Micronutrients in Energy and Amino Acid Metabolism

Learning Objectives

- Identify the functions, bioavailability, requirements, and food sources of these micronutrients.
- Describe how they are absorbed, transported, stored, and excreted
- Identify deficiency and toxicity symptoms for each.

Vitamins Classification

- **Fat Soluble Vitamins**
  - Vitamin A
  - Vitamin D
  - Vitamin E
  - Vitamin K

- **Water Soluble Vitamins & Choline**
  - Vitamin C
  - B Vitamins
    - Thiamin
    - Riboflavin
    - Niacin
    - Pantothenic acid
    - Biotin
    - Vitamin B-6
    - Folate (folic acid)
    - Vitamin B-12
  - Choline

A Bit of History

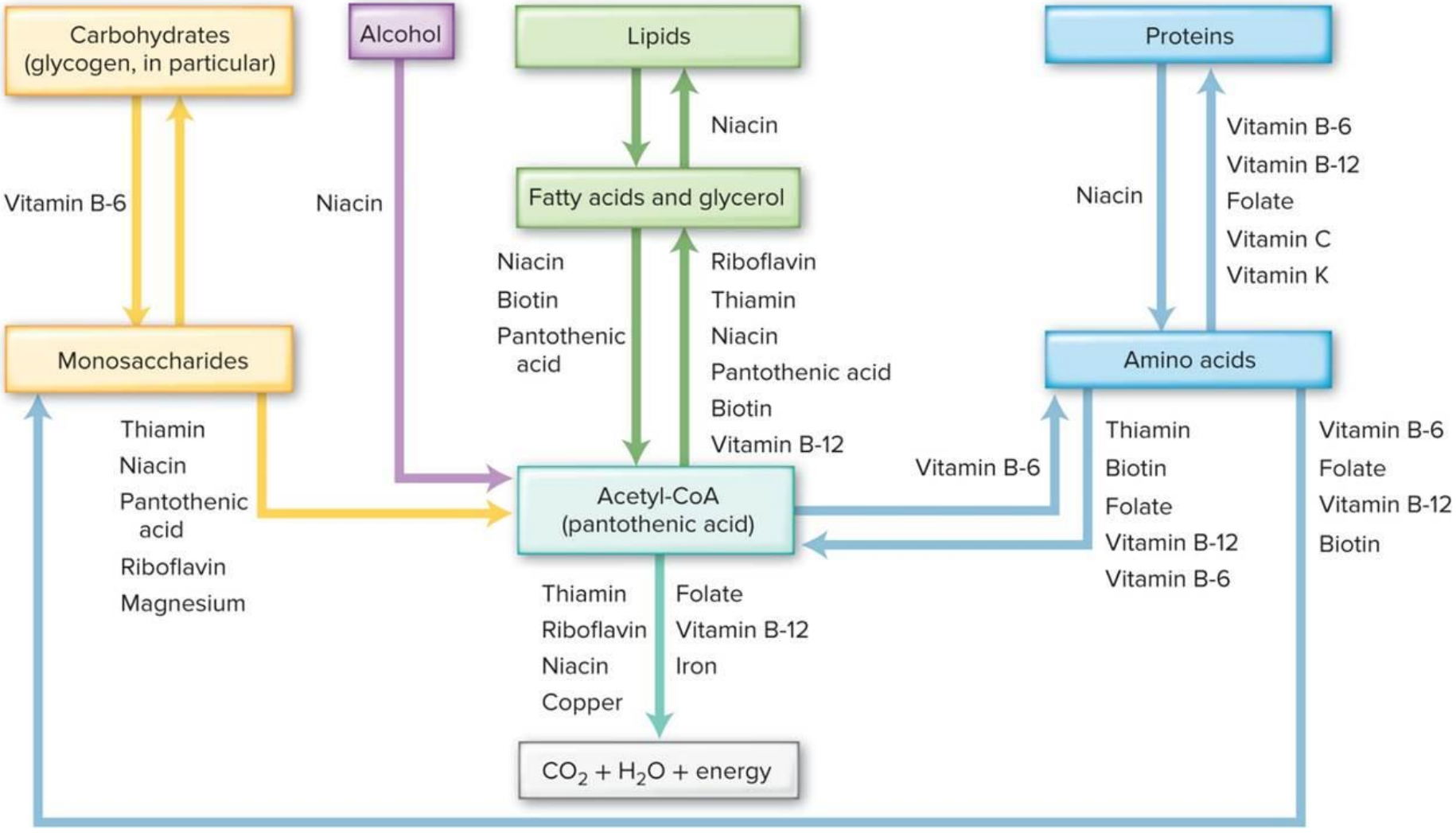
- Vitamin originated from the word “vital-amines”
- Our understanding of vitamins continues to evolve
- B vitamins were determined to be a complex of nutrients rather than independent because of their similar properties
- Missing vitamins were reclassified or determined not to be vitamins

Kazimierz Funk
Polish Biochemist

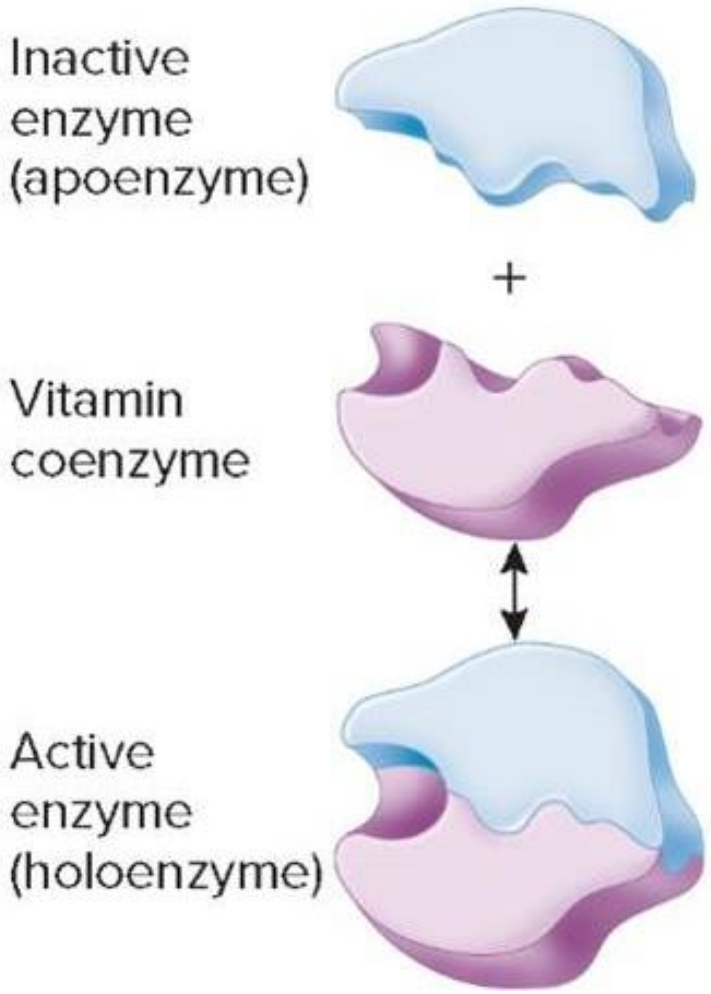
Regulation of Energy Metabolism

- Many vitamins and minerals are needed for metabolism:
  - Thiamin
  - Riboflavin
  - Niacin
  - Pantothenic acid
  - Vitamin B-6
  - Biotin
  - Folate
  - Vitamin B-12
  - Iron
  - Copper

Vitamins and Minerals Involved in Metabolic Pathways



The Enzyme-Coenzyme Interaction



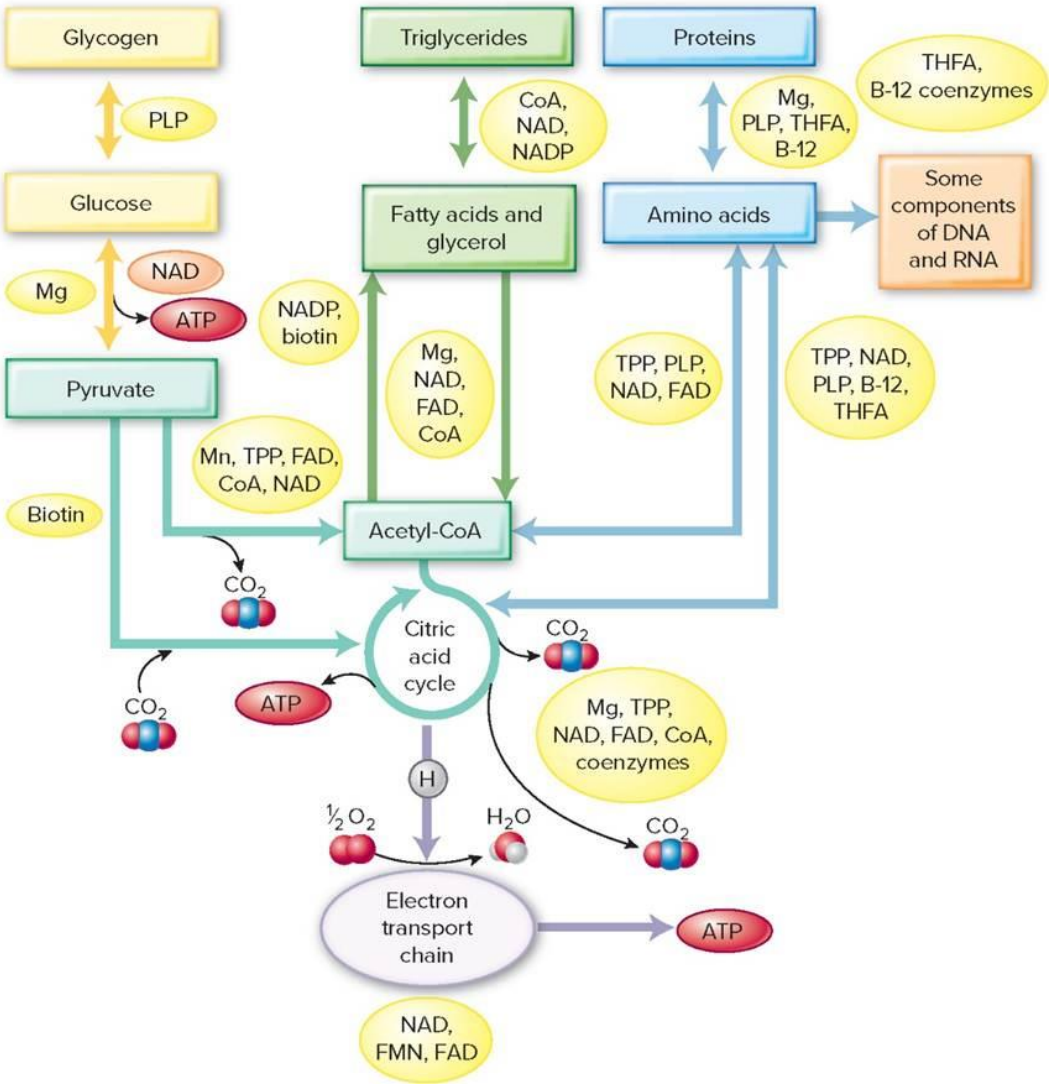
Apoenzyme: inactive form of enzyme

Cofactor: substance that combines with an inactive form of an enzyme to activate it (e.g., metals, vitamins)

- Coenzyme: organic cofactor

Holoenzyme: active enzyme

B-Vitamins in Metabolic Pathways



Jump to long description

TABLE 8-2 ▶ Summary of the Water-Soluble Vitamins and Choline

Vitamin	Major Functions	RDA or Adequate Intake	Dietary Sources*	Deficiency Symptoms	Toxicity Symptoms
Thiamin	• Coenzyme of carbohydrate metabolism • Nerve function	*Men:* 1.2 milligrams *Women:* 1.1 milligrams	• Sunflower seeds • Pork • Whole and enriched grains • Dried beans • Peas	*Beriberi* • Nervous tingling • Poor coordination • Edema • Heart changes • Weakness	• None
Riboflavin†	• Coenzyme of carbohydrate metabolism	*Men:* 1.3 milligrams *Women:* 1.1 milligrams	• Milk • Mushrooms • Spinach • Liver • Enriched grains	• Inflammation of the mouth and tongue • Cracks at the corners of the mouth • Eye disorders	• None
Niacin	• Coenzyme of energy metabolism • Coenzyme of fat synthesis	*Men:* 16 milligrams (NE) *Women:* 14 milligrams (NE)	• Mushrooms • Bran • Tuna • Salmon • Chicken • Beef • Liver • Peanuts • Enriched grains	*Pellagra* • Diarrhea • Dermatitis • Dementia • Death	• Headache • Itching • Flushing of skin • Damage to the GI tract or liver • Upper Level is 35 milligrams from supplements, based on flushing of skin.
Pantothenic acid	• Coenzyme of energy metabolism • Coenzyme of fat synthesis	5 milligrams	• Mushrooms • Liver • Broccoli • Eggs *Most foods have some*	No natural deficiency disease or symptoms	• None

TABLE 8-2 ▶ Summary of the Water-Soluble Vitamins and Choline

Vitamin	Major Functions	RDA or Adequate Intake	Dietary Sources*	Deficiency Symptoms	Toxicity Symptoms
Biotin	• Coenzyme of glucose production • Coenzyme of fat synthesis	30 micrograms	• Cheese • Egg yolks • Cauliflower • Peanut butter • Liver	• Dermatitis • Tongue soreness • Anemia • Depression	• Unknown
Vitamin B-6†	• Coenzyme of energy metabolism, especially protein • Neurotransmitter synthesis • Red blood cell synthesis *Many other functions*	*Men (up to 50 years):* 1.3 milligrams *Women (up to 50 years):* 1.3 milligrams	• Animal protein foods • Spinach • Broccoli • Bananas • Salmon • Sunflower seeds	• Headache • Anemia • Convulsions • Nausea • Vomiting • Flaky skin • Sore tongue	• Difficulty walking • Numbness or tingling in hands or feet • Upper Level is 100 milligrams, based on nerve destruction.
Folate (folic acid)†	• Coenzyme involved in DNA synthesis *Many other functions*	400 micrograms (DFE)	• Green leafy vegetables • Orange juice • Organ meats • Sprouts • Sunflower seeds	• Macrocytic • Inflammation of tongue • Diarrhea • Poor growth • Depression	• None likely • Upper Level for adults is set at 1000 micrograms for synthetic folic acid (exclusive of food folate), based on masking of B-12 deficiency.

Thiamin (Vitamin B-1)

Functions:

- Metabolism of carbohydrates
- Metabolism of branched-chain amino acids

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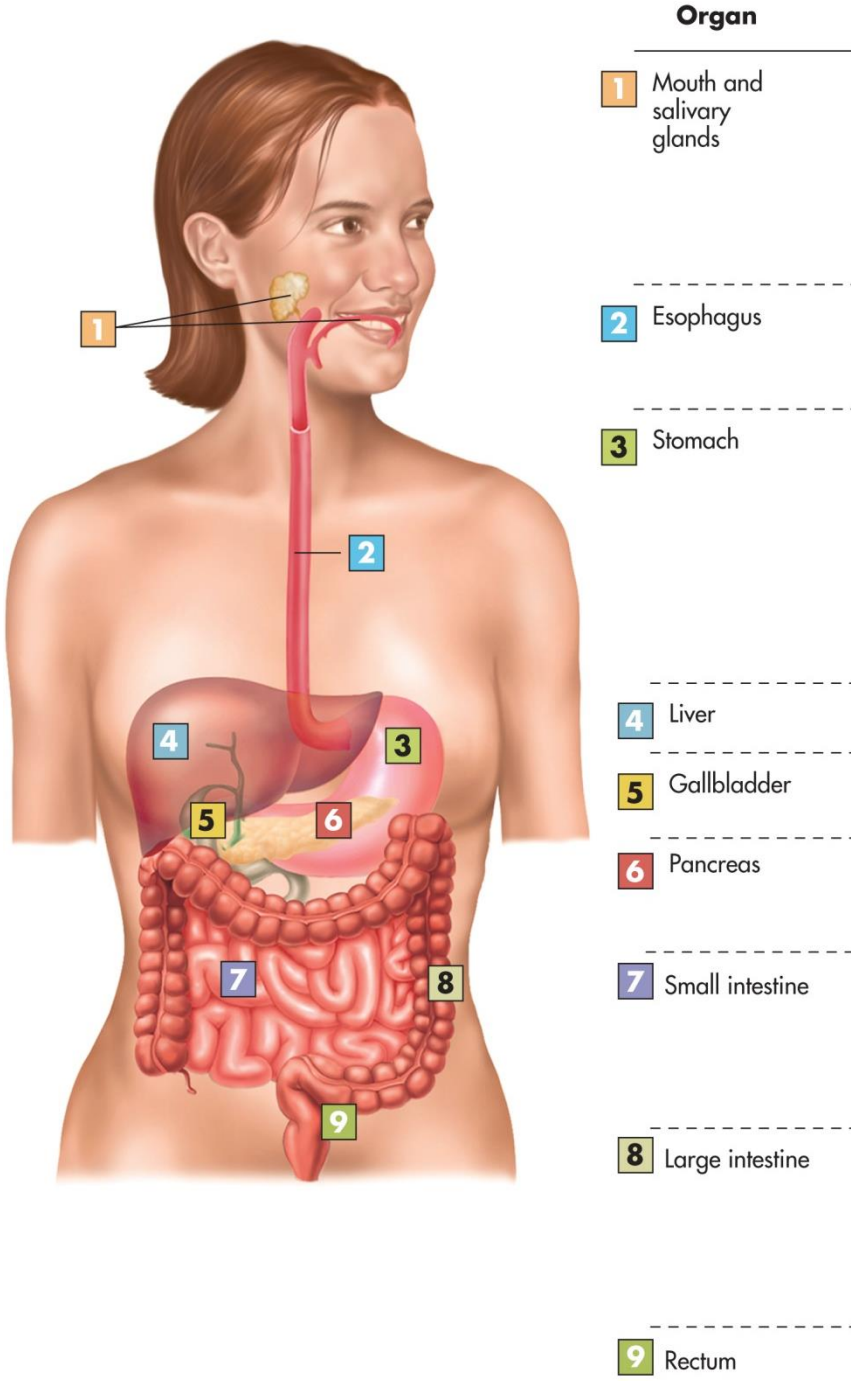
Thiamin in the Body

- Actively absorbed from the small intestine
- Transported in coenzyme form by red blood cells
- Only a small amount is stored in the muscles, brain, liver, and kidneys
- Excreted via urine



Thiamin Deficiency: Beriberi

Dry beriberi:

- Affects peripheral nervous & muscular systems
  - Peripheral neuropathy
  - Weakness
  - Muscle pain
  - Anorexia
  - Confusion

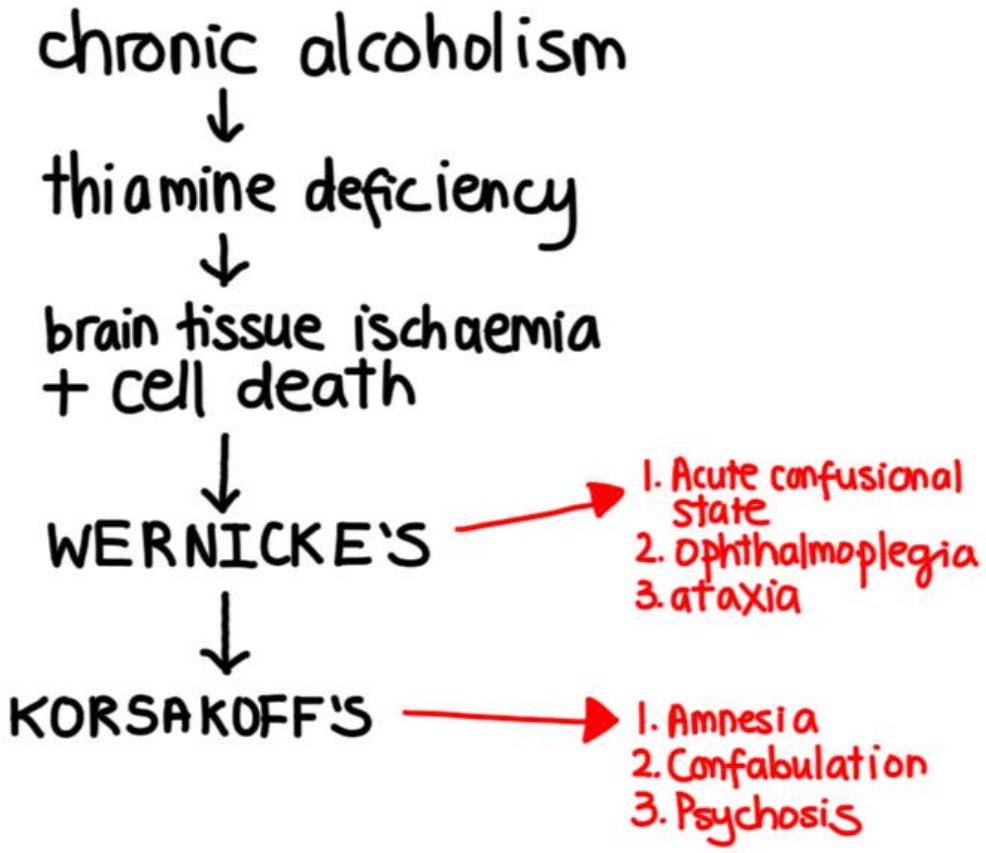
Wet beriberi:

- Affects cardiovascular system
  - Enlargement of heart
  - Difficulty breathing
  - Edema

Thiamin Deficiency: Wernicke-Korsakoff Syndrome

Related to alcohol abuse

- Decreased thiamin absorption
- Increased thiamin excretion
- Poor dietary intake of thiamin
- Affects central nervous system
  - Changes in vision
  - Ataxia
  - Impaired mental function



TAKE-HOME POINTS

- Consider WE in any patient with a potential nutritional deficiency or chronic alcohol use disorder
- If a patient has 2 or more of the following, start thiamine 500 mg IV TID and admit for further parenteral thiamine repletion.
  a. Dietary deficiency
  b. Oculomotor abnormalities
  c. Cerebellar dysfunction
  d. Amnesia or altered mental status
- Prevent, diagnose, and treat WE aggressively as Korsakoff syndrome is permanent and devastating.

Functions of Riboflavin

Energy metabolism:

- Citric acid cycle

B-vitamin metabolism:

- Formation of niacin from tryptophan (F A D)
- Activation of vitamin B-6 coenzyme (F M N)
- Folate metabolism (F A D)

Antioxidant:

- Glutathione reductase (F A D)

Vitamin	Major Functions	RDA or Adequate Intake	Dietary Sources*	Deficiency Symptoms	Toxicity Symptoms
Riboflavin†	• Coenzyme of carbohydrate metabolism	*Men:* 1.3 milligrams *Women:* 1.1 milligrams	• Milk • Mushrooms • Spinach • Liver • Enriched grains	• Inflammation of the mouth and tongue • Cracks at the corners of the mouth • Eye disorders	• None

Riboflavin in the Body

- HCl in stomach releases bound riboflavin
- Absorbed by active transport or facilitated diffusion from the small intestine (60-65% efficiency)
- Transported through blood by protein carriers
- Converted to coenzyme form mainly in small intestine, liver, heart, and kidneys
- Minor storage in liver, kidneys, and heart
- Excreted via urine

Riboflavin Deficiency: Ariboflavinosis

- Rare
- 2 months of deficient intake
- Assessment:
  - R B C s
  - Glutathione reductase activity
- At-risk populations:
  - Alcoholism
  - Avoidance of dairy
  - Cancer
  - Cardiovascular disease
  - Diabetes

Riboflavin Deficiency: Ariboflavinosis

Symptoms:

- Inflamed throat
- Stomatitis
- Glossitis
- Angular cheilitis
- Seborrheic dermatitis
- Anemia
- Fatigue
- Confusion
- Headaches

Niacin (Vitamin B-3)

Forms:

- Nicotinic acid (niacin)
- Nicotinamide (niacinamide)

Functions:

- Coenzymes (N A D $^{+}$ and N A D P $^{+}$)
- Catabolism of energy-yielding nutrients (N A D $^{+}$)
- Fatty acid biosynthesis (N A D P H)

Niacin in Foods

Two sources:

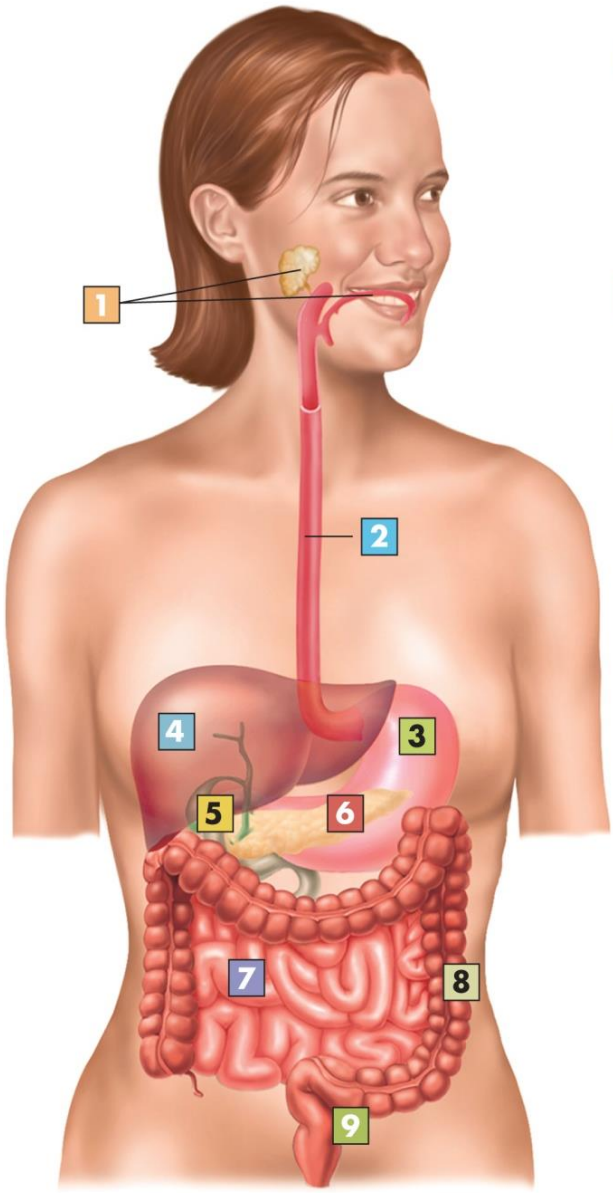
- Direct (preformed in foods)
- Indirect (synthesized from tryptophan)

Heat stable

Vitamin	Major Functions	RDA or Adequate Intake	Dietary Sources*	Deficiency Symptoms	Toxicity Symptoms
Niacin	• Coenzyme of energy metabolism • Coenzyme of fat synthesis	*Men:* 16 milligrams (NE) *Women:* 14 milligrams (NE)	• Mushrooms • Bran • Tuna • Salmon • Chicken • Beef • Liver • Peanuts • Enriched grains	*Pellagra* • Diarrhea • Dermatitis • Dementia • Death	• Headache • Itching • Flushing of skin • Damage to the GI tract or liver • Upper Level is 35 milligrams from supplements, based on flushing of skin.

Niacin in the Body

- Absorbed in the small intestine
  - Low bioavailability of protein-bound niacin in some grains (e.g., corn)
- Transported through bloodstream to liver and body cells
- Stored to small extent in liver
- Converted to coenzyme form in body tissues
- Excreted via urine



Organ

1 Mouth and salivary glands

2 Esophagus

3 Stomach

4 Liver

5 Gallbladder

6 Pancreas

7 Small intestine

8 Large intestine

9 Rectum

Niacin Deficiency

Pellagra (“rough skin”):

- Dermatitis
- Diarrhea
- Dementia
- Death

At-risk populations:

- Associated with corn-based diets
  - Niacin bound to protein
  - Corn is poor source of tryptophan
- Alcoholics

Pharmacological Use of Niacin

High doses of niacin have been used for many years to:

- Increase H D L-cholesterol
- Lower L D L-cholesterol
- Lower triglyceride levels

Aim is to reduce the risk of stroke and heart attack

Recent research does not support this use

Niacin-containing medications are no longer recommended for most individuals with cardiovascular disease

Biotin

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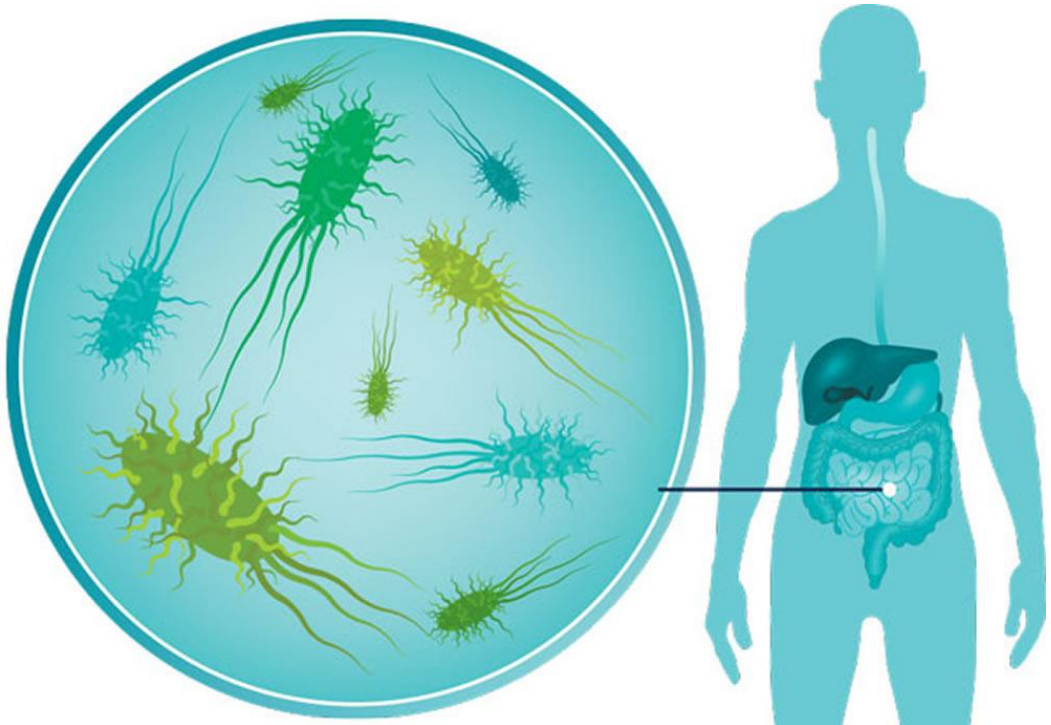
Biotin	• Coenzyme of glucose production • Coenzyme of fat synthesis	30 micrograms	• Cheese • Egg yolks • Cauliflower • Peanut butter • Liver	• Dermatitis • Tongue soreness • Anemia • Depression	• Unknown

Biotin Sources

- Free biotin or biocytin
  - Nutrient databases are incomplete
- Bacterial synthesis in large intestine



Biotin in the Body

- Absorbed from small intestine
- Minor amount of storage:
  - Muscles
  - Liver
  - Brain
- Excreted via bile and urine

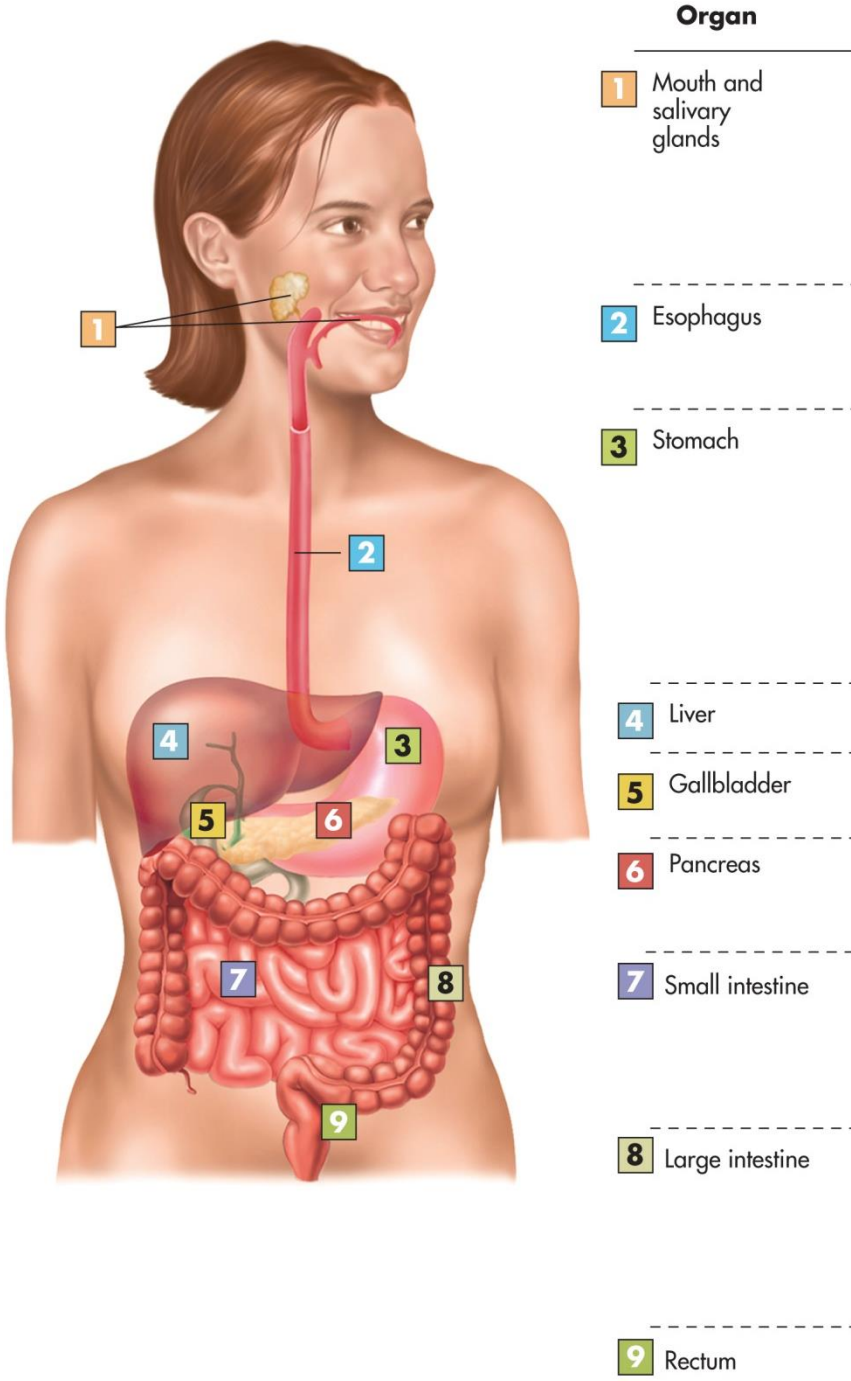


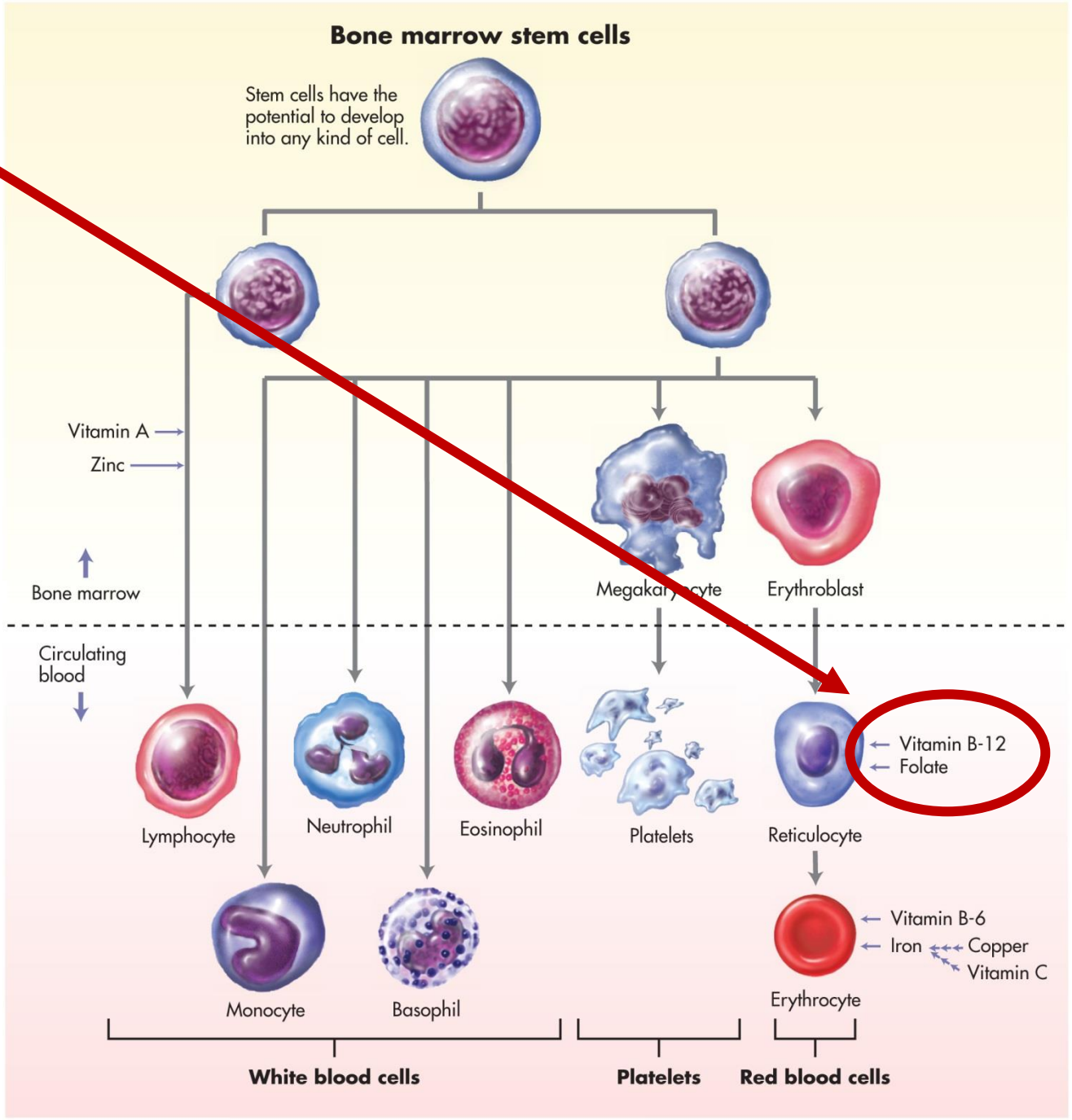
TABLE 8-2 ▶ Summary of the Water-Soluble Vitamins and Choline

Vitamin	Major Functions	RDA or Adequate Intake	Dietary Sources*	Deficiency Symptoms	Toxicity Symptoms
Folate (folic acid)†	• Coenzyme involved in DNA synthesis *Many other functions*	400 micrograms (DFE)	• Green leafy vegetables • Orange juice • Organ meats • Sprouts • Sunflower seeds	• Macrocytic • Inflammation of tongue • Diarrhea • Poor growth • Depression	• None likely • Upper Level for adults is set at 1000 micrograms for synthetic folic acid (exclusive of food folate), based on masking of B-12 deficiency.

Folate (B9):

- **Cell division**
- Metabolism of amino acids
- DNA formation

Folic acid: synthetic form of folate added to fortified foods

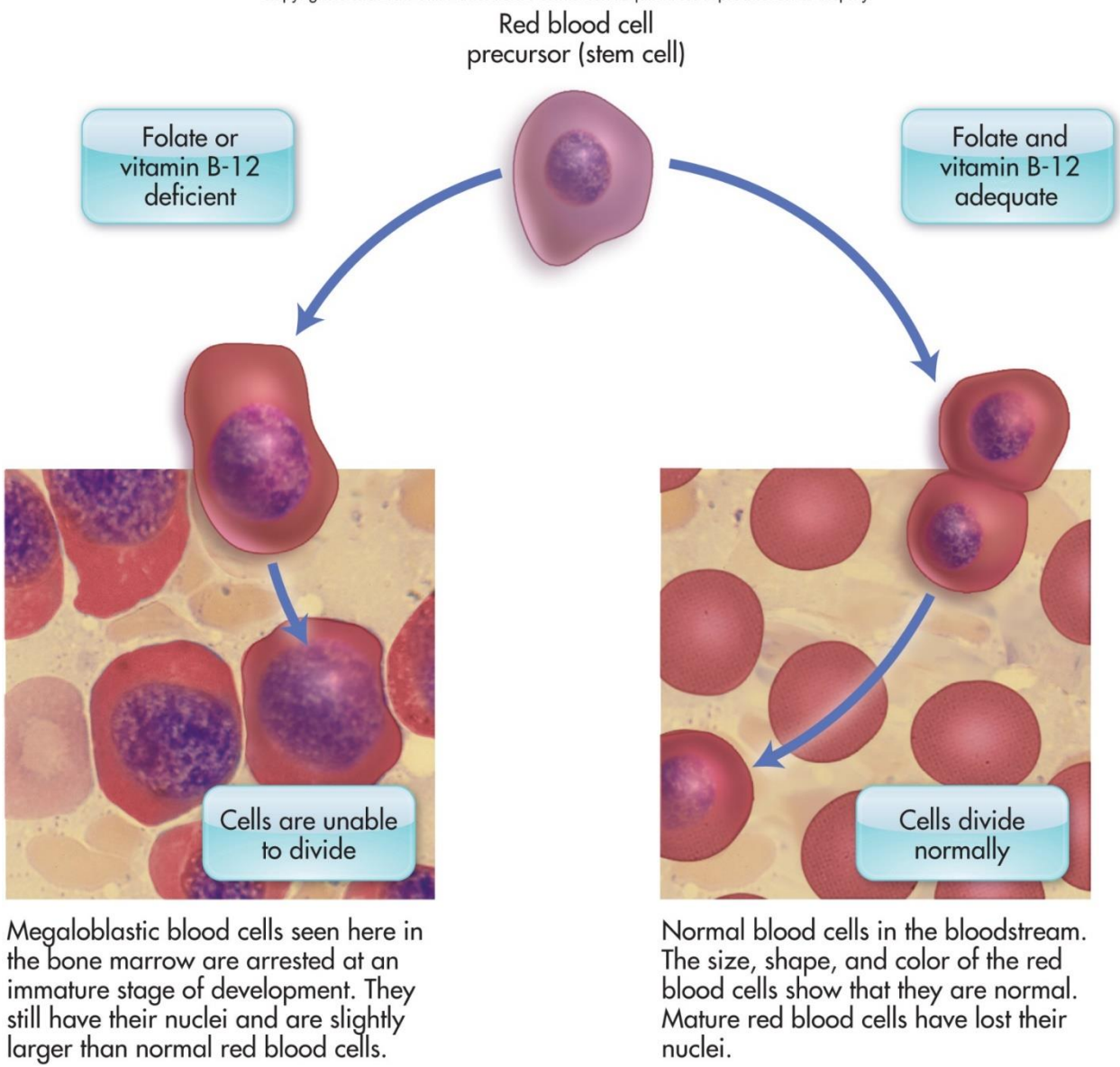


Folate deficiency → megaloblastic anemia (aka macrocytic anemia)

- Immature cells can't divide because they can't form new DNA
- Cells grow larger because insufficient DNA for nuclei to divide
- Large immature form: megaloblast

Symptoms:

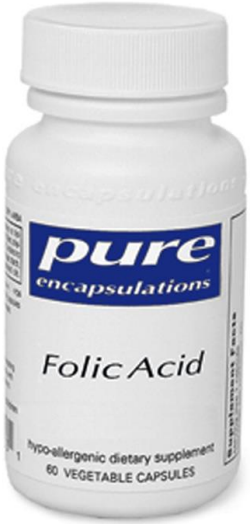
- Tongue inflammation
- Diarrhea
- Poor growth
- Mental confusion
- Depression
- Nerve dysfunction



Megaloblastic blood cells seen here in the bone marrow are arrested at an immature stage of development. They still have their nuclei and are slightly larger than normal red blood cells.

Normal blood cells in the bloodstream. The size, shape, and color of the red blood cells show that they are normal. Mature red blood cells have lost their nuclei.

Getting Enough Folate



- RDA: 400 mcg/day
- Pregnancy RDA: 600 mcg/day
  - Low folate levels in pregnant woman linked to neural tube defects in fetus
    (ex: spina bifida, anancephaly)
  - Neural tubes close within first 28 days of pregnancy
  - Recommended that 6 weeks BEFORE pregnancy all women have 400 mcg/day
- Very susceptible to heat: cooking destroys 50-90% folate
- 1998, FDA mandated fortification of grain products
  - Has increase intakes by 200 mcg/day
  - Decreased neural tube defects 15% to 20%

J Nutr. 2002 Aug;132(8 Suppl):2367S-2372S.

Metabolic interactions of alcohol and folate.

Halsted CH[1], Villanueva JA, Devlin AM, Chandler CJ.

…*chronic alcohol exposure impairs folate absorption by inhibiting expression of the reduced folate carrier and decreasing the hepatic uptake and renal conservation of circulating folate.*

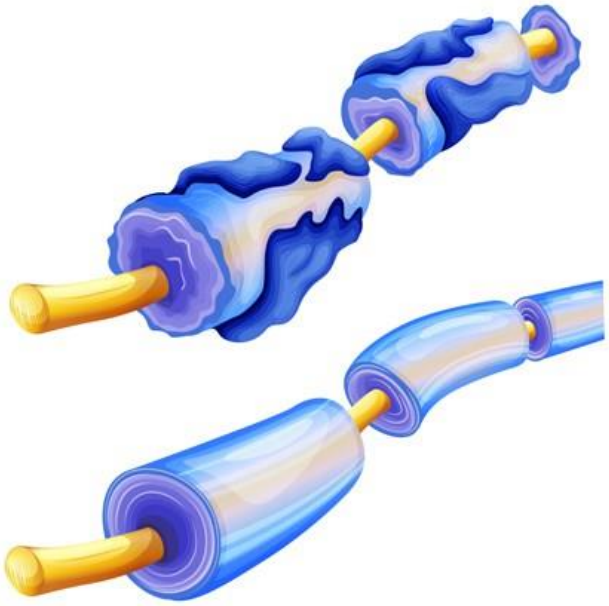
…*folate deficiency accelerates alcohol-induced changes in hepatic methionine metabolism while promoting enhanced oxidative liver injury…*

Avoiding Too Much Folate

- UL for only refers to folic acid
  - Natural form, folate, has limited absorption
- UL: 1 mg/day (1,000 mcg)
- Large doses of folate can mask vitamin B-12 deficiency symptoms

Vitamin	Major Functions	RDA or Adequate Intake	Dietary Sources*	Deficiency Symptoms	Toxicity Symptoms
Vitamin B-12†	• Coenzyme of folate metabolism • Nerve function *Many other functions*	2.4 micrograms *Older adults and vegans should use fortified foods or supplements.*	• Animal foods (not natural in plants) • Organ meats • Oysters • Clams • Fortified, ready-to-eat breakfast cereals	• Macrocytic anemia • Poor nerve function	• None

Vitamin B-12



- Also known as: cobalmin or cyanocobalmin
- Can be stored in liver
- Functions in folate metabolism
- Maintaining myelin sheath that insulates neurons from each other
- B-12 in food bound to protein, can't be absorbed
- Requires **Intrinsic Factor (IF)** for absorption

Vitamin B-12: Deficiency

- Destruction of parts of myelin sheath
  - Neurological symptoms:
    - Irregular muscle actions
    - Impaired reflexes
    - Eventual paralysis and, perhaps, death
- Pernicious anemia
  - anemia from lack of B12 absorption
- Only found in foods of animal origin
  - vegans at risk for deficiency
- Elderly encouraged to have synthetic form because of low Intrinsic Factor production with increasing age
- Gastric bypass recipients also need a supplement

Chocolate Chia Seed Pudding

- 1 cup non dairy milk
- 2-3 tablespoons cacao powder
- 2-3 tablespoons pure maple syrup or 2-3 dates
- 1 tsp vanilla
- ¼ cup chia seeds
- Add ingredients to blender and blend.

Recipe from: https://detoxinista.com/chocolate-chia-pudding-vegan-paleo/

Easy Energy Bites

INGREDIENTS

2/3 cup creamy peanut butter
1/2 cup semi-sweet chocolate chips
1 cup old fashioned oats
1/2 cup ground flax seeds
2 tablespoons honey

INSTRUCTIONS

1. Combine all 5 ingredients in a medium bowl. Stir to combine. Place in the refrigerator for 15-30 minutes so they are easier to roll.

https://chefsavvy.com/5-ingredient-peanut-butter-energy-bites/#wprm-recipe-container-27489