Vitamins and their role in metabolism and transfer of 1C residues

1st week

Vitamin deficiency

- **decrease of intake**

- **defects of absorption** - diseases of intestinal mucosa
  - decreased bile secretion

- **effects of drugs** - antivitamins
  - suppression of intestinal bacterial flora

- **liver diseases** - decreased storage capacity
  - decreased activation

- **increased requirement and utilization** - pregnancy
  - lactation
  - growth
  - infections diseases
  - alcoholism

Water soluble vitamins

Ascorbate – scurvy, fragility of bones and capillaries

B-complex

Energy releasing

Thiamine (B_1) – Beri-beri, inflammation of nerves, degeneration of nerves, muscle pains, seizures, **THIAMINASES** (coffee, tea)

Riboflavin (B_2)

Niacin (B_3) – dermatitis
dementia

Biotin diarrhea

Pantothenic acid

Hemopoetic

Folic acid (B_9) – megaloblastic anaemia in pregnancy – developmental defects

Cobalamin (B_{12}) - megaloblastic anaemia defects of CNS

AA metabolism

Pyridoxine (B_6) – skin inflammation, increased excitability, seizures

Lipid soluble vitamins

Hypovitaminoses

Retinol (A) - night blindness, anaemia
Retinal
Retinoic acid - increased ceratinization
- defects in regeneration of skin and mucosae
→ infections

Cholecalciferol (D) - rickets

Tocopherol (E) - newborns: fragility of capillaries, hemolytic anaemia
- adults: erythrocytes and muscles damage

Vitamin K - bleeding

Lipid soluble vitamins

Hypervitaminoses

Vitamin A	- skin, liver - intracranial pressure increase - congenital malformations
Cholecalciferol (D)	- lack of appetite, diarrhea, vomiting - soft tissues calcification (vessels, kidneys)

		Metabolism of		
vitamin	**active form**	**Carbohydrates**	**Lipids**	**Amino acids**
B_1	**TDP**	pyruvate dehydrogenase complex		branched-chain α-keto acid oxidation
		α-ketoglutarate dehydrogenase complex		
		transketolase (PPP)		
B_2	**FAD**	pyruvate dehydrogenase complex		branched-chain α-keto acid oxidation
		α-ketoglutarate dehydrogenase complex succinate dehydrogenase		
			acylCoA dehydrogenase	
	FMN			amino acid oxidases

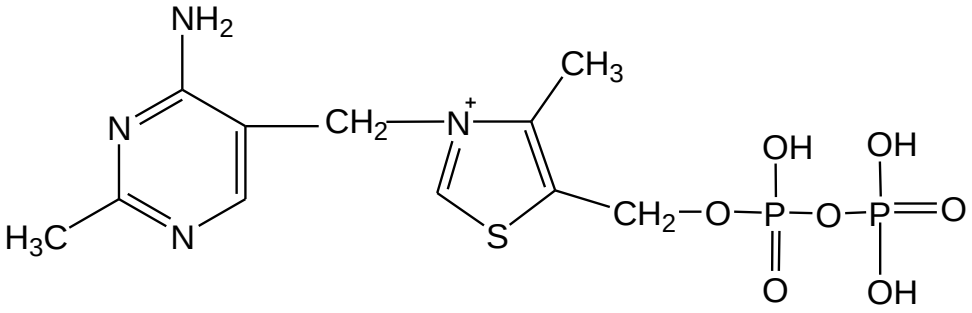
		Metabolism of		
vitamin	**active form**	**Carbohydrates**	**Lipids**	**Amino acids**
B_3	**NAD^+**	pyruvate dehydrogenase complex		branched-chain α-keto acid oxidation
		α-ketoglutarate dehydrogenase complex		
		glyceraldehyde-3P dehydrogenase	hydroxyacylCoA dehydrogenase	glutamate dehydrogenase
		lactate dehydrogenase		
		malate dehydrogenase isocitrate dehydrogenase		
	$NADP^+$	glucose-6P-dehydrogenase (PPP)	malic enzyme	
		(PPP) 6-phosphoglucono lactonate-dehydrogenase		
	NADPH		cytochrome P_{450} reductase ketoacyl-reductase enoyl-reductase HMG-CoA-reductase	

		Metabolism of		
vitamin	**active form**	**Carbohydrates**	**Lipids**	**Amino acids**
B_5	**CoA**	acetylCoA		
		succinylCoA		
			acylCoA	
H (B_7)	**biotin**	pyruvate carboxylase	acetylCoA carboxylase	
			propionylCoA carboxylase	
B_6	**pyridoxal phosphate (PLP)**	glycogen phosphorylase		transaminases
				serine dehydratase
				cystein desulfhydrase
				decarboxylases of AA

Vitamin B_1

coenzyme form: **thiamine pyrophosphate**: - oxidative decarboxylation of 2-ketoacids
- transketolase

thiamine triphosphate: nerve impulse transmission



Hypovitaminosis B_1:

glucose ⟶ pyruvate ⟶// acetyl-CoA ↓ ATP (CNS, myocard later)

2-ketoglutarate

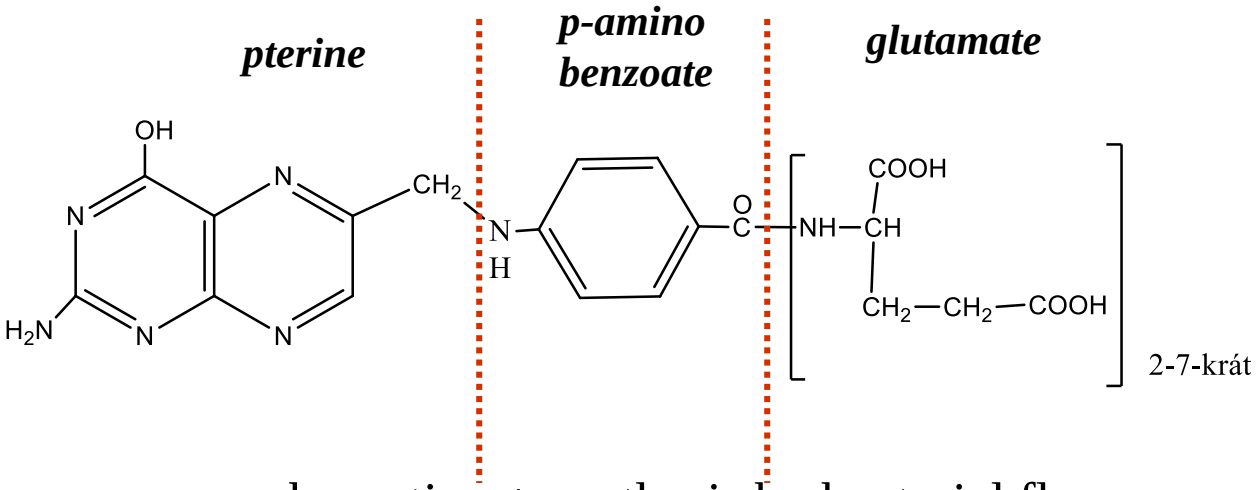
oxoacids from VAL, LEU, iLEU

BERI-BERI:

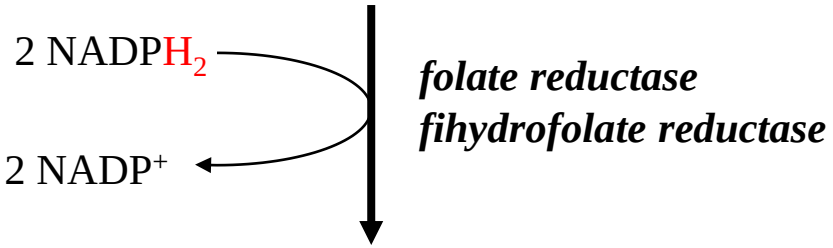
1. inflammation of nerves, defects in reflexes
   degenerative changes in central + peripheral NS
   paralysis, muscle pains
2. defects in cardiovascular system
3. fatigue, anorexia

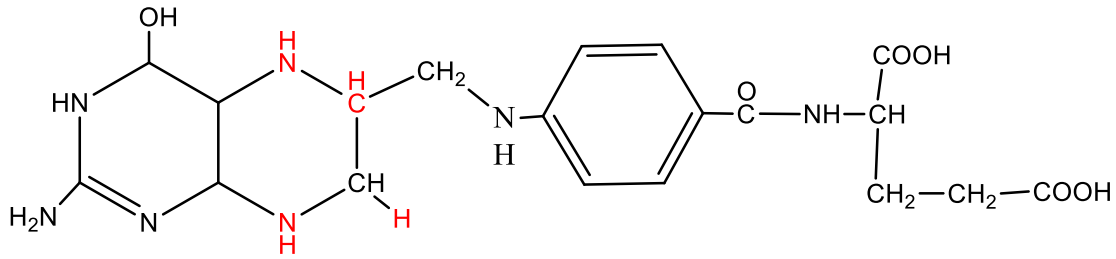
Folic acid

coenzyme form: **tetrahydrofolate**



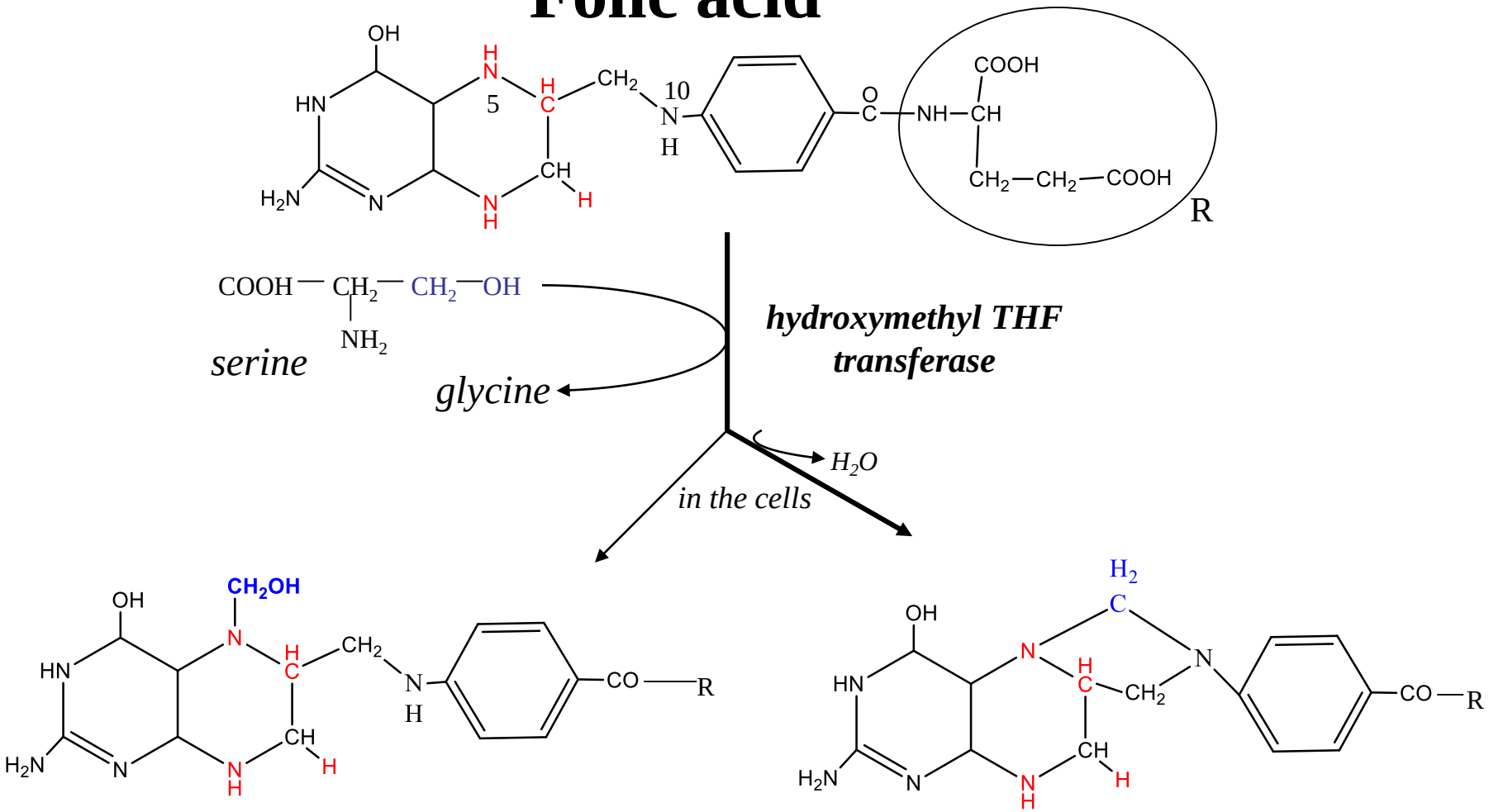
absorption + synthesis by bacterial flora





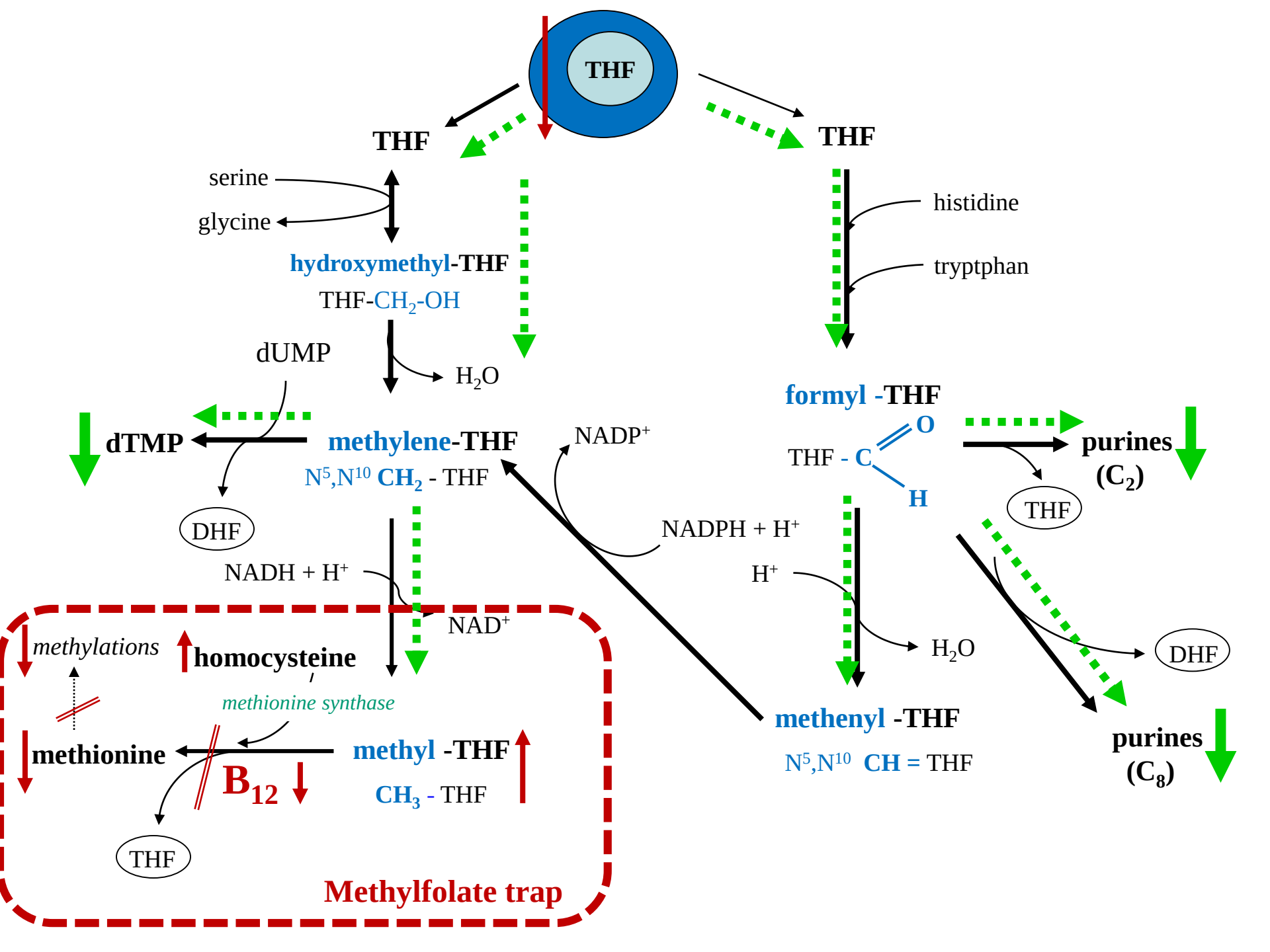
tetrahydrofolate

Folic acid



N^5-hydroxymethyl-THF
or N^{10}-hydroxymethyl-THF

N^5,N^{10}-methylene-THF

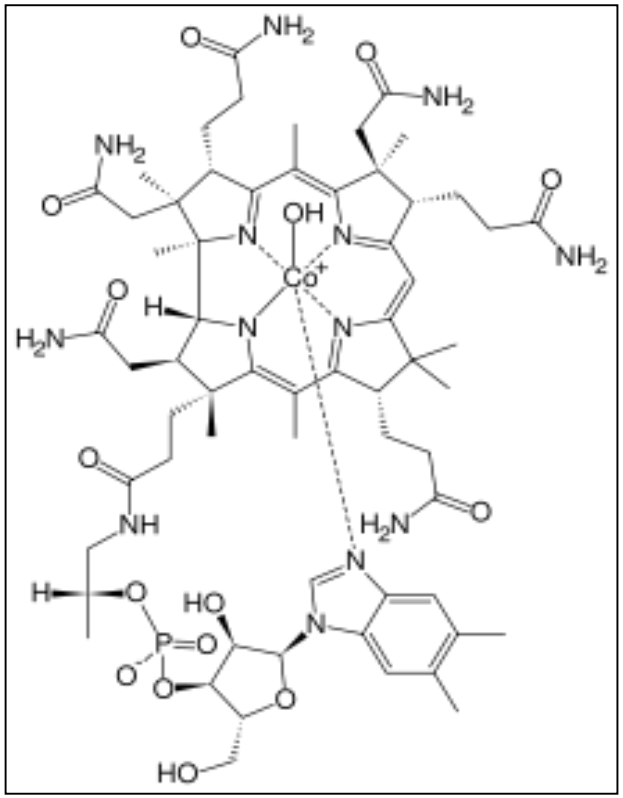

THF
THF
THF
serine
glycine
hydroxymethyl-THF
THF-CH2-OH
dUMP
H2O
histidine
tryptphan
formyl -THF
THF - C
O
H
dTMP
methylene-THF
N5,N10 CH2 - THF
NADP+
purines
(C2)
THF
DHF
NADPH + H+
H+
NADH + H+
NAD+
H2O
DHF
methylations
homocysteine
methionine synthase
methionine
B12
methyl -THF
CH3 - THF
methenyl -THF
N5,N10 CH = THF
purines
(C8)
THF
Methylfolate trap

Vitamin B_{12}

coenzyme form: **cobalamine**

coenzyme: - methylmalonyl-CoA mutase

- methioninesynthase (from homocysteine)



absorption

food

stomach → B_{12}-intrinsic factor

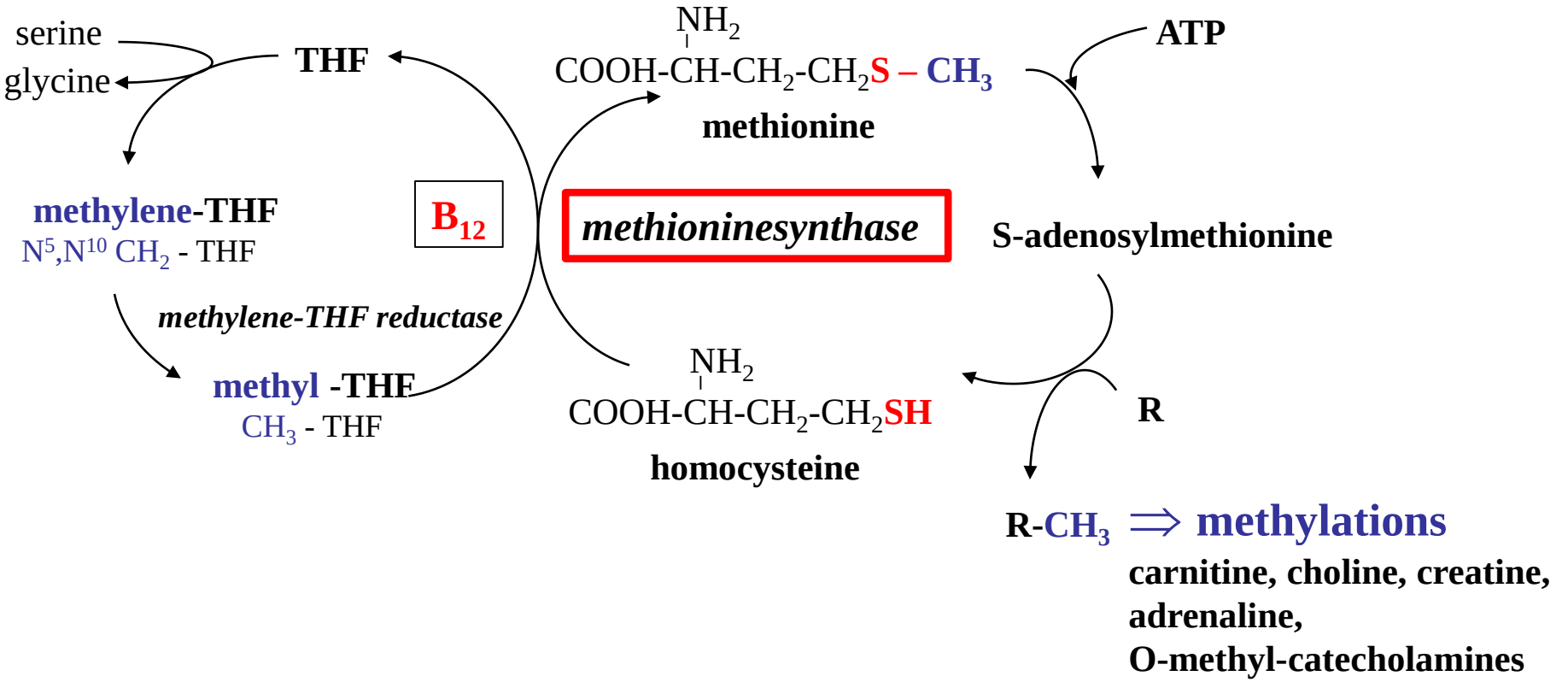
ileum → receptor protein

blood → B_{12}-transcobalamin

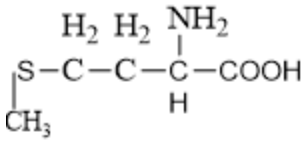
cells → B_{12} by receptors to the cells

Deficiency: mainly caused by deficiency of intrinsic factor ⇒ pernicious anaemia

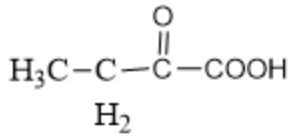
Vitamin B_{12}


serine
glycine
THF
NH2
COOH-CH-CH2-CH2S – CH3
methionine
ATP
methylene-THF
N5,N10 CH2 - THF
B12
methioninesynthase
S-adenosylmethionine
methylene-THF reductase
methyl -THF
CH3 - THF
NH2
COOH-CH-CH2-CH2SH
homocysteine
R
R-CH3 ⇒ methylations
carnitine, choline, creatine,
adrenaline,
O-methyl-catecholamines

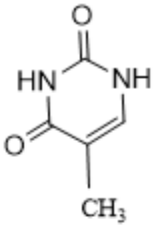
Vitamin B_{12}



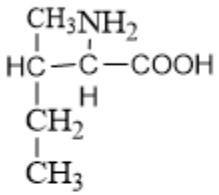
methionine



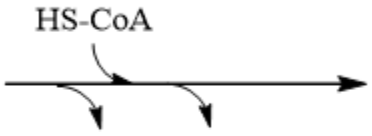
2-oxo- butyric acid

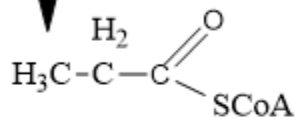


Thymine



isoleucine



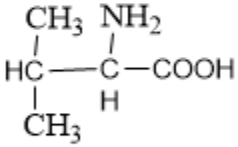


propionyl-CoA

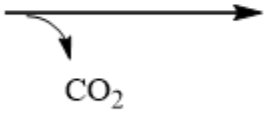
Cholesterol

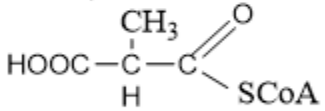
carboxylic acids with an odd number of C

CO_2
biotin
propionyl-CoA carboxylase



valine

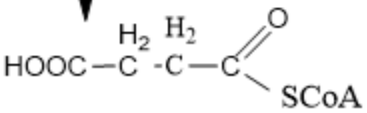




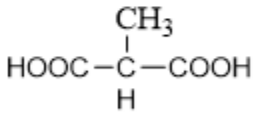
methylmalonyl-CoA

B_{12}

methylmalonyl-CoA mutase



succinyl-CoA



Methylmalonic acid

blood

urine

Hypovitaminoses: folic acid, B_{12}

1.) methylfolate-Trap: decreased synthesis of purines „de novo“
- decreased methylation of dUMP on dTMP
- increased homocysteine and decreased methionine

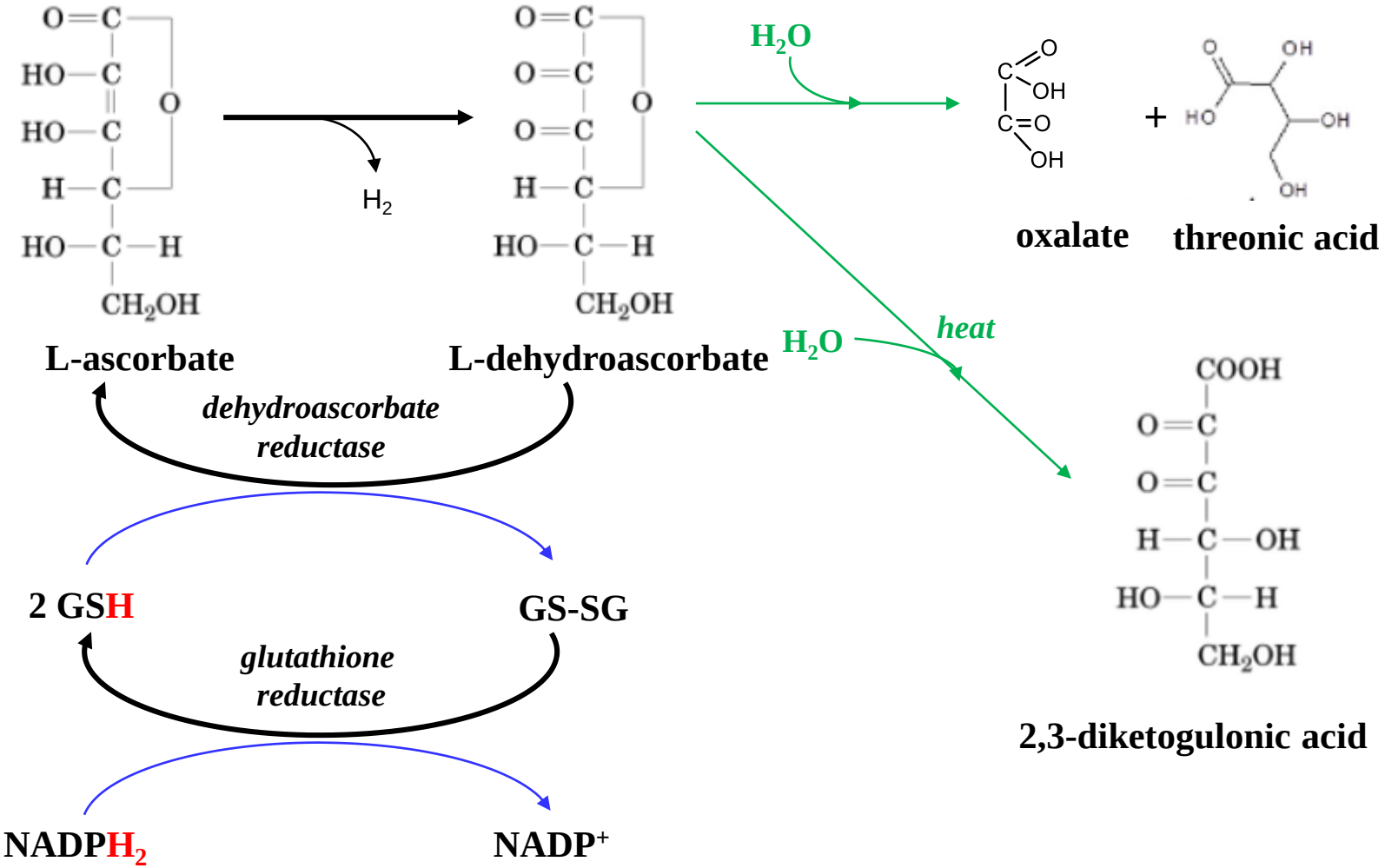
- **megaloblastic anemia (large Ery, full of hemoglobin, but a small number) ⇒ weakness, fatigue**
- **bioch. finding: increased serum and urine homocysteine, incresed urine methylmalonate**
- **Leu and Thromb. decrease**
- **inflammations, mucous membranes ulcerations (cell division decrease)**
- **Methionine decrease ⇒ choline decrease ⇒ reduced acetylcholine production**
- **hyperhomocysteinemia**

2.) methylmalonyl-CoA $\xrightarrow{B_{12}}$ succinyl-CoA (KC)

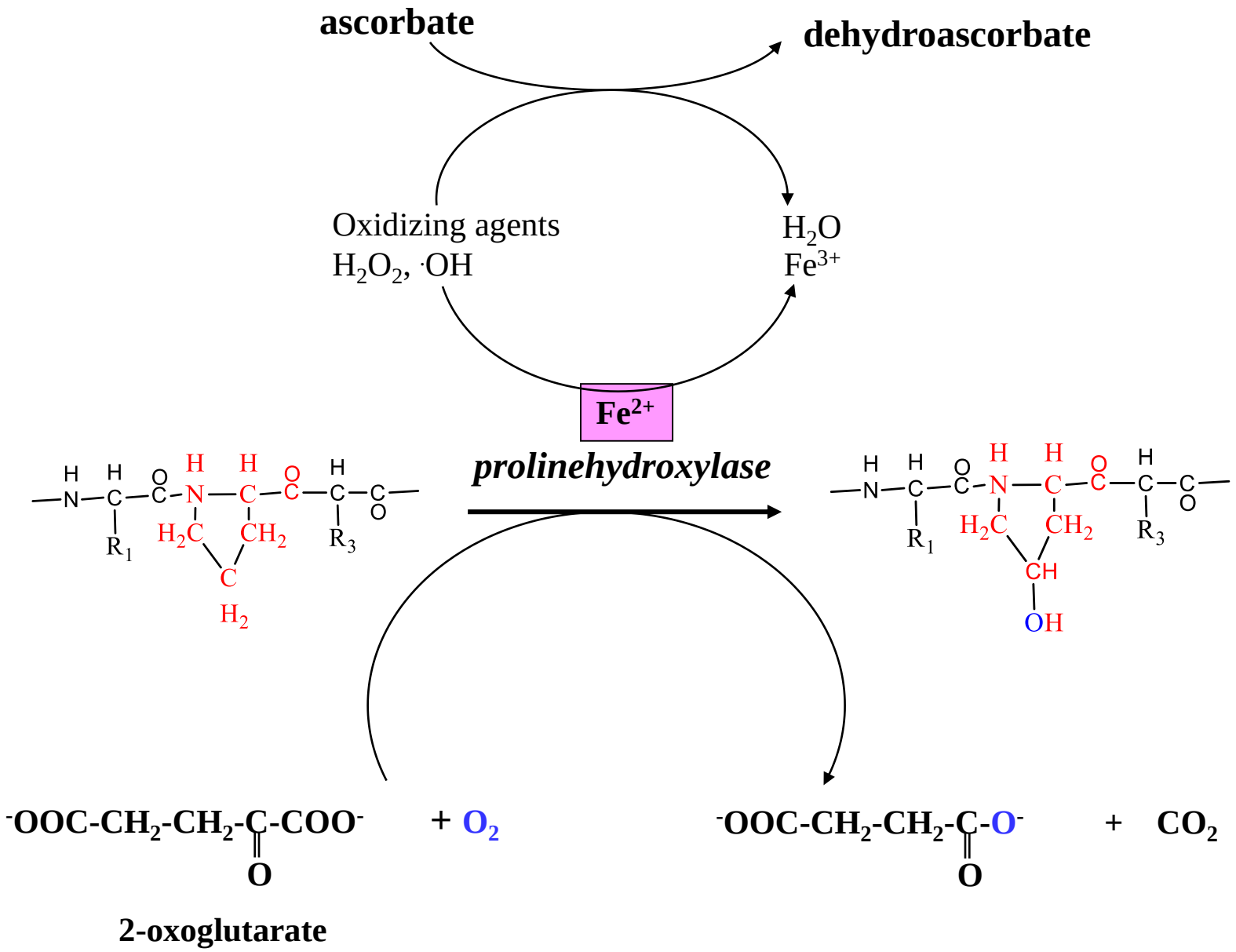
- **CNS disorders: much methylmalonyl-CoA ⇒ competition with malonyl-CoA at FA synthesis ⇒ branched FA (demyelination?)**
- **cardiovascular system: blood homocysteine increase – storage in walls vessels ⇒ arteriosclerosis (especially with elevated cholesterol)**

Vitamin C

function: - dopamine-β-hydroxylase (monooxygenase)
- proline post-translational modification
- hydroxylation – corticoids, cholesterol breaking-down
- maintenance of Fe^{2+} - hemoglobín, Fe^{2+} absorption



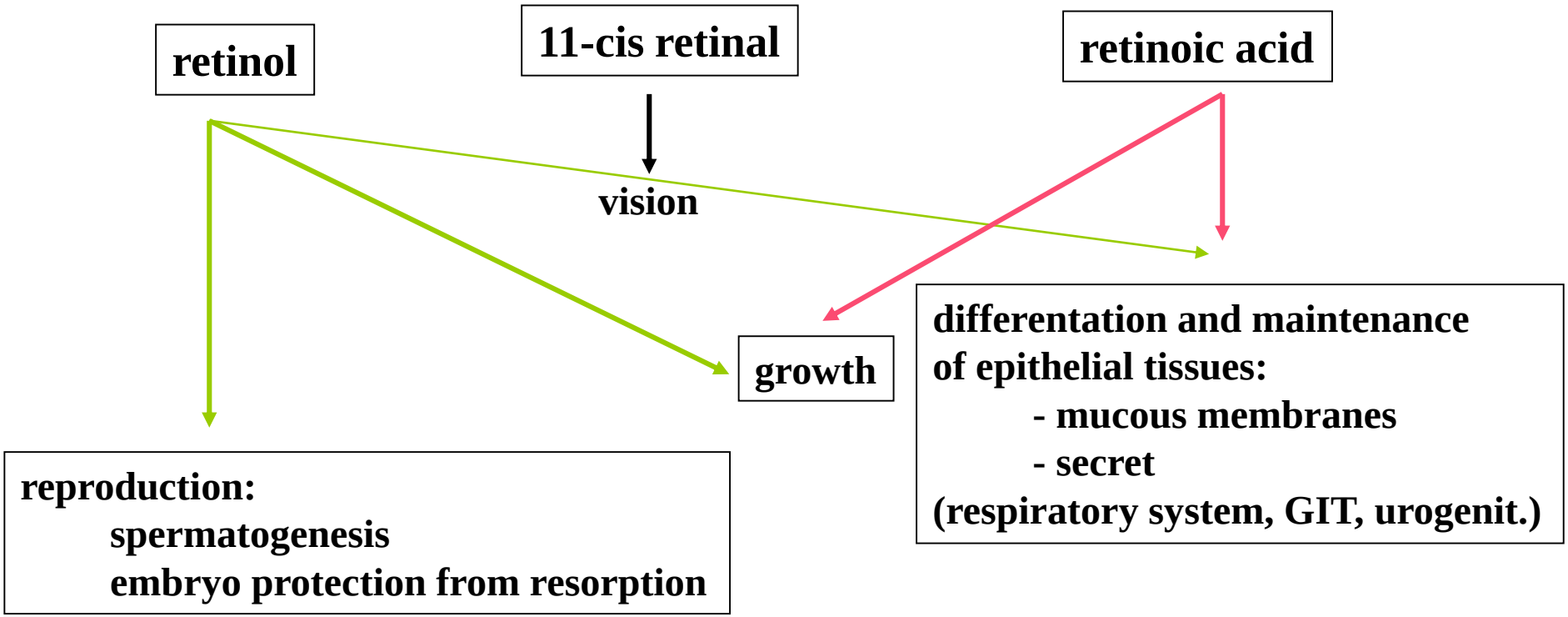
Vitamin C


ascorbate
dehydroascorbate
Oxidizing agents
H_2O_2, ·OH
H_2O
Fe^{3+}
Fe^{2+}
prolinehydroxylase
$^-OOC-CH_2-CH_2-C-COO^-$
O
+ O_2
$^-OOC-CH_2-CH_2-C-O^-$
O
+ CO_2
2-oxoglutarate

Vitamin A

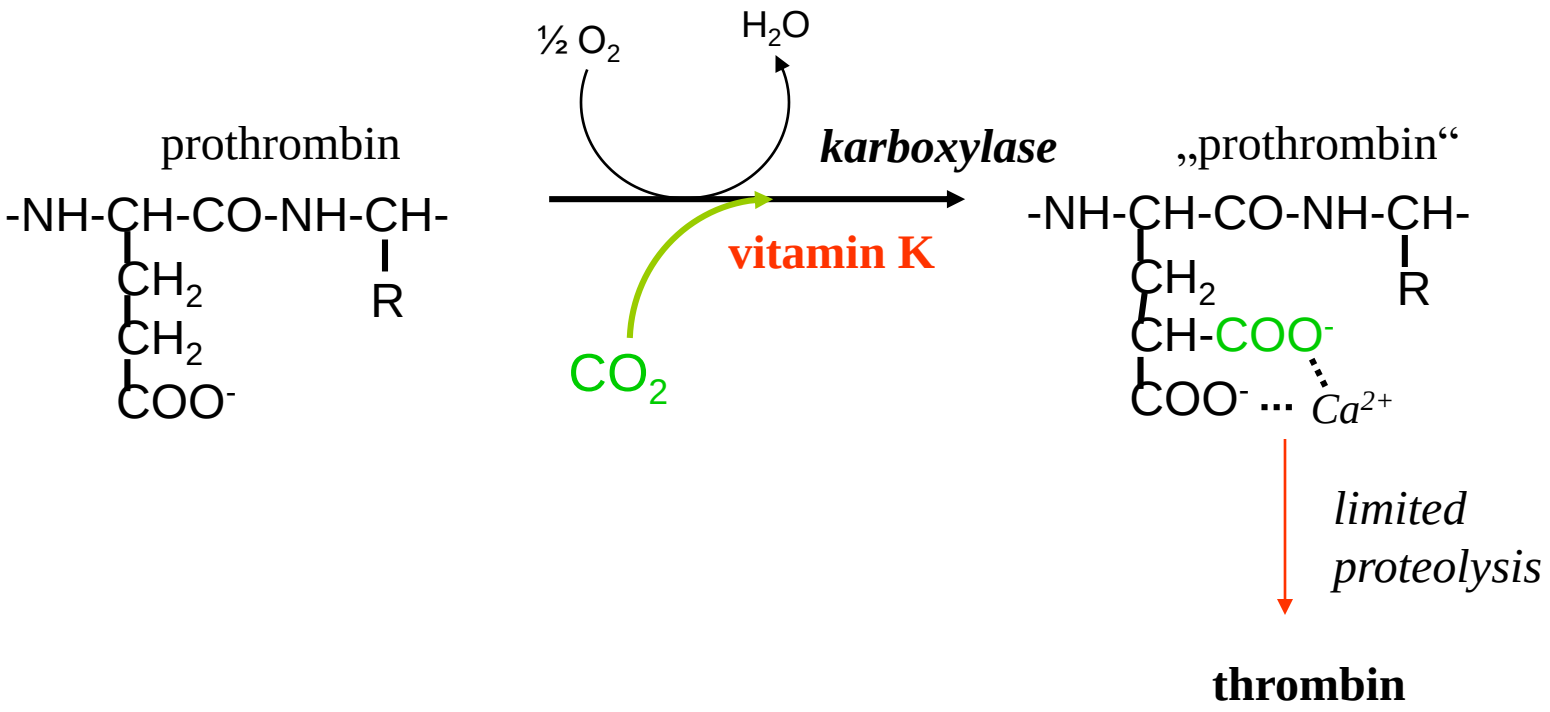
resources: - retinol esters – animal (liver, kidney)
- β-carotene – plants (less than 20%) → retinal

function: - cancer protection
- β-carotene (antioxidative effects)
- vitamin A (growth regulation)



Vitamin K

function: - **blood clotting regulation**
- liver prothrombin production and secretion
- participates in the activation of prothrombin to thrombin
(vitamin K- dependent carboxylation of glutamic acid in the liver ER



By the same mechanism (glutamic acid γ-carboxylation) it activates osteocalcin production together with vitamin D. The osteocalcin is necessary for Ca^{2+} binding in bones.

Vitamins and oral health

Vitamin A - ensures the integrity of mucous membranes, salivary glands, teeth and bones
- deficiency → xerostomia (dry mouth), increased infectious diseases, disturbed tooth growth
- excess → exfoliative cheilitis (inflammation of the lips associated with peeling skin), impaired healing and gingivitis

Vitamin D - important in the process of synthesis and mineralization of dentin and bone tissue
- protects against chronic gingivitis

Vitamin K - it participates in the process of calcium storage and mineralization of bones and teeth together with vitamin D

Vitamin C - important in the process of collagen and dentin formation, keeps it strong and healthy connective tissues of the gums
- deficiency → scurvy: gingivitis and bleeding gums, tooth loss

Vitamins of B-complex - angular cheilitis (corners inflammation), glossitis, aphthae, gingivitis and periodontitis