INE INSTITUTE OF NUTRITIONAL ENDOCRINOLOGY

Micronutrients: Vitamin B5

Dr. Ritamarie Loscalzo

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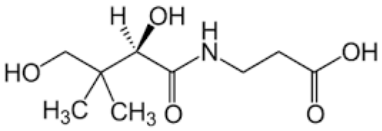
B Vitamins At a Glance

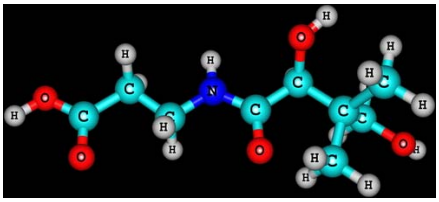
Letter	Names	Notes/Actions
B1	Thiamin, Benfotiamine	Energy, heart, muscle, and nerve function
B2	Riboflavin, R 5'-Phosphate	Energy, red blood cells, vision
B3	Niacin, Nicotinic Acid, Niacinamide	Energy, nerve function, circulation and heart
B4	Choline, Adenine, Carnitine	Loosely considered as B vitamins - cell membranes, memory, neuromuscular
B5	Pantothenic Acid	Coenzyme A, adrenals, skin
B6	Pyridoxine, Pyridoxal 5'-Phosphate	Brain and nerve, hormones, protein synthesis
B7	Biotin	Hair, metabolism
B8	Inositol	Loosely considered a B vitamin
B9	Folate, Methylfolate, Folinic Acid	Red blood cell production, DNA repair, brain
B10	Pteroylmonoglutamic Acid (PABA – Para-aminobenzoic Acid)	Really a form of folate, skin protector
B11	Salicylic Acid	Not technically a vitamin, loosely categorized
B12	Cobalamin	Red blood cells, DNA repair, nervous system

Vitamin B5 General Info

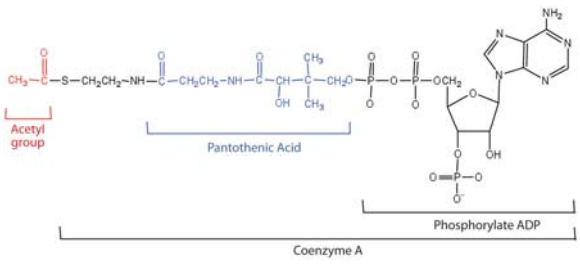
- ✓Water-soluble B vitamin
- ✓Also known as **pantothenic acid or pantothenate**
- ✓Consists of B-alanine and pantoic acid joined by peptide bond
- ✓Name derived from Greek word “panthos” meaning **everywhere** (vitamin B5 is present in virtually all foods)
- ✓Part of coenzyme A **(CoA)**

Vitamin B5 Chemical Structure

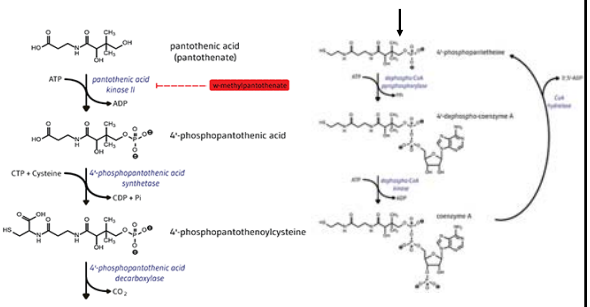




Vitamin B5 Coenzyme Form



CoA Synthesis from Pantothenic Acid



http://www.dritamarie.com/go/LPIVitaminB5 This link leads to a website provided by the Linus Pauling Institute at Oregon State University. Dr. Ritamarie Loscalzo is not affiliated or endorsed by the Linus Pauling Institute or Oregon State University.

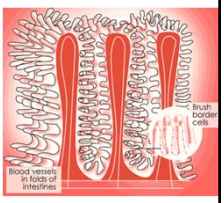
Coenzyme A Synthesis

- ✓ Five-step process
- ✓ Requires four molecules of ATP
- ✓ Made from pantothenate and cysteine

1. Phosphorylated to 4'-phosphopantothenate by enzyme pantothenate kinase
2. A cysteine is added to 4'-phosphopantothenate by phosphopantothenoylcysteine synthetase to form 4'-phospho-N-pantothenoylcysteine
3. Decarboxylated by phosphopantothenoylcysteine decarboxylase to 4'-phosphopantetheine
4. 4'-phosphopantetheine is adenylylated to form dephospho-CoA by phosphopantetheine adenylyltransferase
5. Dephospho-CoA is phosphorylated to coenzyme A by the enzyme dephosphocoenzyme A kinase

Vitamin B5 Absorption

- ✓ Occurs in food in **free and bound forms**: 85% bound to CoA
- ✓ Absorbed mainly in **jejunum**
- ✓ **High concentrations:** passive diffusion
- ✓ **Low concentrations:** sodium dependent multi-vitamin carrier
- ✓ CoA hydrolyzed to **pantetheine** then pantothenic acid by phosphatases and pyrophosphatases



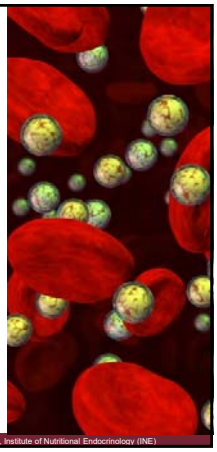
- ✓ Shares an intestinal carrier/transporter with **biotin and lipoic acid**
- ✓ Panthenol, the alcohol form used in many multivitamins, is also absorbed and converted to pantothenate
- ✓ Pantothenate absorption **decreases to 10%** when intake exceeds 10 times the recommended intake (in pill form)

Vitamin B5 Transport and Storage

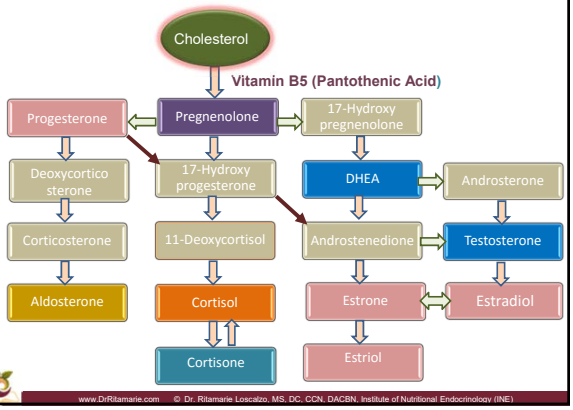
- ✓ Absorbed into intestinal epithelial cells
- ✓ Enters the portal circulation
- ✓ Free form in blood serum
- ✓ Higher concentrations in the red blood cells than in the blood serum
- ✓ **Active transport uptake by:**
  - ➢ Heart
  - ➢ Muscle
  - ➢ Brain
  - ➢ Liver
- ✓ Passive diffusion into all other tissues
- ✓ **Found in cells as**
  - ➢ 4'-phosphopantothenate
  - ➢ Pantetheine
- ✓ **Most pantothenate is used to synthesize CoA**
  - ➢ Liver
  - ➢ Kidney
  - ➢ Adrenal
  - ➢ Brain
  - ➢ Heart

Vitamin B5 Roles

- ✓ Metabolism of protein, fat, and carbohydrates
- ✓ Krebs cycle
- ✓ Production of cholesterol
- ✓ Production of adrenal hormones
- ✓ Production of sex hormones
- ✓ Production of bile
- ✓ Production of hemoglobin
- ✓ Reducing inflammation
- ✓ Maintaining healthy levels of blood lipids
- ✓ Methylation

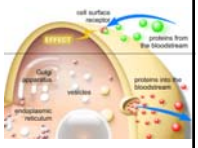


Vitamin B5 Role in Hormones



Acetylation and Proteins

- ✓ CoA was named for its role in acetylation reactions
- ✓ **Acetylation of proteins** alters their overall charge, their three-dimensional structure, and their function
- ✓ Regulates the **activity of peptide hormones**, including those produced by the pituitary gland
- ✓ Regulates function and half-life of many signaling molecules, **transcription factors,** and enzymes
- ✓ **Acetylation of histones** plays a role in the regulation of gene expression by facilitating transcription



http://www.drritamarie.com/go/LPIVitaminB5

Acetylation and Lipids

- ✓ Acetylation is important in formation of **sphingolipids (myelin sheath), phospholipids, and fatty acids**
- ✓ **Fatty acid synthase (FAS)** requires pantothenic acid dependent acyl-carrier protein (ACP) in the form of 4'-phosphopantetheine
- ✓ **Acetyl-CoA, malonyl-CoA, and ACP** are all required for the synthesis of fatty acids
- ✓ 4'-phosphopantetheine is required for 10-formyltetrahydrofolate dehydrogenase (FDH) needed to form **tetrahydrofolate**, an essential cofactor in the metabolism of nucleic acids and amino acids

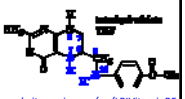


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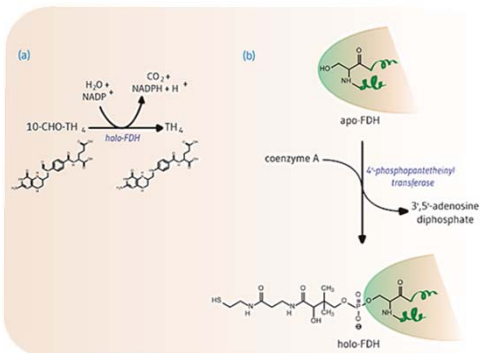
Figure 3. 4'-Pantetheinylation of Formyltetrahydrofolate Dehydrogenase (FDH)



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Vitamin B5, Lipids, and Cardiovascular Disease

- ✓ 900 mg/day shown to **lower LDL cholesterol** and triglycerides, reducing the risk of cardiovascular disease

Donati C, Bertieri RS, Barbi G. Clin Ter 1989 Mar 31;128(6):411-22, PMID: 2524328
http://www.drritamarie.com/go/PMID2524328

- ✓ Pantetheine supplements appear to **reduce blood levels of triglycerides** and possibly improve cholesterol by 25%
- ✓ Pantetheine **blocks the activity of HMG-CoA** (cholesterol synthesis) by about 50% leading to significantly lower cholesterol production

http://www.drritamarie.com/go/PMID11425046
http://www.drritamarie.com/go/PantetheineTriglycerides
http://www.drritamarie.com/go/PrepareMDPantethine

Vitamin B5 and Lipids

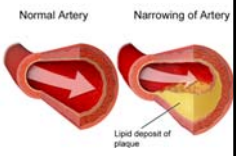
- ✓ **University of Minnesota Medical School Study:**
  - ➢ Healthy, unmedicated adults
  - ➢ **Double-blind, randomized, placebo controlled and cross-over**
  - ➢ Each patient was given placebo, 600 mg, and 900 mg pantetheine for 6 weeks; under these conditions pantethine:
    - Reduced LDL-c by 10-15%
    - Fasted triglycerides by 20-25%
    - Increased HDL-c by 15-20%

MEDICAL SCHOOL
UNIVERSITY OF MINNESOTA

http://www.drritamarie.com/go/PrepareMDPantethine

Vitamin B5 and Artery Health

- ✓ Administered to cholesterol-fed rabbits (0.5% cholesterol diet + 1% pantetheine) for 90 days; results:
  - ➢ **Total cholesterol levels were reduced 64.7%**
  - ➢ HDL/total cholesterol ratio increased
  - ➢ Total aortic area with evident **plaques was reduced by 18.2%**
  - ➢ Microscopic examination: **Reduction in the severity of lesions, both in the aorta and in the coronary arteries**
- ✓ 182 patients with coronary heart disease and stable **angina given** pantetheine, 500 mg/day for 3 weeks; had favorable effects on hemodynamics, lipids, riboflavin, and ascorbic acid



Carrara P, Matturri L, Galbussera M, Lovati MR, Franceschini G, Sirtori CR. Atherosclerosis 1984 Dec;53(3):255-64
http://www.drritamarie.com/go/PrepareMDPantethine

Long-Term Pantetheine Study

- ✓ A one-year clinical trial
- ✓ 24 patients with established dyslipidemia of Fredrickson's types II A, II B, and IV, alone or associated with **diabetes** mellitus
- ✓ Blood lipid assays repeated after 1, 3, 6, 9, and 12 months of treatment
  - ➢ **Consistent and statistically significant reductions in:**
    - Total cholesterol
    - LDL
    - Apolipoprotein B
  - ➢ **Increased levels of:**
    - HDL
    - Apolipoprotein A

Arsenio L, Bodria P, Magnati G, Strata A, Trovato R. Clin Ther 1986;8(5):537-45 PMID: 3094958
http://www.drritamarie.com/go/PMID3094958

Vitamin B5 and Fatty Liver

- ✓ 600 mg/day of pantetheine, 16 outpatients with fatty liver and hypertriglyceridemia for six months or longer
  - ➢ **9/16 pantetheine patients were no longer diagnosed as having fatty liver**
  - ➢ Visceral fat calculated from the CT image was significantly reduced
  - ➢ Subcutaneous fat area increased
  - ➢ **Suggests pantetheine may transfer fat from liver and viscera to subcutaneous**

(Osono Y, Hirose N, Nakajima K, Hata Y. "The effects of pantethine on fatty liver and fat distribution." J Atheroscler Thromb 2000;7(1):55-8)

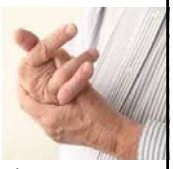
Pantetheine and Cognitive Function

- ✓ In rats that received daily injections, **pantetheine facilitated the learning process and activity levels**
- ✓ Pantetheine **supports BDNF** (Brain Derived Neurotrophic Factor)

http://www.drritamarie.com/go/PMID16797865

Morisaki N, Matsuoka N, Shirai K, Sasaki N, Saito Y, Kumagai A. "Effect of pantethine on fatty acid oxidation in microvessels of rat brain." Tohoku J Exp Med 1983 Sep;141(1):41-5

Other Uses of Vitamin B5



- ✓ Large daily doses of pantothenic acid were helpful to **relieve symptoms of arthritis** *(Haslock DI, Wright V, "Pantothenic acid in the treatment of osteoarthrosis." Rheumatol Phys Med 1971 Feb;11(1):10-3)*
- ✓ Pantetheine used successfully for heart burn, ulcers, and candida infections, and has been used with some success in the management of **certain allergies**

http://www.drritamarie.com/go/DrLamAllergies

- ✓ Rat study: **deficiency of pantothenic acid can cause hair to turn gray and fall out;** no human studies
- ✓ Panthoderm may be helpful in treatment of minor skin injuries

Vitamin B5 Interactions

- ✓ Nutrients that compete for absorption and transport:
  - ➢ Biotin
  - ➢ Lipoic Acid
- ✓ Medications:
  - ➢ **Tetracycline:** Vitamin B5 interferes with the absorption and effectiveness
  - ➢ **Alzheimer's drugs:** Cholinesterase inhibitors: B5 increases the effects leading to severe side effects; should not be taken with B5 unless under a doctor's supervision

Cholinesterase inhibitors include:

- Donepezil (Aricept)
- Memantine hydrochloride (Ebixa)
- Galantamine (Reminyl)
- Rivastigmine (Exelon)

Vitamin B5 RDI

Infants:
- ✓ Birth up to 6 months: 1.7 mg (adequate intake)
- ✓ 7-12 months: 1.8 mg (adequate intake)

Children:
- ✓ 1-3 years: 2 mg a day
- ✓ 4-8 years: 3 mg a day
- ✓ 9-13 years: 4 mg a day

Adults:
- ✓ Males: 14 years and older: 5 mg a day
- ✓ Females: 14 years and older: 5 mg a day

Women who are pregnant or breastfeeding:
- ✓ Pregnant women: 6 mg
- ✓ Breastfeeding women: 7 mg a day

Signs and Symptoms Vitamin B5 Deficiency

- ✓Fatigue
- ✓Muscle cramps
- ✓Plantar Fasciitis
- ✓Irritability
- ✓Hypoglycemia
- ✓Cramps
- ✓Heart palpitations
- ✓Hair loss
- ✓Insomnia
- ✓Intestinal distress
- ✓Joint aches
- ✓Nausea
- ✓Premature graying of hair
- ✓Restlessness
- ✓Vomiting

Impact of Vitamin B5 Excess

- ✓ There is no known toxicity to vitamin B5
- ✓ Excess easily excreted in the urine
- ✓ Diarrhea in very high intakes of 10-20 g/day calcium D-pantothenate for 6 weeks
- ✓ One case report of life-threatening eosinophilic pleuropericardial effusion in an elderly woman who took a combination of 10 mg/day of biotin and 300 mg/day of pantothenic acid for two months

Debourdeau PM, Djezzar S, Estival JL, Zammit CM, Richard RC, Castot AC. Life-threatening eosinophilic pleuropericardial effusion related to vitamins B5 and H. Ann Pharmacother. 2001;35(4):424-426

Top Food Sources of Vitamin B5

Plant-Based

- ✓ Mushrooms
- ✓ Cauliflower
- ✓ Sweet potato
- ✓ Broccoli
- ✓ Beet greens
- ✓ Asparagus
- ✓ Turnip greens
- ✓ Bell peppers
- ✓ Cucumber
- ✓ Celery
- ✓ Avocado
- ✓ Lentils
- ✓ Peas

Animal-Based

- ✓ Chicken
- ✓ Turkey
- ✓ Yogurt
- ✓ Salmon
- ✓ Beef
- ✓ Eggs

Food Preparation Effects on Vitamin B5

- ✓Easily destroyed by heat
- ✓Destroyed by light
  - ➢Store away from light to protect vitamin B5 content
- ✓Can be lost in water when foods are boiled or soaked

WH Foods Vitamin B5 Foods Ranking

Food	Serving Size	Cals	Amount (mg)	DRI/DV (%)
Mushrooms, Shitake	0.50 cup	40.6	2.61	52
Mushrooms, Crimini	1 cup	15.8	1.08	22
Cauliflower	1 cup	28.5	0.63	13
Sweet Potato	1 cup	180.0	1.77	35
Broccoli	1 cup	54.6	0.96	19
Beet Greens	1 cup	38.9	0.47	9
Asparagus	1 cup	39.6	0.40	8
Turnip Greens	1 cup	28.8	0.39	8
Bell Peppers	1 cup	28.5	0.29	6
Cucumber	1 cup	15.6	0.27	5
Celery	1 cup	16.2	0.25	5
Avocado	1 cup	240.0	2.08	42
Lentils	1 cup	229.7	1.26	25
Dried Peas	1 cup	231.3	1.17	23
Chicken	4 oz	187.1	1.09	22
Turkey	4 oz	166.7	1.02	20
Yogurt	1 cup	149.4	0.95	19
Salmon	4 oz	157.6	0.92	18
Rye	0.33 cup	188.5	0.81	16
Beef	4 oz	175.0	0.77	15
Eggs	1 each	77.5	0.70	14
Potatoes	1 cup	160.9	0.65	13
Wheat	1 cup	151.1	0.63	13
Corn	1 each	73.9	0.61	12
Shrimp	4 oz	134.9	0.59	12
Papaya	1 medium	118.7	0.55	11
Winter Squash	1 cup	75.8	0.48	10

http://www.drritamarie.com/qa/WHFVitaminB5Foods

Herbs High In Vitamin B5

Black catnip

Eyebright

Red clover

Alfalfa

Burdock

Nettle

Yellow dock

Risk Factors for Vitamin B5

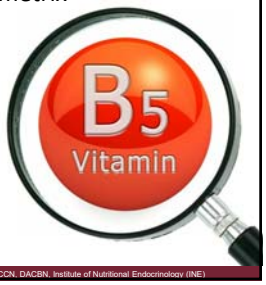
- ✓ **Alcoholics**
  - ➢ Decreased intake
  - ➢ Decreased absorption
  - ➢ Impaired utilization of vitamin B5
- ✓ **Anorexia**
- ✓ Lactose intolerance
- ✓ **Hypothyroid and adrenal fatigue**
  - ➢ The conversion of vitamin B5 into FAD and FMN is impaired
- ✓ Very physically active people (athletes, laborers)
  - ➢ Slightly increased vitamin B5 requirement

What Depletes Vitamin B5?

- ✓ **Stress**
- ✓ **Refined foods**
- ✓ **Alcohol**
- ✓ **Beta Blockers:**
  - ✓ Blocadren
  - ✓ Tenormin
  - ✓ Nadolol
  - ✓ Toprol XL
  - ✓ Inderal
  - ✓ Lopressor
  - ✓ Cartrol
  - ✓ Brevibloc
  - ✓ Sectral
  - ✓ Betapace
  - ✓ Corgard

Assessing Status of Vitamin B5

- ✓ Static serum level not always accurate
- ✓ NutrEval by Genova / Metametrix
- ✓ SpectraCell Labs
- ✓ Diet journal
- ✓ Questionnaires and good history taking for signs and symptoms



Vitamin B5 Supplementation

- ✓ Generally included in multivitamins and B-complex vitamins
- ✓ Available forms:
  - ➢ Pantothenic acid
  - ➢ Panthenol: common in multivitamins
  - ➢ Pantetheine: possibly most effective
  - ➢ Calcium D-pantothenate
- ✓ Capsules, powder, liquid
- ✓ According to Dr. Lam, best with high dose nutritional cocktail of vitamin C, lysine, proline, bioflavonoids, pine bark extract, glycine, carnitine, magnesium, fructooligosaccharides, glutamine, and ascorbyl palmitate

http://www.drritamarie.com/go/DrLamPantothenicAcid

References

- ✓ ***Advanced Nutrition and Human*** **Metabolism** – Gropper, Smith and Groff.
- ✓ Linus Pauling Institute: http://www.drritamarie.com/go/LPIVitaminB5
- ✓ http://www.drritamarie.com/go/DrLamPantothenicAcid
- ✓ Flodin N. Pharmacology of micronutrients. New York: Alan R. Liss, Inc.; 1988.
- ✓ Debourdeau PM, Djezzar S, Estival JL, Zammit CM, Richard RC, Castot AC. Life-threatening eosinophilic pleuropericardial effusion related to vitamins B5 and H. Ann Pharmacother. 2001;35(4):424-426.
- ✓ http://www.drritamarie.com/go/PossibleInteractionsVitaminB5