NUTRITION:

NUTRITIONAL REQUIREMENTS AND PRINCIPLES

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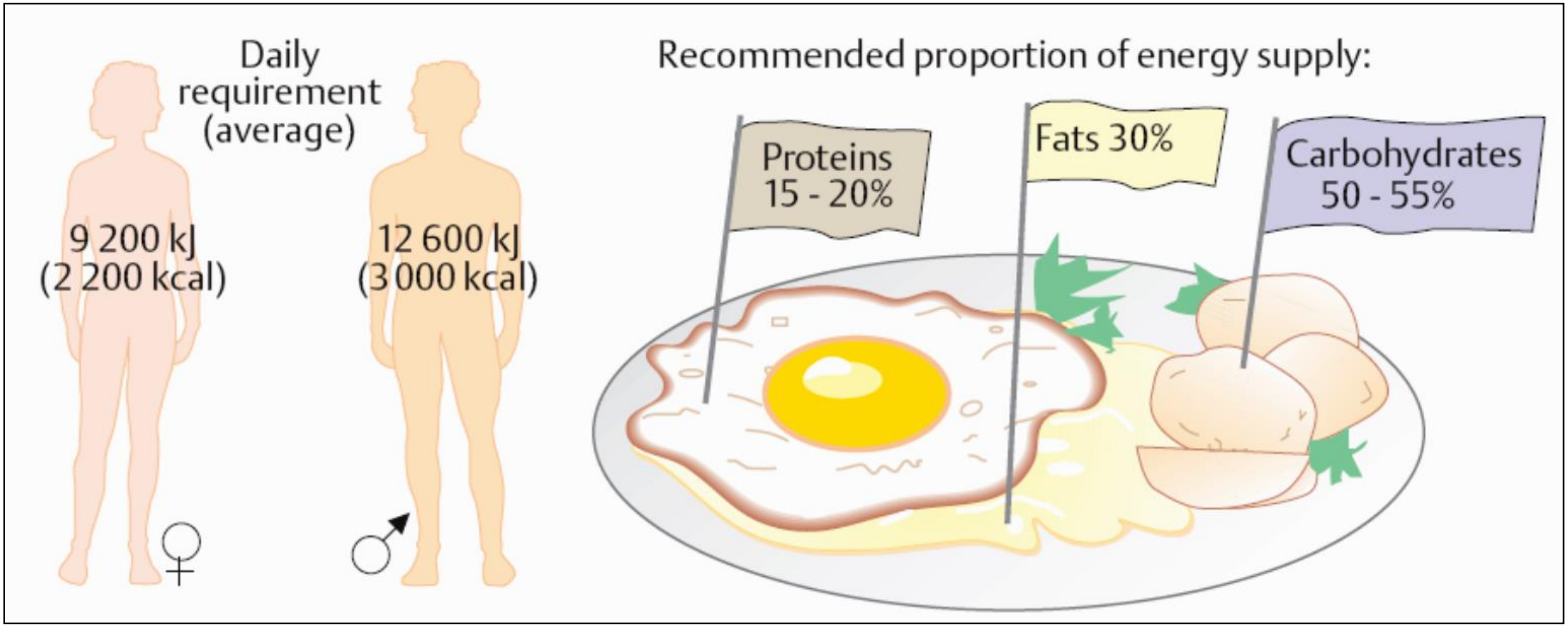
Energy requirement by a human organism

- expressed in kilojoule per day (kJ per day)
- older unit is kilocalorie (kcal: 1 kcal = 4.187 kJ)
- energy required may be estimated taking into account different factors such as age, sex, body weight, and particularly physical activity

Nutrients: proteins, carbohydrates, fats, water, minerals, vitamins

(alcoholic beverages, i.e. ethanol, have caloric value of about 30 kJ g^{-1})



<u>Energy requirements increase with activity</u>

- Calculated using data on **Basal Metabolic Rate (BMR)** → energy expenditure by the body when <u>at rest</u> but <u>no asleep</u>, under controlled conditions;

  - Sedentary activity uses only 1.1-1.2 x BMR; more vigorous activity (climbing stairs, skiing, walking uphill) may use 6-8 x BMR, and marathon up to 20 x BMR!

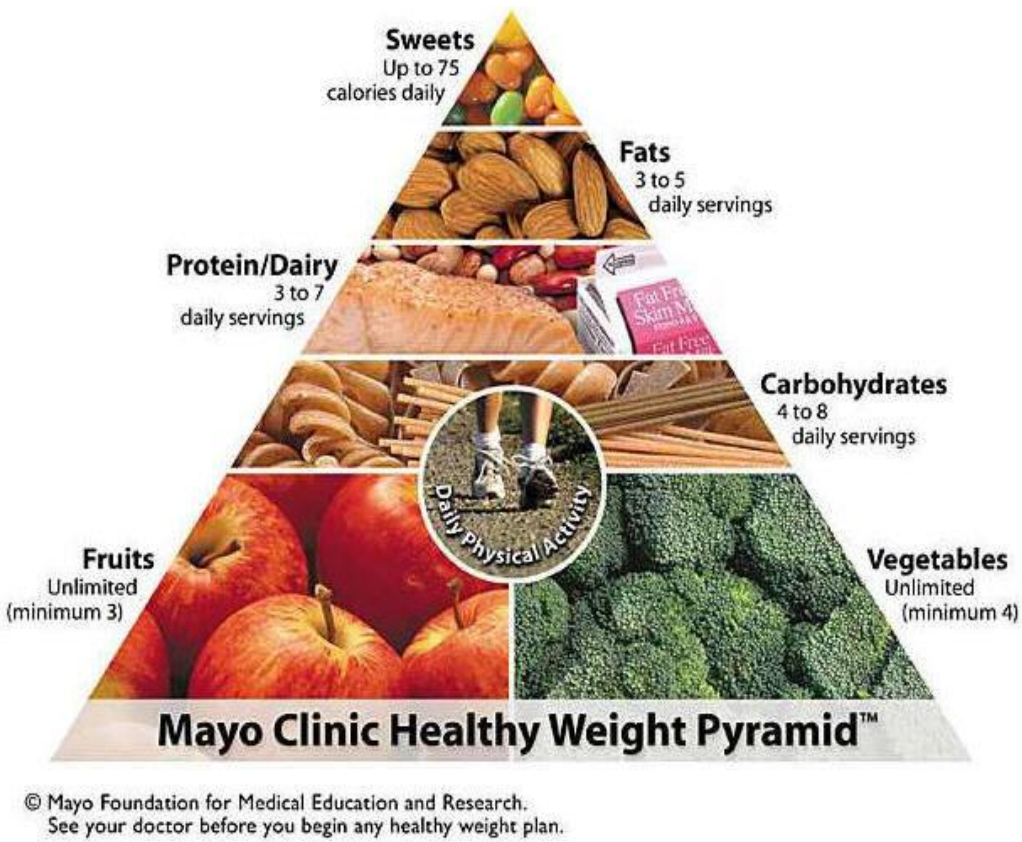
- ultra-endurance triathlon (eg. *Ironman Triathlon)* - total loss of 8500-11500 kcal!

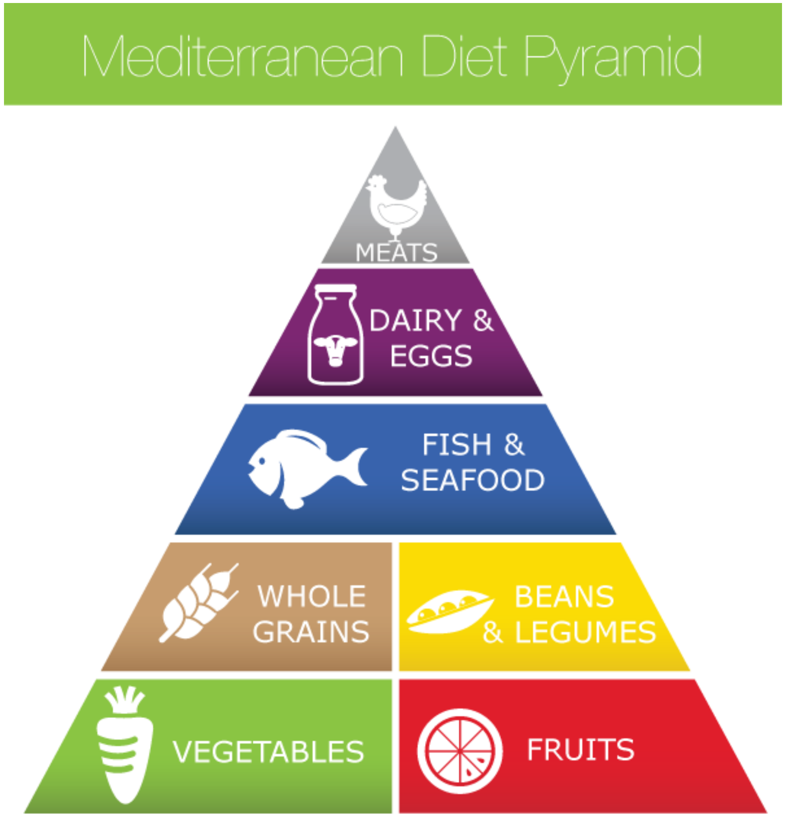
IRONMAN®
swim 3.8 km / bike 180 km / run 42 km
TRIATHLON

Barrero A, Erola P, Bescós R. Energy balance of triathletes during an ultra-endurance event. *Nutrients* 2014;
Guyton, Arthur C. Textbook of medical physiology / Arthur C. Guyton, John E. Hall., 11th ed. 2006

Balanced diet should provide intake of:

- Water
- Metabolic “fuel” (fats and carbohydrates)
- Proteins (growth and transport of tissue protein)
- Dietary fiber
- Essential fatty acids and essential amino acids, minerals, vitamins





Mediterranean Diet influence on reduction of chronic diseases:

- cardiovascular system
- obesity
- respiratory system
- neurological system

- reduced risk of breast cancer

Sofi F, Cesari F, Abbate R, et al. Adherence to Mediterranean diet and health status: meta-analysis. BMJ 2008

Mediterranean diet and life expectancy; beyond olive oil, fruits, and vegetables

Miguel A. Martinez-Gonzalez[a,b] *and Nerea Martin-Calvo*[a,b]

Purpose of review

The recent relevant evidence of the effects of the Mediterranean diet (MedDiet) and lifestyle on health (2015 and first months of 2016).

Recent findings

Large observational prospective epidemiological studies with adequate control of confounding and two large randomized trials support the benefits of the Mediterranean dietary pattern to increase life expectancy, reduce the risk of major chronic disease, and improve quality of life and well-being. Recently, 19 new studies from large prospective studies showed – with nearly perfect consistency – strong benefits of the MedDiet to reduce the risk of myocardial infarction, stroke, total mortality, heart failure, and disability. Interestingly, two large and well conducted cohorts reported significant cardiovascular benefits after using repeated measurements of diet during a long follow-up period. In addition, Prevención con Dieta Mediterránea, the largest randomized trial with MedDiet, recently reported benefits of this dietary pattern to prevent cognitive decline and breast cancer.

Summary

In the era of evidence-based medicine, the MedDiet represents the gold standard in preventive medicine, probably because of the harmonic combination of many elements with antioxidant and anti-inflammatory properties, which overwhelm any single nutrient or food item. The whole seems more important than the sum of its parts.

Keywords

cardiovascular disease, coronary heart disease, feeding trials, nuts, olive oil

Curr Opin Clin Nutr Metab Care 2016;19:401-407

Received: 10 April 2019 | Revised: 8 June 2019 | Accepted: 17 June 2019
DOI: 10.1111/bph.14778

Themed Section: The Pharmacology of Nutraceuticals

BJP BRITISH PHARMACOLOGICAL SOCIETY

REVIEW ARTICLE

Mediterranean diet and health status: Active ingredients and pharmacological mechanisms

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The Mediterranean diet (MedDiet) is one of the most widely described and evaluated dietary patterns in scientific literature. It is characterized by high intakes of vegetables, legumes, fruits, nuts, grains, fish, seafood, extra virgin olive oil, and a moderate intake of red wine. A large body of observational and experimental evidence suggests that higher adherence to the MedDiet is associated with lower risk of mortality, cardiovascular disease, metabolic disease, and cancer. Current mechanisms underlying the beneficial effects of the MedDiet include reduction of blood lipids, inflammatory and oxidative stress markers, improvement of insulin sensitivity, enhancement of endothelial function, and antithrombotic function. Most likely, these effects are attributable to bioactive ingredients such as polyphenols, monounsaturated and polyunsaturated fatty acids, or fibre. This review will focus on both established and less established mechanisms of action of biochemical compounds contained in a MedDiet.

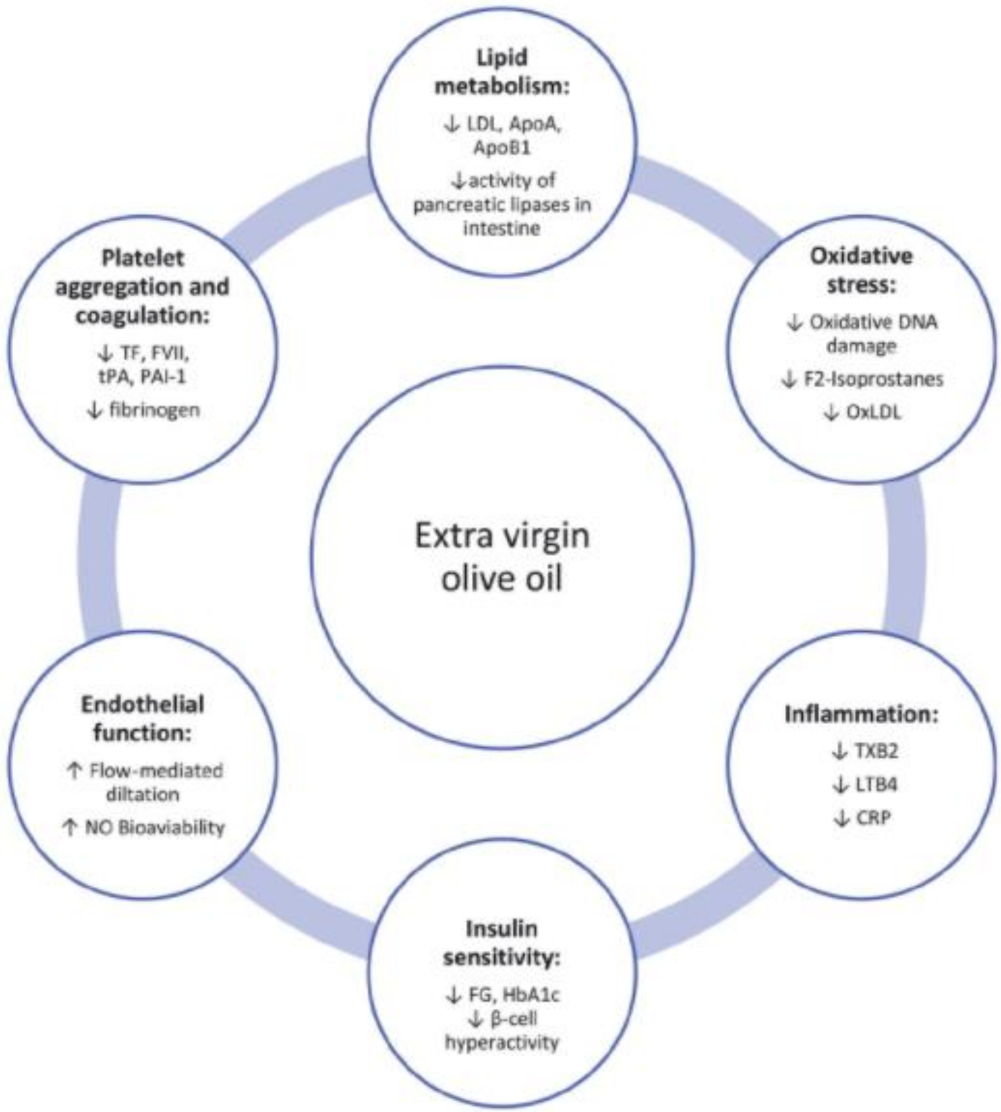


FIGURE 1 Overview of mechanistic properties of extra virgin oil (EVOO). EVOO may provide a beneficial effect for non-communicable disease risk by modifying lipid metabolism, decreasing oxidative stress and inflammation, increasing insulin sensitivity, and improving endothelial function and coagulation. ApoA, apolipoprotein A; ApoB1, apolipoprotein B1; CRP, C-reactive protein; FG, fasting glucose; FVII, coagulation factor VII; OxLDL, oxidized LDL; PAI-1, plasminogen activator inhibitor-1; TF, tissue factor; tPA, tissue plasminogen activator

Disorders related to nutrition/digestion:

- malnutrition / undernourishment
- obesity
- hypovitaminosis
- gastric acid hyperexcretory states → peptic ulcer disease (PUD), gastroesophageal reflux disease (GERD)
- *Helicobacter pylori* bacterial infections
- gallstones (crystallization of cholesterol)
- food intolerance (eg. lactose, food aditives)
- food allergy (eg. peanuts, milk, eggs, gluten-celiac disease)
- GI system diseases (eg. Crohn disease, ulcerative colitis)
- functional GI disorders → irritable bowel syndrom (IBS), constipation

B. Nutrients

	Quantity in body (kg)	Energy content kJ · g^{-1} (kcal · g^{-1})	Daily requirement (g) a	b	c	General function in metabolism	Essential constituents
Proteins	10	17 (4.1)	♂ 37 ♀ 29	55 45	92 75	Supplier of amino acids Energy source	Essential amino acids:: (Daily requirement in mg per kg body weight) Val (14) Leu (16) Ile (12) Lys (12) Phe (16) Trp (3) Met (10) Thr (8) Cys and His stimulate growth
Carbohydrates	1	17 (4.1)	0	390	240-310	General source of energy (glucose) Energy reserve (glycogen) Roughage (cellulose) Supporting substances (bones, cartilage, mucus)	Non-essential nutritional constituent
Fats	10-15	39 (9.3)	10	80	130	General energy source Most important energy reserve Solvent for vitamins Supplier of essential fatty acids	Polyunsaturated fatty acids: Linoleic acid Linolenic acid Arachidonic acid (together 10 g/day)
Water	35-40	0	2400	–	–	Solvent Cellular building block Dielectric Reaction partner Temperature regulator	
Minerals	3	0				Building blocks Electrolytes Cofactors of enzymes	Macrominerals Microminerals (trace elements)
Vitamins	–	–				Often precursors of coenzymes	Lipid-soluble vitamins Water-soluble vitamins

a: Minimum daily requirement b: Recommended daily intake c: Actual daily intake in industrialized nations

CARBOHYDRATES IN NUTRITION

Carbohydrates are non-essential!

Glycemic index - the increase in blood glucose concentration after a test dose of a carbohydrate compared with that after an equivalent amount of glucose.

Glycemic index = 1 for **glucose**, galactose, lactose, maltose, isomaltose, trehalose

Glycemic index < 1 for fructose

Glycemic index = from near 1 to near 0 for starch (variable rate of hydrolysis); 0 for non-starch polysaccharides

Foods that have low glycemic index are considered to be more beneficial (less fluctuation in insulin secretion)

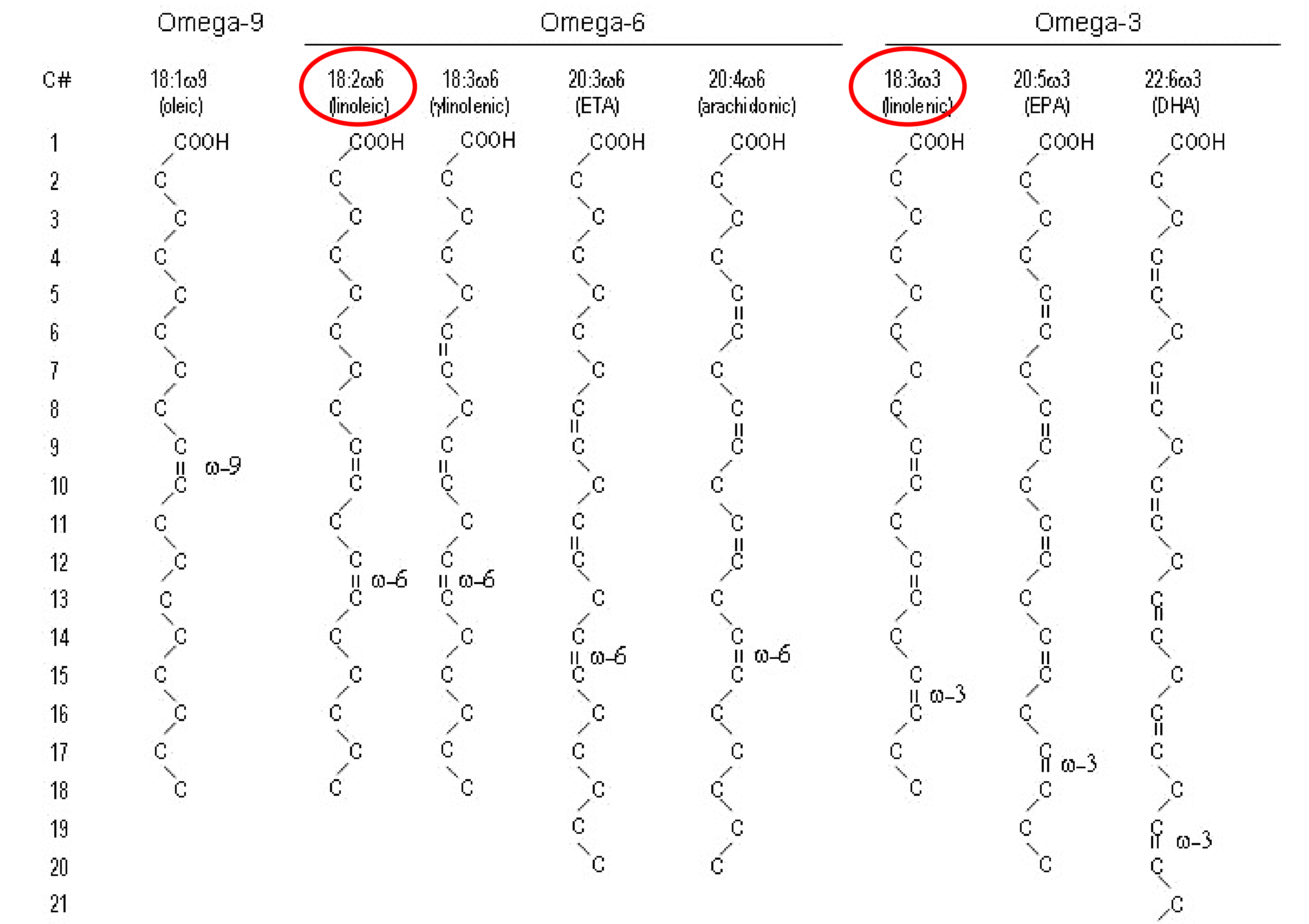
FATS IN NUTRITION

TAGs, cholesterol
Essential fatty acids!

PROTEINS IN NUTRITION

Essential amino acids!

Essential fatty acids: linoleic (18:2) i α-linolenic (18:3)



- **ω3, ω6 i ω9 groups of fatty acids**

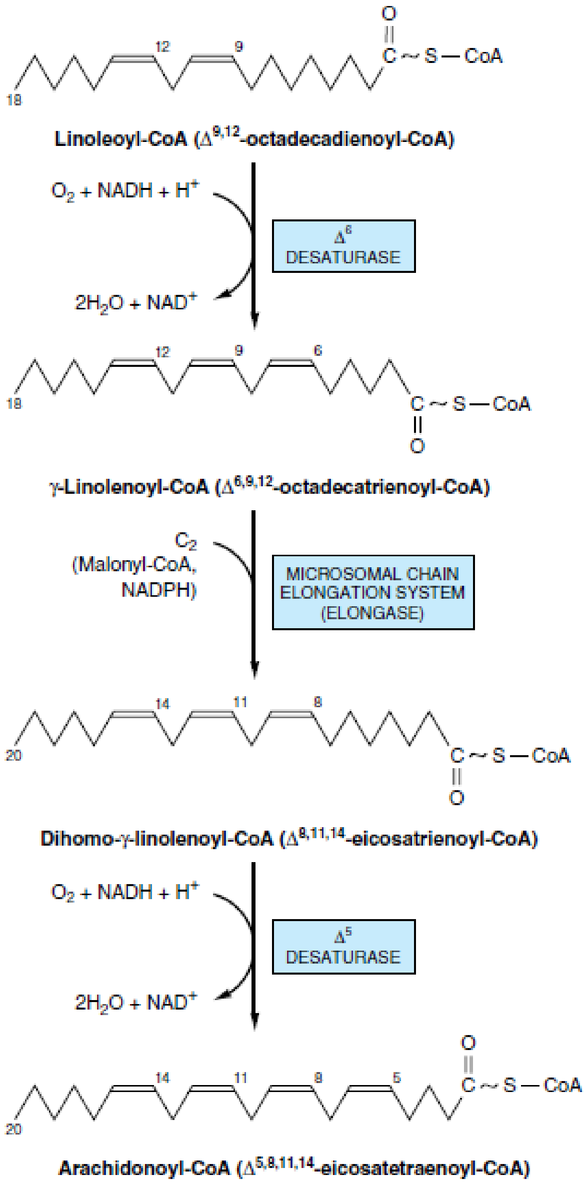


Figure 23–4. Conversion of linoleate to arachidonate. Cats cannot carry out this conversion owing to absence of Δ^6 desaturase and must obtain arachidonate in their diet.

Linoleic acid (18:2, $\Delta^{9,12}$)

↓

γ-Linolenic acid (18:3, $\Delta^{6,9,12}$)

↓

Arachidonic acid (20:4, $\Delta^{5,8,11,14}$)

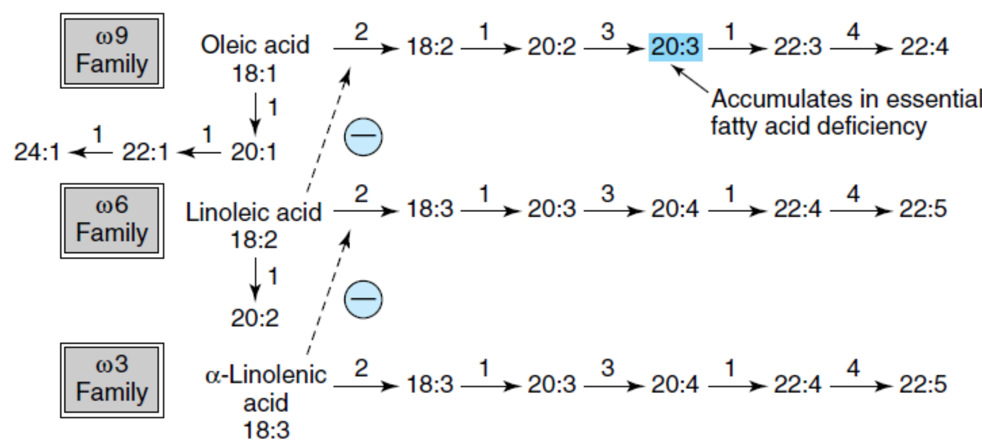


Figure 23–3. Biosynthesis of the ω9, ω6, and ω3 families of polyunsaturated fatty acids. Each step is catalyzed by the microsomal chain elongation or desaturase system: 1, elongase; 2, Δ^6 desaturase; 3, Δ^5 desaturase; 4, Δ^4 desaturase. (⊖, Inhibition.)

EPA = eicosapentanoic acid (ω3, 20:5)
DHA = docosahexanoic acid (ω3, 22:6)

Omega-3 Fatty Acids EPA and DHA: Health Benefits Throughout Life[1,2]

Danielle Swanson,[3] Robert Block,[4] and Shaker A. Mousa[3,5*]

[3]*The Pharmaceutical Research Institute, Albany College of Pharmacy and Health Sciences, Rensselaer, NY;* [4]*Department of Community and Preventive Medicine, and Division of Cardiology, Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY;* [5]*College of Medicine, King Saud University, Riyadh, Saudi Arabia*

ABSTRACT

Omega-3 [(n-3)] fatty acids have been linked to healthy aging throughout life. Recently, fish-derived omega-3 fatty acids EPA and DHA have been associated with fetal development, cardiovascular function, and Alzheimer's disease. However, because our bodies do not efficiently produce some omega-3 fatty acids from marine sources, it is necessary to obtain adequate amounts through fish and fish-oil products. Studies have shown that EPA and DHA are important for proper fetal development, including neuronal, retinal, and immune function. EPA and DHA may affect many aspects of cardiovascular function including inflammation, peripheral artery disease, major coronary events, and anticoagulation. EPA and DHA have been linked to promising results in prevention, weight management, and cognitive function in those with very mild Alzheimer's disease. *Adv. Nutr. 3: 1–7, 2012.*

EPA = eicosapentanoic acid (ω3, 20:5)
DHA = docosahexanoic acid (ω3, 22:6)

Swanson D, Block R, Mousa SA. Omega-3 fatty acids EPA and DHA: health benefits throughout life. Adv Nutr 2012;3:1-7.

Essential amino acids

RDA, mg/kg per day (*Recommended Dietary Allowances*)

- from FAO/WHO/UNU (Food and Agriculture Organization/World Health Organization/United Nations University) recommendations for adults (1985):

Threonine	**7**
Tryptophan	**3.5**
Valine	**10**
Histidine	**8-12**
Lysine	**12**
Phenylalanine	**14**
Leucine	**14**
Isoleucine	**10**
Methionine	**13**

- nutritionally essential: **„T**hese **T**en **V**aluable **A**mino-acids **H**ave **L**ong **P**reserved **L**ife **I**n **M**an**"**

Threonine, Tryptophan, Valine, Arginine, Histidine (semiessential), Lysine, Phenylalanine, Leucine, Isoleucine, Methionine

Young VR, Borgonha S. Nitrogen and Amino Acid Requirements: The Massachusetts Institute of Technology Amino Acid Requirement Pattern. J Nutr, 2000

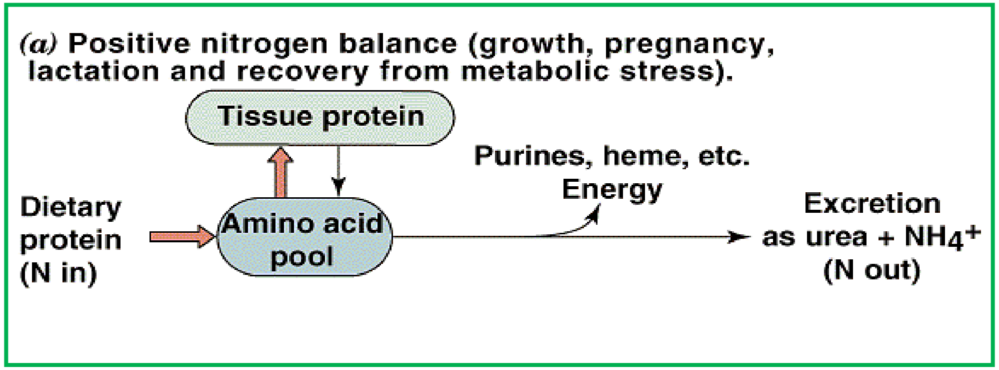
Protein requirement may be determined by measuring nitrogen balance

- difference between intake and output of nitrogenous compounds

- healthy individuals - **nitrogen balance in equilibrium** (intake = output)

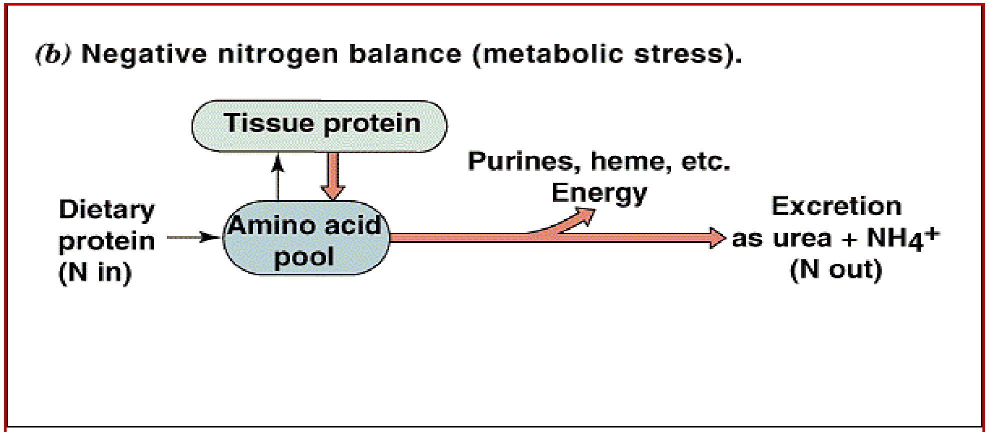
a) positive balance

- more intake than output (growth, pregnancy, lactation)



b) negative balance

- nitrogen loss (infection, stress, damage)

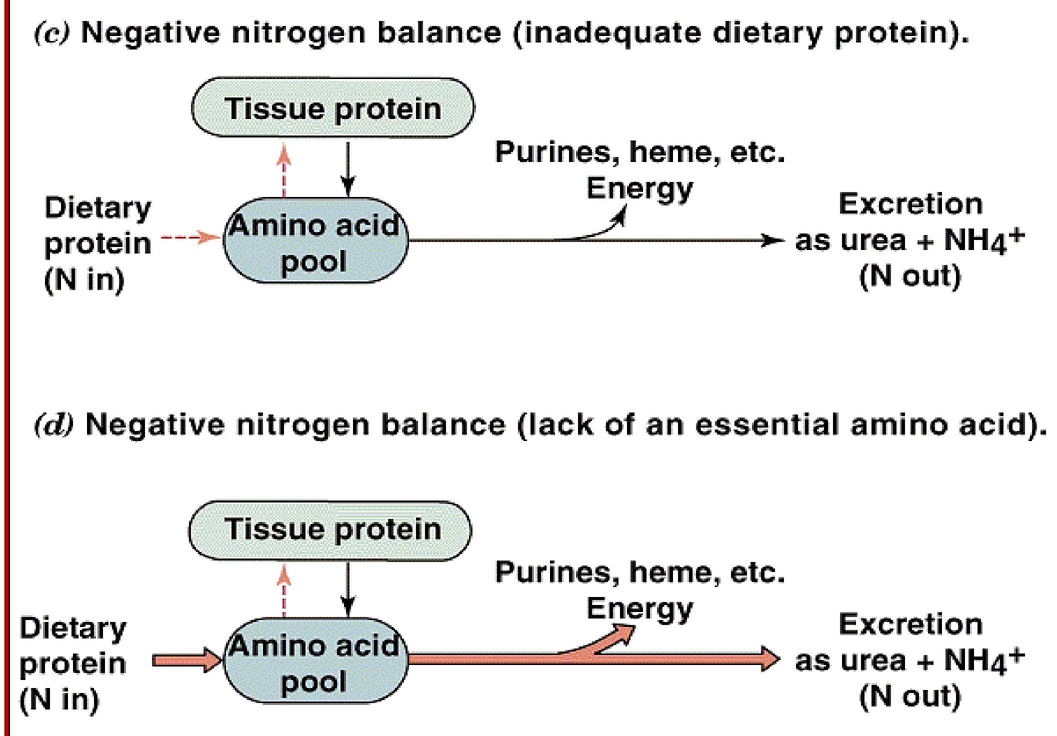


c) <u>negative balance</u>

- inadequate dietary protein

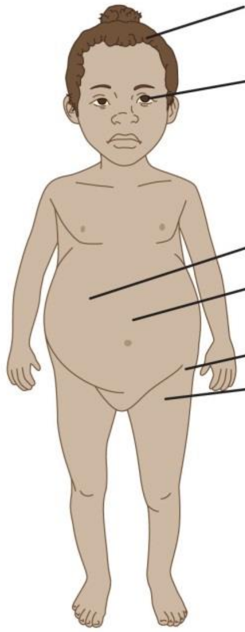
d) <u>negative balance</u>

- lack of essential amino acids



- <u>two extreme forms of undernutrition</u>:

- **kwashiorkor** - severe protein malnutrition
  - „edematous malnutrition" - decreased plasma proteins concentration - fluid retention, leading to edema
  - occurs only in children
  - areas of famine or poor food suplies
  - the name is derived from the Ga language (Ghana), translated as "the sickness the baby gets when the new baby comes" or "the disease of the deposed child"



Slika 54-19. Neki od glavnih znakova kvašiorkora.

- **marasmus** - extreme energetic deficiency
  - the outcome of prolonged negative energy balance
  - body's fat reserves exhausted
  - wastage of muscles and loss of protein from the heart, liver, and kidneys

WATER

- The most important essential inorganic nutrient in the diet
- In adults, the body has a **daily** requirement of **2-3 L of water** (supplied from drinks, water contained in solid/liquid foods, and from the *oxidation water* produced in the respiratory chain).
- The daily production of *oxidation water* is approximately 800-900 g.
- Water is distributed between extracellular, intracellular and transcellular space.

	Content * (g)	Major source	Daily requirement (g)	Functions/Occurrence
Water	35 000-40 000	Drinks Water in solid foods From metabolism 300g	1200 900	Solvent, cellular building block, dielectric, coolant, medium for transport, reaction partner

MINERALS AND TRACE ELEMENTS

Mineral	Content * (g)	Major source	Daily requirement (g)	Functions/Occurrence
Macroelements (daily requirement >100 mg)				
Na	100	Table salt	1.1-3.3	Osmoregulation, membrane potential, mineral metabolism
K	150	Vegetables, fruit, cereals	1.9-5.6	Membrane potential, mineral metabolism
Ca	1 300	Milk, milk products	0.8	Bone formation, blood clotting, signal molecule
Mg	20	Green vegetables	0.35	Bone formation, cofactor for enzymes
Cl	100	Table salt	1.7-5.1	Mineral metabolism
P	650	Meat, milk, cereals, vegetables	0.8	Bone formation, energy metabolism, nucleic acid metabolism
S	200	S-containing amino acids (Cys and Met)	0.2	Lipid and carbohydrate metabolism, conjugate formation

MINERALS AND TRACE ELEMENTS

Mineral	Content * (g)	Major source	Daily requirement (g)	Functions/Occurrence
Microelements (trace elements)			(mg	
Fe	4-5	Meat, liver, eggs, vegetables, potatoes, cereals	10	Hemoglobin, myoglobin, cytochromes, Fe/S clusters
Zn	2-3	Meat, liver, cereals	15	Zinc enzymes
Mn	0.02	Found in many foodstuffs	2-5	Enzymes
Cu	0.1-0.2	Meat, vegetables, fruit, fish	2-3	Oxidases
Co	<0.01	Meat	Traces	Vitamin B_{12}
Cr	<0.01		0.05-0.2	Not clear
Mo	0.02	Cereals, nuts, legumes	0.15-0.5	Redox enzymes
Se		Vegetables, meat	0.05-0.2	Selenium enzymes
I	0.03	Seafood, iodized salt, drinking water	0.15	Thyroxin
Requirement not known				Metals / Non-metals
F		Drinking water (fluoridated), tea, milk	0.0015-0.004	Bones, dental enamel

Classification of essential minerals according to their function

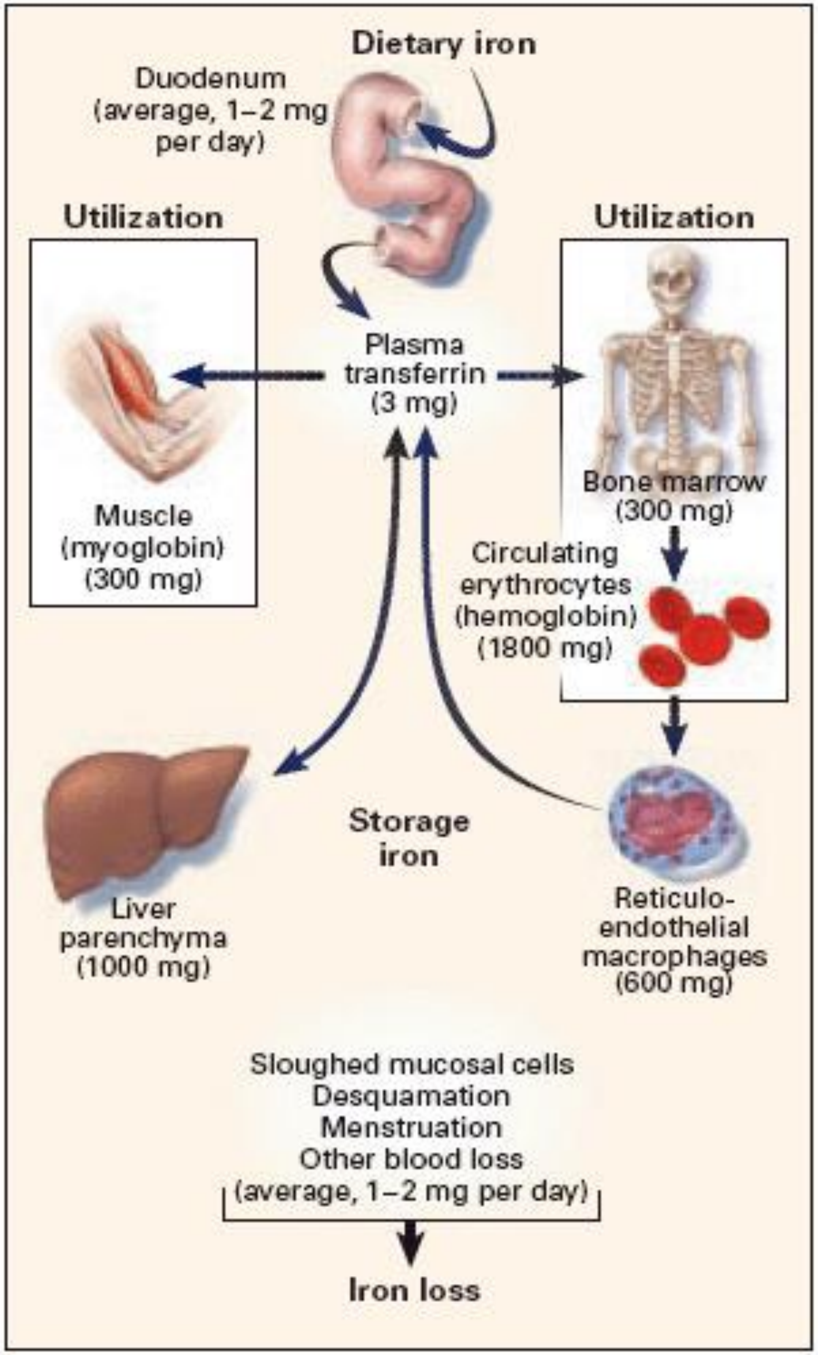
Function	Mineral
Structural function	Calcium, magnesium, phosphate
Involved in membrane function: principal cations of extracellular- and intracellular fluids, respectively	Sodium, potassium
Function as prosthetic groups in enzymes	Cobalt, copper, iron, molybdenum, selenium, zinc
Regulatory role or role in hormone action	Calcium, chromium, iodine, magnesium, manganese, sodium, potassium
Known to be essential, but function unknown	Silicon, vanadium, nickel, tin
Have effects in the body, but essentiality is not established	Fluoride, lithium
Without known nutritional function but toxic in excess	Aluminum, arsenic, antimony, boron, bromine, cadmium, cesium, germanium, lead, mercury, silver, strontium

Iron (Fe)

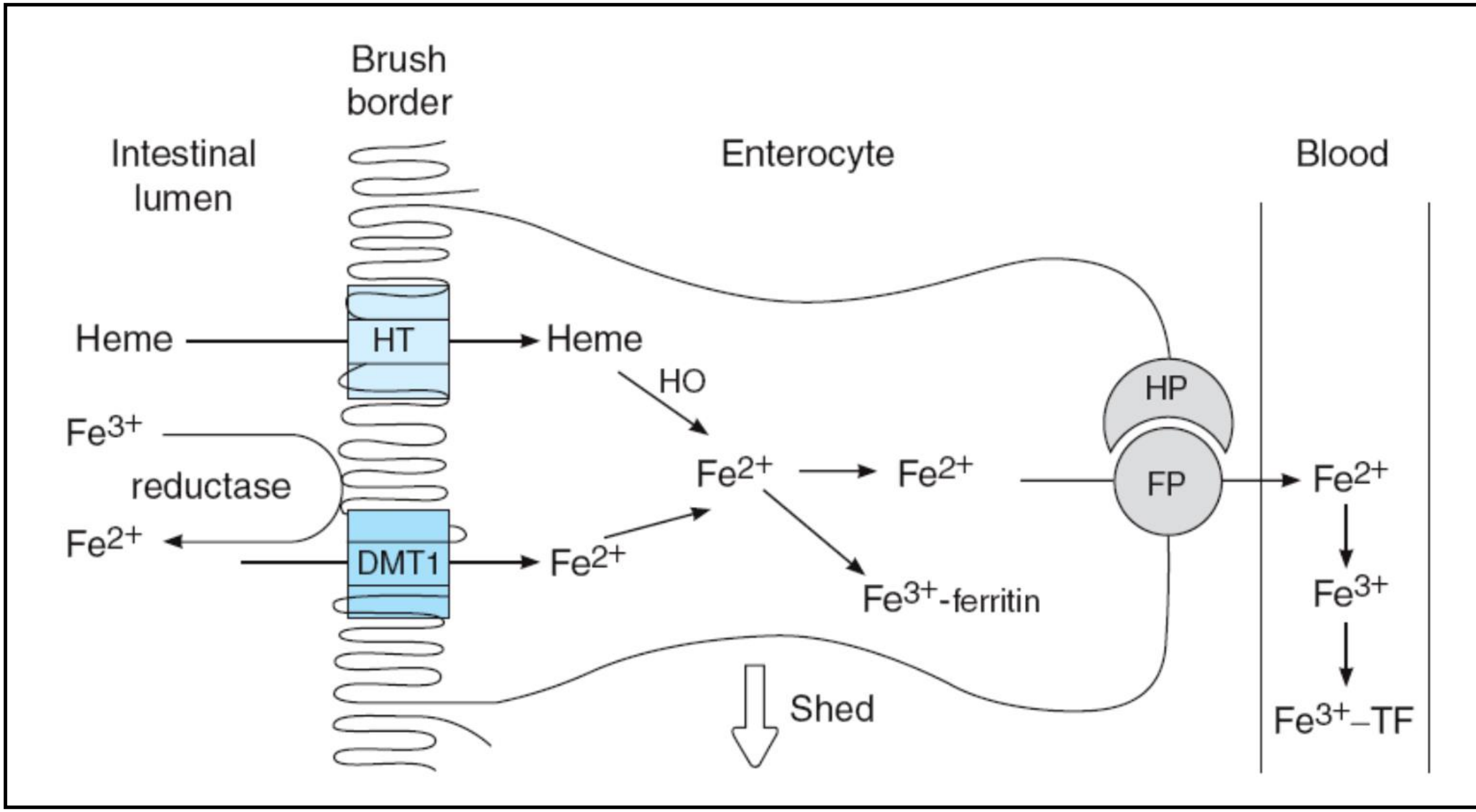
Distribution of iron in a 70-kg adult male.

Transferrin	3–4 mg
Hemoglobin in red blood cells	2500 mg
In myoglobin and various enzymes	300 mg
In stores (ferritin and hemosiderin)	1000 mg
Absorption	1 mg/d
Losses	1 mg/d

[1] In an adult female of similar weight, the amount in stores would generally be less (100–400 mg) and the losses would be greater (1.5–2 mg/d).



Absorption of heme and non-heme iron and transport of iron



HT- heme transporter; DMT1 – apical membrane iron transporter; HO – heme oxidase; TF – transferrin; FP – basolateral Fe transporter

- Iron is absorbed in reduced state, so the presence of reducing agents enhance absorption of iron (vitamin C). Ethanol and fructose also enhance iron absorption.
- Heme iron from meat is more available than inorganic iron, but **iron absorption** from both sources **is impaired by calcium (milk!)**

- for students who asked about fructose as an enhancer of iron absorption:

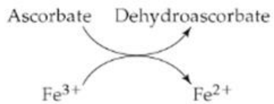
S. S. Gropper, Jack L. Smith: Advanced Nutrition and Human Metabolism, Cengage Learning, 5th Ed, 2009

However, if the iron chelate/ligand is strongly bonded and insoluble, iron is not absorbed but is excreted in the feces as part of the chelate.

Enhancers of Iron Absorption Some dietary factors that have been found to enhance nonheme iron absorption include:

- sugars, especially fructose and sorbitol
- acids, such as ascorbic, citric, lactic, and tartaric
- meat, poultry, and fish or their digestion products
- mucin

Ascorbic acid (vitamin C), along with citric, lactic, and tartaric acids, for example, acts as a reducing agent and forms a chelate with nonheme ferric iron at an acid pH.



This chelate (a ferrous ascorbate chelate if vitamin C served as the reducing agent) remains soluble in the small intestine and thus can improve intestinal absorption of nonheme iron.

Meat, poultry, and fish factors that enhance nonheme iron absorption have not been clearly identified. Digestion products from animal tissues high in the contractile proteins actin and myosin promote iron absorption [5]. These proteins are digested into peptides that contain relatively large amounts of the amino acid cysteine, which is believed to serve as a ligand to facilitate iron absorption [5]. Another amino acid histidine also may chelate iron to enhance its absorption. Meat is further suspected to improve iron absorption by stimulating intestinal secretions [5].

The amount of iron available for absorption can be estimated from the quantity of vitamin C and meat, fish, or poultry that is ingested with the nonheme iron source, assuming ~500 mg body iron stores. Seventy-five units of ascorbic acid or meat, fish, or poultry (MFP) factor (one unit = 1.3 g raw or 1 g cooked meat, fish, or poultry or 1 mg ascorbic acid) has been shown to maximize iron absorption when consumed with the iron source [6]. Units in excess of 75 seem to have no further benefit. The absence of enhancing factors predicts a nonheme iron absorption of only 2% to 3%, but 75 units of these factors can increase absorption of nonheme iron to 8% (some suggest up to 20% if the person is also iron deficient) [7].

Mucin, an endogenously synthesized chelator, is a small protein made in both gastric and intestinal cells. Gastric mucin (sometimes called gastroferrin) is released into the lumen of the gastrointestinal tract, and some mucin is also found on the brush border membrane of mucosal cells in the intestine. Chelation of iron by mucin facilitates iron absorption. Mucin binds multiple ferric iron atoms at an acid pH and maintains ferric iron solubility in the alkaline pH of the small intestine. Histidine, ascorbic acid, and fructose, other chelators of iron, are thought to donate the iron to mucin in the small intestine. In addition to iron, mucin also binds and facilitates absorption of zinc and chromium.

Inhibitors of Iron Absorption Many dietary factors inhibit iron absorption, including:

- polyphenols such as tannin derivatives of gallic acid (in tea and coffee)
- oxalic acid (in spinach, chard, berries, chocolate, and tea, among other sources)
- phytates, also called phytic acid, inositol hexaphosphate, or polyphosphate (in maize, whole grains, legumes)
- phosvitin, a protein containing phosphorylated serine residues found in egg yolks
- nutrients such as calcium, calcium phosphate salts, zinc, manganese, and nickel

Polyphenols are found in fairly high concentrations in both tea and coffee. These phenolic compounds, when consumed with a source of iron, can reduce iron absorption over 60%. Coffee consumption, with or just after a meal, may reduce iron absorption by 40% [8].

Phytates and oxalates use oxygen to bind with many minerals, including not only iron but also zinc, copper, and calcium. The phytate mineral and oxalate mineral complexes are insoluble and poorly absorbed. Fermentation of bread reduces the phytate content and improves the absorption of some minerals, but, in general, mineral absorption is better without the presence of phytates or oxalates. (Figure 12.10, in the section on zinc, shows the structures of both phytate and oxalate.)

Several nutrients, when ingested in large amounts, can reduce absorption of nonheme iron. Calcium and phosphorus are thought to interact with iron and inhibit its absorption through $Fe:Ca:PO_4$ chelate formation at the intestinal mucosa. Alternately, the inhibitory effect of calcium on iron absorption may be within the intestinal mucosal cells at a step in iron transport that is common for both heme and nonheme iron transport [9]. Several studies [9–12] have demonstrated that calcium in amounts of 300 to 600 mg and in the forms of calcium phosphate, calcium citrate, calcium carbonate, and calcium chloride, when given with up to 18 mg iron as ferrous sulfate or when incorporated into food, substantially decreases iron absorption by up to 70%. Similar reductions in iron absorption have been shown with milk ingestion [11]. Thus, those with iron deficiency who need to maximize iron absorption from a supplement should not take the iron supplement with a source of calcium.

Zinc and iron also interact and may negatively affect each other's absorption. The two minerals are thought to

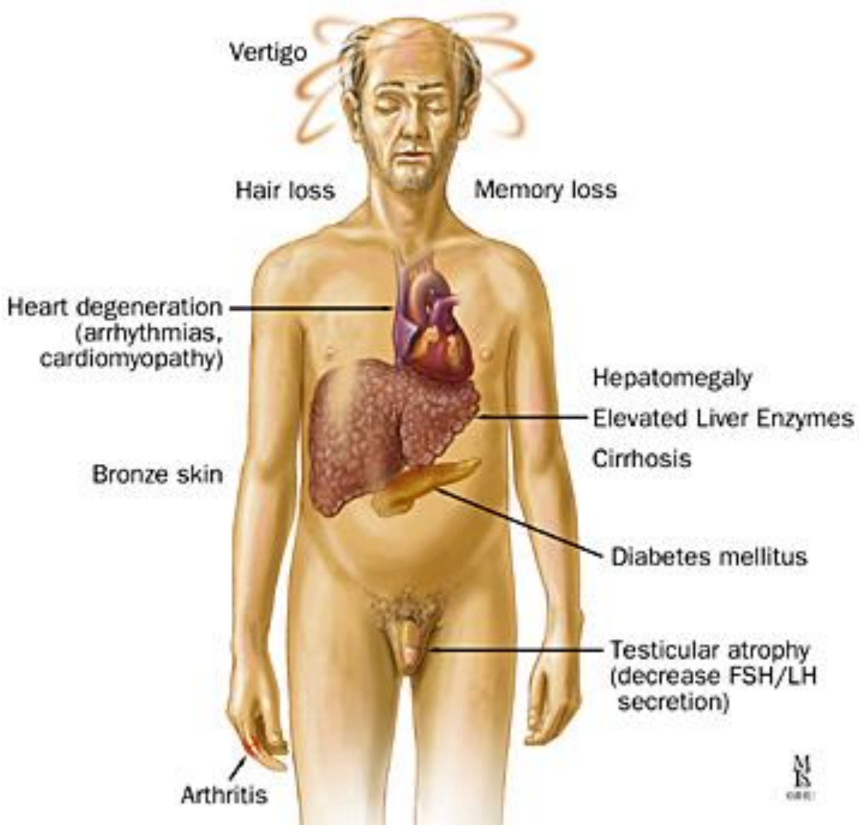
Iron absorption is limited and strictly controlled!

Disorders of iron metabolism:

- <u>Anemia</u>

- <u>Hemosiderosis</u>
  - iron overload disorder
  - accumulation of **hemosiderine** - complex containing ferritin, denatured ferritin and iron

- <u>Hemochromatosis</u>
  - high total iron concentration
  - tissue damage



Disorder of copper metabolism

<u>Wilson's disease</u>: hereditary disorder of copper metabolism (hepatolenticular degeneration) - copper accumulation leading to liver damage and central nervous system disorders

<u>Symptoms</u>:

- chronic liver inflammation, motoric disturbances similar to Parkinson's disease, psychiatric disorders
- copper colored Keyser-Fleischer ring around the iris
- low **ceruloplasmin** concentrations (α-globuline, transports 90% of copper)

VITAMINS

I. Lipid-soluble vitamins:

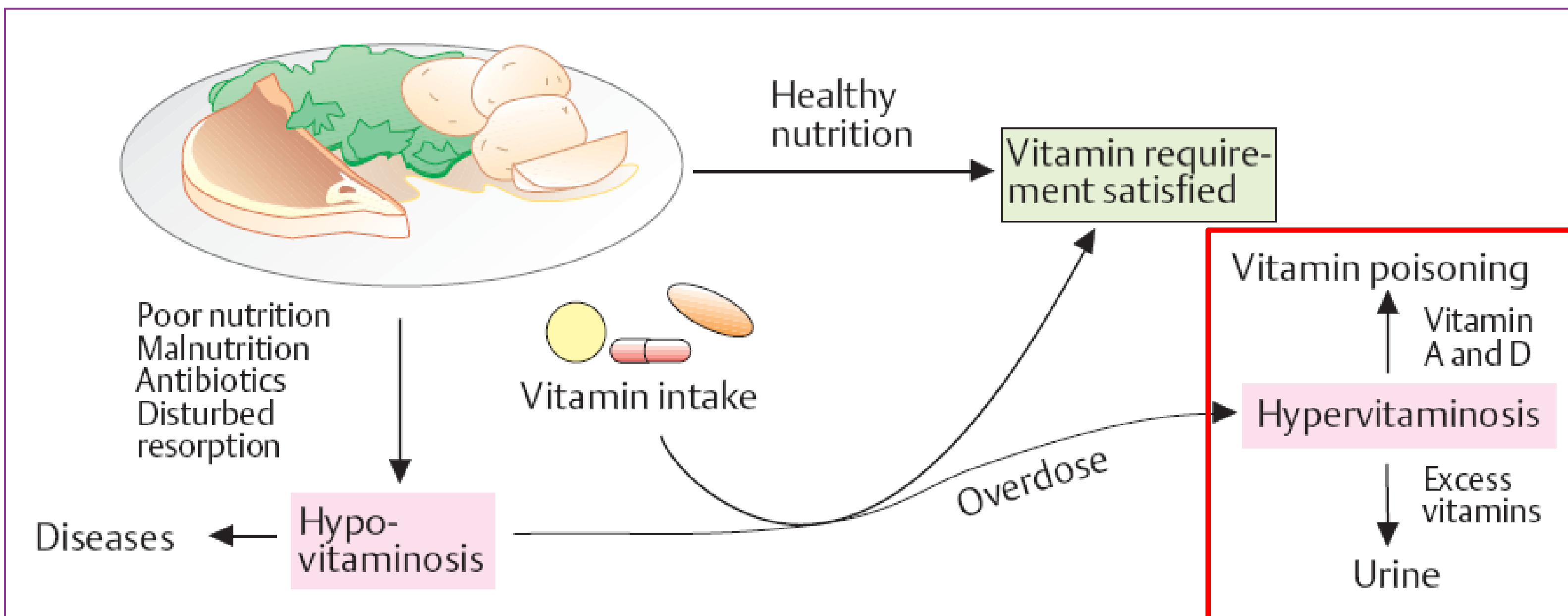
A, D, E, K

II. Water-soluble vitamins:

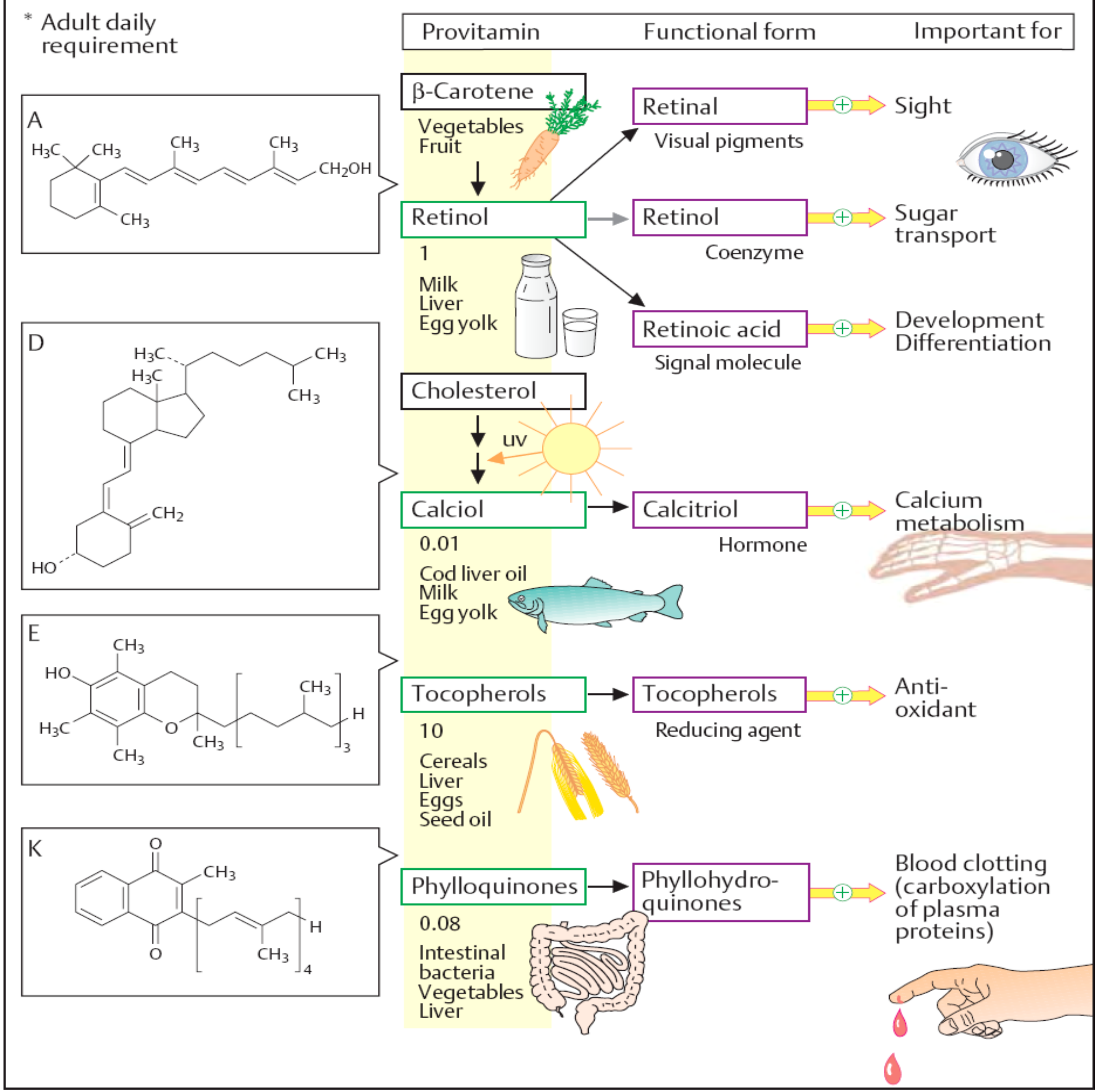
B_1, B_2, B_6, B_{12}, C, H

Roles of vitamins:

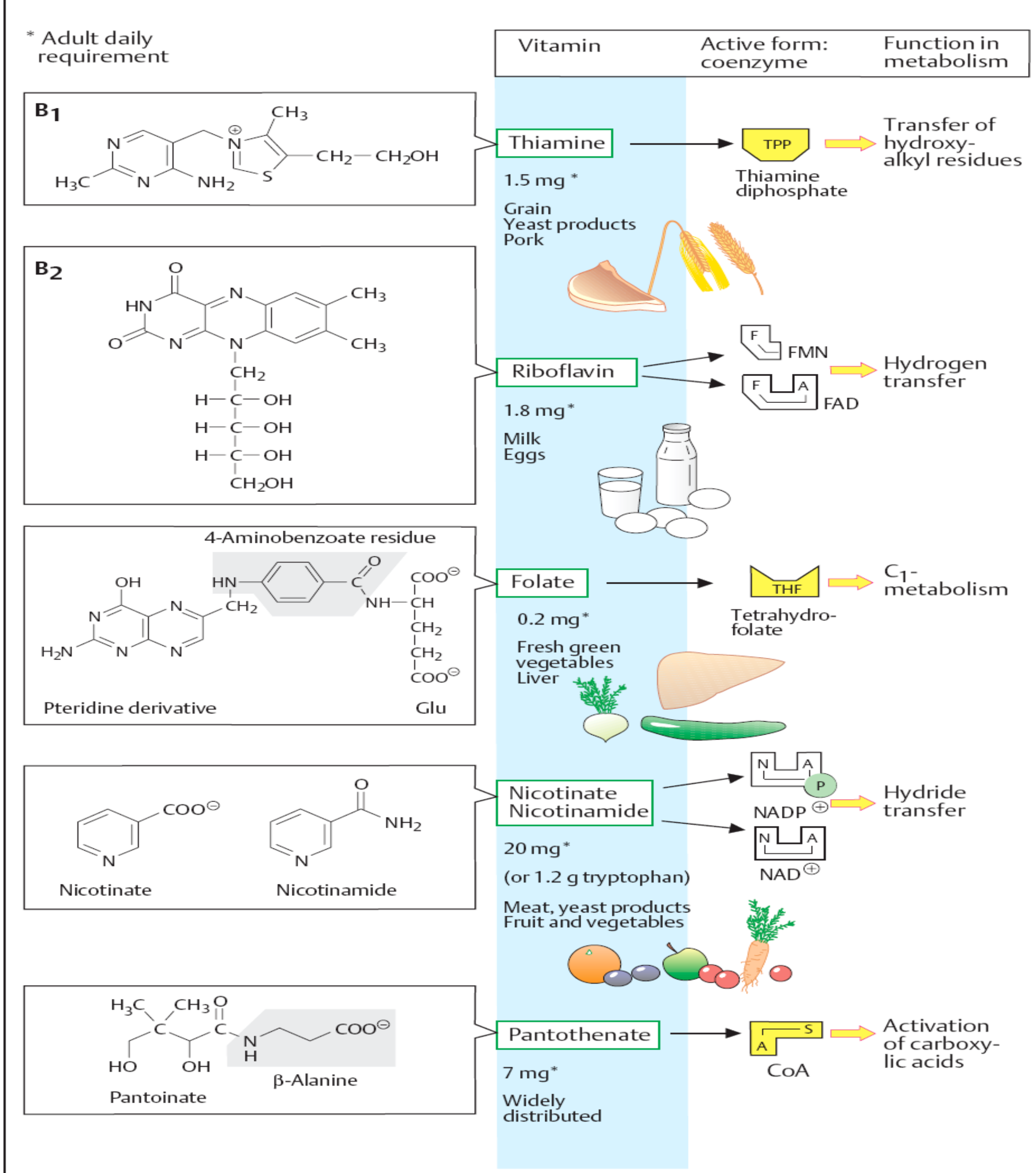
- Precursors of coenzymes
- Precursors of hormones
- Antioxidants



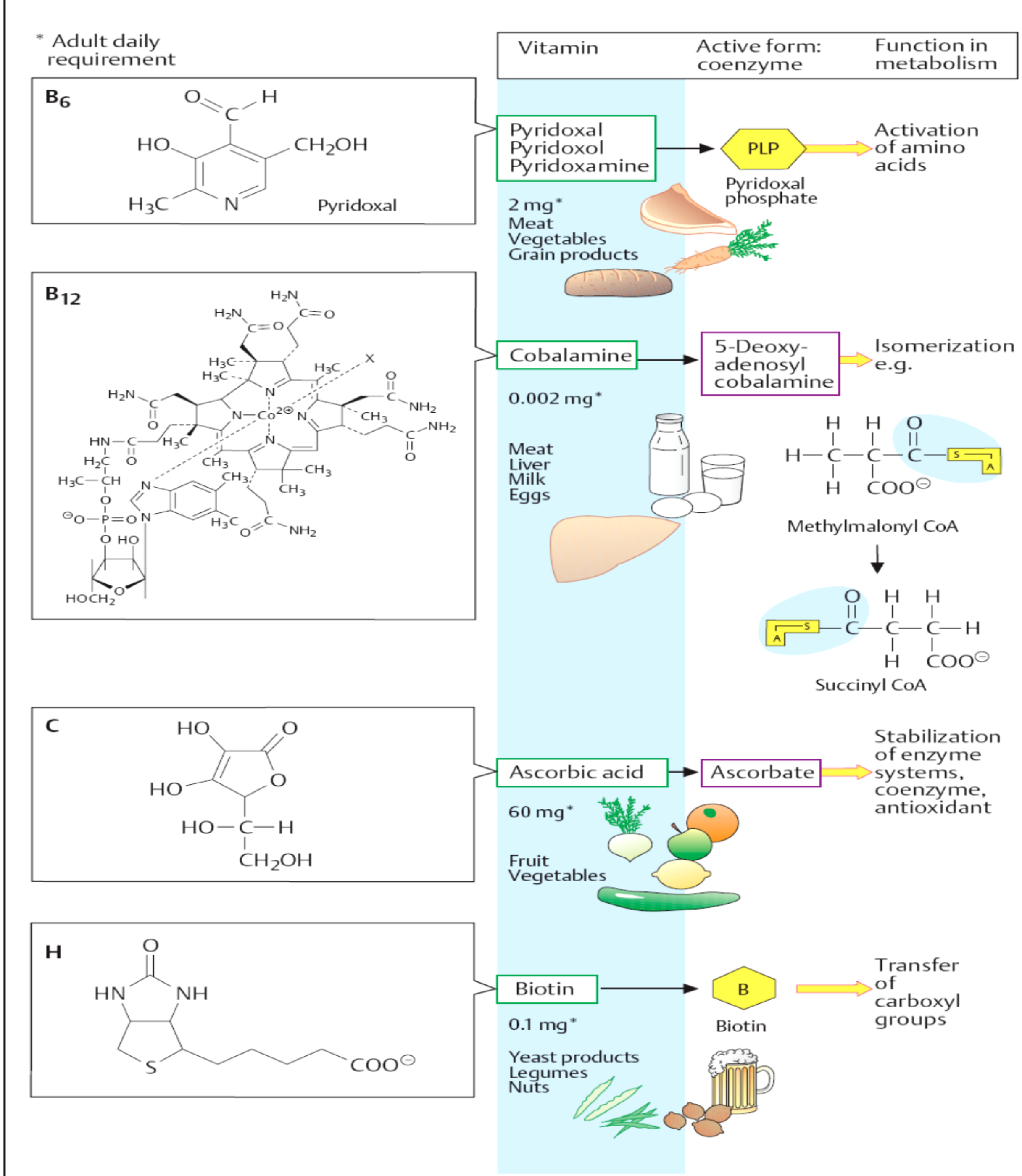
B. Lipid-soluble vitamins



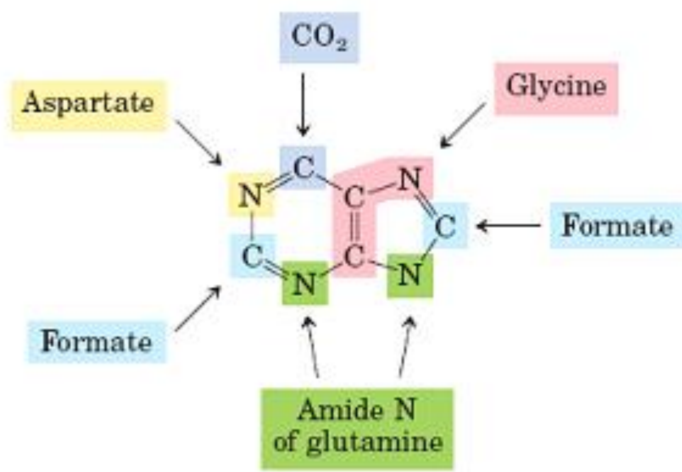
A. Water-soluble vitamins I

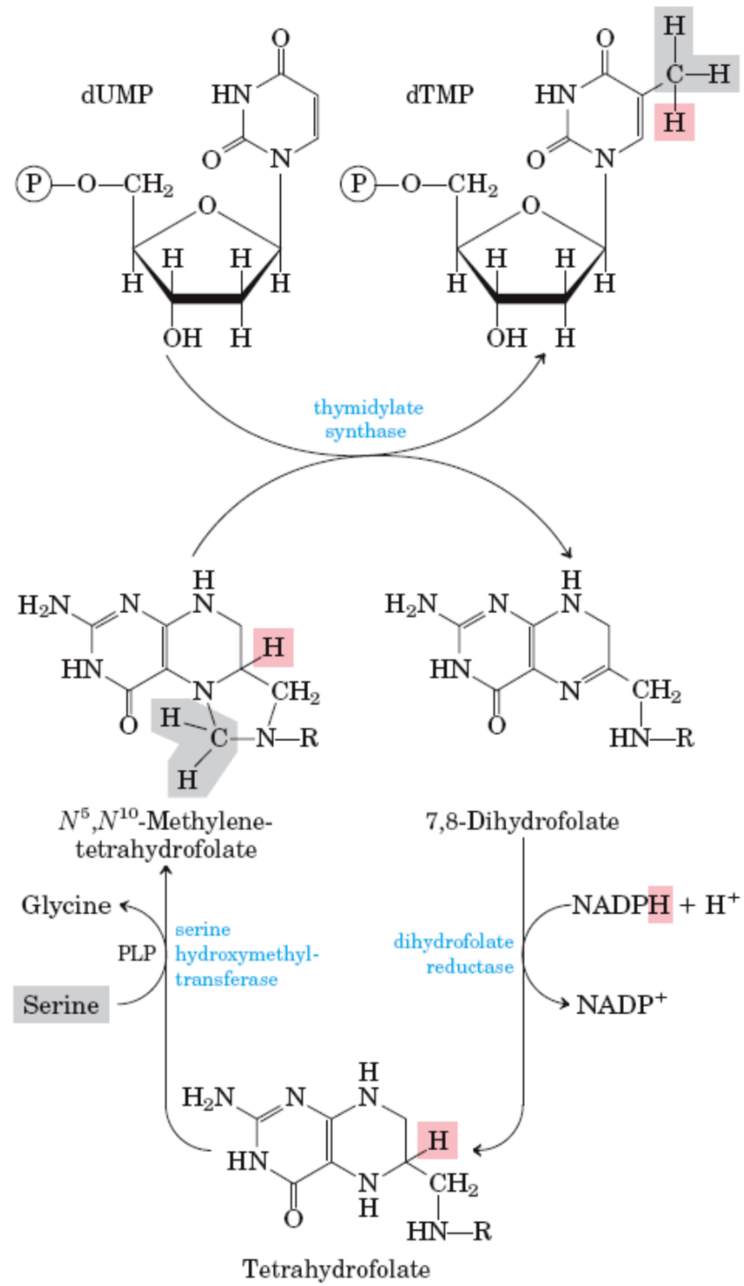


A. Water-soluble vitamins II

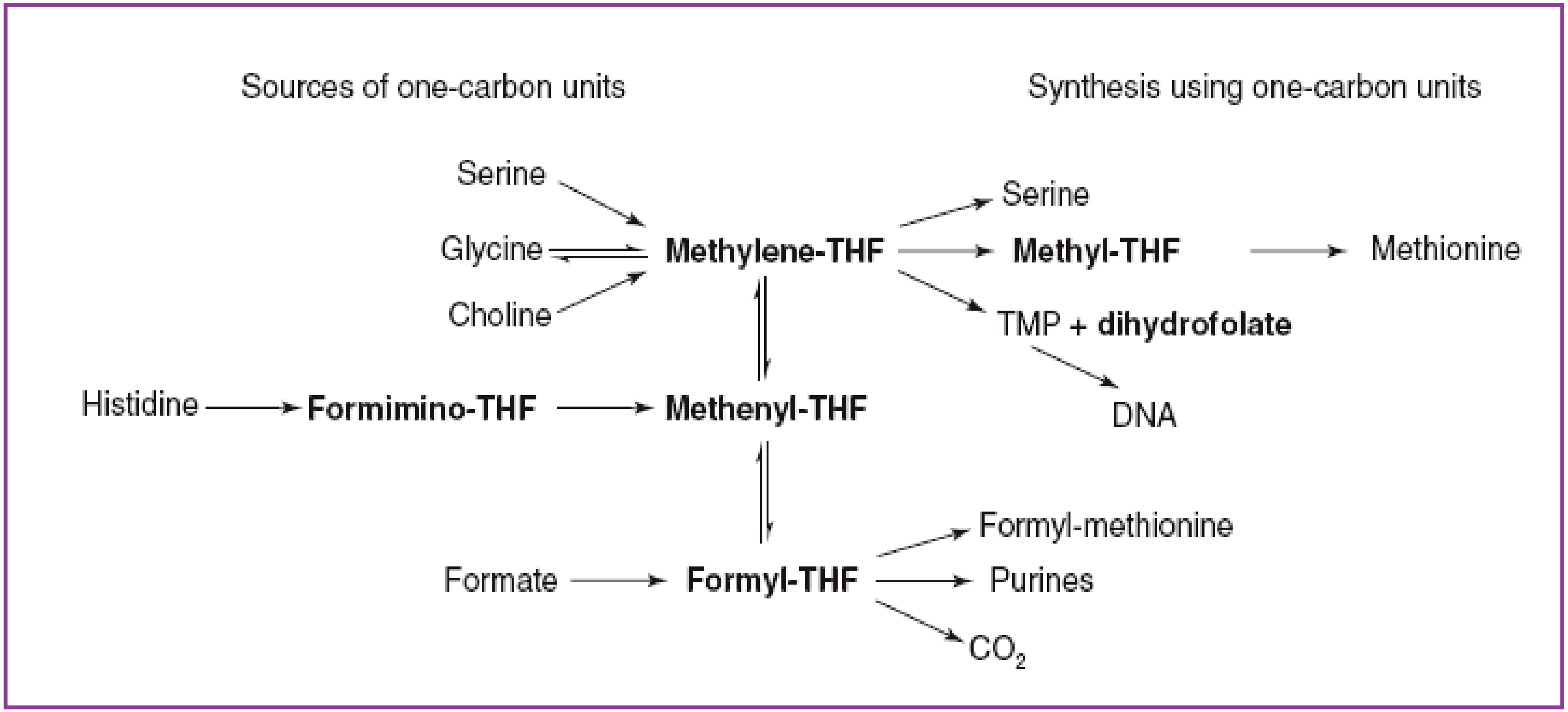


Folate, and its coenzyme form **tetrahydrofolate (THF)** (C_1 metabolism) – role in purine synthesis *de novo*, and synthesis of deoxyribonucleotide dTMP



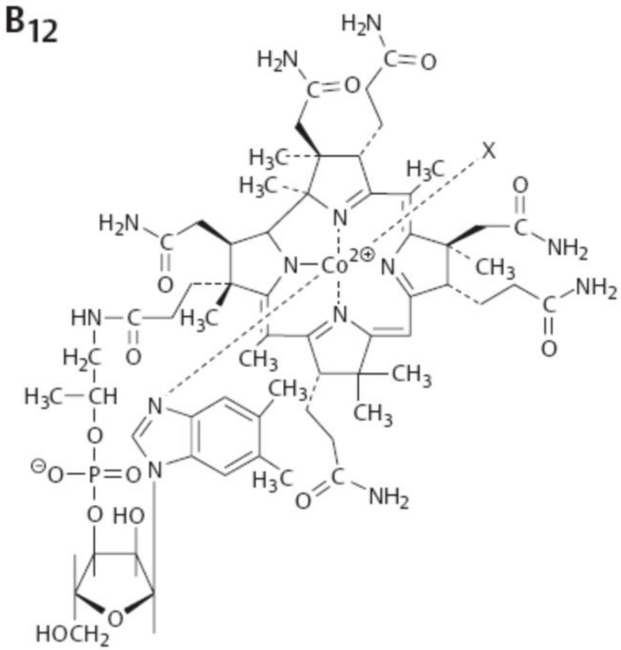


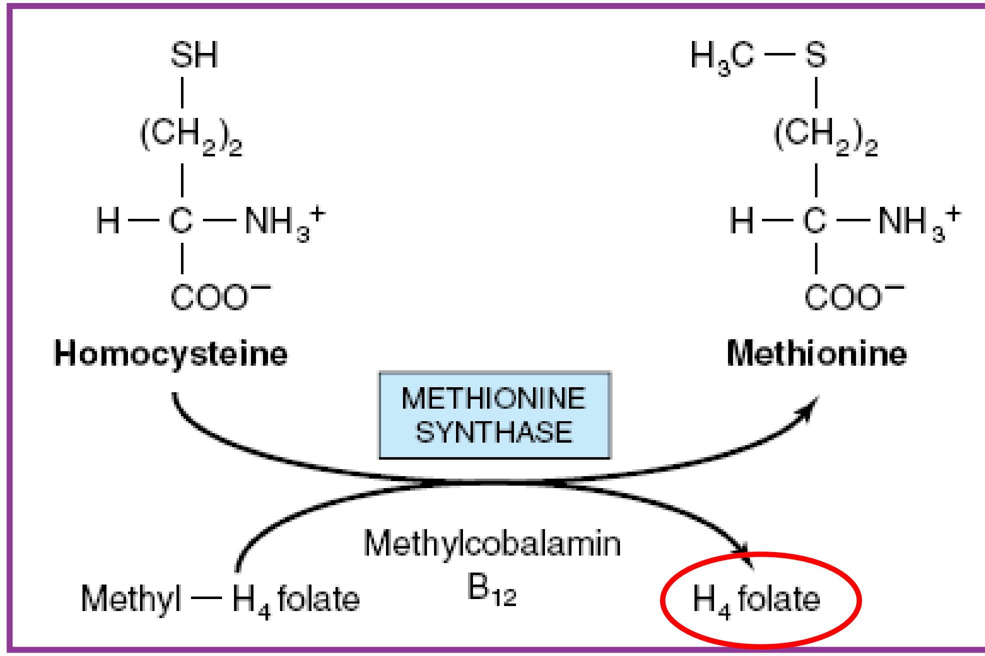
Utilization of folate



- mammals unable to synthesize folic acid!

- **<u>folic acid deficiency</u>** during prenatal development can lead to ***spina bifida***, a birth defect (developmental disorder) - incomplete neural tube closing
- high amount of THF is necessary during frequent cell divisions; folic acid supplementation during pregnancy reduces the risk for 70%
- folic acid deficiency also leads to **megaloblastic anemia** (inhibition of DNA synthesis during RBC production; hypersegmented neutrophils)

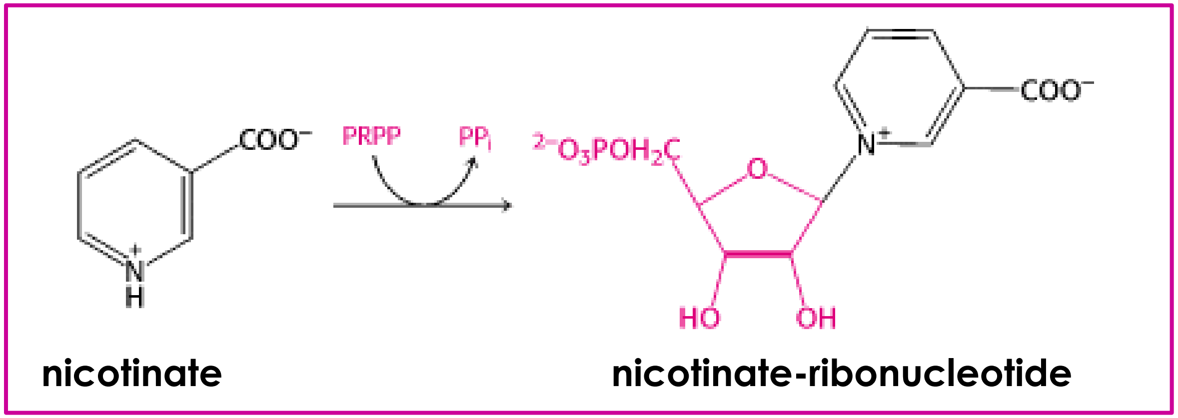




Vitamin B_{12} (cobalamin) – extrinsic factor, needs ***intrinsic factor (IF** or **gastric IF)*** for absorption; deficiency of *intrinsic factor* and thus of vitamin B_{12} results with alteration in folate metabolism which impairs erythropoiesis and leads to **pernicious anemia** or **vitamin B_{12} deficiency anemia.**

Nicotinate (niacin, vitamine B_3) may be synthesized from dietary **tryptophane**

- essential for NAD and NADP formation



- **pellagra**

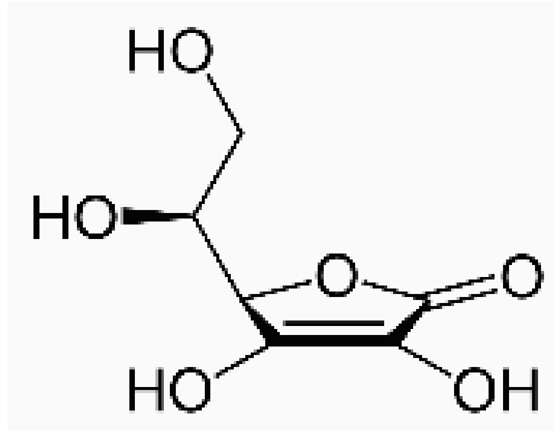
- niacin (vitamine B_3) and/or tryptophane deficiency
- symptoms: photosensitive dermatitis, diarrhea, dementia

→ ***"3 D": Dermatitis, Diarrhea, Dementia***

- treatment: niacine supplementation

- **pediatric pellagra** (malnutrition)

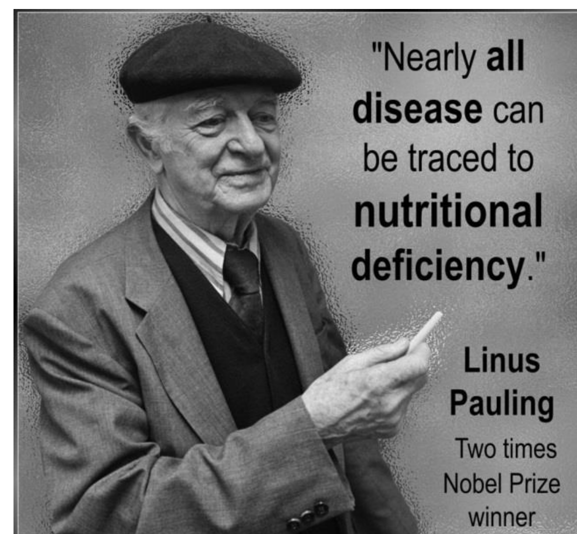
- after nursing period - food rich in starch, low in proteins



Humans, apes and guinea pigs have lost the ability to synthesize ascorbate.

SCURVY

- this disease is the consequence of vit. C hypovitaminosis (why?)



Vitamin		Functions	Deficiency Disease
A	Retinol, β-carotene	Visual pigments in the retina; regulation of gene expression and cell differentiation; β-carotene is an antioxidant	Night blindness, xerophthalmia; keratinization of skin
D	Calciferol	Maintenance of calcium balance; enhances intestinal absorption of Ca^{2+} and mobilizes bone mineral	Rickets = poor mineralization of bone; osteomalacia = bone demineralization
E	Tocopherols, tocotrienols	Antioxidant, especially in cell membranes	Extremely rare—serious neurologic dysfunction
K	Phylloquinone, menaquinones	Coenzyme in formation of γ-carboxyglutamate in enzymes of blood clotting and bone matrix	Impaired blood clotting, hemorrhagic disease
B_1	Thiamin	Coenzyme in pyruvate and α–ketoglutarate, dehydrogenases, and transketolase; poorly defined function in nerve conduction	Peripheral nerve damage (beriberi) or central nervous system lesions (Wernicke-Korsakoff syndrome)
B_2	Riboflavin	Coenzyme in oxidation and reduction reactions; prosthetic group of flavoproteins	Lesions of corner of mouth, lips, and tongue; seborrheic dermatitis
Niacin	Nicotinic acid, nicotinamide	Coenzyme in oxidation and reduction reactions, functional part of NAD and NADP	Pellagra—photosensitive dermatitis, depressive psychosis
B_6	Pyridoxine, pyridoxal, pyridoxamine	Coenzyme in transamination and decarboxylation of amino acids and glycogen phosphorylase; role in steroid hormone action	Disorders of amino acid metabolism, convulsions
	Folic acid	Coenzyme in transfer of one-carbon fragments	Megaloblastic anemia
B_{12}	Cobalamin	Coenzyme in transfer of one-carbon fragments and metabolism of folic acid	Pernicious anemia = megaloblastic anemia with degeneration of the spinal cord
	Pantothenic acid	Functional part of CoA and acyl carrier protein: fatty acid synthesis and metabolism	
H	Biotin	Coenzyme in carboxylation reactions in gluconeogenesis and fatty acid synthesis	Impaired fat and carbohydrate metabolism, dermatitis
C	Ascorbic acid	Coenzyme in hydroxylation of proline and lysine in collagen synthesis; antioxidant; enhances absorption of iron	Scurvy—impaired wound healing, loss of dental cement, subcutaneous hemorrhage

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