PRINCIPALS OF RECOMMENDED NUTRITION

- Quantitative aspect
- Qualitative aspect
- **Special components of diet**
- Aesthetic aspect
- Socio-economic aspect

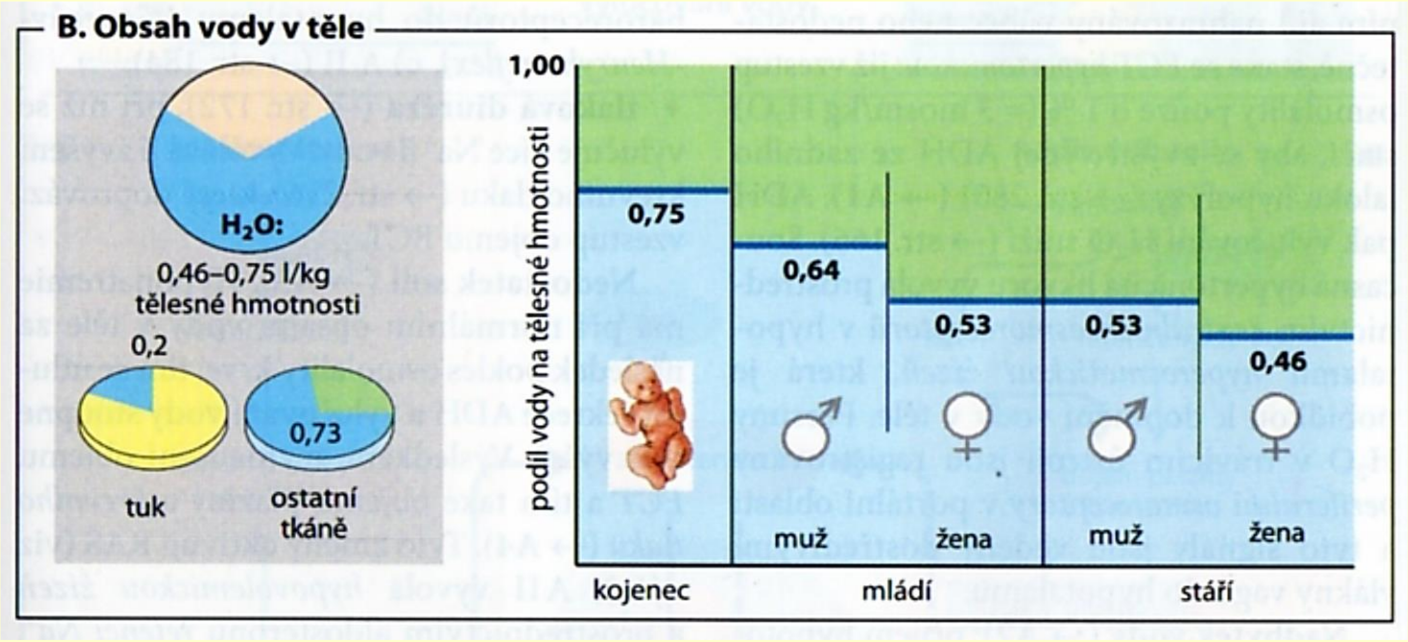
WATER, VITAMINS, MINERALS IN NUTRITION

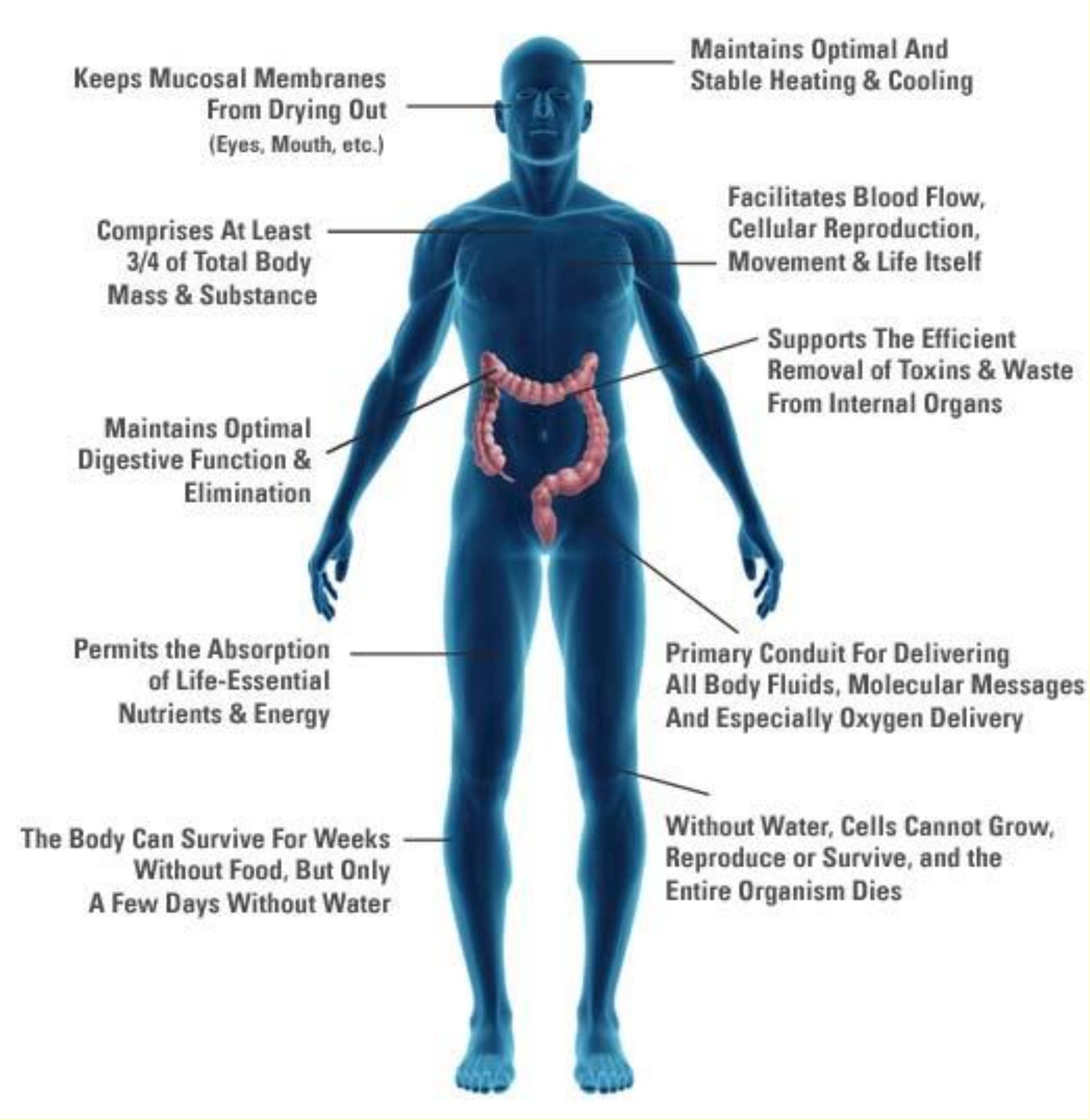
WATER

- 50-70% of body mass, newborns
- 2/3 intracellularly, 1/3 extracellularly
- metabolism
- compartmentalisation
- phylogenetic view

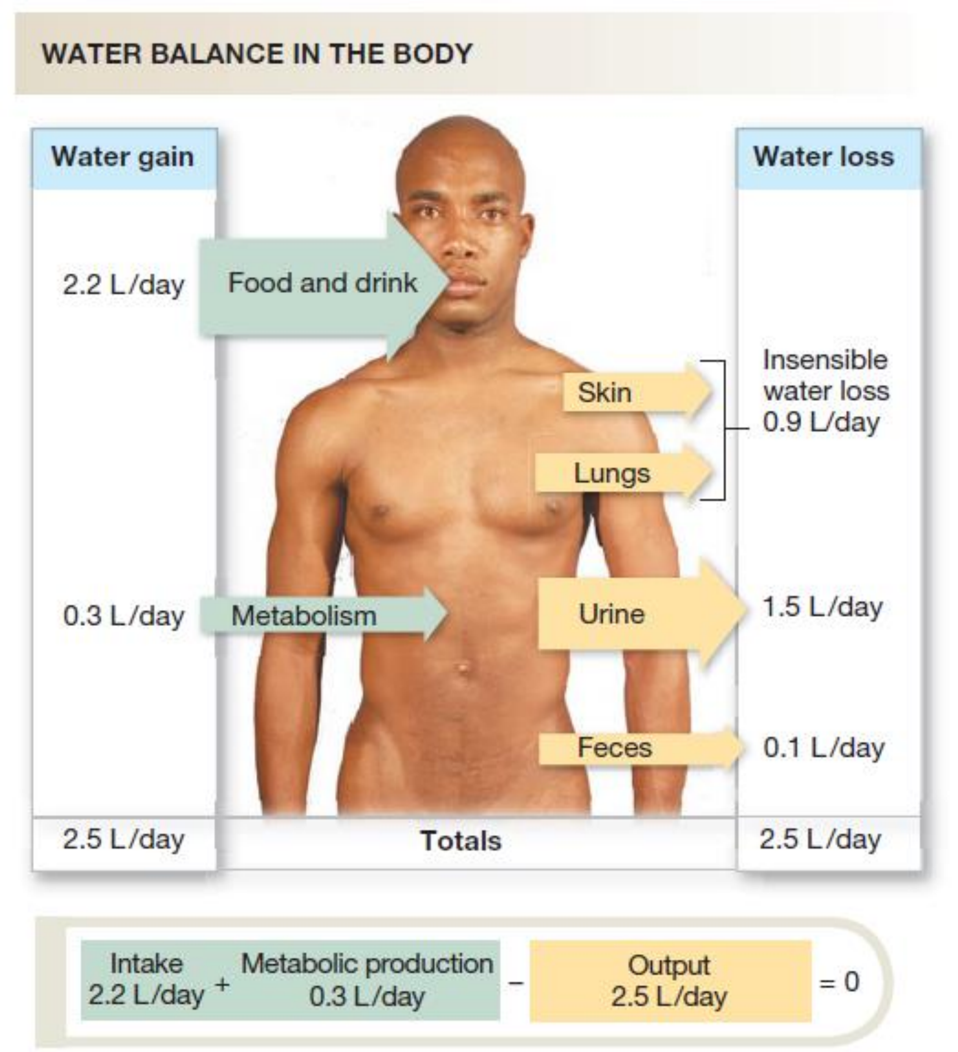
Water and its functions in the human body

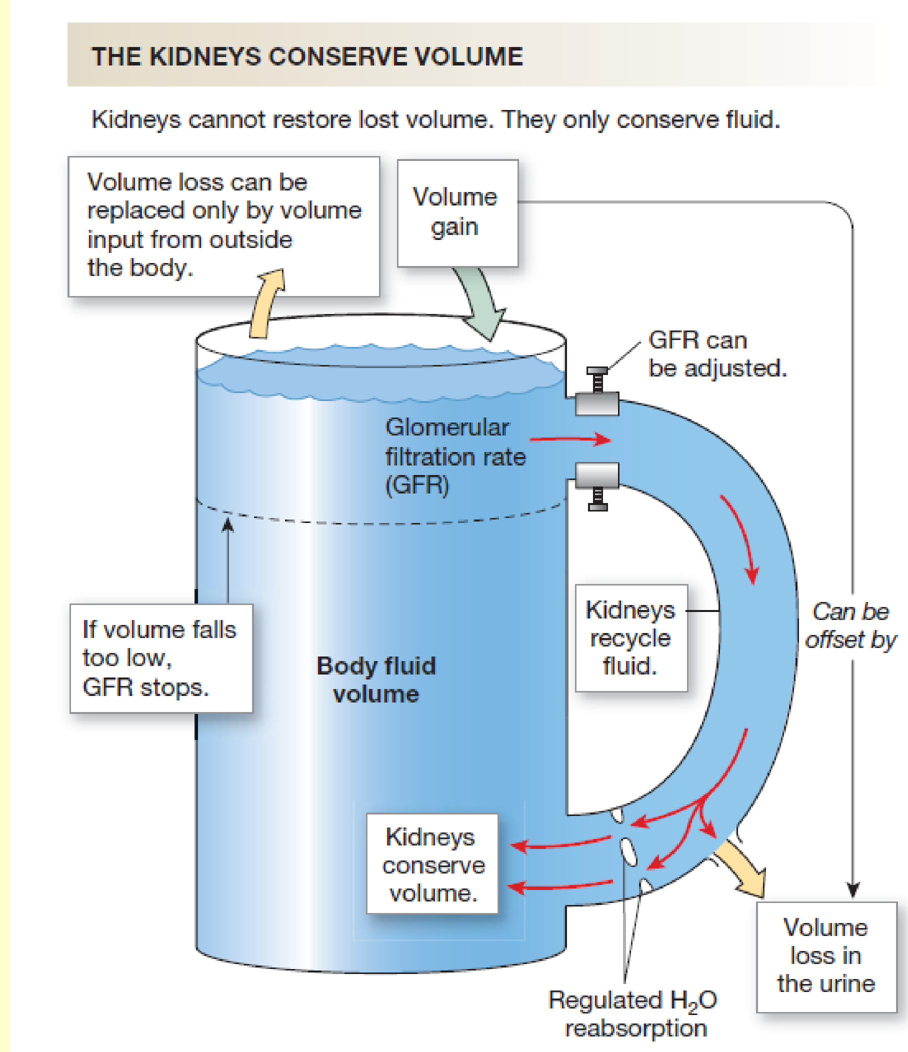
- The transport medium, solvent, wetting and protection of the mucous membranes
- Age, sex, weight

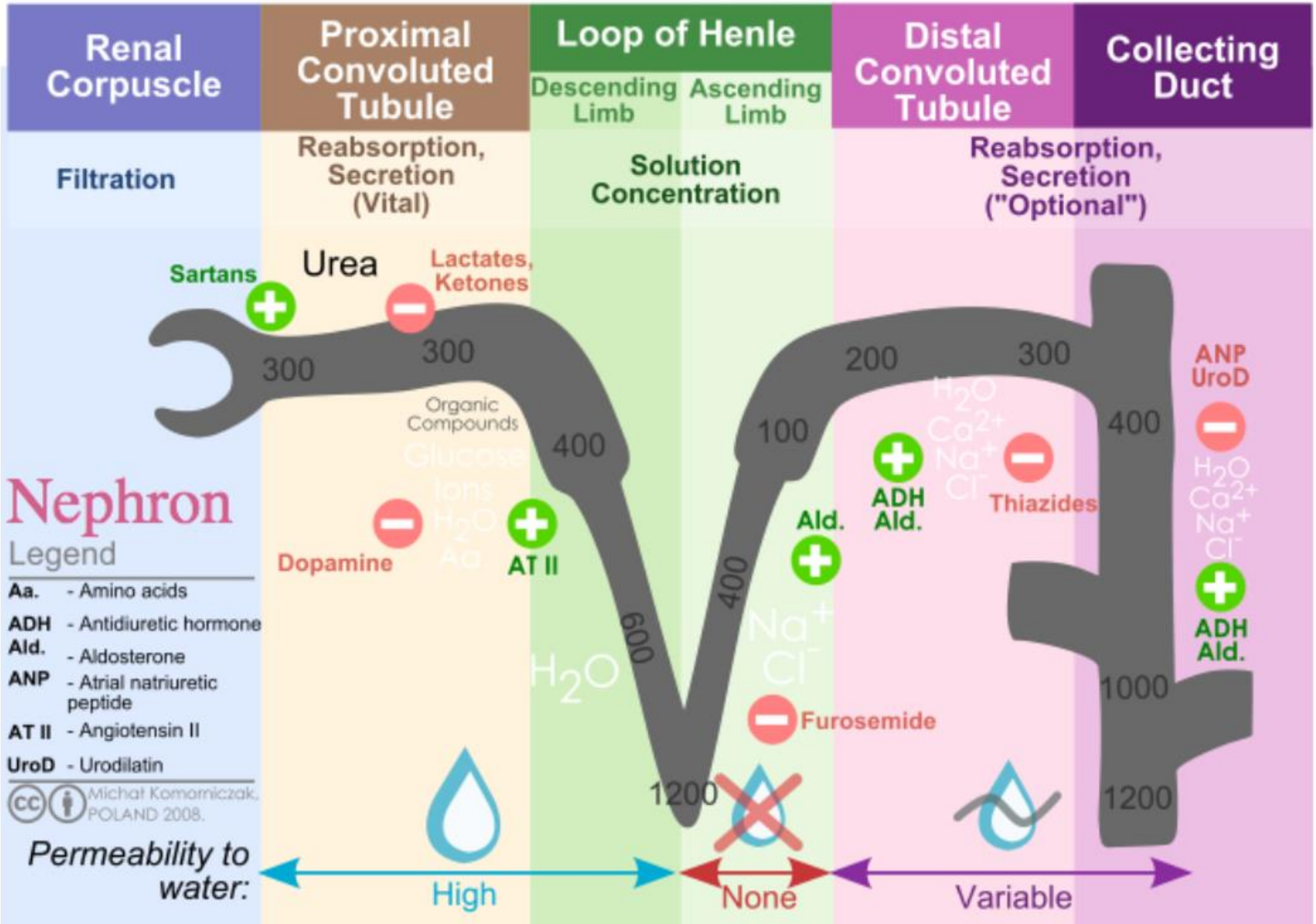




Keeps Mucosal Membranes From Drying Out (Eyes, Mouth, etc.)
Maintains Optimal And Stable Heating & Cooling
Comprises At Least 3/4 of Total Body Mass & Substance
Facilitates Blood Flow, Cellular Reproduction, Movement & Life Itself
Supports The Efficient Removal of Toxins & Waste From Internal Organs
Maintains Optimal Digestive Function & Elimination
Permits the Absorption of Life-Essential Nutrients & Energy
Primary Conduit For Delivering All Body Fluids, Molecular Messages And Especially Oxygen Delivery
The Body Can Survive For Weeks Without Food, But Only A Few Days Without Water
Without Water, Cells Cannot Grow, Reproduce or Survive, and the Entire Organism Dies

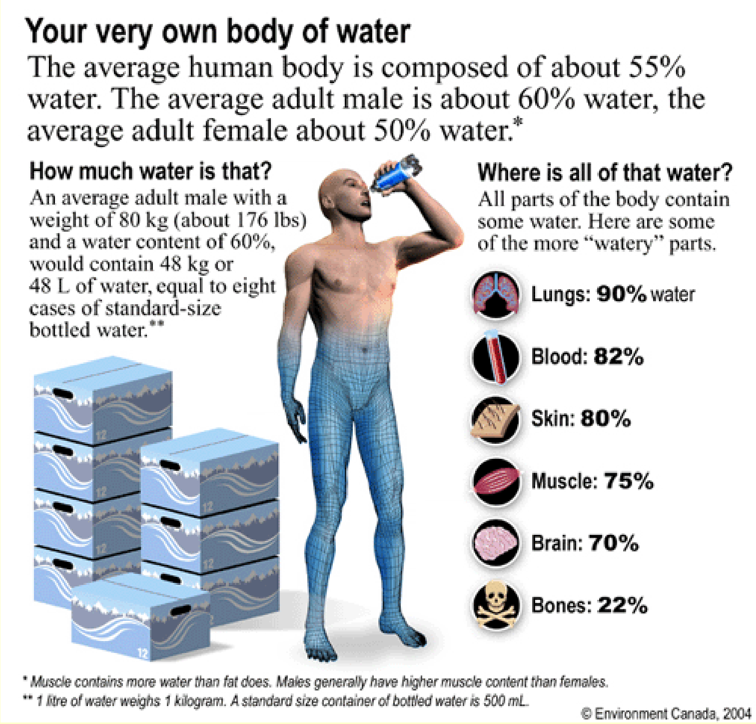

WATER BALANCE IN THE BODY
Water gain
Water loss
2.2 L/day
Food and drink
Skin
Lungs
Insensible water loss 0.9 L/day
0.3 L/day
Metabolism
Urine
1.5 L/day
Feces
0.1 L/day
2.5 L/day
Totals
2.5 L/day
Intake 2.2 L/day
+
Metabolic production 0.3 L/day
−
Output 2.5 L/day
= 0

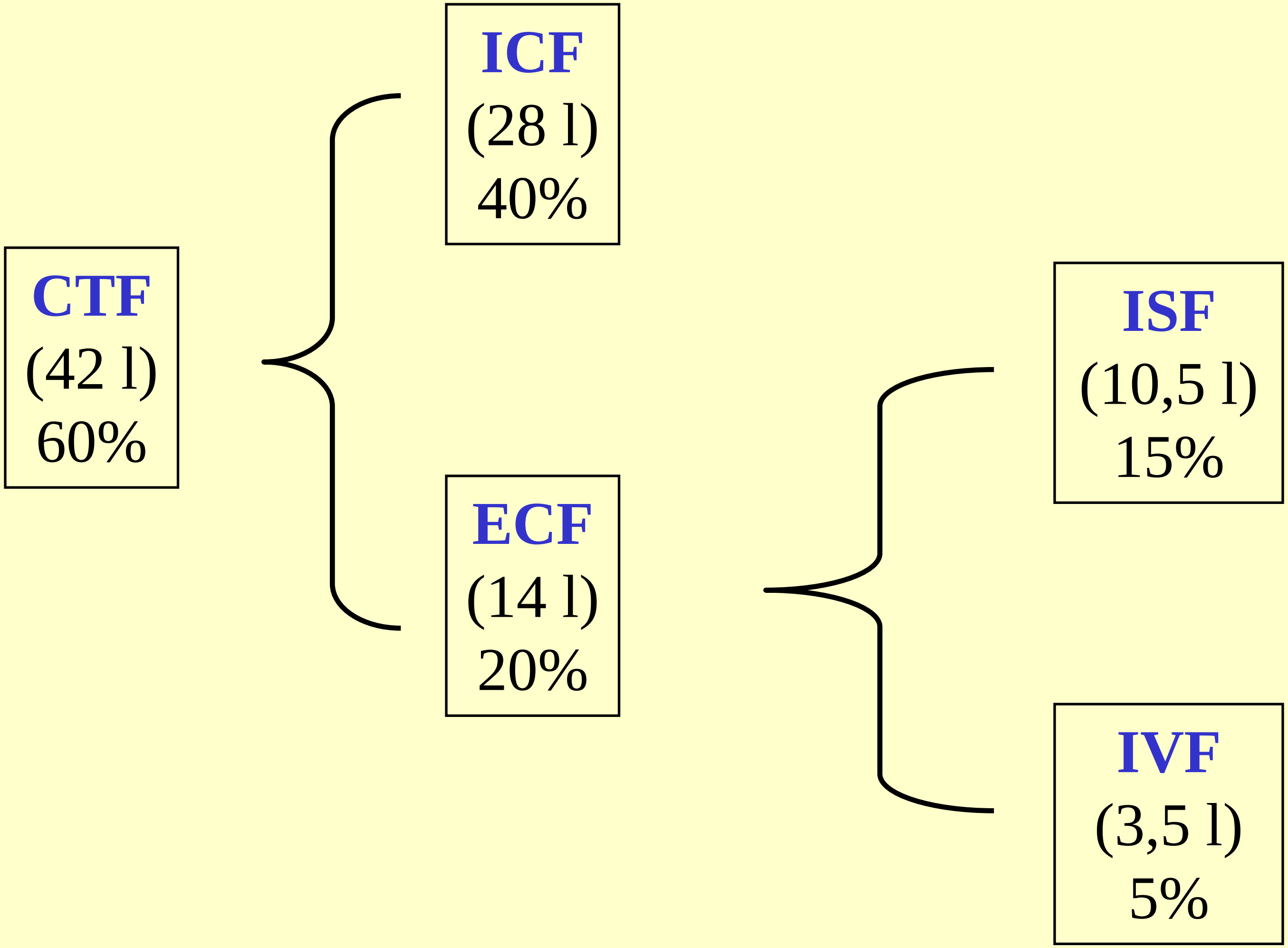

THE KIDNEYS CONSERVE VOLUME
Kidneys cannot restore lost volume. They only conserve fluid.
Volume loss can be replaced only by volume input from outside the body.
Volume gain
GFR can be adjusted.
Glomerular filtration rate (GFR)
If volume falls too low, GFR stops.
Body fluid volume
Kidneys recycle fluid.
Can be offset by
Kidneys conserve volume.
Regulated H_2O reabsorption
Volume loss in the urine


Renal Corpuscle
Proximal Convoluted Tubule
Loop of Henle
Descending Limb
Ascending Limb
Distal Convoluted Tubule
Collecting Duct
Filtration
Reabsorption, Secretion (Vital)
Solution Concentration
Reabsorption, Secretion ("Optional")
Sartans
Urea
Lactates, Ketones
300
300
400
600
1200
400
100
200
300
400
1000
1200
Organic Compounds
Glucose
Ions
H_2O
Aa.
Dopamine
AT II
H_2O
Ald.
Na^+
Cl^-
Furosemide
ADH
Ald.
H_2O
Ca^{2+}
Na^+
Cl^-
Thiazides
ANP
UroD
H_2O
Ca^{2+}
Na^+
Cl^-
ADH
Ald.
Nephron
Legend
Aa. - Amino acids
ADH - Antidiuretic hormone
Ald. - Aldosterone
ANP - Atrial natriuretic peptide
AT II - Angiotensin II
UroD - Urodilatin
Michał Komorniczak, POLAND 2008.
Permeability to water:
High
None
Variable

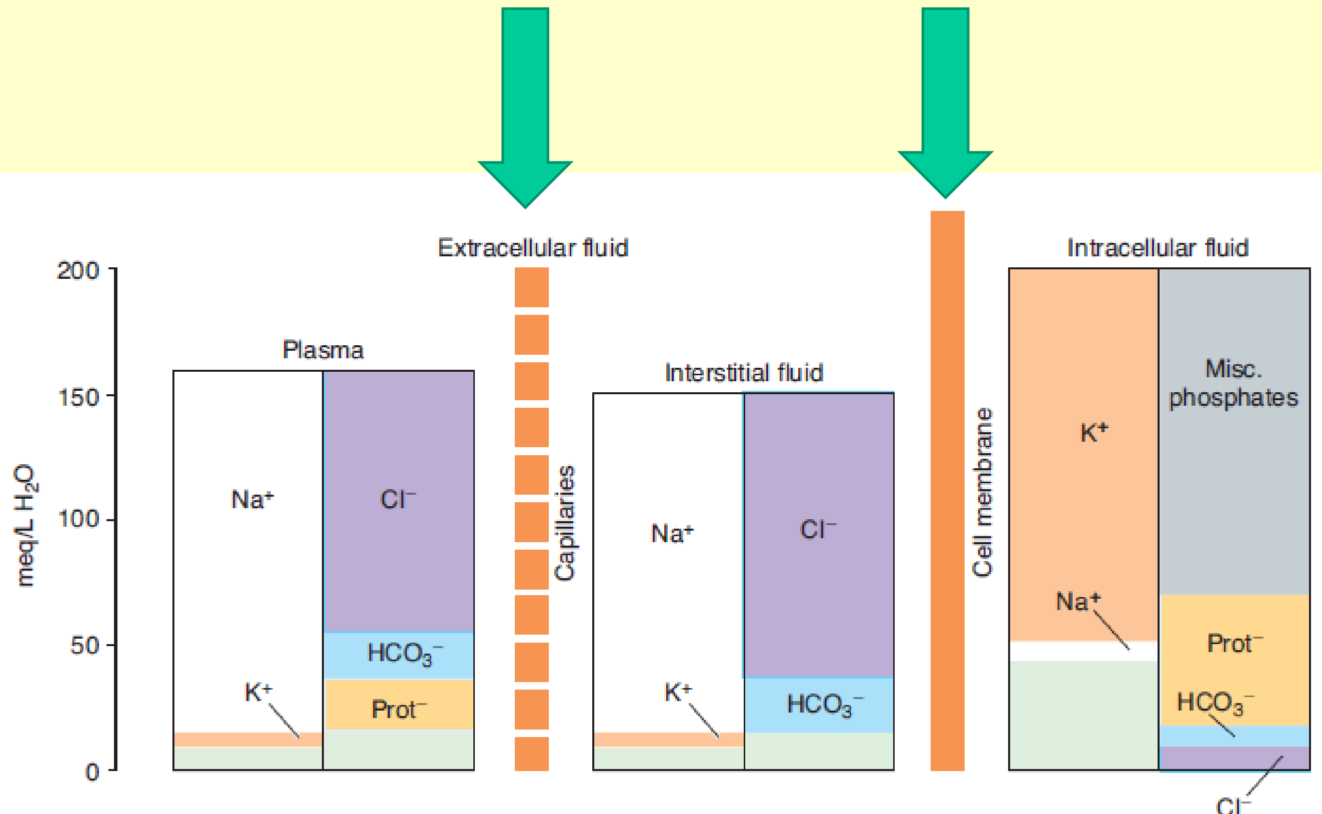
The water content in different tissues (male, 70 kg)

	% of water
blood	83%
muscle tissue	76%
skin	72%
bones	22%
fats	10%
tooth enamel	2%





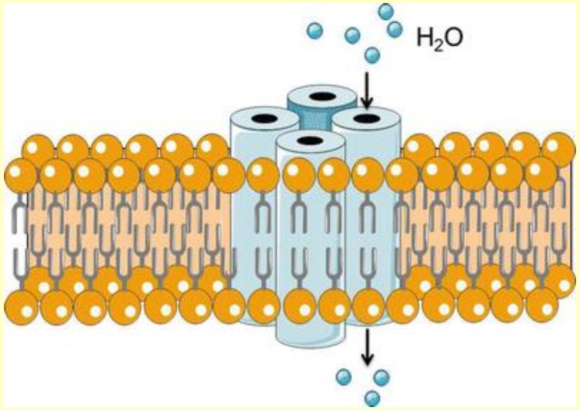
Clinical examination: evaluation of extracellular (plasmatic) levels of electrolytes (Na, K)

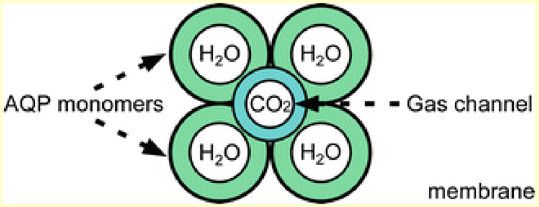


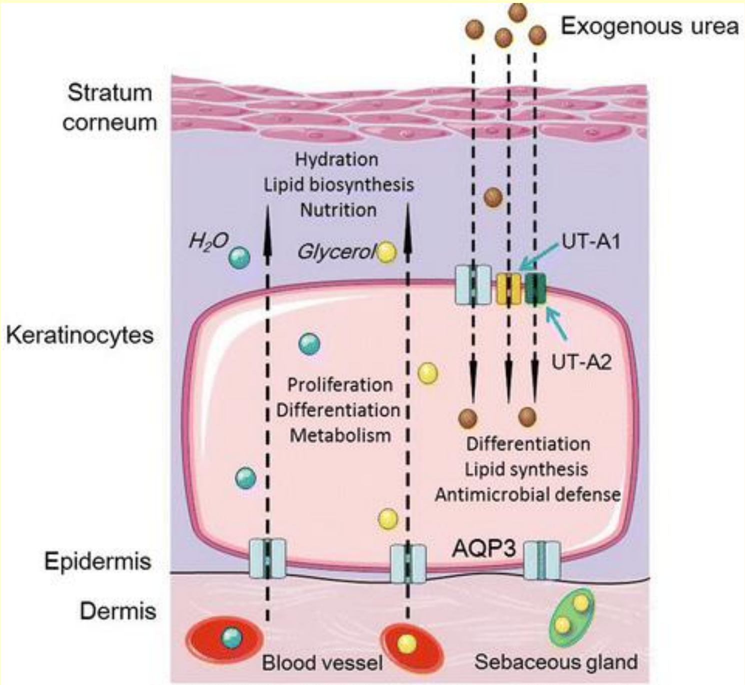
B

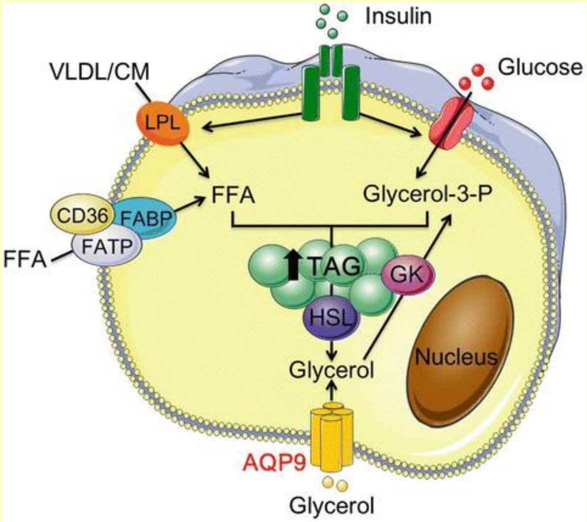
FIGURE 1–1 **Organization of body fluids and electrolytes into compartments. A)** Body fluids are divided into Intracellular and extracellular fluid compartments (ICF and ECF, respectively). Their contribution to percentage body weight (based on a healthy young adult male; slight variations exist with age and gender) emphasizes the dominance of fluid makeup of the body. Transcellular fluids, which constitute a very small percentage of total body fluids, are not shown. Arrows represent fluid movement between compartments. **B)** Electrolytes and proteins are unequally distributed among the body fluids. This uneven distribution is crucial to physiology. $Prot^-$, protein, which tends to have a negative charge at physiologic pH.

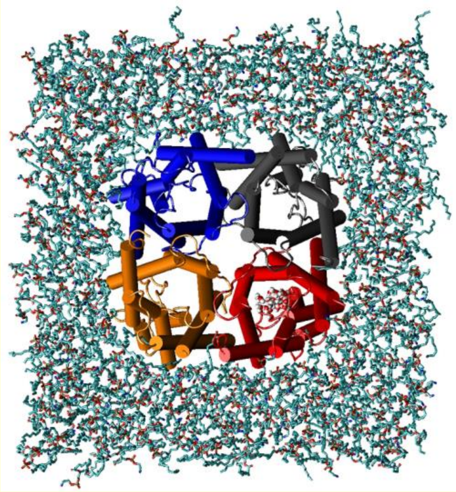
Aquaporins

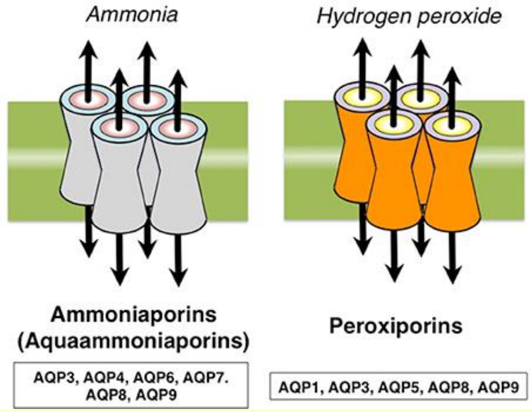

H_2O

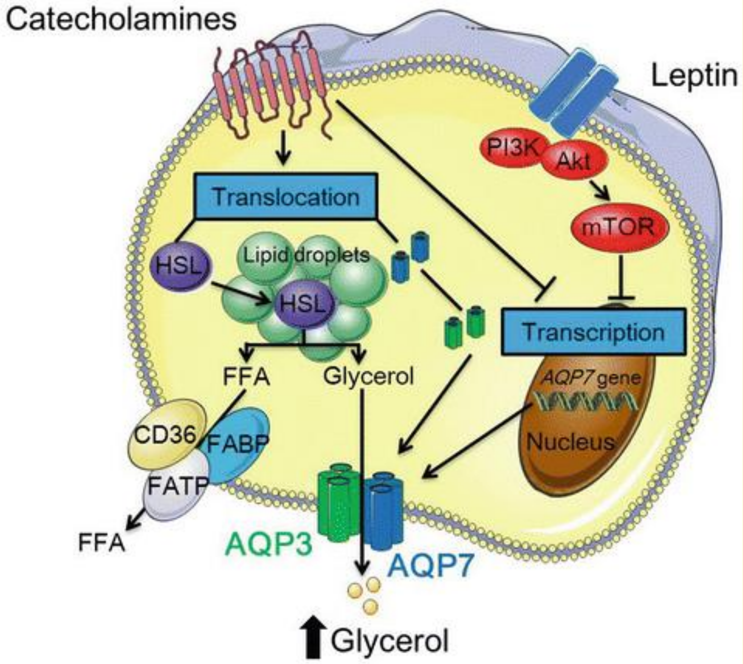

AQP monomers
H_2O
H_2O
CO_2
Gas channel
H_2O
H_2O
membrane


Exogenous urea
Stratum corneum
Hydration
Lipid biosynthesis
Nutrition
H_2O
Glycerol
UT-A1
Keratinocytes
UT-A2
Proliferation
Differentiation
Metabolism
Differentiation
Lipid synthesis
Antimicrobial defense
Epidermis
AQP3
Dermis
Blood vessel
Sebaceous gland

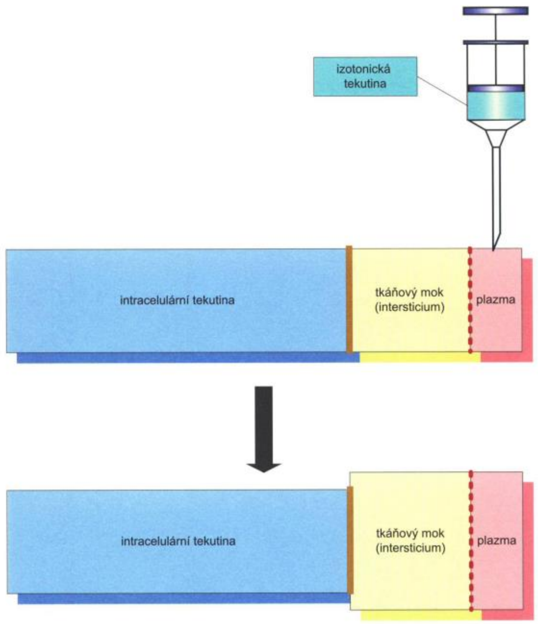

Insulin
VLDL/CM
Glucose
LPL
FFA
Glycerol-3-P
CD36
FABP
FATP
FFA
TAG
GK
HSL
Glycerol
Nucleus
AQP9
Glycerol



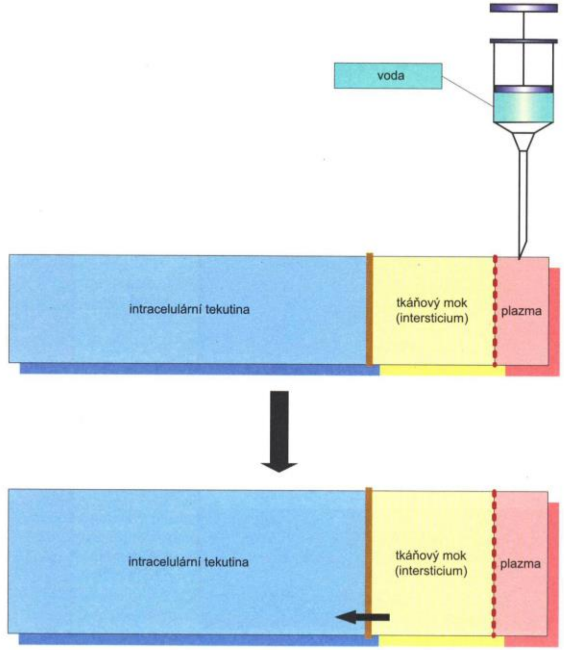

Ammonia
Hydrogen peroxide
Ammoniaporins (Aquaammoniaporins)
AQP3, AQP4, AQP6, AQP7. AQP8, AQP9
Peroxiporins
AQP1, AQP3, AQP5, AQP8, AQP9


Catecholamines
Leptin
PI3K
Akt
Translocation
mTOR
HSL
Lipid droplets
HSL
Transcription
FFA
Glycerol
AQP7 gene
CD36
FABP
Nucleus
FATP
FFA
AQP3
AQP7
Glycerol

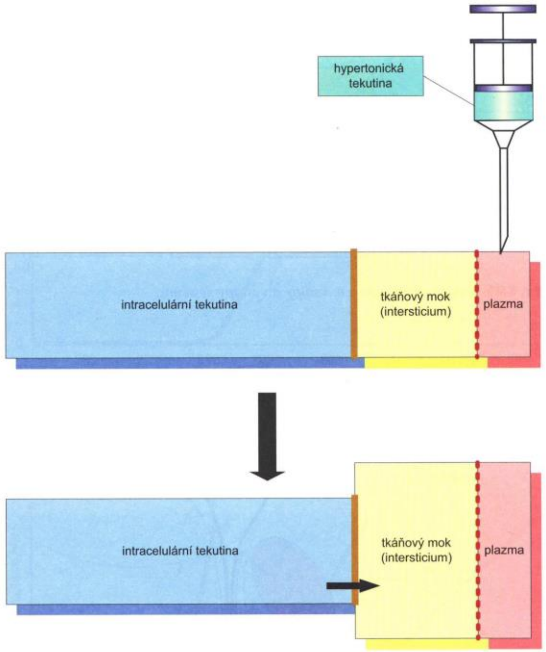
System	AQP protein localisation	Role of aquaporins in transcellular water flow	References
Nervous	Retina — AQP4	Suggested role in Muller cell water balance.	[64]
	Olfactory epithelium — AQP4	Membrane permeability - link to olfaction.	[65]
	Inner ear — AQP4 (hensons, claudius and Inner Succlus cells), AQP1 (fibrocytes)	AQP4 mediated transcellular water flow in to Henson cells exiting via AQP4 on basal membrane of Claudius cells	[66]
	Brain — AQP4 astrocytes, AQP1 (choroid plexus)	AQP4 at astrocyte end feet for BBB water permeability. AQP1 secretion of CSF, AQP4 absorption of CSF	[62,47]
	Spinal cord — AQP1, AQP4, AQP8	Localisation of AQPs suggests transcellular water flow from perivascular space to interstitium, into central canal	[54]
Renal (kidney)	Proximal tubule — AQP1 (apical and basolateral), AQP7 (apical of convoluted and straight)	Water reabsorption, importance of AQP7 unknown	[9,69]
	Renal collecting duct cells — AQP2 (apical, sub apical vesicles), AQP3 and AQP4 (basolateral)	Urine concentration by AQP2 AVP mediated water absorption - AQP3 and 4 exit pathways into blood	[63,68]
	Descending thin limb of henle — AQP1	Water reabsorption	[9]
	Descending vasa recta — AQP1	Water reabsorption	[9]
	Connecting tubule — AQP3	Water homeostasis	[9]
Integumentary	Skin — AQP1 (endothelia of dermis), AQP3 + 10 (keratinocytes of epidermis), AQP5 (sweat glands)	Homeostasis, glycerol or water transport for skin hydration, sweat excretion	[96–98]
	Fat — AQP7 (adipocytes)	Glycerol transport	[102]
Cardiovascular	Blood vessels — AQP1 strongly expressed in endothelia outside of brain	i.e. Airspace-Capillary osmotic water permeability and heart vasculature	[112]
	Cardiomyocytes — AQP4	Absorption of excess water from interstitial space into to capillaries	[113]
Respiratory	Lung alveolar epithelium — AQP5 (apical membrane)	Transcellular water flow route for water absorption and secretion in airway, Role in airway hydration	[117]
	Airway epithelial lining — AQP3 and AQP4	Possibly provide route for water into capillaries of airway	[87]
	Airway sub-mucosal glands — AQP5 (apical membrane)	Fluid secretions into lumen of submusosal glands for mucous production and hydration	[119]
Reproductive	Ovarian granulosa cells — AQP7, AQP8, AQP9	Transcellular water flow in folliculogenesis	[2]
	Epididymis	Transepithelial water transport and sperm concentration	[129,135,137,138]
	Sperm — AQP3, AQP7	CVR to prevent swelling and to aid mobility	[41]
Digestive	Salivary Glands — AQP5 (acinar cells, intercalated duct cells), AQP8 (myoepithelial cells)	Transcellular water transfer in process of primary saliva secretion	[87,147]
	Oesophagus — AQP3 (stratified epithelia)	Intracellular osmolarity and CVR to water deprived cells	[143]
	Stomach — AQP3 (stratified epithelia), AQP4 (BLM parietal cells), AQP5 (pyloric gland)	Provide water to cells facing harsh conditions, AQP4 - gastric acid secretion, AQP5 transcellular water secretion for mucous production	[141,143,144]
	Small intestine — AQP4, AQP9 (goblet cells)	Transcellular colonic fluid transport, AQP9 aids in mucous secretion	[149]
	Colon — AQP3 (simple + stratified epithelia of distal colon), AQP4 (surface epithelia)	Water absorption from intestine and colonic fluid transport	[144,149]
	Liver — AQP1 (cholangiocytes), AQP8 (hepatocytes), AQP9 (sinusoidol membrane of hepatocyte)	AQP8 — osmotic driven water transfer and homeostasis, AQP9 — glycerol uptake from blood released by AQP7	[82,152]
	Pancreas — AQP1 (inter/intralobular ducts), AQP8 (acinar cells)	AQP1 — Transcellular water transfer and pancreatic juice secretion, AQP8 — Pancreatic juice secretion	[146]
Musculoskeletal	Muscle fibres — AQP4	Contraction-induced muscle swelling	
	Articular cartilage — AQP1, AQP3	Involved in cell swelling during mechanistic load	[160]
	Intervertebral disc — AQP1, AQP3 (nucleus pulposus cells)	AQP1 and 3 involved in NP cell swelling during mechanistic load	[159]
	Osteoclasts — AQP9	AQP9 osteoclast differentiation and cell fusion — increase in cell volume	[154,156]



Obr. 8.42 *Při příjmu izotonické tekutiny se tekutina rozprostře mezi intravaskulární a extravaskulární část extracelulárního kompartmentu, do intravaskulárního kompartmentu tekutina nepřechází, protože bariéra je pro ionty nepropustná, a voda nepřechází, protože obě strany bariéry jsou izotonické*



Obr. 8.43 *Při příjmu čisté vody se voda rozprostře do všech kompartmentů, aby vyrovnala jejich osmolaritu*



Obr. 8.44 *Při příjmu hypertonické tekutiny přechází voda do extracelulárního prostoru z prostoru intracelulárního, aby vyrovnala osmolaritu obou kompartmentů*

table 5-1 Body Water and Body Fluid Compartments

Body Fluid Compartment	Fraction of TBW*	Markers Used to Measure Volume	Major Cations	Major Anions
TBW	1.0	Tritiated H_2O D_2O Antipyrene		
ECF	1/3	Sulfate Inulin Mannitol	Na^+	Cl^- HCO_3^-
Plasma	1/12 (1/4 of ECF)	RISA Evans blue	Na^+	Cl^- HCO_3^- Plasma protein
Interstitial	1/4 (3/4 of ECF)	ECF–plasma volume (indirect)	Na^+	Cl^- HCO_3^-
ICF	2/3	TBW–ECF (indirect)	K^+	Organic phosphates Protein

*Total body water (TBW) is approximately 60% of total body weight, or 42 L in a 70-kg man. ECF = extracellular fluid; ICF = intracellular fluid; RISA = radioiodinated serum albumin.

HOMEOSTASIS

•**Izoionia** – concentration of ions

•**Izotonia** – osmotic concentration

•**Izohydria** – ratio between acids and bases

•**Izovolemia** –ECL volume (volumoreceptors or baroreceptors,

RAS, ADH)

- Izovolemia
- **Hypovolemia (dehydratation)**
- Hypervolemia (hyperhydratation)

Cause – result

Complex disorders!

EXAMINATIONS AT HYDRATATION DISORDERS

1. **Anamnesis** – diseases of kidneys, GIT, DM, DI, drugs, intake and output=balance, body mass changes, etc.

2. **Laboratory examinations**: electrolytes, blood osmolality, RBCC, total plasmatic proteins; Astrup examination

OBJECTIVE EXAMINATIONS

1. Skin changes
2. Body mass changes
3. Diuresis changes (oliguria, anuria, polyuria)
4. Respiration disorders (respiratory acidosis, alkalosis; secondary changes – Kussmaul breathing)
5. CNS disorders (changes of reflexes, muscle tonus, paresthesias, changes of consciousness, coma)
6. Central venous pressure changes (filling of neck veins)
7. Circulation changes: dehydratation – tachycardia, hypotonia

CAUSES OF HYDRATATION DISORDERS

1. Disturbance of normal intake of water and ions
2. Disturbance of normal circulation of water and ionts between ECL and GIT
3. Disturbance of cell metabolism
4. Disturbance of loss of water and ions
5. Excessive loss of water (and ions) by skin

DEHYDRATATION

= decreased volume of body fluids accompanied by lack of sodium

HYPERTONIC DEHYDRATATION = loss of (only) water

Bigger lack of water than sodium. Disorders of intake and big losses.
Cell dehydratation.
Thirst. Decreased skin turgor. CNS symptoms.
Hydratation.

IZOTONIC DEHYDRATATION = isonatremic

Causes – bleeding, diuretics, „blind spaces“
Hypovolemic syndrome: decreased diuresis, symptoms of dehydratation.

HYPOTONIC DEHYDRATATION

Always bigger deficiency of sodium than water.
Cell hyperhydratation.
Losses by GIT, kidneys.
Hypovolemic syndrome, CNS symptoms.

HYPERHYDRATATION

= increased volume of extracellular fluid

HYPOTONIC HYPERHYDRATATION – **water intoxication**

Cell hyperhydratation. Decreased osmolality.
Excessive intake of liquids (dialysed patient, patient with kidney disorders), hyperproduction of ADH

IZOTONIC HYPERHYDRATATION

Increased volume of ECF. Osmolality stabile.
Heart failure, nefrotic syndrome, liver cirrhosis.
Oedemas and water withholding in serose cavities.

HYPERTONIC HYPERHYDRATATION = hypernatremic

Rare. Increase of ECF caused by sodium abundance. Osmolality increases.
Primary hyperaldosteronism.

table 5-2 Changes in Volume and Osmolarity of Body Fluids

Type	Key Examples	ECF Volume	ICF Volume	ECF Osmolarity	Hct and Serum [Na^+]
Isosmotic volume expansion	Isotonic NaCl infusion	↑	No change	No change	↓ Hct –[Na^+]
Isosmotic volume contraction	Diarrhea	↓	No change	No change	↑ Hct –[Na^+]
Hyperosmotic volume expansion	High NaCl intake	↑	↓	↑	↓ Hct ↑ [Na^+]
Hyperosmotic volume contraction	Sweating Fever Diabetes insipidus	↓	↓	↑	–Hct ↑ [Na^+]
Hyposmotic volume expansion	SIADH	↑	↑	↓	–Hct ↓[Na^+]
Hyposmotic volume contraction	Adrenal insufficiency	↓	↑	↓	↑ Hct ↓[Na^+]

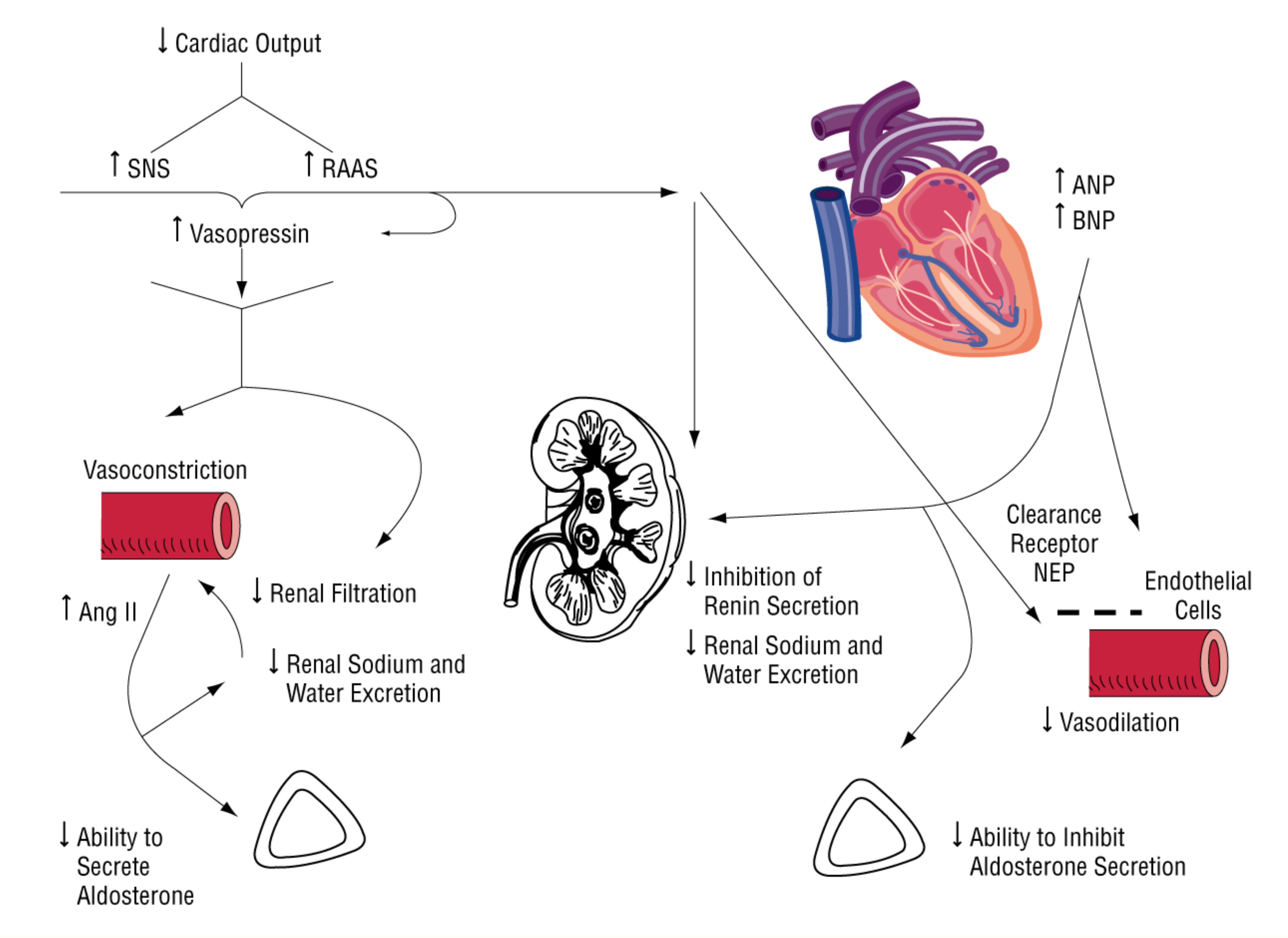
– = no change; ECF = extracellular fluid; Hct = hematocrit; ICF = intracellular fluid; SIADH = syndrome of inappropriate antidiuretic hormone.

SIADH = syndrome of inappropriate antidiuretic hormone secretion)

Regulation of ECV

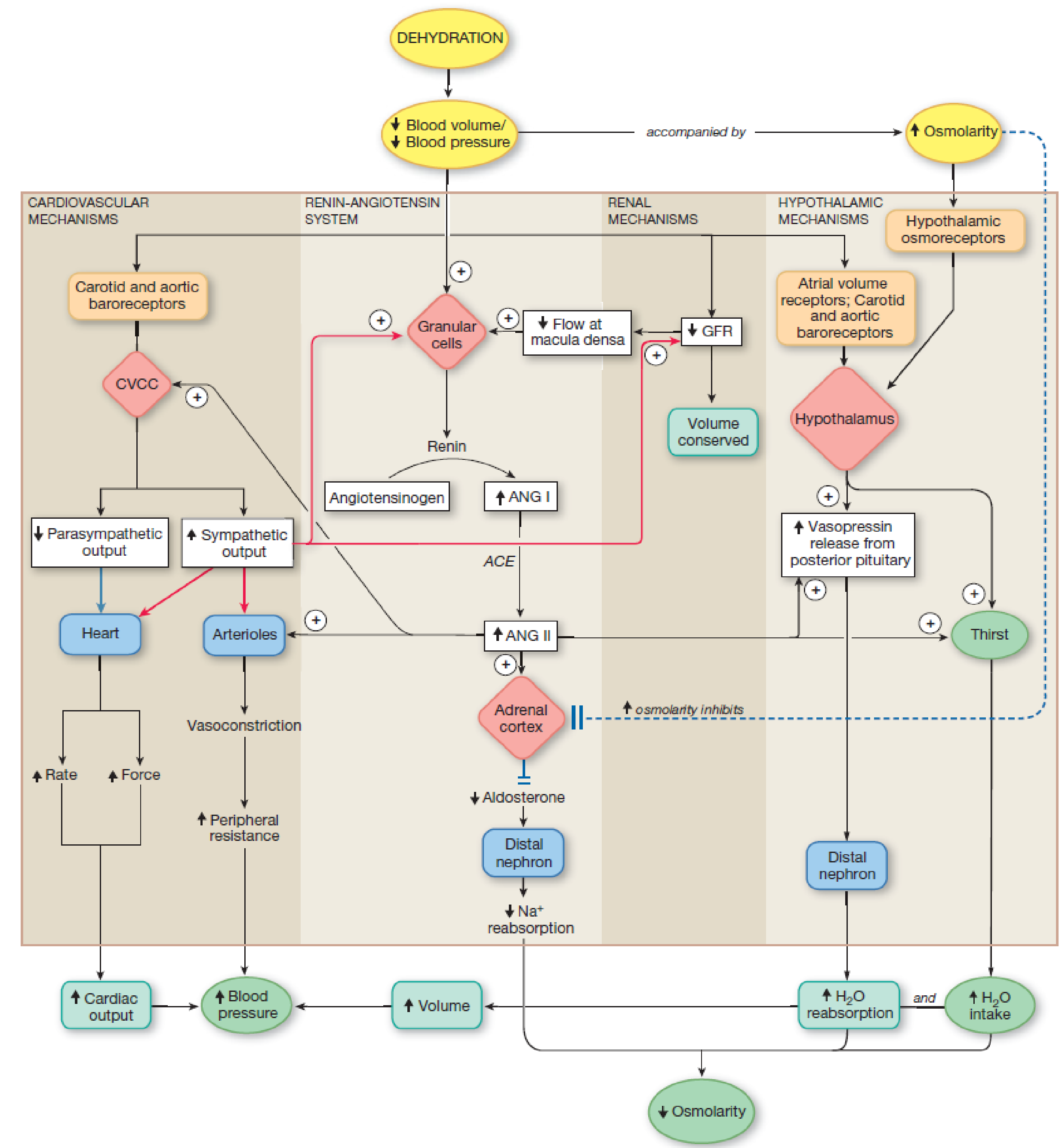
- Change in circulation (capacity)
- Change in volume of IVF – (movement of water, diuresis)
- Sympaticus
- RAS/aldosterone (mineralocorticoids)
- NPs
- Dopamine
- Urodilatin; guanylin, uroguanylin (intestinal epithelium - stimulation of sodium and potassium ion excretion)

RAAS

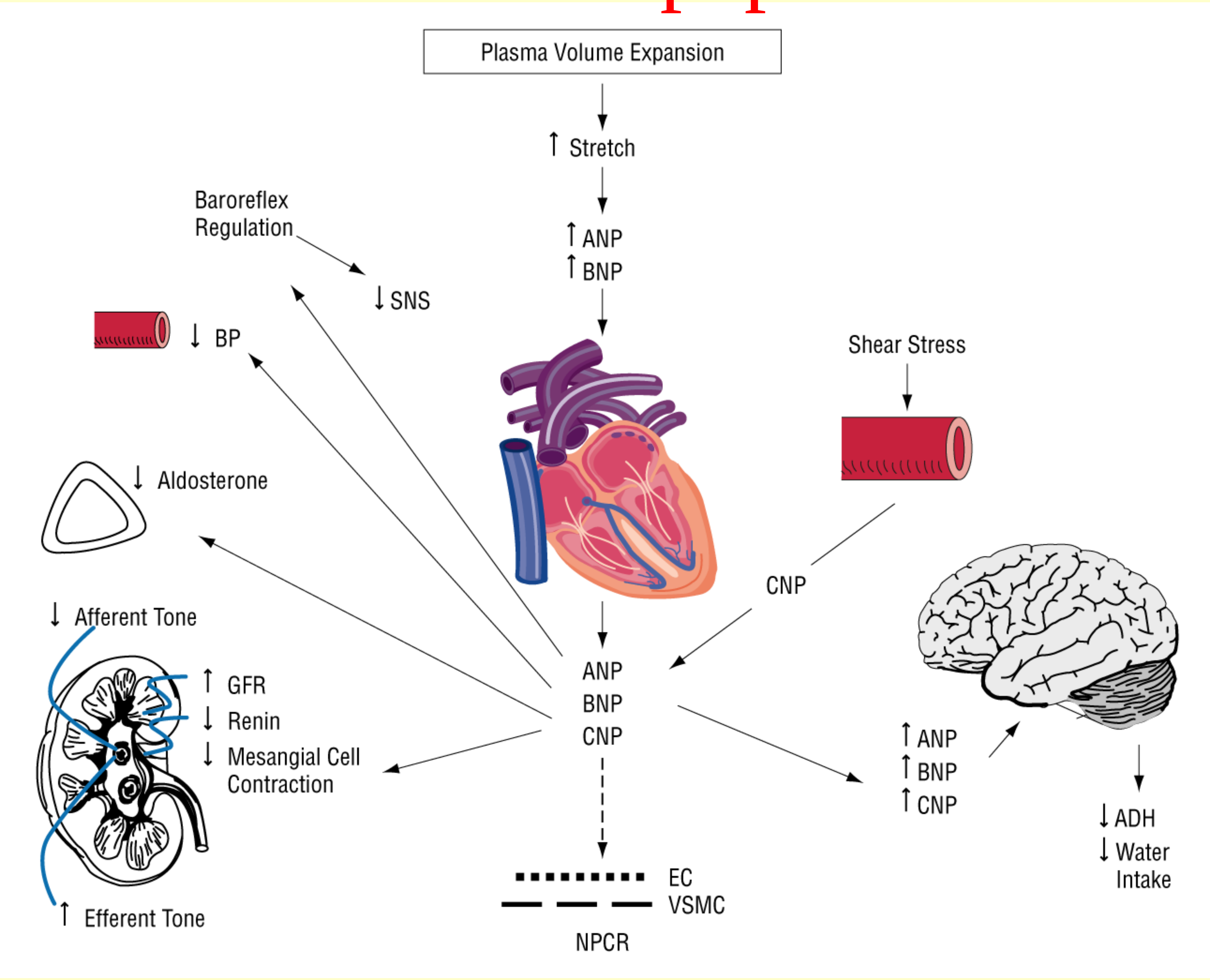


↓ Cardiac Output
↑ SNS
↑ RAAS
↑ Vasopressin
↑ ANP
↑ BNP
Vasoconstriction
↑ Ang II
↓ Renal Filtration
↓ Renal Sodium and Water Excretion
↓ Inhibition of Renin Secretion
↓ Renal Sodium and Water Excretion
Clearance Receptor NEP
Endothelial Cells
↓ Vasodilation
↓ Ability to Secrete Aldosterone
↓ Ability to Inhibit Aldosterone Secretion

HOMEOSTATIC COMPENSATION FOR SEVERE DEHYDRATION



Natriuretic peptides



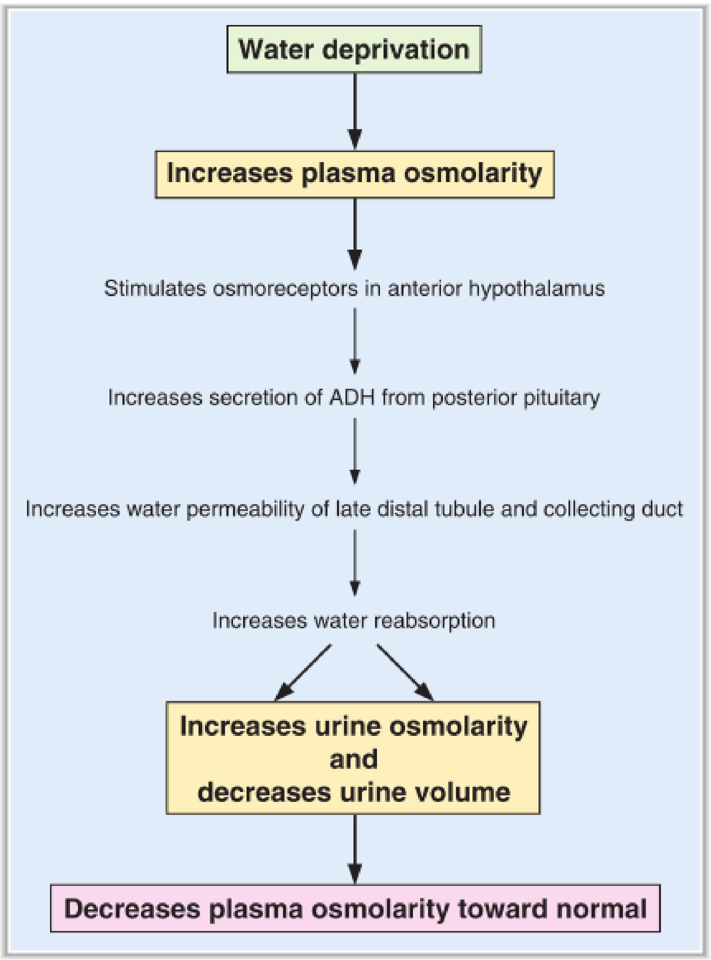


FIGURE 5-14 Responses to water deprivation. ADH = antidiuretic hormone.

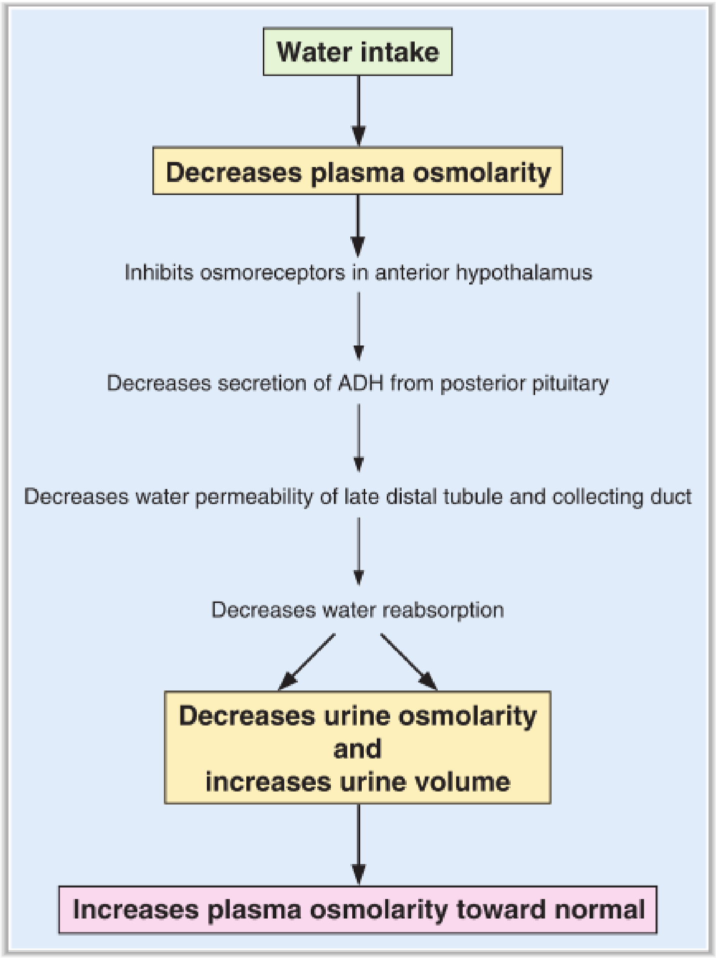


FIGURE 5-15 Responses to water intake. ADH = antidiuretic hormone.

VITAMINS

= all organic compounds of diet, necessary for life, health and growth; NO source of energy

HYPOVITAMINOSIS (AVITAMINOSIS)
HYPERVITAMINOSIS

1. Decrease supply in diet
2. Food intake disorders
3. Absorption disorders
4. Increased consumption
5. Store organ diseases

1. Increased supply in diet – usually **iatrogenic**

SOLUBLE

→ in water: diffusion, D, J; **vit.B_{12}** - I

→ in lipids: deficient absorption in disorders of lipids absorption (pancreatic enzymes or bile missing)

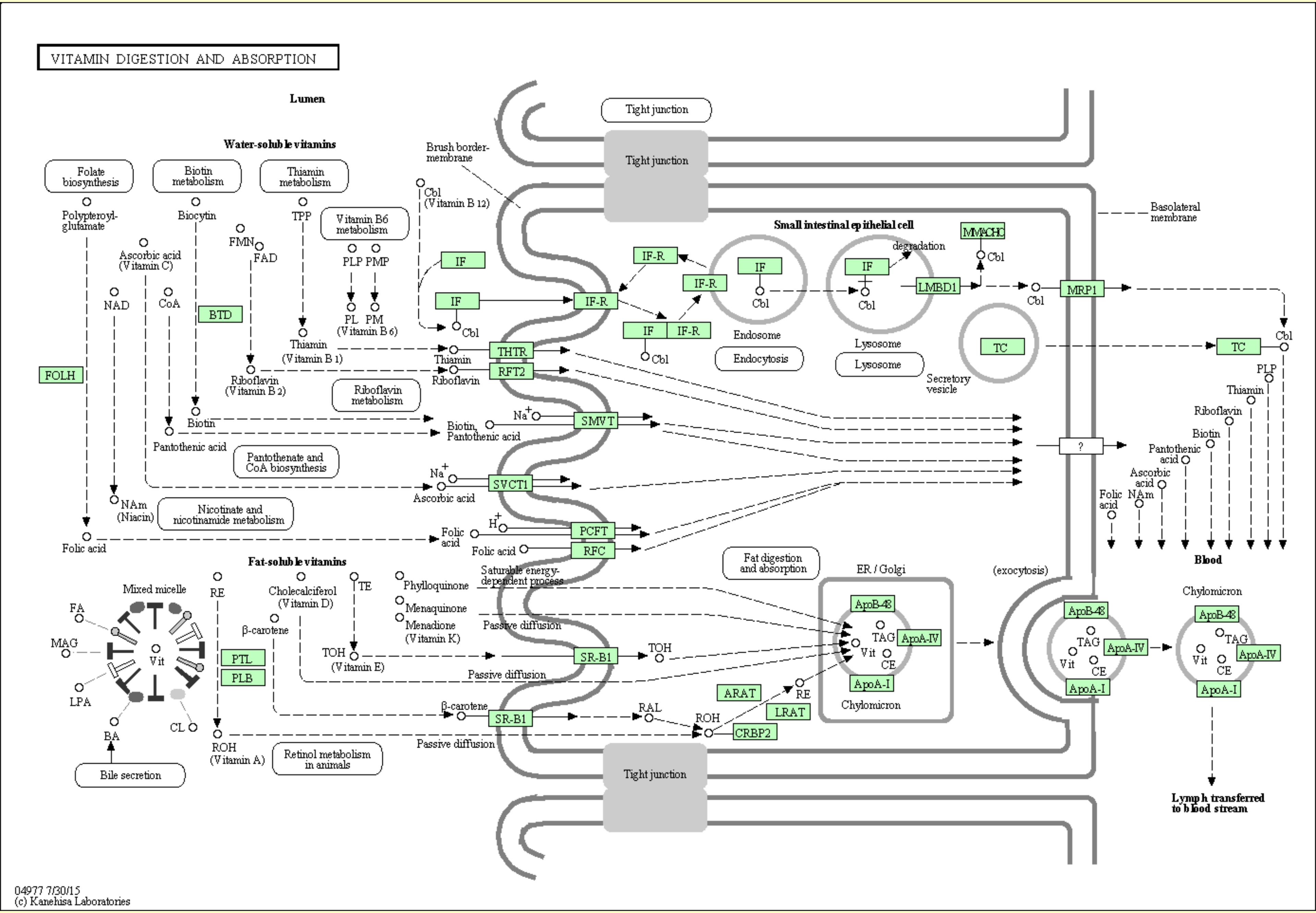
HYPOVITAMINOSES

Folic acid – disorders of embryo development (clefts)
B_{12} – pernicious anaemia
C – scurvy (scorbutus)
D – rickets (rhachitis, English disease, English sickness)
E – fertility problems
K - haemorrhage

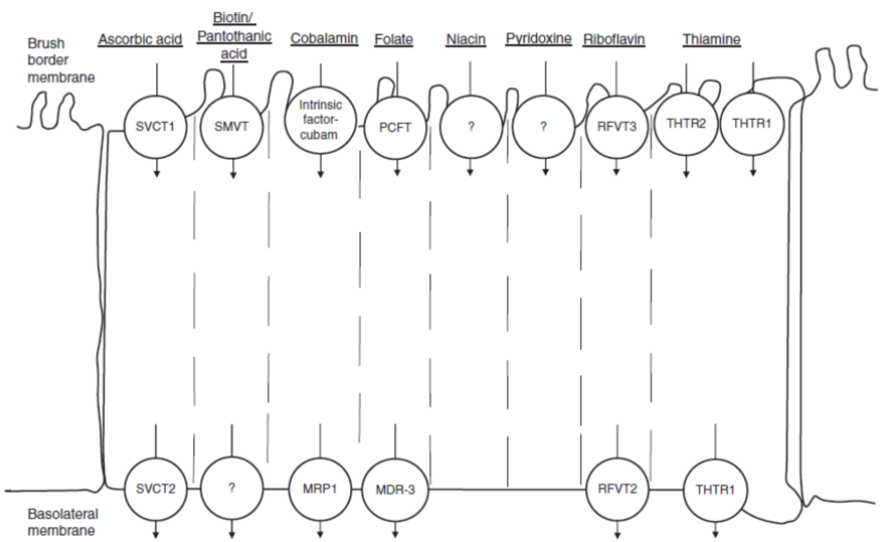
HYPERVITAMINOSES

A – teratogenic effects
D – kidney failure
K – anaemia, GIT disorders
B_6 – peripheral polyneuropathy

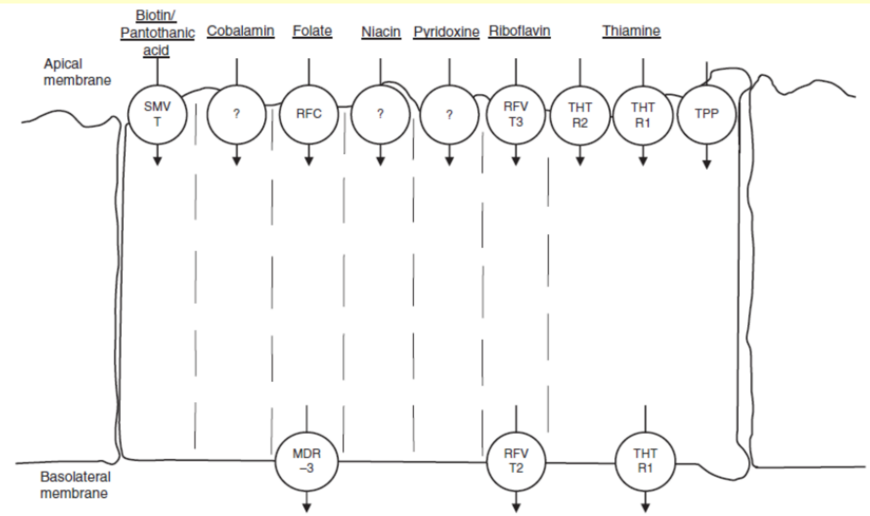
Vitamin	Species	Place of absorption	Transport mechanism	Maximal absorption capacity in humans / day	Daily dose
C	Humans, guinea pig	Ileum	Active	>5000mg	<50mg
Biotin	Hamster	Small intestine	Active	?	?
Cholin	Guinea pig, hamster	Small intestine	Facilitated diffusion	?	?
Folic acid (pteroylglutamate)	Rat	Jejunum	Facilitated diffusion	> 1000µg (dose)	100-200µg
Folic acid (5-methyltetrahydrofolate)	Rat	Jejunum	Diffusion	> 1000µg (dose)	100-200µg
Nicotinic acid	Rat	Jejunum	Facilitated diffusion	?	10-20mg
Pantothenic acid		Small intestine	?	?	(?)10mg
B_6 (pyridoxine)	Rat, hamster	Small intestine	Diffusion	> 50mg (dose)	1-2mg
B_2 (riboflavin)	Humans, rat	Jejunum	Facilitated diffusion	10-12mg (dose)	1-2mg
B_1 (thiamine)	Rat	Jejunum	Active	8-14mg	Approx. 1mg
B_{12}	**Humans, rat, hamster**	**Distal ileum**	**Active**	**6-9µg**	**3-7µg**



VITAMIN DIGESTION AND ABSORPTION
Lumen
Water-soluble vitamins
Folate biosynthesis
Biotin metabolism
Thiamin metabolism
Vitamin B6 metabolism
Polypteroyl-glutamate
Biocytin
TPP
FMN
FAD
PLP PMP
PL PM (Vitamin B 6)
Ascorbic acid (Vitamin C)
NAD
CoA
BTD
Cbl (Vitamin B 12)
IF
Thiamin (Vitamin B 1)
Riboflavin (Vitamin B 2)
Riboflavin metabolism
FOLH
Biotin
Pantothenic acid
Pantothenate and CoA biosynthesis
NAm (Niacin)
Nicotinate and nicotinamide metabolism
Folic acid
Brush border-membrane
Tight junction
Small intestinal epithelial cell
IF-R
Endosome
Endocytosis
Lysosome
degradation
LMBD1
MMACHC
MRP1
TC
Secretory vesicle
Basolateral membrane
THTR
RFT2
SMVT
SVCT1
PCFT
RFC
Na+
H+
Biotin, Pantothenic acid
Ascorbic acid
Folic acid
?
PLP
Thiamin
Riboflavin
Biotin
Pantothenic acid
Ascorbic acid
Folic acid
NAm
Cbl
Blood
Fat-soluble vitamins
Mixed micelle
FA
MAG
LPA
BA
CL
Vit
Bile secretion
RE
ROH (Vitamin A)
Retinol metabolism in animals
Cholecalciferol (Vitamin D)
β-carotene
TE
TOH (Vitamin E)
Phylloquinone
Menaquinone
Menadione (Vitamin K)
PTL
PLB
Saturable energy-dependent process
Passive diffusion
SR-B1
TOH
RAL
ROH
ARAT
LRAT
CRBP2
Fat digestion and absorption
ER / Golgi
ApoB-48
TAG
ApoA-IV
CE
ApoA-I
Chylomicron
(exocytosis)
Lymph transferred to blood stream
04977 7/30/15
(c) Kanehisa Laboratories



Obr. 1: Transportní systémy pro hydrofilní, ve vodě rozpustné vitamíny, v tenkém střevě. Jednotlivé transportéry jsou označeny používanými zkratkami. V případě otazníku nebyl doposud transportní systém identifikován. Převzato - https://www.researchgate.net/publication/327659030_Gastrointestinal_Handling_of_Water-Soluble_Vitamins - Said, H., Nexø, E.: (2018). Gastrointestinal Handling of Water-Soluble Vitamins. Comprehensive Physiology 8(4):1291-1311.



Obr. 2: Transportní systémy pro hydrofilní, ve vodě rozpustné vitamíny, v tlustém střevě. Jednotlivé transportéry jsou označeny používanými zkratkami. V případě otazníku nebyl doposud transportní systém identifikován. Za povšimnutí stojí absence transportních systémů na bazolaterální membráně, což indikuje nemožnost jejich transportu dále. Výjimku tvoří folát, riboflavin a thiamin, nicméně kapacita těchto transportních systémů je velmi omezená. Převzato - https://www.researchgate.net/publication/327659030_ Gastrointestinal_Handling_of_Water-Soluble_ Vitamins – Said, H., Nexø, E.: (2018). Gastrointestinal Handling of Water-Soluble Vitamins. Comprehensive Physiology 8(4):1291-1311.

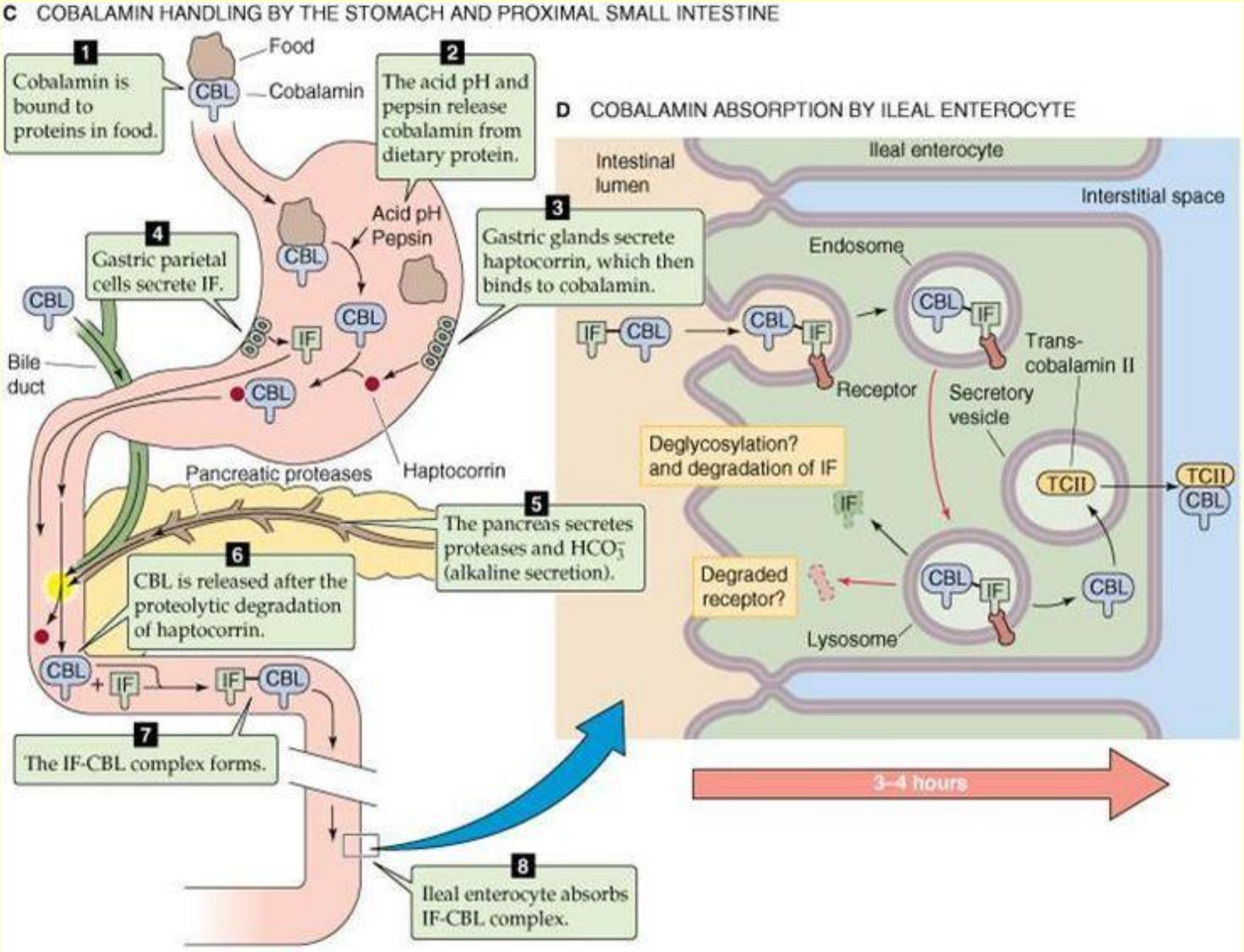
Vitamin	Name	Active Form (co-factor)	Biochemical Function	Physiological/cellular Role
B_5	Pantothenic Acid	Coenzyme A	Acyl Transfer	• Energy production from foodstuff • Fatty acid synthesis
B_6	Pyridoxine	Pyridoxal Phosphate (PLP)	• Transamination • Racemization • Decarboxylation • β/γ-Elimination	• Amino acid breakdown • Glycogen breakdown
B_7	Biotin	Biotin	Carboxylation	• Glucose & fatty acid synthesis • Leucine synthesis
B_9	Folic Acid	Tetrahydrofolate (THF)	One-Carbon Group Transfer	Amino Acid & nucleotide synthesis
B_{12}	Cobalamin	Coenzyme B_{12}	• Intramolecular Rearrangements • Methyl transfer	• Nucleotide synthesis • Amino acid metabolism • Fatty acids breakdown • Folic acid regeneration
C	Ascorbic Acid	Ascorbic Acid	Proline Hydroxylation	Collagen synthesis
			Reduction	Antioxidation
D	Calciferol	Calcitriol	Gene expression	Bone growth

VITAMIN B_{12}

- Daily dose is close to absorption capacity
- Synthesised by bacteria in colon – BUT there is not absorption mechanism
- Store in liver (2-5mg)
- In bile 0,5-5μg / day, reabsorbed
- Daily loss – 0,1% of stores → stores will last for 3-6 years

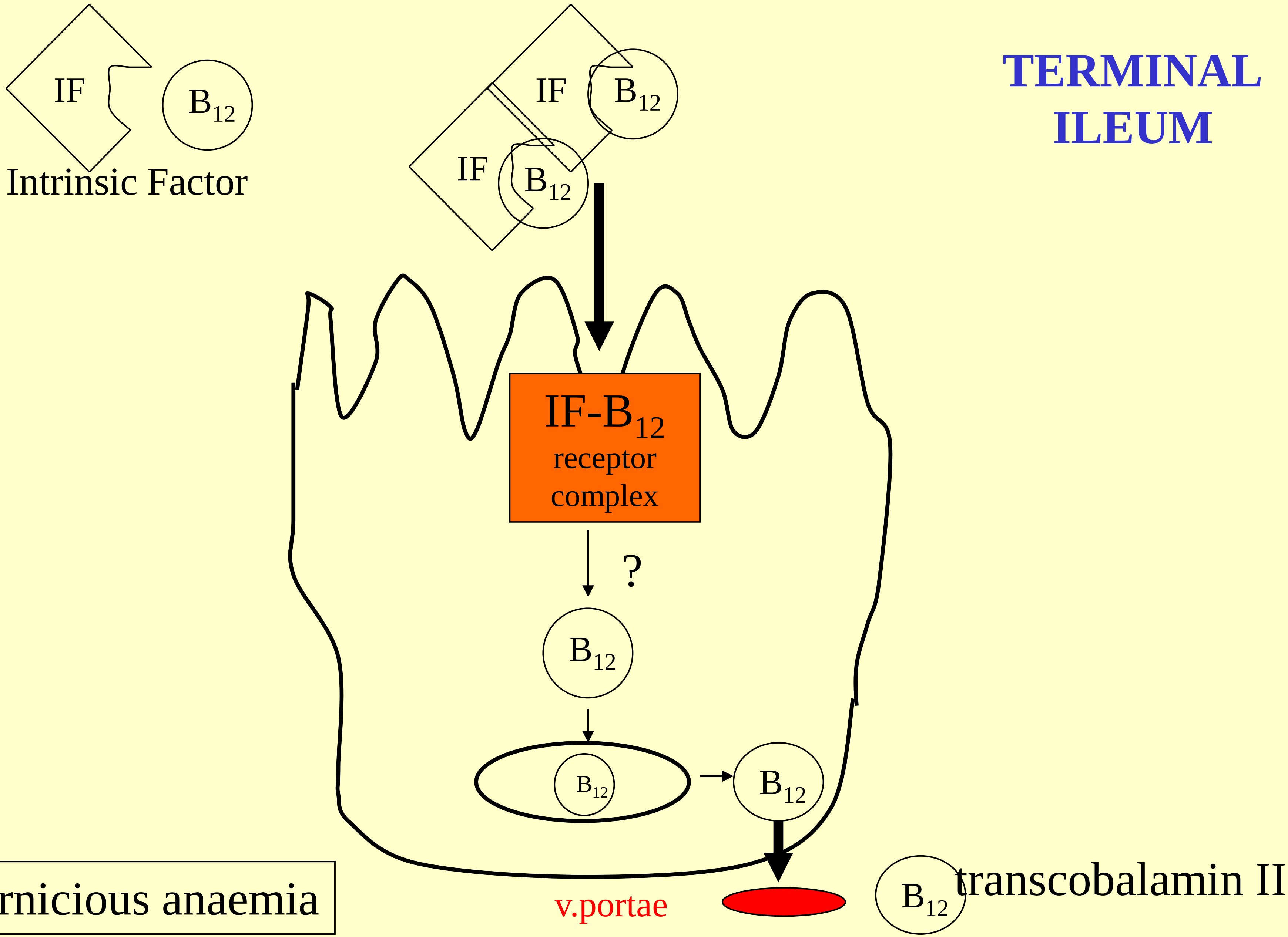
ABSORPTION

1. **Gastric phase**: B_{12} is bound to proteins, low pH and pepsin release it; bound to glycoproteins – **R-proteins** (saliva, gastric juice), almost pH-undependable; intrinsic factor (**IF**) – parietal cells of gastric mucosa; most of vitamin bound to R-proteins
2. **Intestinal phase:** pancreatic proteases, cleavage of R-B_{12}, bound to IF (resistant to pancreatic proteases)

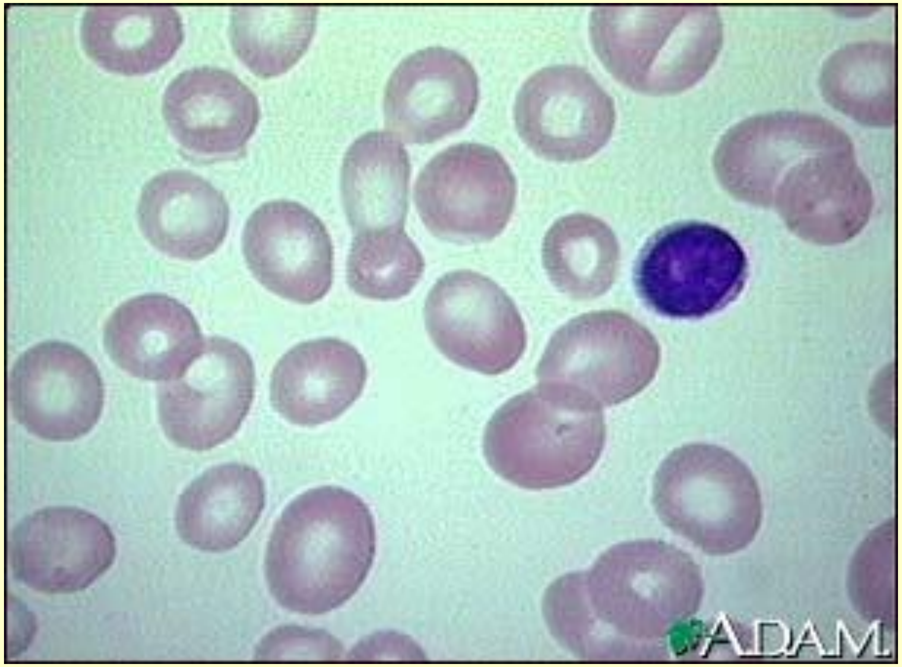

C COBALAMIN HANDLING BY THE STOMACH AND PROXIMAL SMALL INTESTINE
1
Cobalamin is bound to proteins in food.
Food
CBL
Cobalamin
2
The acid pH and pepsin release cobalamin from dietary protein.
Acid pH
Pepsin
3
Gastric glands secrete haptocorrin, which then binds to cobalamin.
4
Gastric parietal cells secrete IF.
IF
Bile duct
Haptocorrin
Pancreatic proteases
5
The pancreas secretes proteases and HCO_3^- (alkaline secretion).
6
CBL is released after the proteolytic degradation of haptocorrin.
7
The IF-CBL complex forms.
8
Ileal enterocyte absorbs IF-CBL complex.
D COBALAMIN ABSORPTION BY ILEAL ENTEROCYTE
Intestinal lumen
Ileal enterocyte
Interstitial space
Endosome
Receptor
Trans-cobalamin II
Secretory vesicle
Deglycosylation? and degradation of IF
TCII
Degraded receptor?
Lysosome
3–4 hours

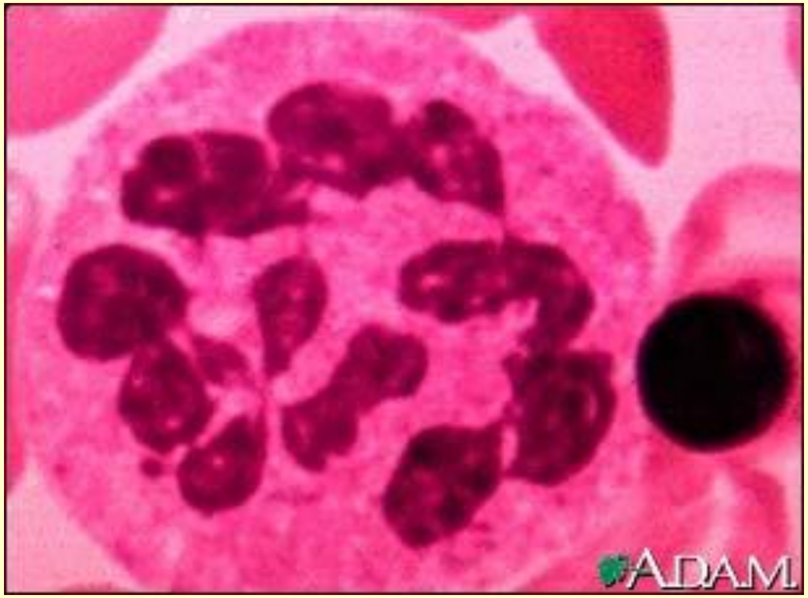
ABSORPTION OF B_{12} VITAMIN

TERMINAL ILEUM



Pernicious anaemia

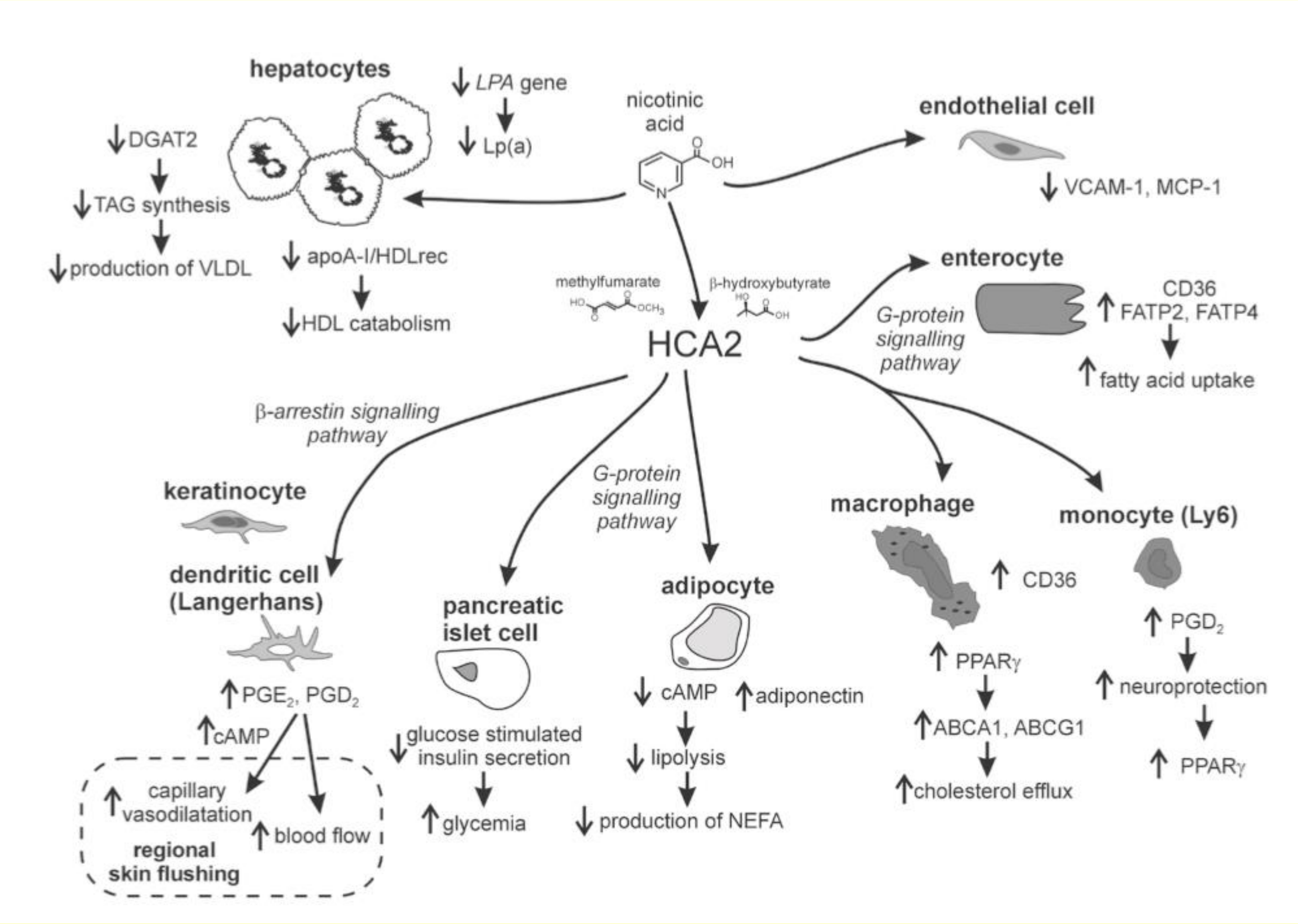




BERI-BERI (B_1)

"The first clinical descriptions of beriberi were by Dutch physicians, Bontius (1642) and Nicolaas Tulp (1652). Tulp treated a young Dutchman who was brought back to Holland from the East Indies suffering from what the natives of the Indies called beriberi or "the lameness." Tulp's description of beriberi was a detailed one, but he had no clues that it was a dietary deficiency disease. This discovery came more than two hundred years later. Nicholaas Tulp (1593-1674) is best remembered as the central figure in Rembrandt's famous painting, "The Anatomy Lesson" (1632).

Niacin

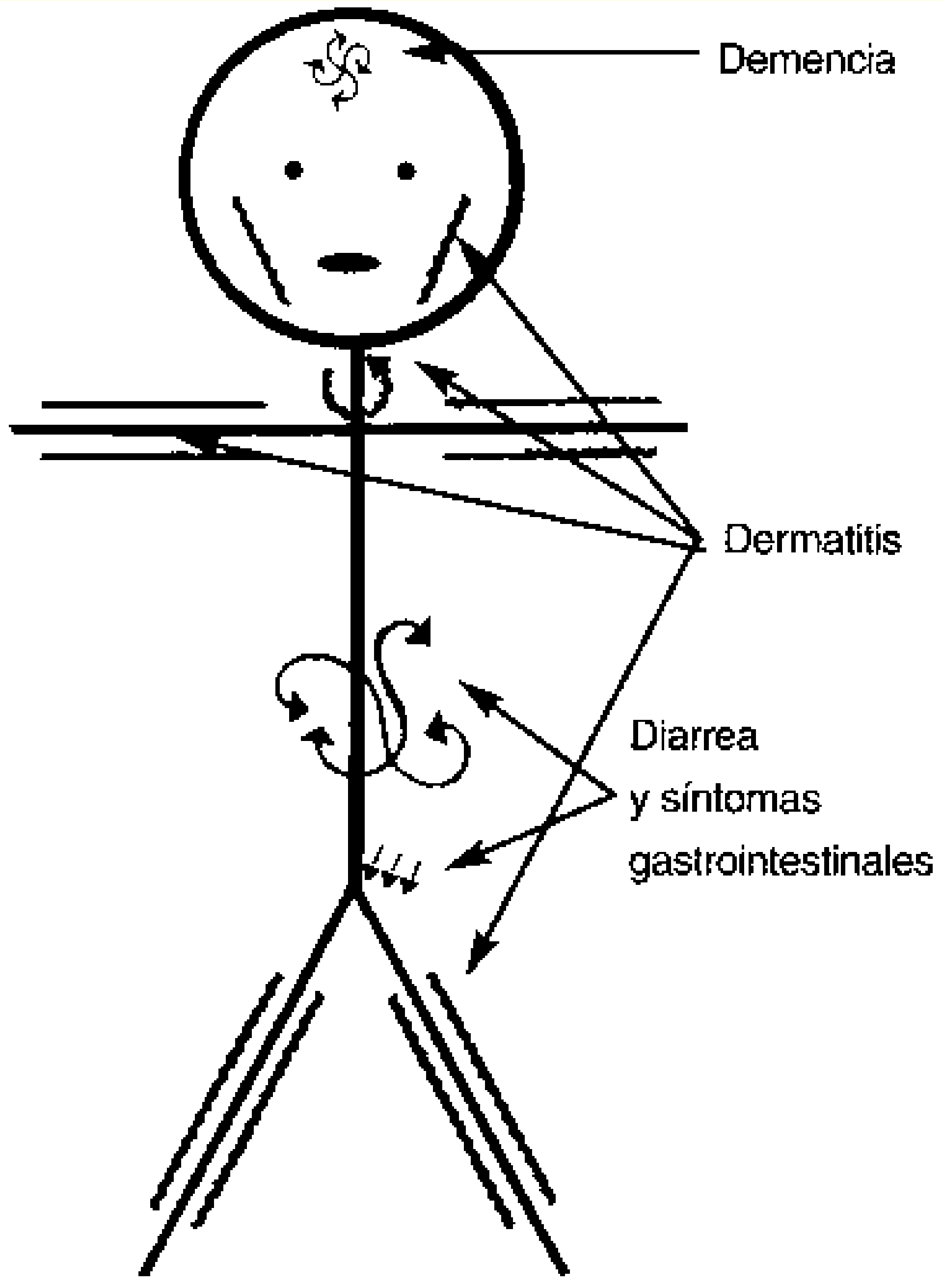


HCA2 = hydroxycarboxylic acid receptor 2

PELAGRA

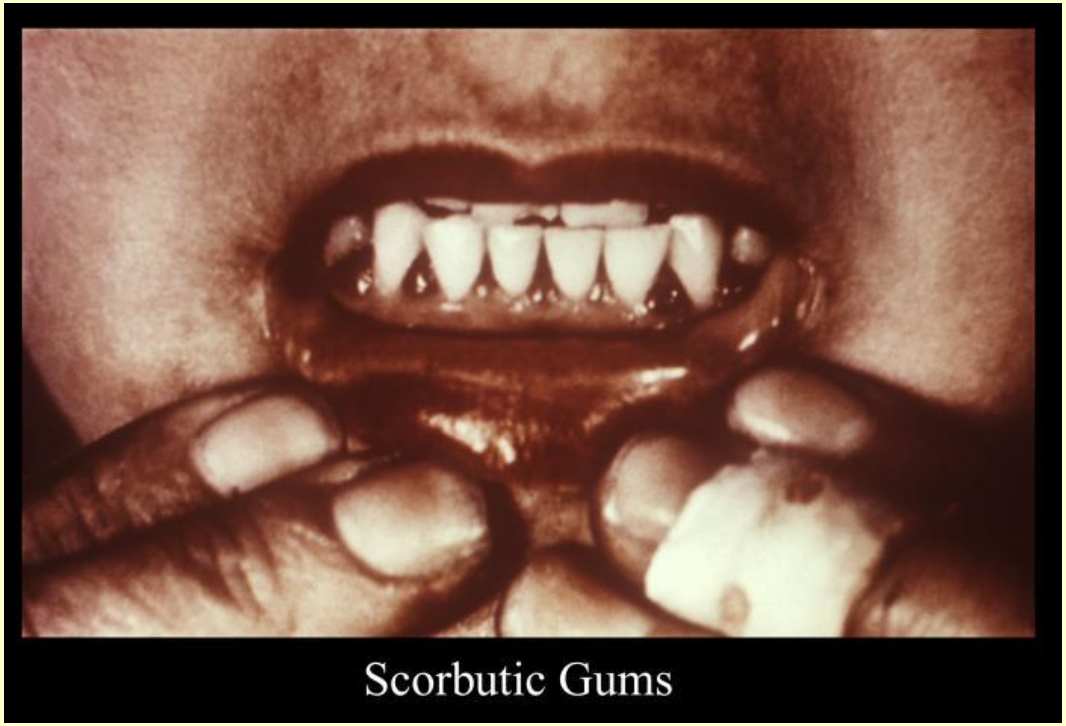
(3 D disease)

(niacin)



Vitamin C

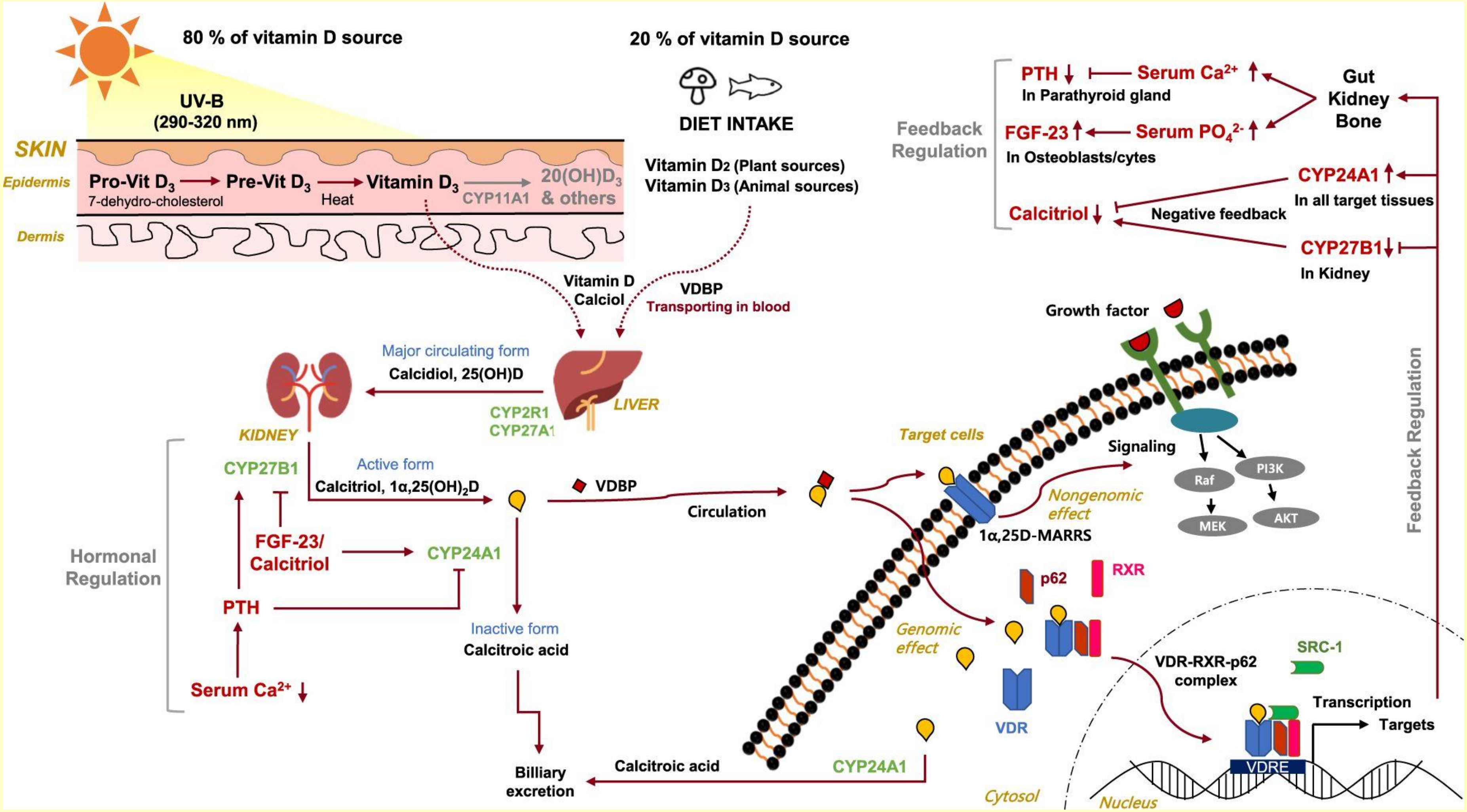
scurvy



20 – 30 weeks

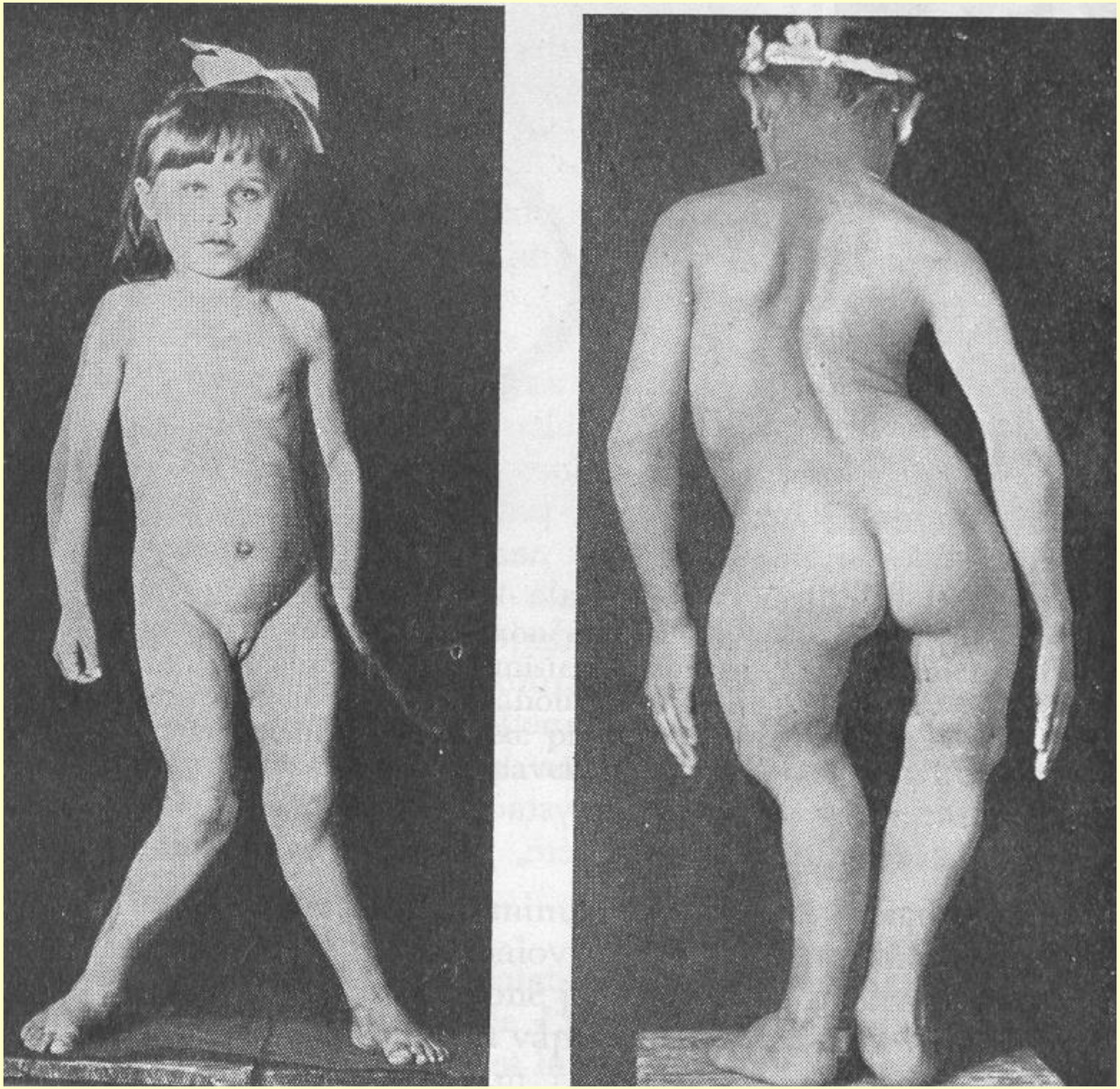
- Long bone growth disorders - ossification disorders - fracture healing disorders
- Fragility of vascular capillaries
- Very serious cases - fever, death

Vitamin D



80 % of vitamin D source
UV-B
(290-320 nm)
SKIN
Epidermis
Dermis
Pro-Vit D3 → Pre-Vit D3 → Vitamin D3 → 20(OH)D3 & others
7-dehydro-cholesterol
Heat
CYP11A1
20 % of vitamin D source
DIET INTAKE
Vitamin D2 (Plant sources)
Vitamin D3 (Animal sources)
Vitamin D
Calciol
VDBP
Transporting in blood
Major circulating form
Calcidiol, 25(OH)D
LIVER
CYP2R1
CYP27A1
KIDNEY
CYP27B1
Active form
Calcitriol, 1α,25(OH)2D
VDBP
Circulation
FGF-23/
Calcitriol
CYP24A1
Hormonal
Regulation
PTH
Serum Ca2+
Inactive form
Calcitroic acid
Billiary
excretion
Calcitroic acid
CYP24A1
Feedback
Regulation
PTH
In Parathyroid gland
Serum Ca2+
Gut
Kidney
Bone
FGF-23
Serum PO4 2-
In Osteoblasts/cytes
CYP24A1
In all target tissues
Calcitriol
Negative feedback
CYP27B1
In Kidney
Growth factor
Target cells
Signaling
PI3K
Raf
MEK
AKT
Nongenomic
effect
1α,25D-MARRS
p62
RXR
Genomic
effect
VDR
VDR-RXR-p62
complex
SRC-1
Transcription
Targets
VDRE
Cytosol
Nucleus
Feedback Regulation

RICKETS



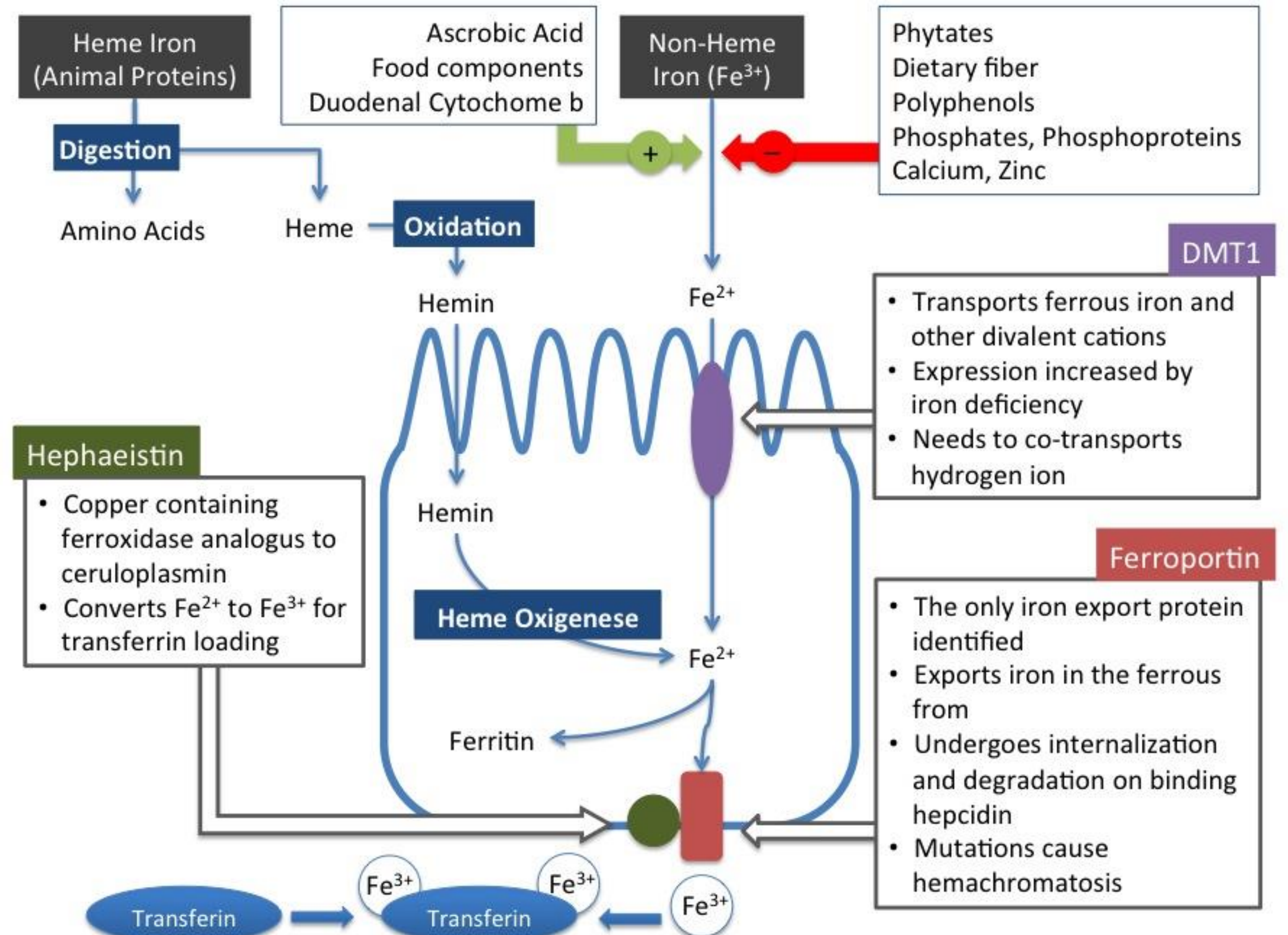
Mineral	Daily need (dose)
Na	3,0 g
K	1,0 g
Cl	3,5 g
Ca	1,2 g
P	1,2 g
Fe	18,0 mg
J	150,0 μg
Mg	0,4 g
Co	?
Cu	?
Mn	?
Zn	15 mg

Coenzyme of metabolic reactions of saccharides; deficiency – increased irritability of CNS, peripheral vasodilatation, arrhythmias; excess – suppresses electrical activity of CNS and skeletal muscle

Part of enzymes (carboanhydrase in erythrocytes, lactatedehydrogenase, peptidases)

MINERALS AND TRACE ELEMENTS

1. Arsenic
2. Chrome – experimental deficiency, glucose oral test is of diabetic character
3. Cobalt – part of enzymes, vit.B_{12}; poisoning by cobalt (beer), cobalt cardiomyopathy
4. Copper – impairment of cytochromoxidase (experiment), melanoma – increase of radiosensitivity when copper is depleted; vessel wall damage
5. Fluorine
6. Iodine
7. Iron
8. Manganese – catalyses similar reactions as Mg, stored in mitochondria, β1-globulintransmanganin
9. Molybdenum – in xantinoxidase and flavoproteins, defficiency in humans???
10. Nickell
11. Selenium – antioxidant, in diet bound to proteins (alcoholism, liver cirrhosis)
12. Silicon
13. Vanadium
14. Zinc – part of metalloenzymes, proteosynthesis (ribosomes);deficiency-Middle East (parasites, fytates in diet); testes atrophy, immune disorders; in DM 50% of stores Zn (insulin stored in pancreas together with Zn)


Heme Iron (Animal Proteins)
Ascrobic Acid
Food components
Duodenal Cytochome b
Non-Heme Iron (Fe^{3+})
Phytates
Dietary fiber
Polyphenols
Phosphates, Phosphoproteins
Calcium, Zinc
Digestion
+
−
Amino Acids
Heme
Oxidation
DMT1
Hemin
Fe^{2+}
• Transports ferrous iron and other divalent cations
• Expression increased by iron deficiency
• Needs to co-transports hydrogen ion
Hephaeistin
• Copper containing ferroxidase analogus to ceruloplasmin
• Converts Fe^{2+} to Fe^{3+} for transferrin loading
Hemin
Ferroportin
Heme Oxigenese
Fe^{2+}
• The only iron export protein identified
• Exports iron in the ferrous from
• Undergoes internalization and degradation on binding hepcidin
• Mutations cause hemachromatosis
Ferritin
Transferin
Fe^{3+}
Transferin
Fe^{3+}
Fe^{3+}

Iron: Factors Affecting Absorption

Physical State (bioavailability)	**heme > Fe^{2+} > Fe^{3+}**
Inhibitors	phytates, tannins, soil/clay (pica), laundry starch, iron overload, antacids
Competitors	lead, cobalt, strontium, manganese, zinc
Facilitators	ascorbate, citrate, amino acids, iron deficiency, stomach acid, high altitude, exercise, pregnancy