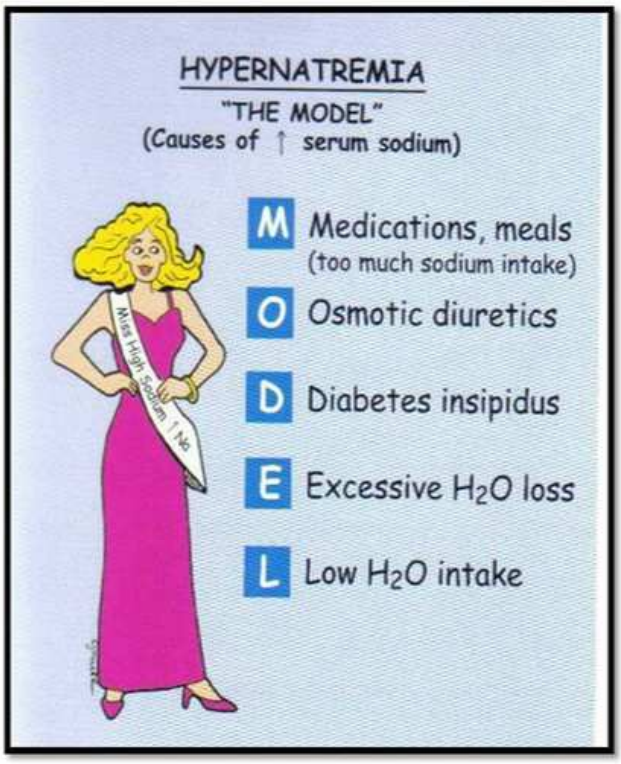
- **Proximal tubule.** 70- 75% actively reabsorbed by ATP pumps an energy dependent process. Water is iso-osmotically absorbed
- **Thick ascending limb** 15 to 25% ;Chloride ions (Cl-) are actively reabsorbed + Na; fluid is diluted to 50 to 100 mmol/kg
- **Distal convoluted tubule.** 1 -5% aldosterone (see below).
- **Collecting duct.** 1-2% aldosterone

- Increased intravascular volume (or effective arterial blood volume) → **renal sodium excretion** (decreased aldosterone plus increased ANP) .

- Decreased blood volume → **renal sodium retention** (increased aldosterone, decreased ANP)

Hypernatremia - Causes

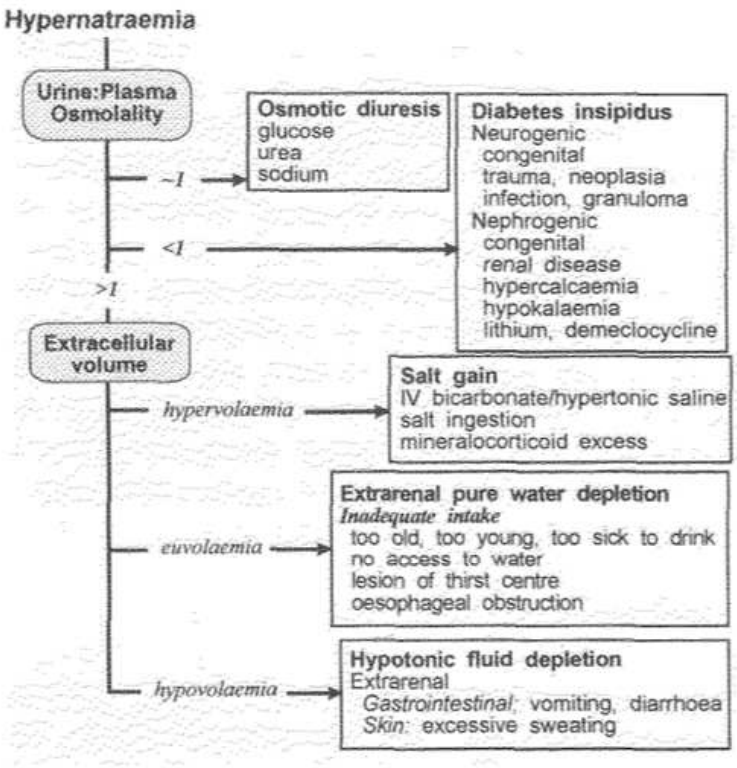
(1) Pure H2O depletion (euvolaemic)
Subject too old, too young, or too sick to drink
Access to water denied, Oesophageal obstructions
Thirst centre lesions, Inappropriate iv therapy.
(2) Na + H2O depletion (hypovolaemic; hypotonic fluid loss)
Extrarenal: GIT: vomiting, diarrhoea, Skin: excessive sweating
Renal: Osmotic diuresis: glucose, mannitol; Diuretic therapy
Diabetes insipidus: neurogenic, nephrogenic
(3) Salt gain (hypervolaemic; without proportional gain in water)
- Iatrogenic: iv hypertonic salineisodium bicarbonate
- Salt ingestion: intentional, accidental
- Primary mineralocorticoid excess (Conn sy.)



Hypernatremia - Manifestations

- **Euvoleamic:** More water depleted urine volume low + very concentrated (of high osmolality). Clinically the subjects do not appear dehydrated or hypervolaemic (oedemarous) .
- **Hypovoleamic**:inadequate fluid intake+ losing hypotonic fluid (more water than salt) high pulse rate, hypotension,

- Clinic: intracellular dehydration → **intracerebral damage (minor),** hyperkalaemia (redistribution from cells) **diminished insulin secretion** (? cause) → hyperglycaemia.



Hyponatraemia - Causes

(1) Euvolaemic (TBNa normal)

a) Pseudohyponatraemia (eutonic), Hyperlipidaemia (↑↑TG > 30 mmol/l)

b) Excess intracellular solute (hypertonic) hyperglycaemia (Glu 40 mmol/l)

c) Acute water overload (hypotonic): rapid water intake+ ▯ADH): + stress (post-surgery, psychogenic), hypothyroidism, cortisol deficiency

d) Chronic water overload (hypotonic): SIADH, drugs, renal failure, hypothyroidism, hypocortisolism

(2) Hypovolaemic (TBNa decreased)

a) Extrarenal causes (hypotonic) GIT: vomiting, diarrhoea; Skin: bums

b) Renal causes (hypotonic): Diuretic therapy, Addison's dis, Salt-losing nephritis

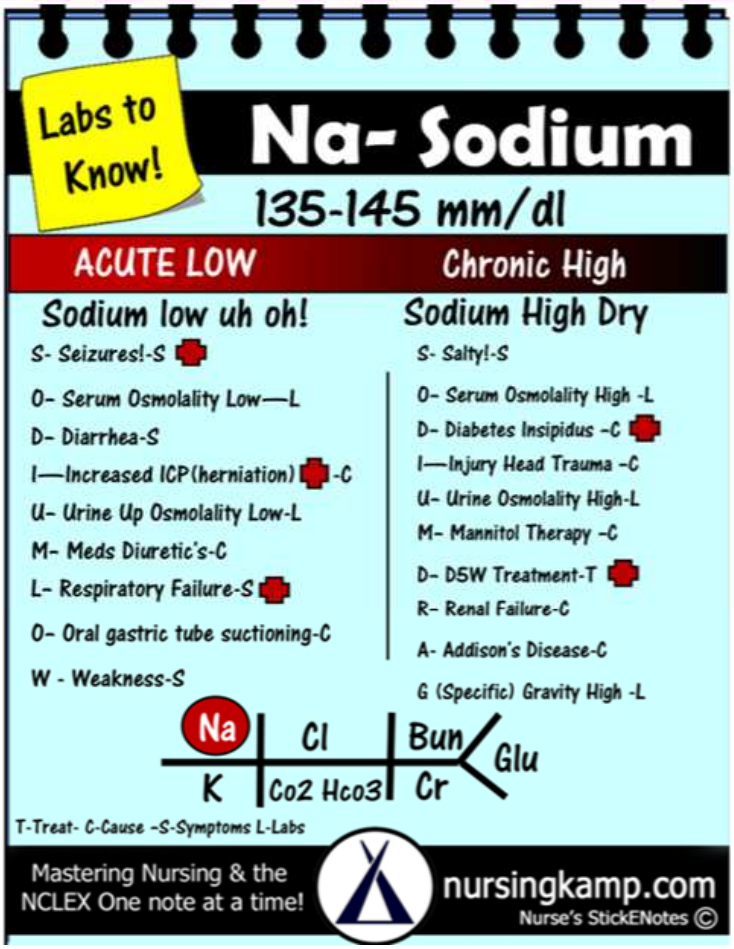
(3) Hypervolaemic (TBNa increased; edematous)

Cardiac failure, Nephrotic syndrome, Liver cirrhosis (hypotonic):

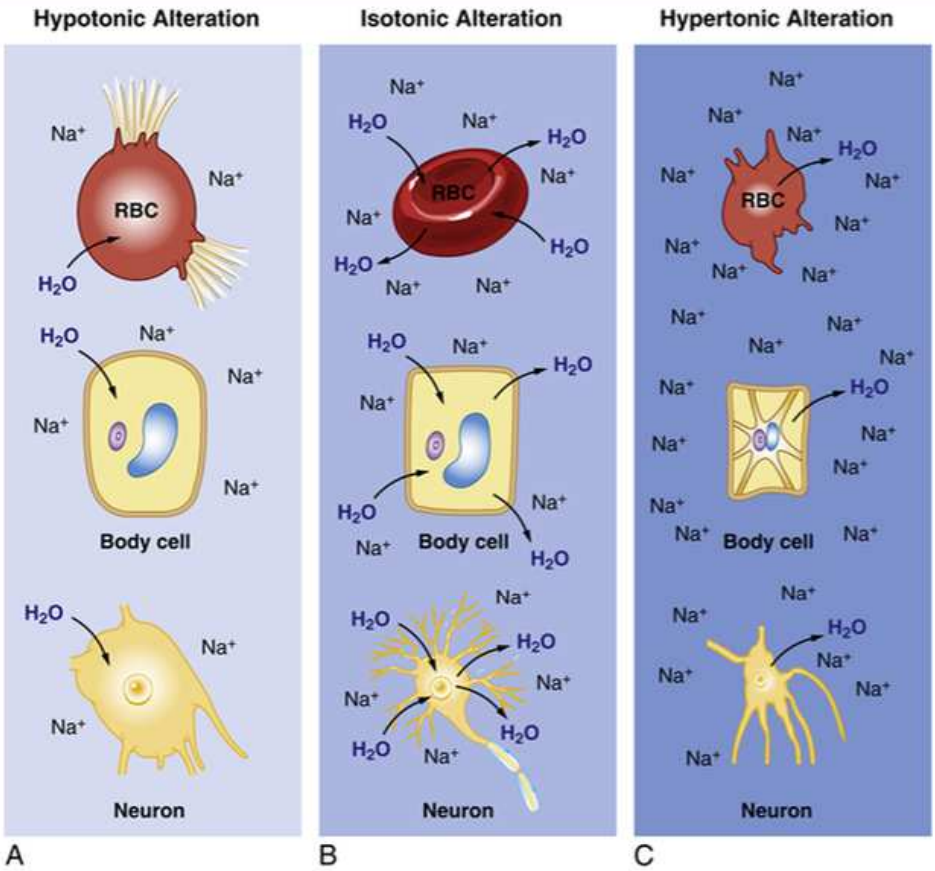
-

Hyponatremia - Manifestations

- **Na (S) < 130 mmol/L** If extracellular Na content remains constant, hyponatraemia will only occur if the extracellular **water content is increased** (i.e., sustained positive water balance (water intake>output).→ **decreased water excretion**
- Clinic: **cellular oedema** → cerebral confusion, decreased mentation, convulsions.



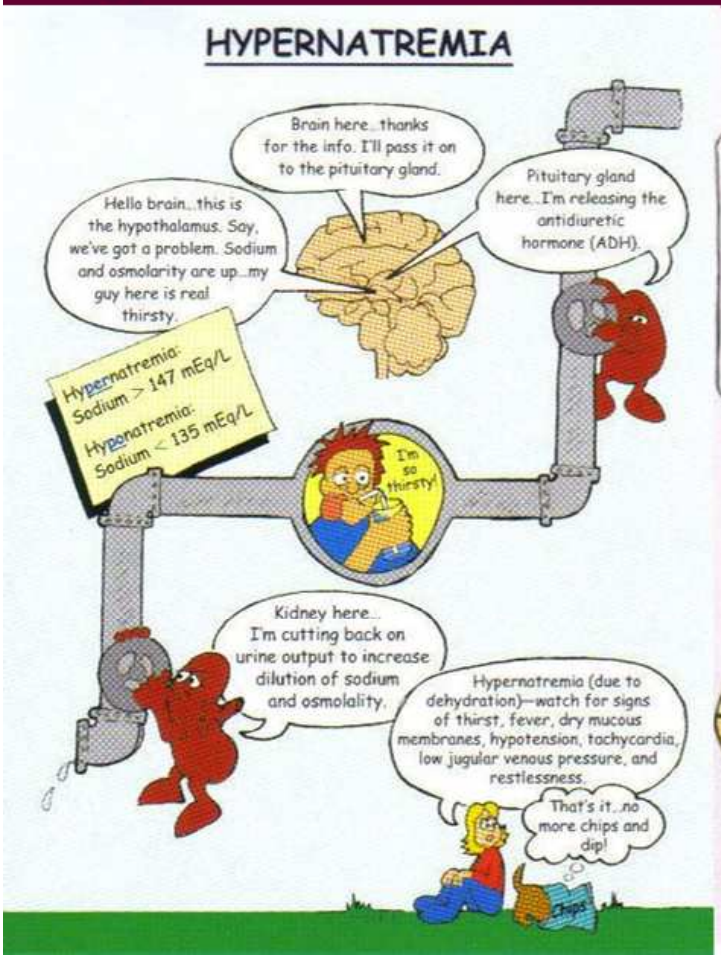
Osmotic effects

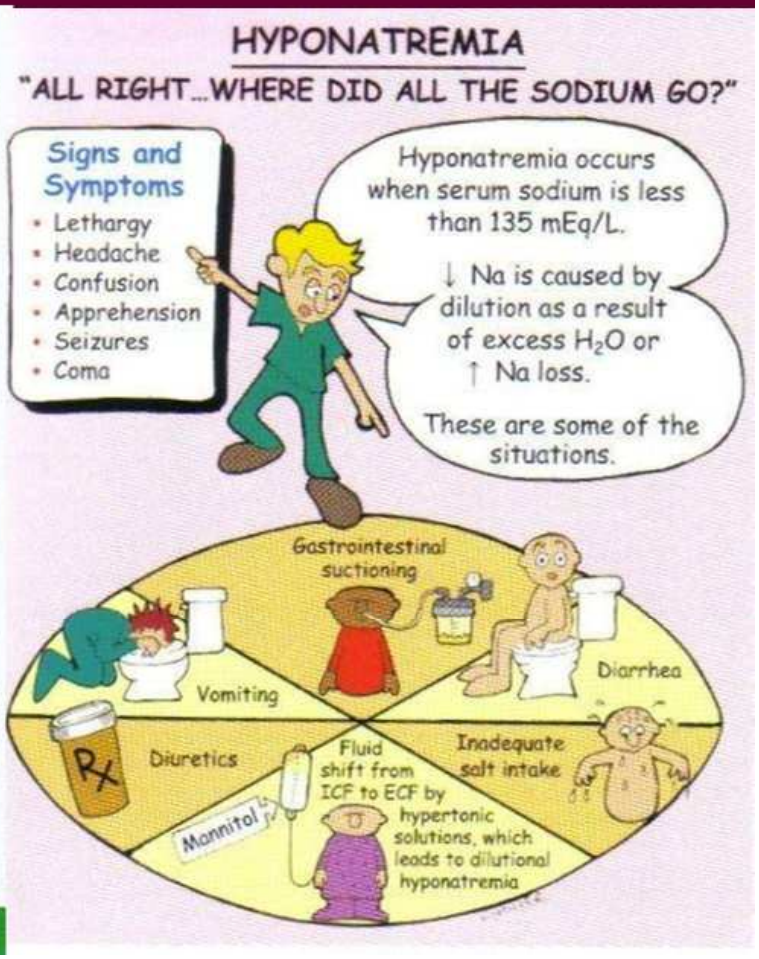


Hypotonic – swelling
Plasmoptysis in plants (certain level needed);
Cell lysis in animal cells – swelling and membrane tearing

Hypertonic – shrinkening
Desmolasmolysis in plants- membrane detach from the wall
Plasmorhisis in animal cell – shrinkening of the cells

Hyponatremia vs hypernatremia

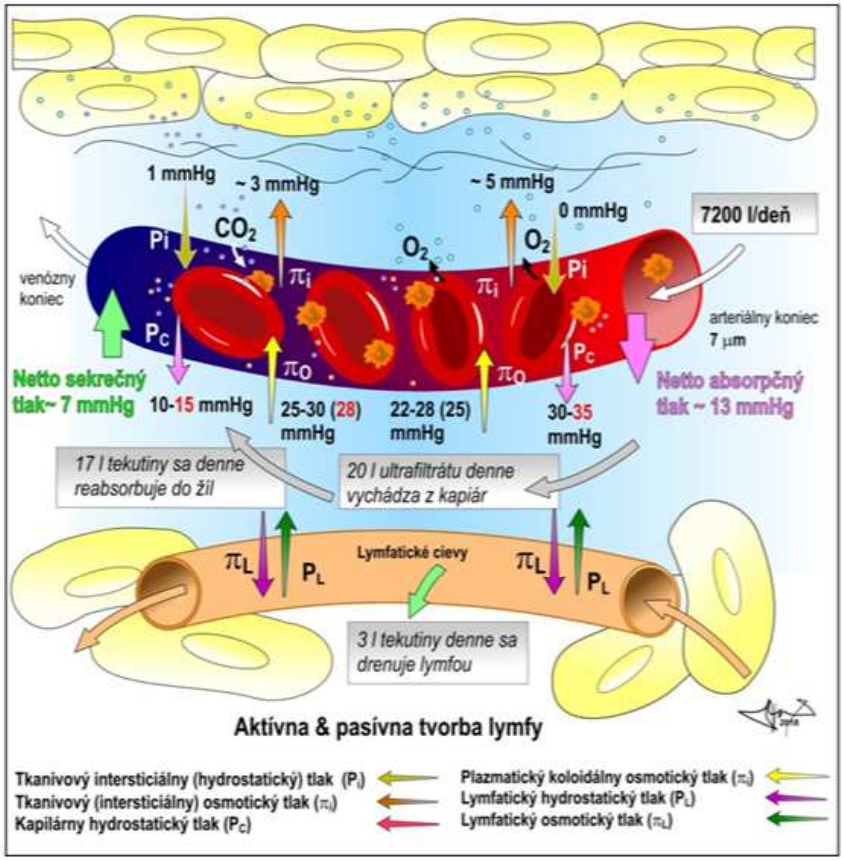




Edemas

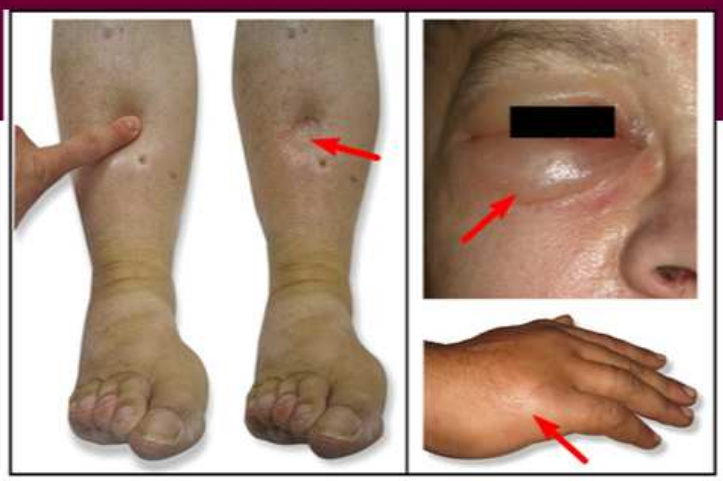
Edemas - Mechanisms

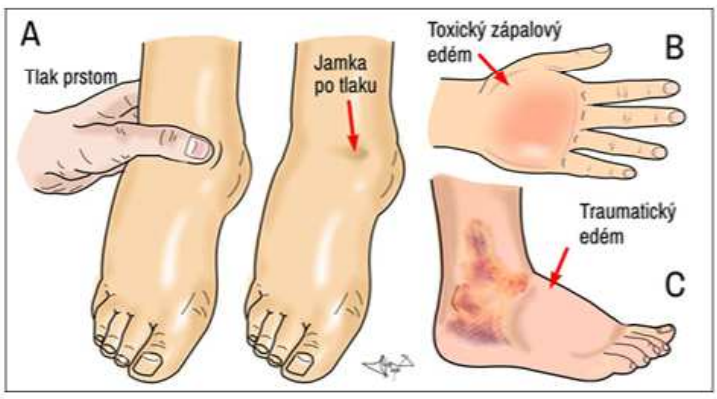
- **Hydrostatic blood pressure Pc**
e.g. venous occlusion, hypertension, renal retention of water + ions
- **Hydrostatic lymphatic press. PL**
e.g. lymph stasis (lymphadenitis), filiriasis, trauma, surgery, tumor)
- **Oncotic blood pressure Πo**
low albumin content (e.g. liver dis., proteinuria, kwasiorkor)
- **Osmotic tissue pressure Πι**
e.g. inflammation
- **Osmotic lymphatic pressure Π L**

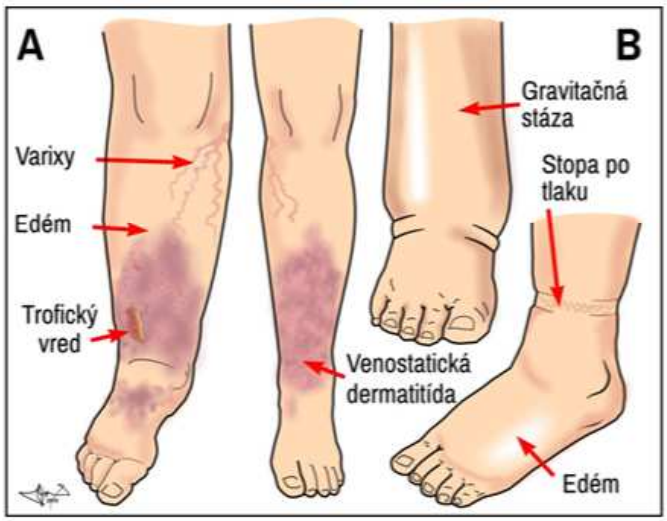


Forms of edema

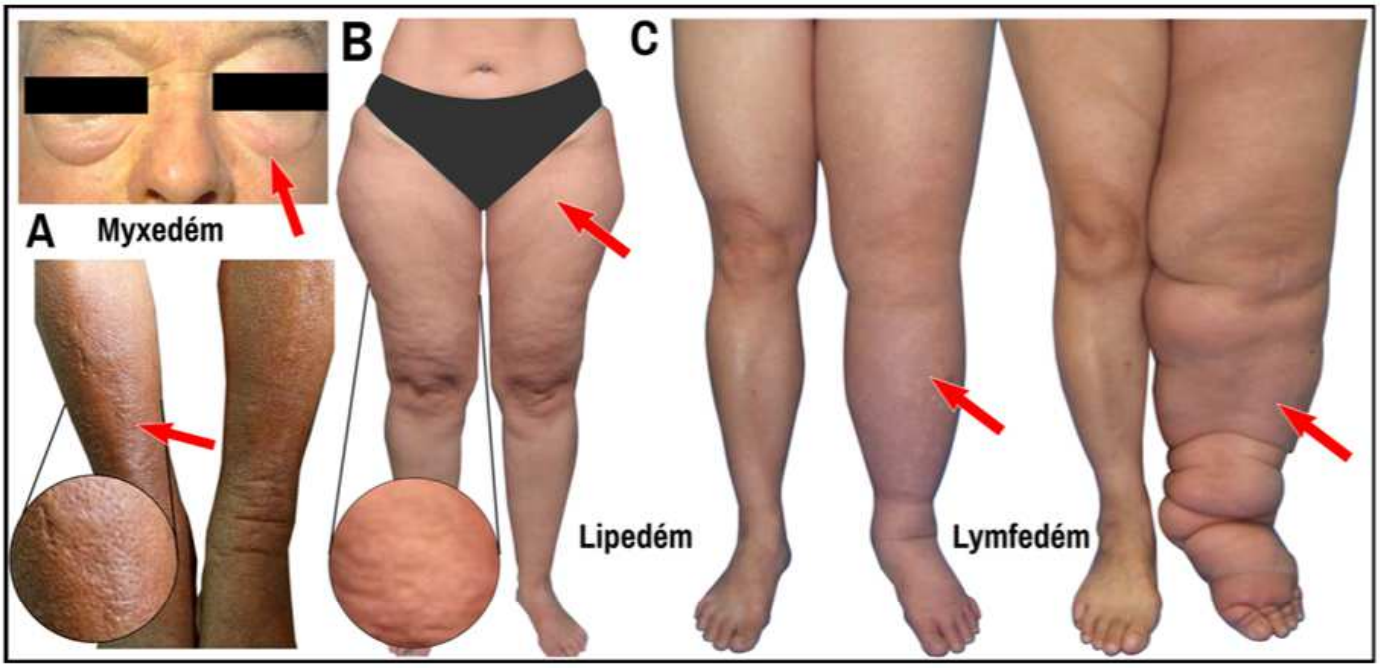
- **Traumatic edema** - damage to the tissue and vasculature – leak
- **Inflammatory edema** – imllamm. transudate or exudate (+ allergy, autoim.)
- **Hypoosmolar edema** – nephritic sy., kwasiorkor, hepatic failure
- **Cardiac edema** – right heart failure, congestive failure (pitting edema)
- **Venostatic edema** - failure of venous reeurn (trombophlebitis, phlebotrombosis)





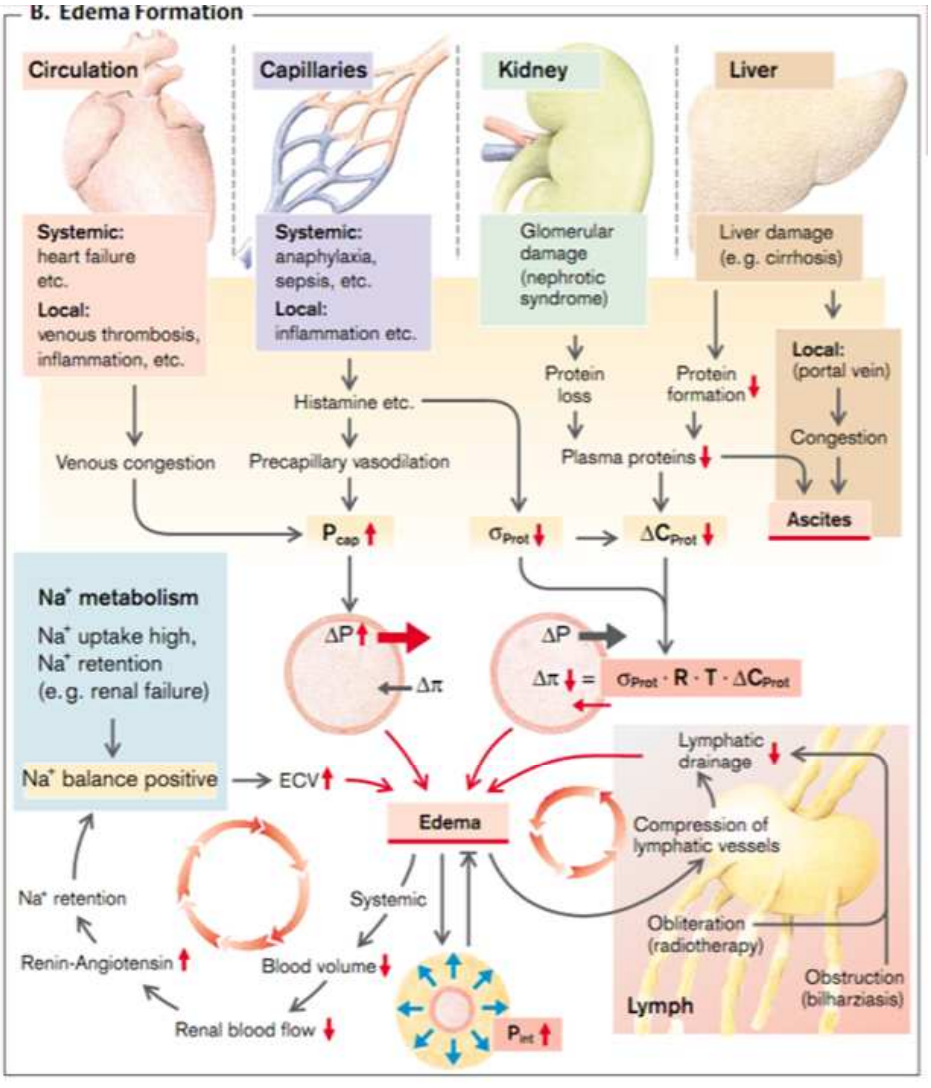


Edemas



- **Lymphedema –** impaired lymphatethic drainage (unilateral, bilateral)
- **Myxdema** – not a real edema ; change in compoisition of interstitial tissue (thyroid dis.)
- **Lipedema -** not a real edema; prominent local fat tissue accumalation

Edemas

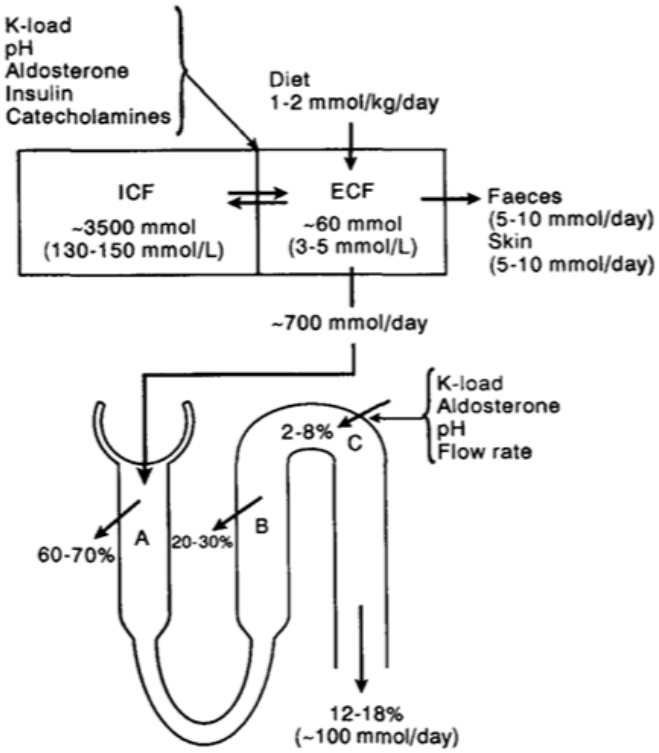


Potassium

Potassium

- TB(K^+) 3000- 3500 mmol; K^+(IC) 120-150 mmol/l; **K^+ (S) 3.5-5.0 mmol/l = 2-3%TB** = 70-80 mmol,
- Intake: diet (single meal = 50 mmol of K+
- 50% of added K^+ goes into cells; 40% is excreted by the kidneys (2 to 3 hours) + 10%.rest in ECF.
- **Insulin cellular K+ uptake independent of Glu glucose) → Insulin to treat hyperkalaemia**.
- Insulin deficiency (DM type I) --> results in potassium 'leaking' from cells.
- **Catecholamines.** release of K' from the liver 1 increase cellular K' uptake → hypokalaemia.
- **Aldosterone**. release of K^+ by the distal renal tubular cells (→ hypokalemia), large gut cells, sweat gland cells and mammary gland cells
- **Alkalosis** → hypokalaemia (cell uptake of K+ exchange for H+), **Acidosis** (hyperchloraemic not due to organic acids)→ hyperkalaemia

Handling with potassium



Hypokalemia - Causes

Hypokalemia = [K'] (S) < 3.5 mmol/l, is the commonest disorder of potassium homeostasis

A. Decreased intake
- Adrenal steroids, Chronic laxative abuse

B. Extrarenal loss (GIT)
- Vomiting, Severe diarrhea, Laxatives
- Gastric outlet obstruction

C. Transcellular Shifts
- Metabol.alkalosis, Insulin overdose
- Catechoamines, salbutamol, Ba toxicity, ephedrine, Periodic paralysis

D. Renal loss
- Mineralocorticoid excess, Bartter's synd., Renal tubul.acidosis; Mg deficiency,
- Levodopa, ATB (gentamicin, amino-glycosides, penicillin), Thiazides + loop diuretics, acetozolamide

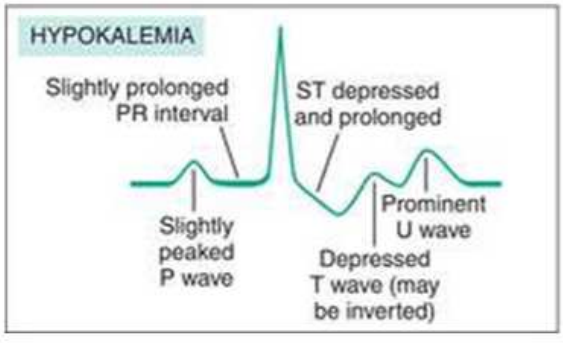
E. Endocrine
- Diabetic ketoacidosis

HYPOKALEMIA – DRUG INDUCED

TRANSCELLULAR K SHIFT	⇑ RENAL K LOSS	⇑ K LOSS IN STOOL
Epinephrine	Acetazolamide	Phenolphthalein
Pseudoephedrine	Thiazides	Na polystrene sulfonate
Salbutomol	Loop diuretics	
Theophylline	Fludrocortisone	
Ritodrine	Pencillin	
Verapamil	Aminoglycoside	
Chloroquine	Amphotericin B	
Insulin overdose	Cisplatin	

Hypokalemia - Manifestation

Hypokalemia is fast and dangerous !!!
- Nervous sy.: Lethargy, confusion, drowsiness
- Muscle weakness, fatigue, paralysis Loss of tendon reflexes
- **CVS:** tachyarrhythmis, irregular rhythm;
- ST depression + T(flatening/ inversion), In
- severe cases: U high ; wide QRS and QT
- Bradycardia, postural hypotension
- **GIT**: nausea, vomiting, smooth muscle weakness: slow motility, paralytic ileus)
- Polyuria, nocturia (hypokalaemic nephropathy)



Hyperkalemia - Causes

(1) Pseudohyperkalaemia
- Haemolysis, Leucocytosis, Thrombocytosis

(2) Excess intake to ECF (very rare)
- Oral or IV therapy

(3) Intra->extracellular shifts
- Metabolic acidosis (inorganic), Insulin deficiency; Diabetes, $\alpha + \beta 2$- agonists
- Drugs: digoxin toxicity, succinylcholine
- Cell shrink: (hypertonicity: glucose, sodium)
- Hyperkalaemic periodic paralysis; excercise
- Tissue necrosis:crush sy., burns, malignancy

(4) Decreased renal excretion
- ***Renal failure:*** Acute (oliguria), Chronic
- Defect of cortical collecting tubule

(4) Decreased renal excretion *(cont.)*
- ***Drugs:*** Potassium-sparing diuretics: amiloride, Prostaglandin inhibitors (NSAIDs)

- ***Mineralocorticoid deficiency syndromes***

- Low cortisol/ aldosterone: Addison's dis. Adrenal hyperplasia, C21 -hydroxylase defect
- Selective aldosterone deficiency: Hypore-ninaemic hypoaldosteronism, Prostaglandin inhibition (indomethacin), triamterene, spironolactone

- ***Mineralocorticoid resistant syndromes***

- Interstitial nephritis, Sickle cell disease
- Obstructive uropathy , Systemic lupus erythrematosus, Amyloidosis, Pseudohypoaldosteronism.

Hyperkalemia - Causes

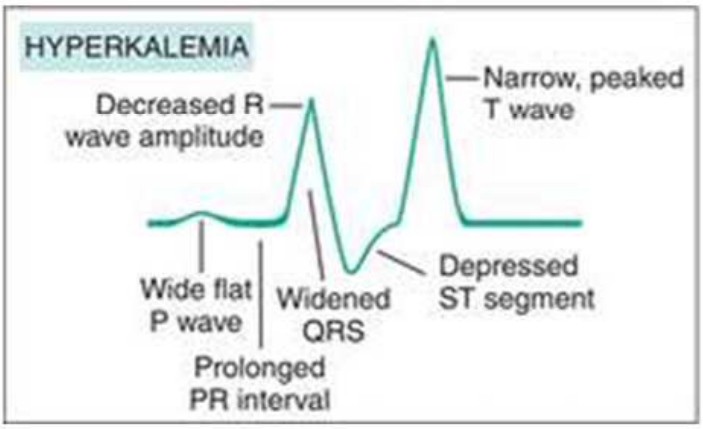
Spurious
- Thrombocytosis (> 1,000,000/mm^3)
- Leukocytosis (> 50,000/mm^3)
- Hemolysis
- Repeated fist-clenching with tourniquet in place

Endogenous
- Impaired potassium excretion
  - Renal insufficiency or failure
- Metabolic acidosis
  - Pseudohypoaldosteronism type II (also known as Gordon's syndrome; familial hyperkalemia and hypertension)
  - Mineralocorticoid deficiency (including Addison's disease)
  - Hyporeninemic hypoaldosteronism (type IV renal tubular acidosis)
  - Hereditary enzyme deficiencies
- Excessive potassium load
  - Chemotherapy causing tumor lysis
  - Muscle breakdown (rhabdomyolysis)
  - Massive tissue breakdown (burns, trauma)
  - Blood administration (particularly with large transfusions of older "bank" blood)
  - Renal tubular acidosis
  - Hemolysis
  - Diet (rarely the sole cause), salt substitutes

Exogenous
- Drug-induced hyperkalemia
  - Potassium supplements
  - Drugs that block the sodium channel in the distal nephron (trimethoprim, pentamidine)
  - Potassium-sparing diuretics (amiloride, triamterene)
  - Drugs that block sodium, potassium-ATPase activity in the distal nephron (cyclosporine)
  - Drugs that block aldosterone production (ACEis, ARBs)
  - Drugs that antagonize triggering of the mineralocorticoid (aldosterone) receptors (spironolactone, eplerenone, finerenone)
  - Antibiotics (including penicillin G, penicillin derivatives, trimethoprim)
  - Azole antifungals
  - NSAIDs (including selective COX-2 inhibitors)
  - ß-blockers
  - Heparin
  - Tacrolimus
  - Succinylcholine
  - Digoxin
  - Arginine, lysine
- Herbal supplements
  - Milkweed, lily of the valley, Siberian ginseng, Hawthorn berries
  - Preparations from dried toad skin or venom (traditional and folk medicines such as Bufo, Chan Su, Senso)
- Impaired transcellular shift-insulin deficiency
- Hypertonicity (as occurs in uncontrolled diabetes)

Hyperkalemia – Manifestations

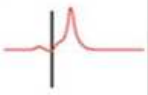
- **Nerv.sy.:**
  - Muscle twitches / cramps, paresthesia
  - Irritability, anxiety, hyperreflexia
- **CVS:**
  - Hypotension, decreased contractility
  - Dysrhythmias, irregular rhythm
  - **Peak T (typical)**
  - **Wide QRS, ST neg. P wave wide**
- Other: diarrhea, respiratory distress

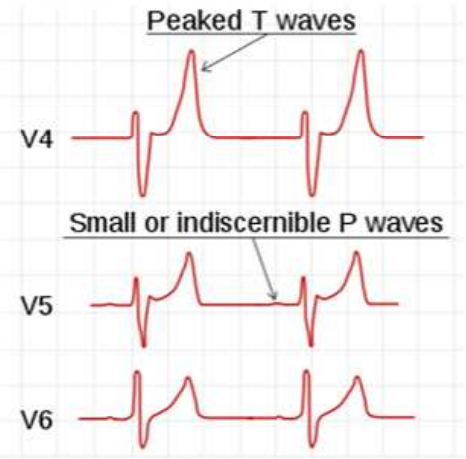


Medications that can cause hyperkalemia	
Medication	**Mechanism**
Nonselective beta-adrenergic blockers	Interferes with beta-2-mediated intracellular potassium uptake
ACE inhibitor, ARB, K^+sparing diuretics	Inhibition of aldosterone or the ENaC channel
Digitalis	Inhibition of the Na-K-ATPase pump
Cyclosporine	Blocks aldosterone activity
Heparin	Blocks aldosterone production
NSAIDs	Decreases renal perfusion resulting in decreased K^+delivery to the collecting ducts
Succinylcholine	Causes extracellular leakage of potassium through acetylcholine receptors

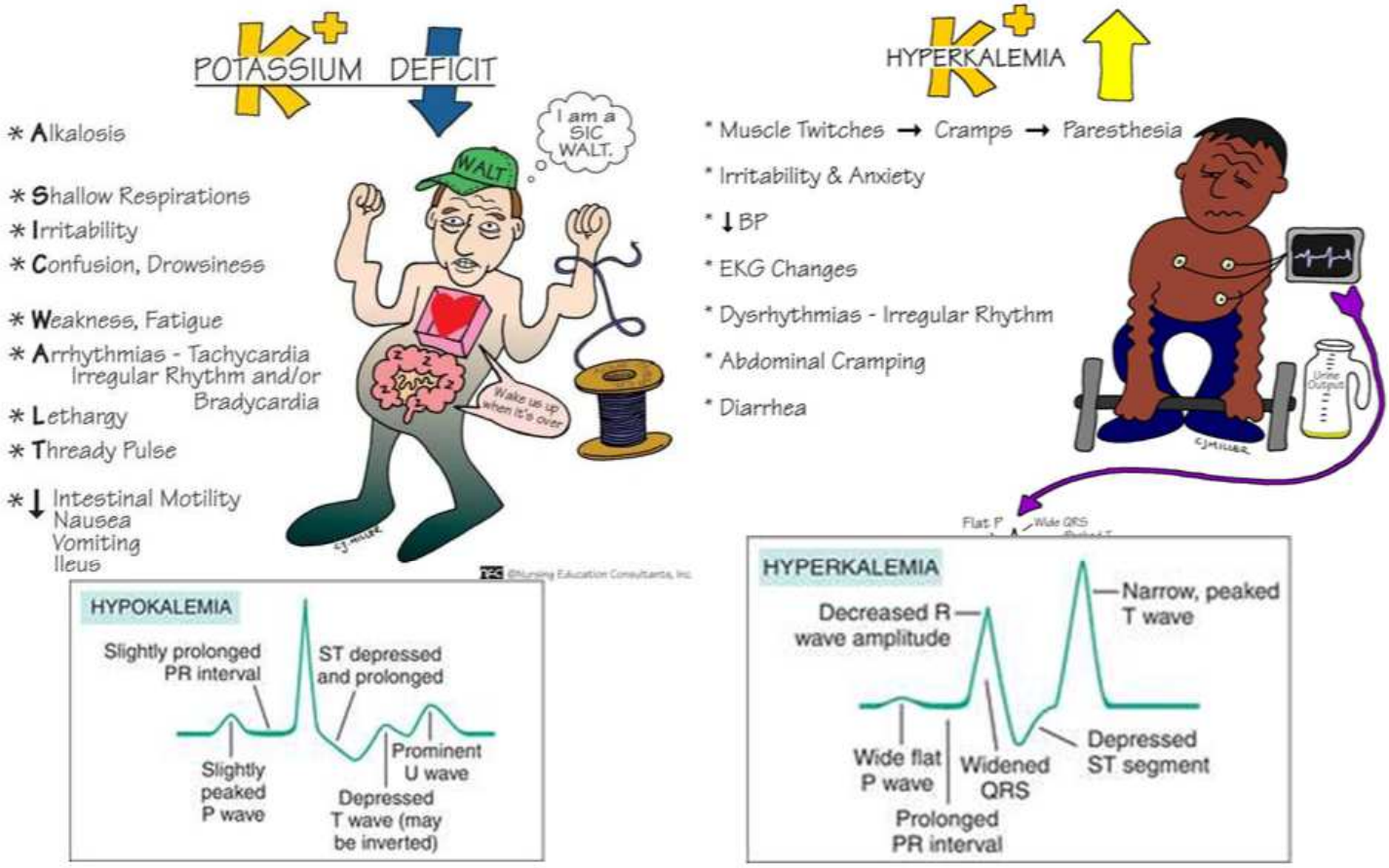
Hyperkalemia – Manifestations in ECG

- $K^+(S)$ >5.5 mmol/L: repolarization abnormalities: **Peaked T waves** = the earliest sign)
- $K^+(S)$ >6.5 mmol/ L: progressive paralysis of the atria: **P wave widens and flattens, PR segment lengthens, P waves eventually disappear**
- $K^+(S)$ >7.0 mmol/ L: is associated with conduction abnormalities and bradycardia; Prolonged QRS interval with bizarre morphology; High-grade **atrioventricular block with** slow junctional and ventricular escape rhythms; **conduction block** (bundle branch blocks, fascicular blocks); **sinus bradycardia** or **slow atrial fibrillation**; sine wave appearance (a pre-terminal rhythm)
- $K^+(S)$ > 9.0 mmol/l; may cause cardiac arrest due to asystole; ventricular fibrillation

Serum Potassium	Typical ECG Appearance	Possible ECG Abnormalities
Mild (5.5-6.5 mEq/L)		Peaked T waves Prolonged PR segment
Moderate (6.5-8.0 mEq/L)		Loss of P wave Prolonged QRS complex ST-segment elevation Ectopic beats and escape rhythms
Severe (> 8.0 mEq/L)		Progressive widening of QRS complex Sine wave Ventricular fibrillation Asystole Axis deviations Bundle branch blocks Fascicular blocks

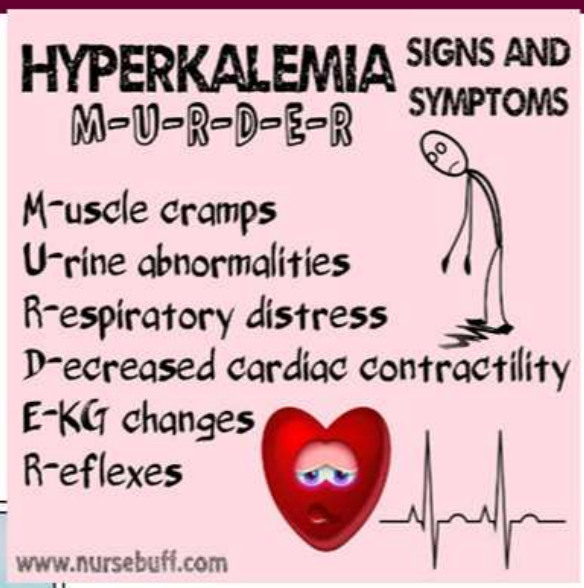


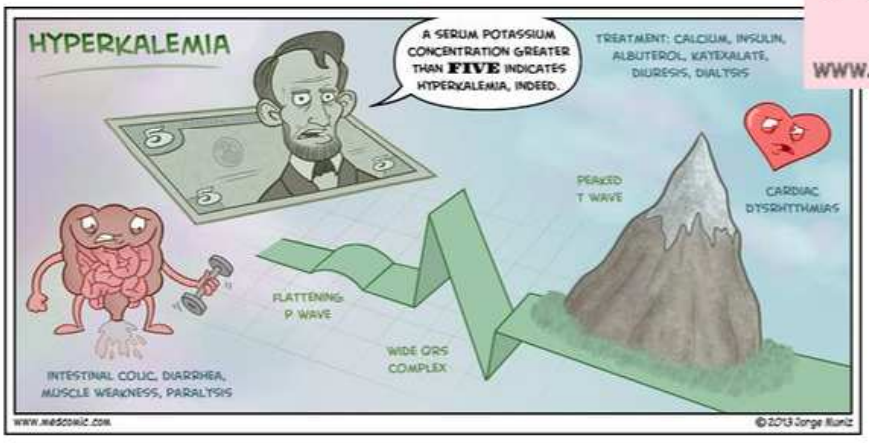
Hypokalemia and hyperkalemia - manifestations



Hyperkalemia

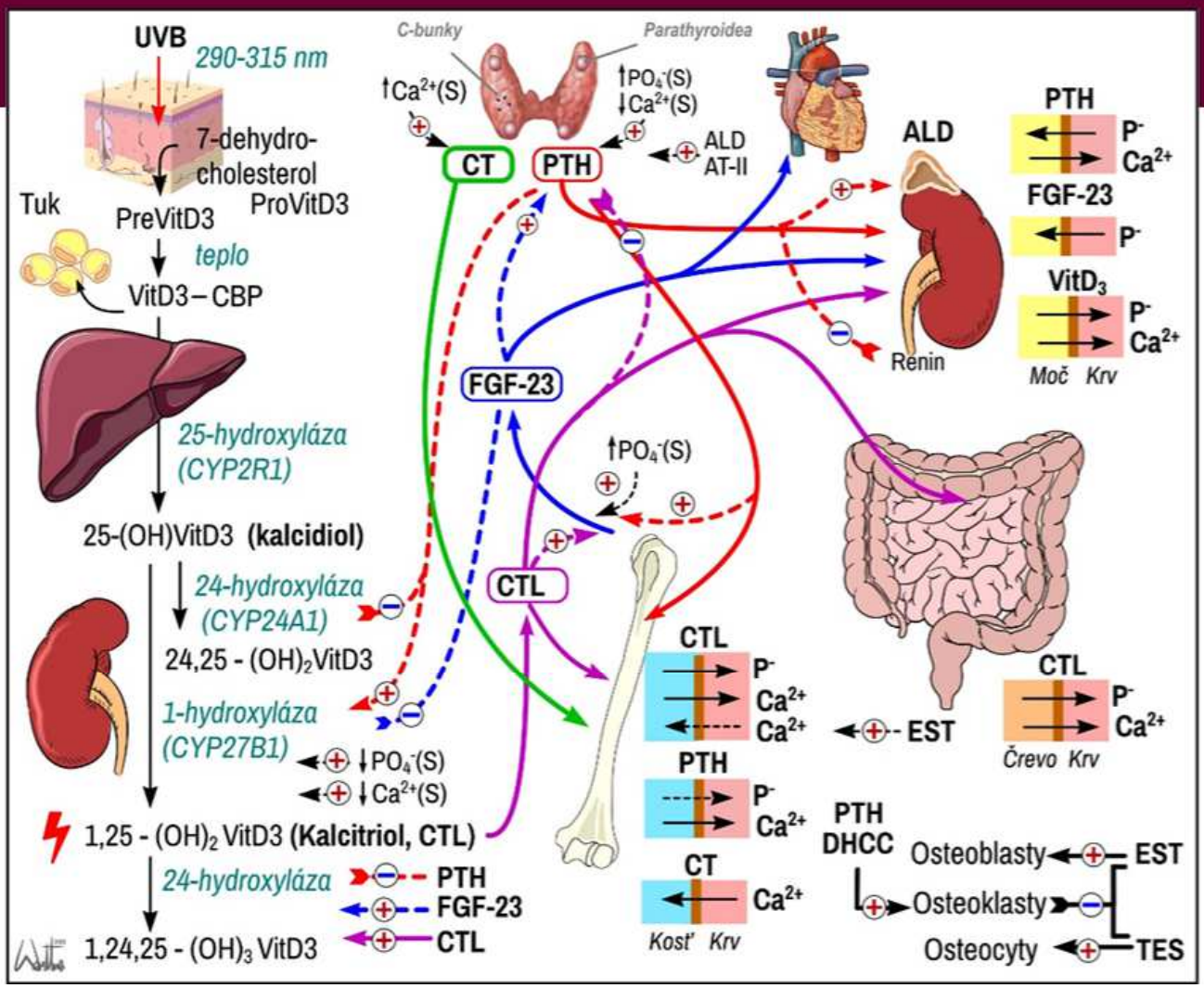
Serum potassium	Typical ECG appearance	Possible ECG abnormalities
Mild (5.5-6.5 mEq/L)		Peaked T waves Prolonged PR segment
Moderate (6.5-8.0 mEq/L)		Loss of P wave Prolonged QRS complex ST-segment elevation Ectopic beats and escape rhythms
Severe (>8.0 mEq/L)		Progressive widening of QRS complex Sine wave Ventricular fibrillation Asystole Axis deviations Bundle branch blocks Fascicular blocks

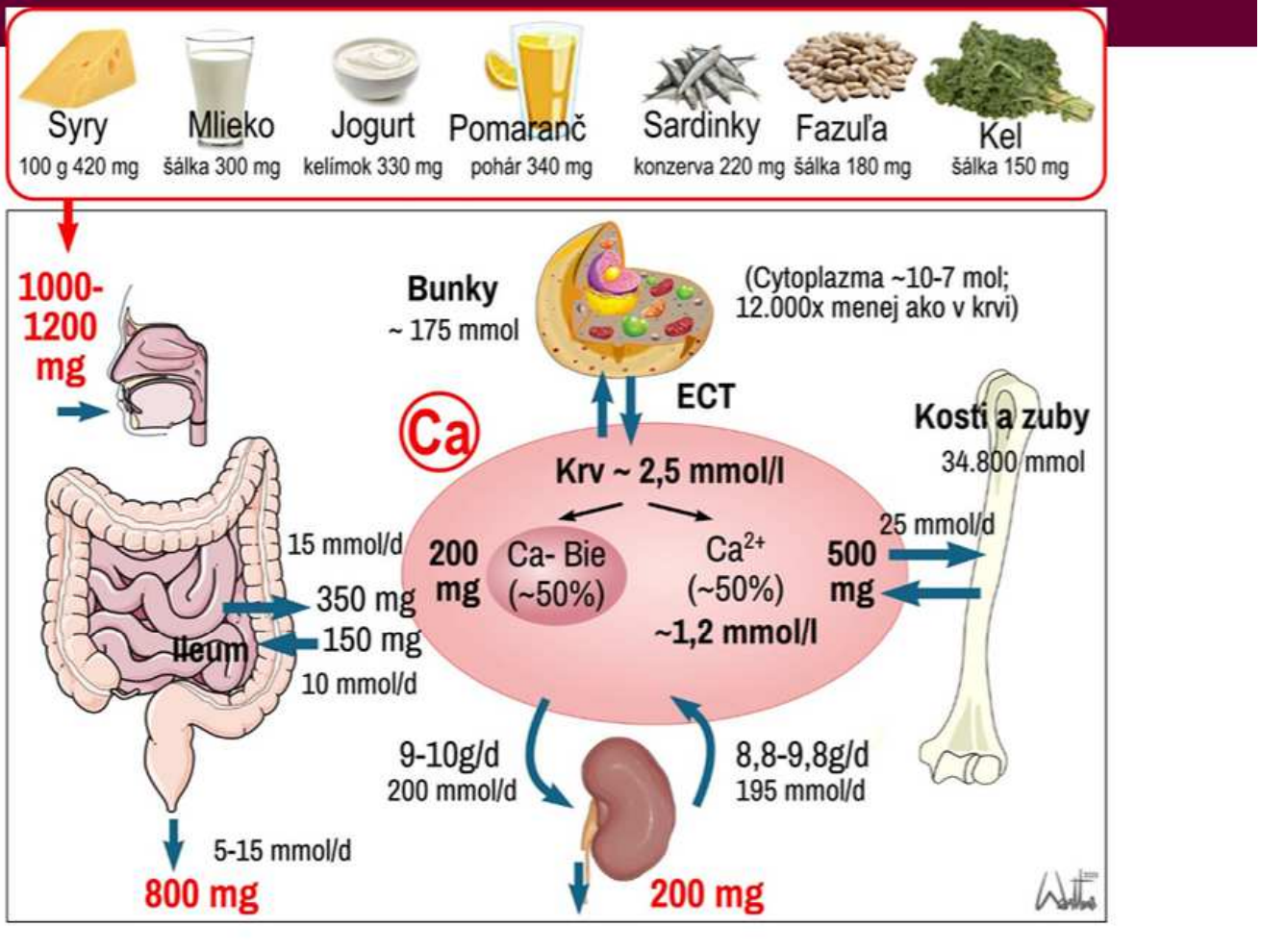


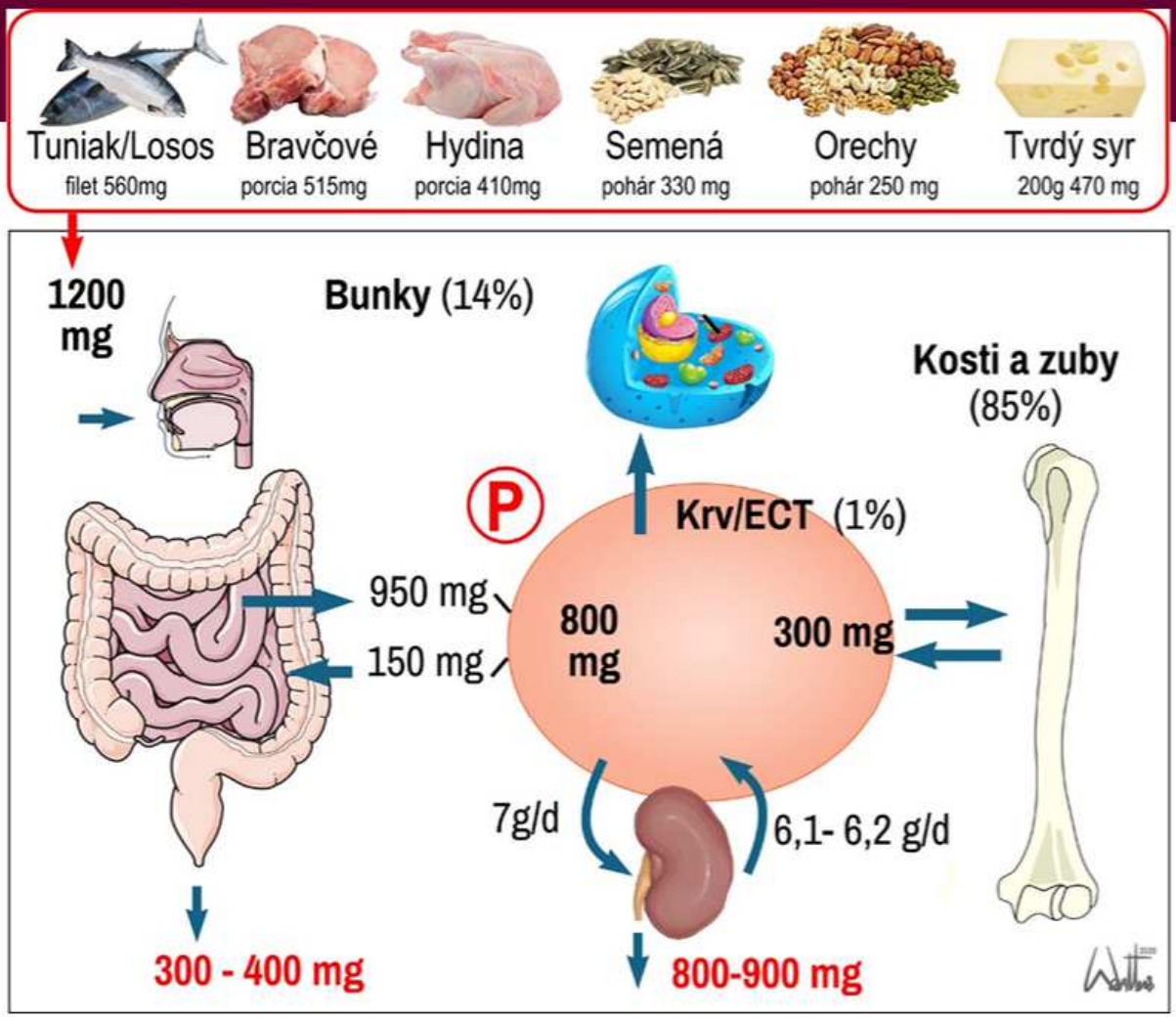


Normal range	Causes of elevation	Causes of decline
Sodium (Na): 135 – 145 mEq/L	**Hypernatremia:** Excessive loss of water through GI system, lungs, or skin; fluid restriction, certain diuretics, hypertonic IV solutions, tube feeding; hypothalamic lesions, hyperaldosteronism, corticosteroid use, Cushing's syndrome, diabetes insipidus	**Hyponatremia:** Congestive heart failure, cirrhosis, nephrosis, excess fluid intake, syndrome of inappropriate antidiuretic hormone secretion (dilutional hyponatremia); sodium depletion, loss of body fluids without replacement, diuretic therapy, laxatives, nasogastric suctioning, hypoaldosteronism, cerebral salt-wasting disease
Potassium (K): 3.5 – 5.0 mEq/L	**Hyperkalemia:** Aldosterone deficiency, sodium depletion, acidosis, trauma, hemolysis of red blood cells, potassium-sparing diuretics	**Hypokalemia:** Lack of dietary intake of potassium, vomiting, nasogastric suctioning, potassium-depleting diuretics, aldosteronism, salt-wasting kidney disease, major GI surgery, diuretic therapy with inadequate potassium replacement
Calcium (Ca): 8.5 – 10.5 mg/dL	**Hypercalcemia:** Excessive vitamin D, immobility, hyperparathyroidism, potassium-sparing diuretics, ACE inhibitors, malignancy of bone or blood	**Hypocalcemia:** Hypoparathyroidism, malabsorption, insufficient or inactivated vitamin D or inadequate intake of calcium, hypoalbuminemia, diuretic therapy, diarrhea, acute pancreatitis, bone cancer, gastric surgery
Magnesium (Mg): 1.5 – 2.5 mg/dL	**Hypermagnesemia:** Excessive use of magnesium-containing antacids and laxatives, untreated diabetic ketoacidosis, excessive magnesium infusions	**Hypomagnesemia:** Malabsorption related to GI disease, excessive loss of GI fluids, acute alcoholism/cirrhosis, diuretic therapy, hyper- or hypothyroidism, pancreatitis, preeclampsia, nasogastric suctioning, fistula drainage

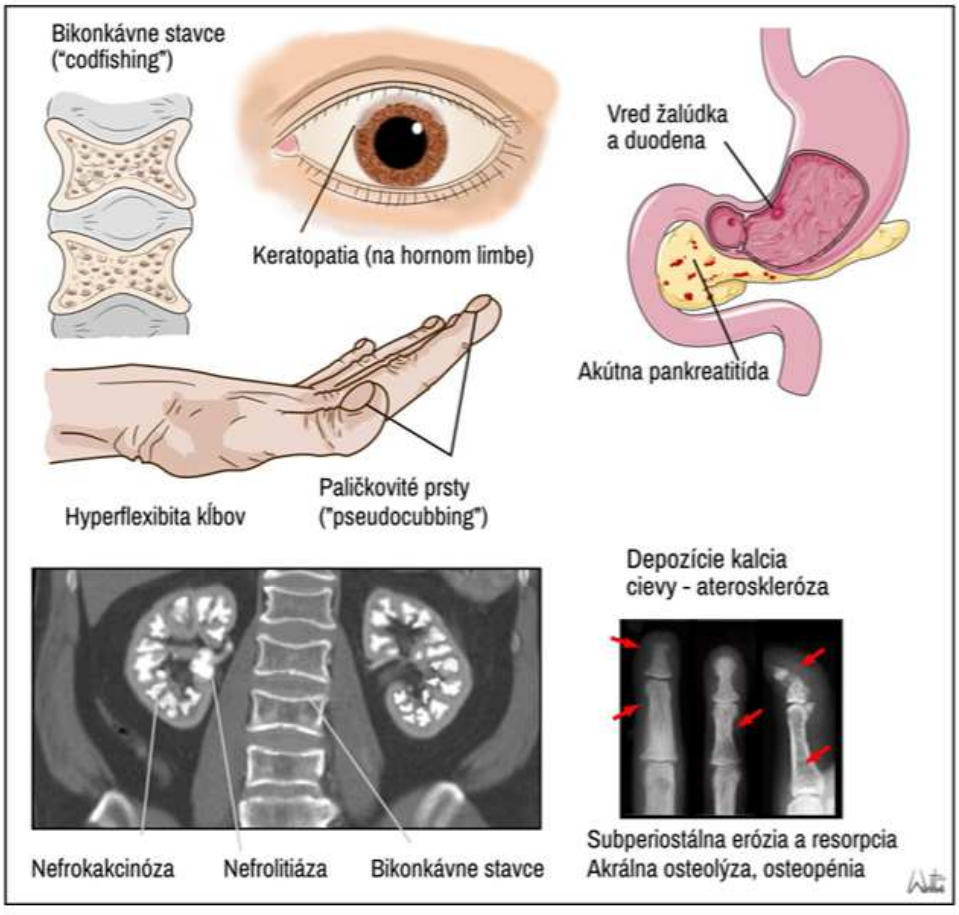
Calcium


UVB
290-315 nm
7-dehydro-cholesterol
Tuk
PreVitD3
ProVitD3
teplo
VitD3 – CBP
25-hydroxyláza (CYP2R1)
25-(OH)VitD3 (kalcidiol)
24-hydroxyláza (CYP24A1)
24,25 - (OH)2VitD3
1-hydroxyláza (CYP27B1)
1,25 - (OH)2 VitD3 (Kalcitriol, CTL)
24-hydroxyláza
1,24,25 - (OH)3 VitD3
PTH
FGF-23
CTL
C-bunky
Parathyroidea
↑Ca2+(S)
↑PO4-(S)
↓Ca2+(S)
CT
PTH
ALD
AT-II
FGF-23
↑PO4-(S)
CTL
↓PO4-(S)
↓Ca2+(S)
ALD
Renin
PTH
P-
Ca2+
FGF-23
P-
VitD3
P-
Ca2+
Moč Krv
CTL
P-
Ca2+
Ca2+
EST
CTL
P-
Ca2+
Črevo Krv
PTH
P-
Ca2+
CT
Ca2+
Kosť Krv
PTH
DHCC
Osteoblasty
EST
Osteoklasty
Osteocyty
TES

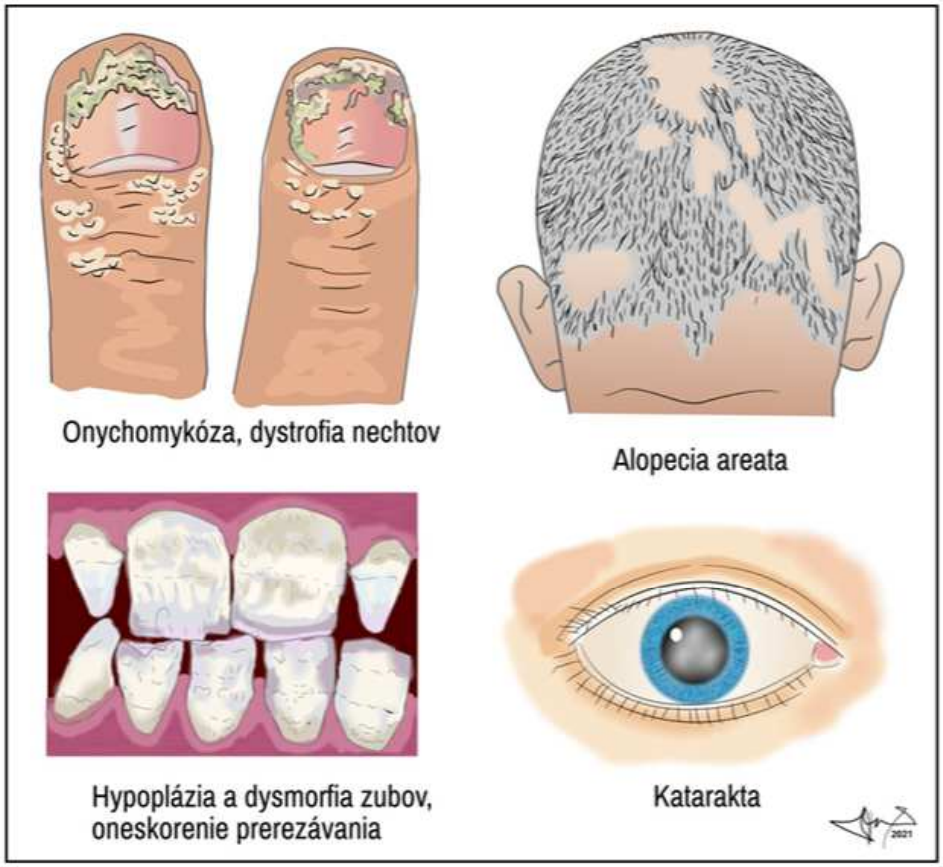

Syry
100 g 420 mg
Mlieko
šálka 300 mg
Jogurt
kelímok 330 mg
Pomaranč
pohár 340 mg
Sardinky
konzerva 220 mg
Fazuľa
šálka 180 mg
Kel
šálka 150 mg
1000-1200 mg
Bunky
~ 175 mmol
(Cytoplazma ~10-7 mol; 12.000x menej ako v krvi)
ECT
Ca
Krv ~ 2,5 mmol/l
Kosti a zuby
34.800 mmol
25 mmol/d
200 mg
Ca- Bie (~50%)
Ca2+ (~50%)
~1,2 mmol/l
500 mg
15 mmol/d
350 mg
150 mg
10 mmol/d
Ileum
9-10g/d
200 mmol/d
8,8-9,8g/d
195 mmol/d
5-15 mmol/d
800 mg
200 mg



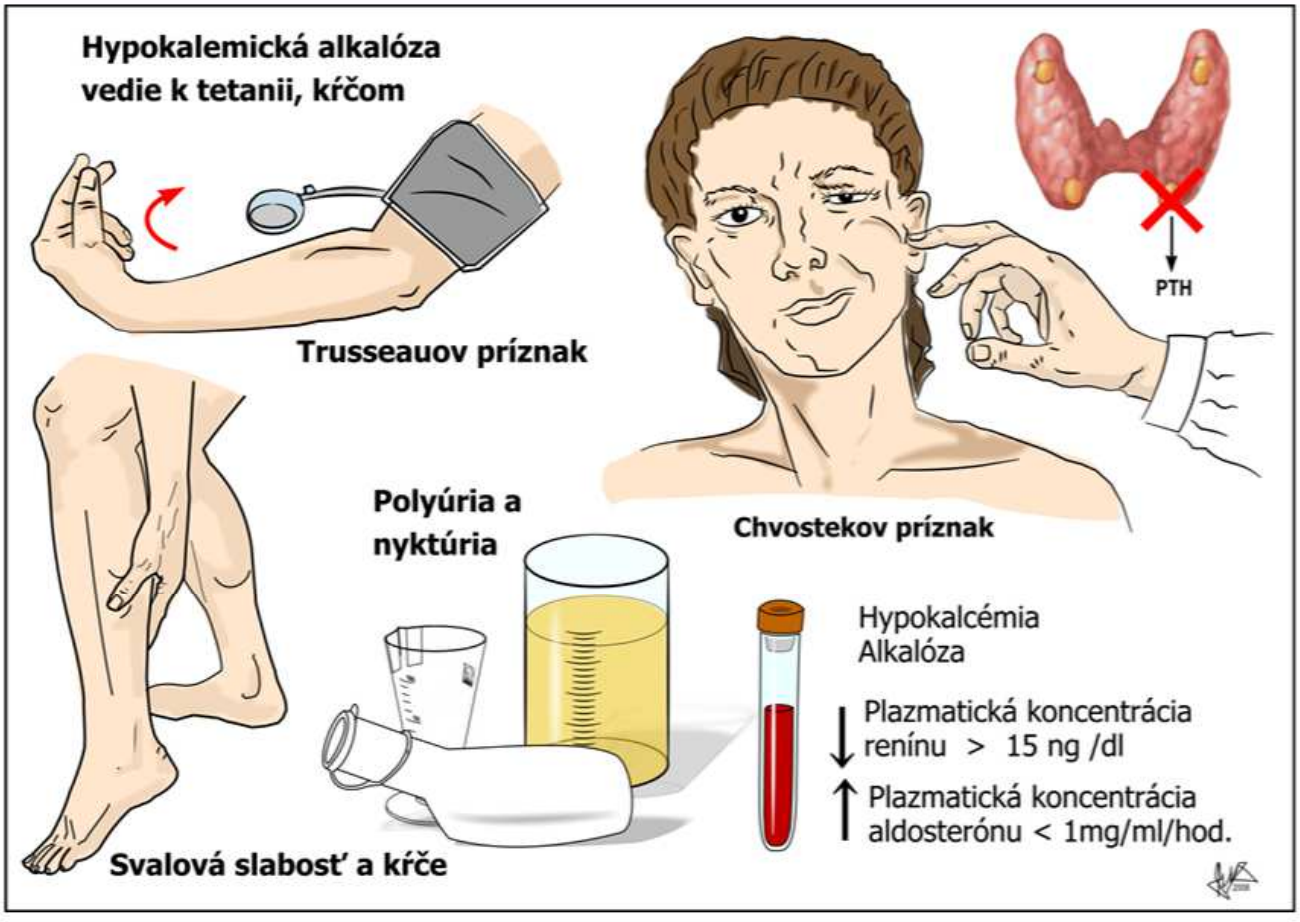
Hypokalcamia



Hypocalcaemia



Hypokalcaemia



Hypercalcemia – Causes 1

- Norm: 2.15 – 2,55 mmol/l ; > 2,60 mmol/l
- Occ: 1% of the general population and 4% of the hospital population
- 95-98% of the causes: malignancy (in hospitalised patients); primary hyperparathyroidism. vitamin D excess

- **Primary hyperparathyroidism**
  25: 10,000 F: M = 3: 1 > 65y
- solitary adenoma (80-90%); chief cell hyperplasia (15%), carcinoma (<2%) MEN II
- asymptomatic, osteoporosis; osteitis fibrosa cystica; hypercalcaemia, hypercalciuria can result in nephrocalcinosis, nephrolitihiasis, and renal failure.

Malignancy
Solid tumours
Breast, bronchus, cervix, ovary kidney
Haematological
Multiple myeloma, leukaemia, Hodgkin's disease, non-Hodgkin's lymphoma

Hyperparathyroidism
Primary, tertiary, Multiple endocrine adenosis

Non-malignant/non-hyperparathyroidism
Vitamin D excess syndromes
Overdose, sarcoidosis, granulomas
Iatrogenic
IV calcium infusion
Increased bone reabsorption
Thyrotoxicosis, immobilisation, vitamin A excess
Renal failure
Post-dialysis, post-acute renal failure
Decreased renal excretion
Familial benign hypercalcaemia, thiazide diuretics, lithium therapy
Miscellaneous
Milk-alkali syndrome, Addison's disease, acromegaly, phaeochromocytoma

Hypercalcemia – Causes2

- **Malignant disease** (-40% of all of hypercalcaemia causes; 20% of subjects with malignancy) abrupt onset of hypercalcaemia (>3.5 mmol/l).
- Most common> Ca of lungs, breast, kidney, myelomas, leukaemias, lymphomas (Hodgkin's dis.)
- *Tu with bone metastases.(40%)* breast cancer (osteoclast-activating factors), multiple myeloma
- *Tu w/o bone metastases.(30-40%)* → hypercalcaemia of malignancy (squamous cell carcinomas of lung, oesophagus), Ca of kidney, ovary|, pancreas). → PTHrP (141 AA)
- Lab: ↑Ca, ↓ PO_4- , ↑ALP, ↓ PTH level.

- **Lymphoma-related hypercalcaemia and vitamin D excess**, Ca^{2+} (> 4.0 mmol/l) increased circulating levels of 1,25-DHCC from 25-HCC causing vitamin D intoxication.

! ↑*Ca,* ↑ *PO_4-* , Hypophosphataemia is characteristic of the humoral hypercalcaemia of malignancy., ALP normal ,

- **Vitamin D excess**

The hypercalcaemia is due to increased gut absorption → suppresses PTH → nhibits renal phosphate excretion → hyperphosphataemia. ALP normal; in lymphomas amd number of granulomatous diseases such as sarcoidosis, tuberculosis, and histoplasmosis, all of which include monocytic cells containing the - 1 ahydroxylase enzyme.

Hypercalcemia – Causes3

Familial benign hypercalcaemia

- hypocalciuric hypercalcaemia, AD, strats < 10 y
- mild hypercalcaemia (<3,00 mmol/L),, hypermagnesaemia, normal oe elevated PTH levels, and relative hypocalciuria.
- that the disorder is due to a mutation of
- the ionised calcium receptor gene.

Thyrotoxicosis

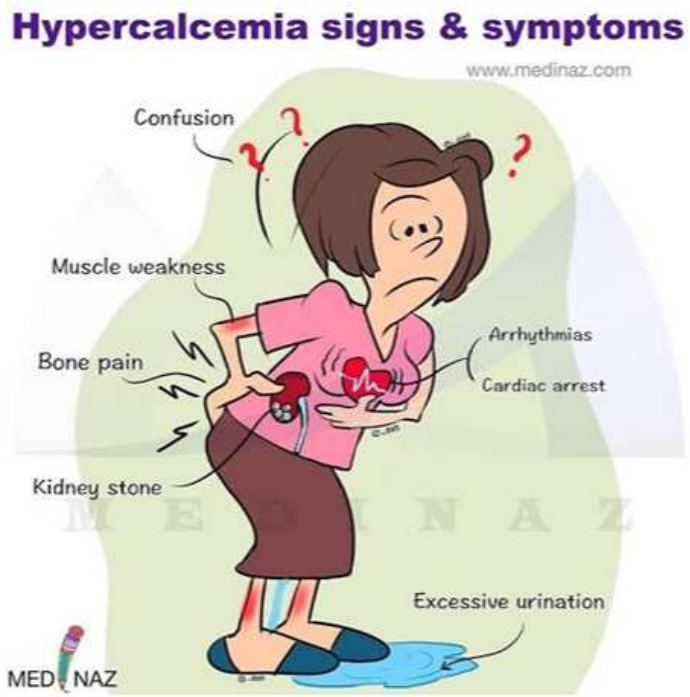
- Thyroid hormones increase the rate of bone turnover

Chronic lithium therapy

- associated with hypothyroidism (due to inhibition of TSH action), diabetes insipidus (interference with AVP activity) and hypercalcaemia.

Hypercalcemia - Manifestations

- *Age and sex* (women over 60 y. familial benign hypercalcaemia usually presents in childhood)
- *Presence or absence of malignancy*
- *Bone pain* (malignancy, primary hyperparathyroidism)
- *Drug history* (particularly vitamin D preparations, lithium, thiazides)
- *Kidney stones* (common in hyperparathyroidism but not in malignancy)
- *Family history* (familial benign hypercalcaemia)



Hypocalcemia - Causes

- Ca (S) <2,15 mmol/L.
- mild degrees 1,90 - 2,10 mmol/l common transient and
- probably of no importance

- Mild hypocalcaemia (1,8-2,00 mmol/l) are : hypoalbuminaemia, renal failure and acute pancreatitis,
- Serious hypocalcaemia (<1.80 mmol/l hypoparathyroidism, vitamin D deficiency sy.

Hypoalbuminaemia
Factitious
EDTA contamination, citrated blood
Decreased intake
Vitamin D deficiency (Table 6.3)
Malabsorption
Inadequate parenteral nutrition
Decreased flux from bone
PTH deficiency: hypoparathyroidism, hypomagnesaemia
Bone resistance to PTH: uraemia, hypomagnesaemia, pseudohypoparathyroidism
Increased bone uptake
Hungry bone syndrome
Vitamin D therapy for osteomalacia
Extra-skeletal sequestration
Acute pancreatitis
Hyperphosphataemia
Renal failure (multifactorial)
Drug therapy
EDTA, calcitonin, mithramycin, phosphates

Hypocalcemia – Causes2

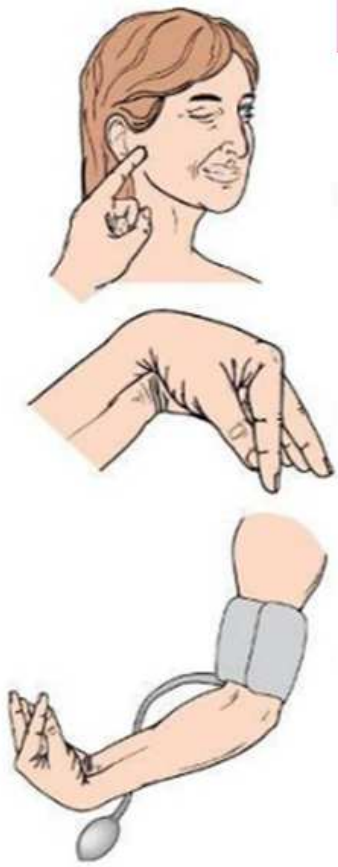
Vitamin D deficiency

- → hypocalcemia, hypophosphatemia, rickets in children, osteomalacia in adults.
- decreased calcium absorption by the gut, i.e. vitamin D + calcium absorption → hypocalcaemia + ↑ PTH secretion + ↑ renal phosphate excretion
- ↑ T osteoblastic activity hypophosphataemia

Environmental
Inadequate exposure to UV light
Nutritional
Decreased intake (dietary deficiency)
Malabsorption syndromes
Decreased 25-hydroxylation
Liver disease
Anticonvulsant therapy (phenytoin)
Decreased 1α-hydroxylation
Renal disease
Endorgan resistance to 1,25-DHCC
Renal disease
Anticonvulsant therapy
Increased clearance of 1,25-DHCC
Nephrotic syndrome, Alcohol, Aminoglutethimide, Phenytoin

Hypocalcemia - Manifestations

- Altered mental status, impaired memory and content, Personality disturbances, hallucinations,
- Weakness, Tetany, Seizures
- Positive Trousseau's or Chvostek's sign
- Laryngeal stridor, Laryngospasm
- Bronchospasm, Dysphagia
- Tingling around the mouth or in the extremities
- Papilledema, hyperkeratosis, coarse brittle hair, dry skin, dental hypoplasia
- Osteodystrophy, rickets, osteomalacia
- Cataracts,
- Cardiac signs- prolonged QT interval, QRS and ST segment changes



Phosphate

Hypophosphatemia - Causes

Severe hypophosphataemia (<0.25 mmol/L:

- Phosphate binding in the gut (AlOH3)
- Hyperalimentation,
- Nutritional recovery syndrome
- Respiratory alkalosis
- Treatment of diabetic ketoacidosis
- Treatment of acute alcoholism
- Recovery from burns

- **Decreased intake.** Phosphate is present bothin food from animals and plants
- hypophosphataemia may occur as a consequence of decreased intake -- ***parenteral nutrition***, inadequate PO4- supplement in the IV fluids.
- aluminium hydroxide - binds phosphate in the gut lumen

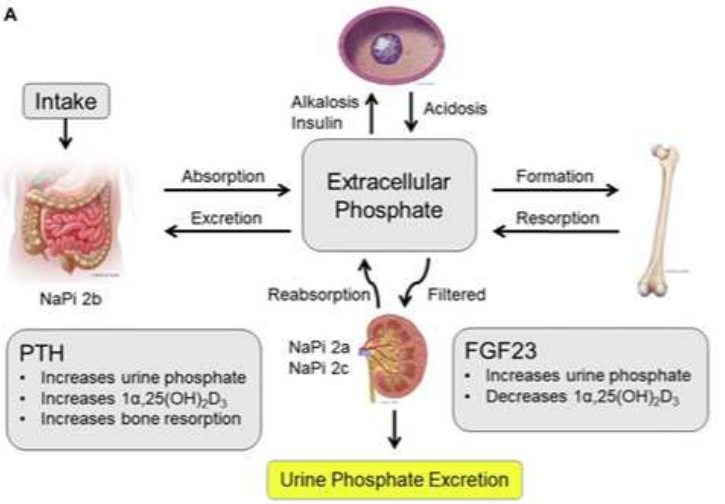
Decreased intake
Starvation, inadequate IV nutrition, malabsorption syndromes, vomiting, aluminium hydroxide therapy

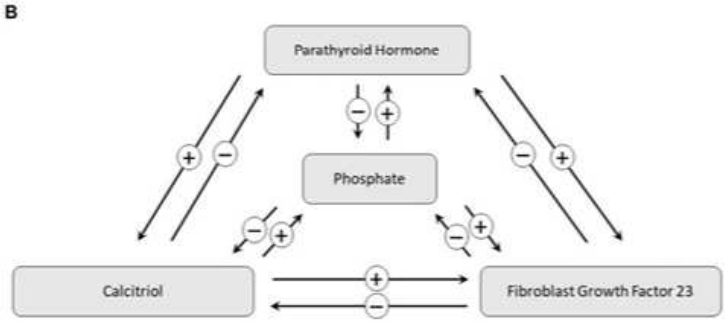
Increased cell uptake
High carbohydrate meal, insulin therapy, nutritional recovery syndrome, respiratory alkalosis

Increased renal excretion
Diuretic therapy, magnesium depletion, renal phosphate leak (Fanconi syndrome, vitamin D-resistant rickets), hyperparathyroidism (primary and secondary)

Multiple causes
Alcoholism, diabetes mellitus, burns, hyperalimentation

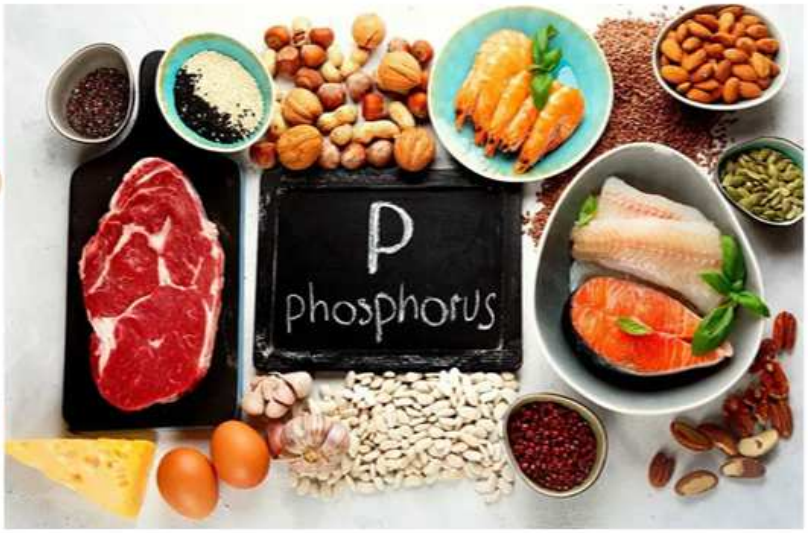
Hypophosphatemia - Causes





Hypophosphatemia - Causes

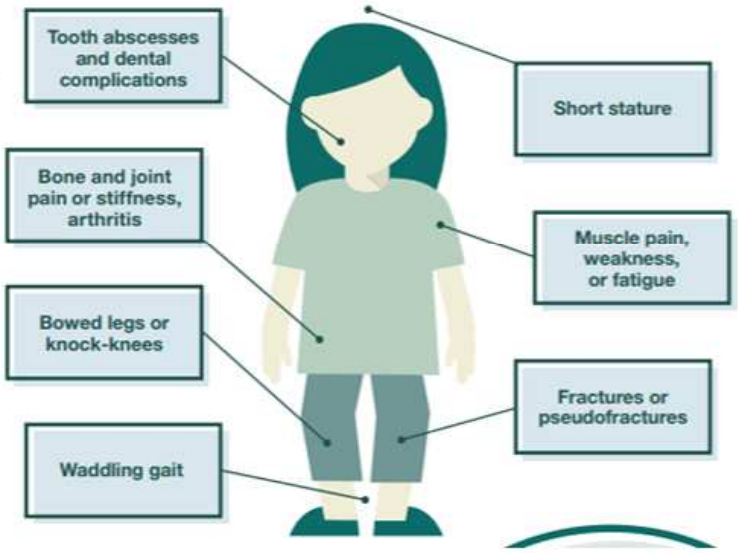
- **Increased cellular uptake:** common causes of severe hypophosphataemia → insulin therapy, respiratory alkalosis.
- **Insulin therapy** → cellular phosphate uptake (hypophosphatemia)
- in the treatment of diabetic ketoacidosis
- with insulin + refeeding after starvation (nutritional recovery syndrome) e.g. or alcoholism).
- **Respiratory alkalosis.** Intracellular alkalaemia → ↑ glycolysis + cellular phosphate uptake
- **Increased renal excretion.** In the Fanconi sy,, familial hypophosphataemic
- rickets (vitamin D resistant type), Diuretics, including osmotic diuretics, and hypomagnesaemia → renal phosphate excretion.



Hypophosphatemia - Manifestations

- Short-term even severe hypophosphataemia, → no appear clinical problems

- Long term phosphate deficiency:
  - Paresthesia, ataxia, coma .
  - Muscle weakness, rhabdomyolysis
  - Increased susceptibility to infection (? defective phagocytosis)
  - Haemolysis (? decreased 2,3-diphosphoglyce rate)
  - Decreased platelet aggregation
  - Osteomalacia



Hyperphosphatemia - Causes

- commonest cause is in vitro leak from red cells or *haemolysis* (factitious hyperphosphataemia); commonest cause pf pathological dosease is *renal failure*.

- **Renal failure.** plasma level begins to rise when the GFR falls to below 20 ml/min (or the plasma creatinine is >*0.35* mmol/l.
- **Tumour calcinosis.** rare AR disorder characterised by hyperphosphataemia,
- normocalcaemia, and deposits of calcium
- phosphate about the large joints.
- **Acromegaly.** increases renal phosphate reabsorption;
- **Cell destruction.** chemotherapy of malignancy, rhabdomyolysis, crush injury
- **Diabetic ketoacidosis** and lactic acidosis

Factitious
Haemolysis
Delay in separation of plasma from red cells
Physiological
Age-related (infancy, childhood)
Increased intake
Oral/IV therapy, Vitamin D overdose
Cell release
Tissue destruction (rhabdomyolysis, crush injury, malignancy, chemotherapy of malignancy)
Bone release (malignancy)
Starvation
Acidaemia (lactic acidosis)
Diabetes mellitus (insulin deficiency)
Decreased renal excretion
Renal failure
Hypoparathyroidism
Growth hormone excess
Volume contraction
Tumour calcinosis
Post-menopause

Hyperphosphatemia - Manifestations

- Persistent *hyperphosphataemia* influences Ca metabolism →
- metastatic calcification due to *in **vivo*** precipitation as calcium phosphate.

- *Hypocalcaemia* due to (a) *in vivo* precipitation, (b)
- decreased gut absorption of calcium (precipitation
- in the gut lumen as insoluble calcium phosphate).

Hyperphosphatemia symptoms:

Tweaking	**T**etany
Calcium	**C**alcification (of soft tissues in lungs, kidneys, and joints)
Can	**C**onvulsions
Clear	**C**ardiac arrest
High	**H**yperneuromuscular activity
Phosphate	**P**rolonged QT interval

Mnemonic by Jenna Batey

How to correct it:

- Limit foods high in phosphate (dairy products, meats, nuts, etc.)
- Eat less process food
- Treat hypoparathyroidism
- Enhance renal excretion through saline diuresis

Nursing implications:

- Diet is especially important for renal failure patients
- Be alert for signs of hypocalcemia (both lab values and symptoms)
- Place patient on continuous cardiac monitoring