

Chad Oler, ND

## **WCA 48 Hr Nutrition Certification Module 1: Day 2**

1

## **Module 1: Day 2**

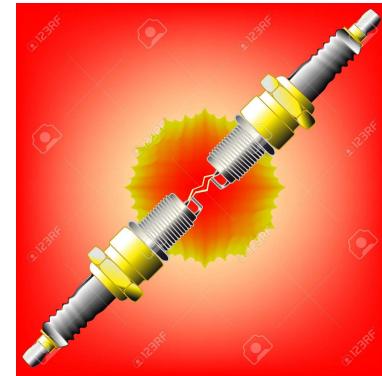
- Micronutrients
  - Water soluble vitamins: RDAs, deficiency, toxicity
  - Fat Soluble vitamins: RDAs, deficiency, toxicity
  - Minerals: RDAs, deficiency, toxicity
  - Metals: RDAs, deficiency, toxicity
  - Phytonutrients
- Non-essential and conditionally essential nutrients
- Efficacy, safety, risks and benefits of glandular products and therapeutic enzymes

2

## Catalysts and Sparkplugs

### ■ Micronutrients

- Vitamins
  - Water soluble – B, C
  - Fat soluble – A, E, D, K
- Minerals
- Antioxidants
- Phytonutrients
- Amino acids
- Conditionally Essential Nutrients



3

			Recommended Dietary Allowance (RDA)																																
Weight kg	Height in	kg lb	cm	VITAMIN A		VITAMIN C		VITAMIN D		VITAMIN E		VITAMIN K		RIBOFLAVIN		NIACIN		VITAMIN B6		FOLATE		VITAMIN B12		CALCIUM		PHOSPHOROUS		MAGNESIUM		IRON		IODINE		SELENIUM	
				PROTEIN	AMINO ACIDS	THIAMIN	NIACIN	VITAMIN A	VITAMIN C	VITAMIN D	VITAMIN E	VITAMIN K	RIBOFLAVIN	NIACIN	VITAMIN B6	FOLATE	VITAMIN B12	CALCIUM	PHOSPHOROUS	MAGNESIUM	IRON	IODINE	SELENIUM	IRON	IODINE	SELENIUM	IRON	IODINE	SELENIUM						
			(kcal)		(g)	(ug)	(mg)	(ug)	(mg)	(mg)	(mg)	(ug)	(ug)	(mg)	(ug)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(ug)	(ug)	(ug)	(ug)						
			Males																																
11-14	45	99	157	62	2500	45	1000	10	10	45	50	1.3	1.5	17	1.7	150	2.0	1200	1200	270	12	15	150	40											
15-18	66	145	176	69	3000	59	1000	10	10	65	60	1.5	1.8	20	2.0	200	2.0	1200	1200	400	12	15	150	50											
19-24	72	160	177	70	2900	58	1000	10	10	70	60	1.5	1.7	19	2.0	200	2.0	1200	1200	350	10	15	150	70											
25-50	79	174	176	70	2900	63	1000	5	10	80	60	1.5	1.7	19	2.0	200	2.0	800	800	350	10	15	150	70											
51+	77	170	173	68	2300	63	1000	5	10	80	60	1.2	1.4	15	2.0	200	2.0	800	800	350	10	15	150	70											
			Females																																
11-14	46	101	157	62	2200	46	800	10	8	45	50	1.1	1.3	15	1.4	150	2.0	1200	1200	280	15	12	150	45											
15-18	55	120	163	64	2200	44	800	10	8	55	60	1.1	1.3	15	1.5	180	2.0	1200	1200	300	15	12	150	50											
19-24	58	128	164	65	2200	46	800	10	8	60	60	1.1	1.3	15	1.6	180	2.0	1200	1200	280	15	12	150	55											
25-50	63	138	163	64	2200	50	800	5	8	65	60	1.1	1.3	15	1.6	180	2.0	800	800	280	15	12	150	55											
51+	65	143	160	63	1900	50	800	5	8	65	60	1.0	1.2	13	1.6	180	2.0	800	800	280	10	12	150	55											
			Pregnant		+300	60	800	10	10	65	70	1.5	1.6	17	2.2	400	2.2	1200	1200	320	30	15	175	65											
			Lactating		+500	65	1300	10	12	65	95	1.6	1.8	20	2.1	280	2.6	1200	1200	355	15	19	200	75											
			1st 6 mo.		+500	62	1200	10	11	65	90	1.6	1.7	20	2.1	260	2.6	1200	1200	340	15	16	200	75											
			2nd 6 mo.		+500	62	1200	10	11	65	90	1.6	1.7	20	2.1	260	2.6	1200	1200	340	15	16	200	75											

4

# Vitamins



- Cannot be synthesized in sufficient quantities and must be obtained through diet
- Classified by their biological and chemical activity, not their structure
  - Each “vitamin” refers to a number of *vitamer* compounds that all show the biological activity associated with a particular vitamin
  - Each set of compounds is grouped under an alphabetized vitamin “generic descriptor” title
    - “Vitamin A” includes retinal, retinol, and four known carotenoids.
  - Vitamers by definition are convertible to the active form of the vitamin in the body and are sometimes interconvertible to one another as well

5

# Vitamins



## Comparison of two types of vitamin

	Fat soluble vitamins	Water soluble vitamins
Solubility in fat	Soluble	Not soluble
Water solubility	Not soluble	Soluble
Absorption	Along with lipids Requires bile salts	Absorption simple (except vitamin B <sub>12</sub> )
Carrier proteins	Present	No carrier proteins (except vitamin B <sub>12</sub> )
Storage	Stored in liver	No storage (except vitamin B <sub>12</sub> )
Deficiency	Manifests only when stores are depleted	Manifests rapidly as there is no storage (except vitamin B <sub>12</sub> )
Toxicity	Hypervitaminosis may result	Unlikely, since excess is excreted
Major vitamins	A, D, E and K	B and C

6

## B Vitamins

- Vitamin B<sub>1</sub> – Thiamin
- Vitamin B<sub>2</sub> – Riboflavin
- Vitamin B<sub>3</sub> – Niacin
- Vitamin B<sub>5</sub> – Pantothenic Acid
- Vitamin B<sub>6</sub> – Pyridoxine
- Vitamin B<sub>7</sub> - Biotin
- Vitamin B<sub>9</sub> - Folic Acid
- Vitamin B<sub>12</sub> – Cobalamin

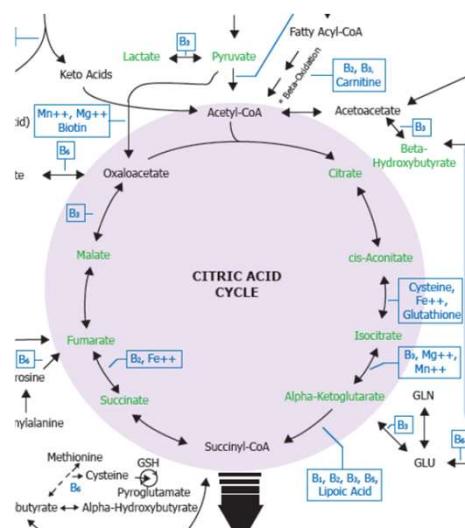


7

## B-Complex: Cell Metabolism

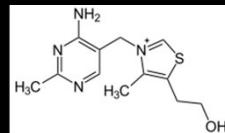


- Energy metabolism
  - B<sub>1</sub> (Thiamin)
  - B<sub>2</sub> (Riboflavin)
  - B<sub>3</sub> (Niacin)
  - B<sub>5</sub> (Pantothenic acid)
  - B<sub>6</sub> (Pyridoxine)
  - B<sub>7</sub> (Biotin)
- Cell formation & division
  - B<sub>5</sub> (Pantothenic acid)
  - B<sub>6</sub> (Pyridoxine)
  - Folic acid
  - B<sub>12</sub> (Cobalamin)



8

## Vitamin B1 - Thiamin



RDA	Age	Thiamin B1 mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	0.6	50-200 mg	<ul style="list-style-type: none"> <li>Up to 8 grams per day have been used with no adverse effects in one case of dementia</li> </ul>
	7-10	0.9		
<b>Males</b>	15-18	1.2	50-200 mg	
	19-24	1.2		
	25-50	1.2		
	50+	1.2		
<b>Females</b>	15-18	1.0	50-200 mg	
	19-24	1.1		
	25-50	1.1		
	50+	1.1		

9

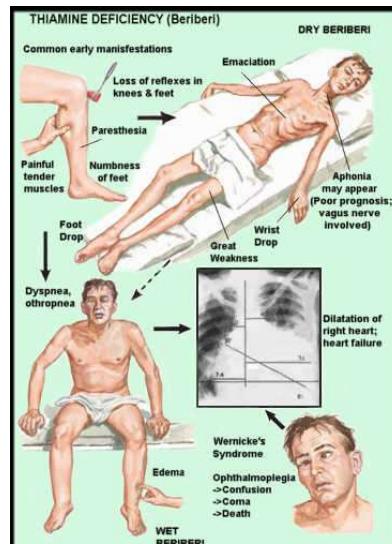
## Vitamin B1 – Thiamin: Functions

- Generation of energy from carbohydrates
  - Necessary for conversion of pyruvate to acetyl coenzyme A (CoA)
  - Necessary for several co-enzymes in Kreb's cycle to generate ATP
- RNA and DNA production
- Neuronal function
  - Formation of neurotransmitters (acetylcholine)
    - Assist with memory and cognition
  - Modulate chloride channels in nervous system

10

## Vitamin B1 – Thiamin: Deficiency

- Beriberi – endemic in Asia due to eating polished white rice
- Affects cardiovascular, nervous, muscular and GI systems
  - Painful/tender muscles, numbness, wrist/foot drop, loss of reflexes, weight loss, weakness, tachycardia, edema, confusion, edema, coma



11

## Vitamin B1 – Thiamin: Food Sources

- Nutritional yeast
- Wheat germ
- Whole grains
- Sunflower seeds
- Brazil nuts
- Almonds
- Peanuts
- Legumes
- Garlic
- Dark leafy greens



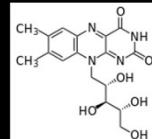
12

## Vitamin B<sub>1</sub> – Thiamin: Therapeutic Considerations

- Consider if exhibit:
  - Dementia, neuropathy, fatigue, confusion, depression, muscle pain, memory loss
  - Excessive alcohol consumption (past or present)
  - Genetic SNPs that inhibit use of thiamin
  - Malabsorption (IBD, IBS, eating disorder)

13

## Vitamin B<sub>2</sub> - Riboflavin

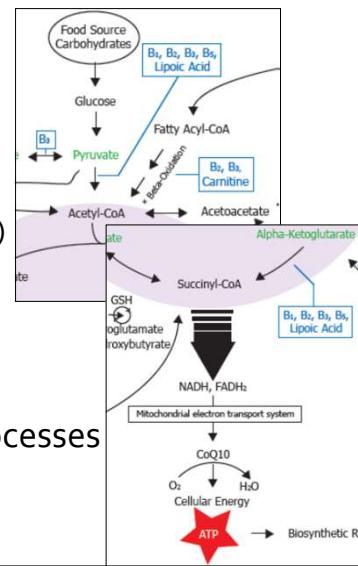


RDA	Age	Riboflavin B2 mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	0.6		<ul style="list-style-type: none"> <li>• Readily excreted</li> </ul>
	7-10	0.9		
<b>Males</b>	15-18	1.3		<ul style="list-style-type: none"> <li>• Toxic only through injection</li> </ul>
	19-24	1.3	50-200mg	
	25-50	1.3		
	50+	1.3		
<b>Females</b>	15-18	1.0		<ul style="list-style-type: none"> <li>• Toxic only through injection</li> </ul>
	19-24	1.1		
	25-50	1.1		
	50+	1.1		

14

## Vitamin B<sub>2</sub> – Riboflavin: Functions

- Energy production
    - Kreb's cycle
    - Electron Transport Chain
      - Flavin adenine dinucleotide (FAD)
    - Breakdown of glucose
    - Catabolism of fatty acids
      - Beta oxidation
  - Required for wide range of processes



15

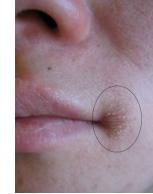
## Vitamin B<sub>2</sub> – Riboflavin: Functions

- Liver Detoxification
    - Necessary for production of cytochrome P450 enzymes & glutathione conjugation
  - Conversion and activation of other vitamins
    - Vitamin B6 – into active form
    - Vitamin A- into active form
    - Folic acid-> 5-MTHF
    - Tryptophan-> Vitamin B<sub>3</sub> (Niacin)

16

## Vitamin B<sub>2</sub> – Riboflavin: Deficiency

- Inflammation of tongue and throat (stomatitis)
- Chapped cracked lips (cheilosis)
- Inflammation of the corners of the mouth (angular stomatitis)
- Oily, scaly skin rashes on scrotum, vulva, mouth
- Eyes – itchy, watery, bloodshot and sensitive to light
- Fatigue
- Failure to thrive/grow
- Anemia – normal RDW & Hgb
- Pregnancy -> congenital heart defects & limb deformities



17

## Vitamin B<sub>2</sub> – Riboflavin: Food Sources

- Nutritional yeast
- Milk, cheese
- Leafy green vegetables
- Liver, kidney
- Eggs
- Legumes
- Mushrooms
- Almonds



18

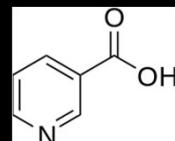
## Vitamin B<sub>2</sub> – Riboflavin: Therapeutic Considerations



- Consider if exhibit:
- Inflammation of tongue/throat, cracked lips/corners of mouth
- Poor diet (multiple deficiencies)
- Anemia – normal RDW & Hgb
- Women taking oral contraceptives
- Excessive alcohol consumption (past or present)
- Malabsorption (IBD, IBS, eating disorder)
- HIV
- Phototherapy to treat jaundice in infants

19

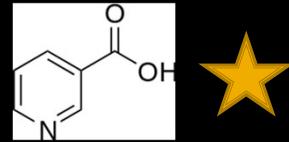
## Vitamin B<sub>3</sub> - Niacin



RDA	Age	Niacin B3 mg	Therapeutic Dosage	Toxic Dosage
Children	4-8	8	• 50mg-200 mg	Readily excreted
	9-13	12		
Males	14-18	16		
	19-30	16		
	31-50	16		
	51+	16		
	14-18	14		
Females	19-30	14		
	31-50	14		
	51+	14		

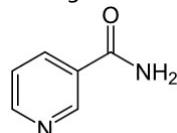
20

## Vitamin B<sub>3</sub> - Niacin



- Two structures

- Nicotinic acid
- Nicotinamide
  - Does not have the same pharmacological and toxic effects as nicotinic acid
  - Does NOT reduce cholesterol or cause flushing



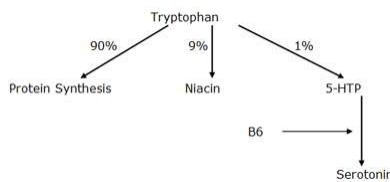
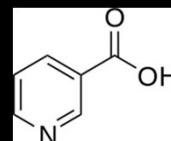
- Two co-enzymes

- Nicotinamide adenine dinucleotide (NAD)
- Nicotinamide adenine dinucleotide phosphate (NADP)

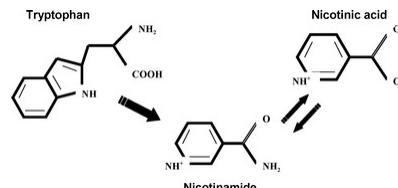
- Both play an important role in energy production & metabolism of glucose, fat and alcohol.

21

## Vitamin B<sub>3</sub> - Niacin



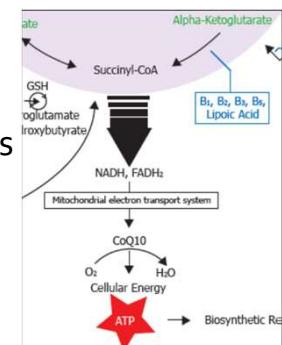
- ❑ Liver can synthesize niacin from tryptophan
- ❑ However, it is inefficient: 60 mg of tryptophan is needed to make 1 mg of niacin.



22

## Vitamin B<sub>3</sub> – Niacin: Functions

- Energy production
  - Kreb's cycle/ Electron Transport Chain
    - Nicotinamide Adenine Dinucleotide (NADH)
  - Catabolism of glucose, fat & protein
  - Breakdown of alcohol
  - Required for wide range of processes

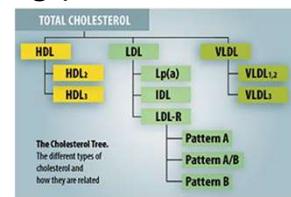


23

## Vitamin B<sub>3</sub> – Niacin: Functions ★



- Cell signaling (NAD)
- DNA repair (NAD)
- Production of steroid hormones in adrenals
- Vasodilation - flushing
- Fatty acid and cholesterol synthesis (NADP)
  - Lowers LDL, Lp(a), VLDL & triglycerides
  - Increases HDL
- Reduces inflammation
- Reduces oxidative stress



24

## Vitamin B3 – Niacin: Deficiency

- Brain, gut, skin most susceptible
- Pellegra – the 4 Ds
  - Dermatitis, diarrhea, dementia and death
  - Hyperpigmentation, thickening of skin, inflammation of mouth & tongue, digestive disturbances, amnesia, delirium
- Psychiatric disturbances
  - Irritability, poor concentration, anxiety, fatigue, restlessness, apathy and depression



25

## Vitamin B3 – Niacin: Food Sources

- Brewer's yeast
- Organ meats
- Chicken
- Beef/venison
- Fish
- Whole grains
- Peanuts/PB
- Legumes



Food sources of Niacin (vitamin B3) include dairy, poultry, fish, lean meat, nuts and eggs

©ADAM

26

## Vitamin B<sub>3</sub> – Niacin: Therapeutic Considerations

- Consider if exhibit:
  - Poverty or malnutrition
  - Chronic use of alcohol
  - Eat corn/maize as staple food (only grain low in niacin)
  - High triglycerides, VLDL, LDL or Lp(a)
  - Low HDL

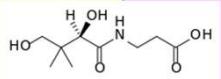
27

## Vitamin B<sub>3</sub> – Niacin: Toxicity

- Flushing is not a sign of toxicity
  - Can occur at 500 mg – 6 grams/day
  - Take with food and avoid alcohol & hot food/drink
- Liver toxicity possible – check liver enzymes
  - Time-released form more likely to cause toxicity
- Can increase uric acid levels (gout)

28

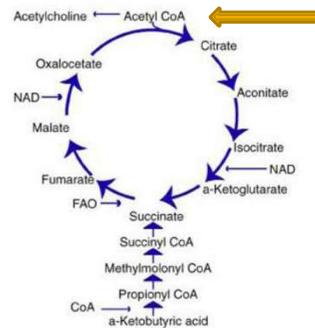
## Vitamin B5 – Pantothenic Acid

RDA	Age	Pantothenic Acid (B5) mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	3	50mg-100 mg	 <ul style="list-style-type: none"> <li>• Intake of 10 gm daily for 6 weeks without consequence</li> </ul>
	7-10	4		
<b>Males</b>	15-18	5	50mg-100 mg	<ul style="list-style-type: none"> <li>• Intake of 10 gm daily for 6 weeks without consequence</li> </ul>
	19-24	5		
	25-50	5		
	50+	5		
<b>Females</b>	15-18	5	50mg-100 mg	<ul style="list-style-type: none"> <li>• Intake of 10 gm daily for 6 weeks without consequence</li> </ul>
	19-24	5		
	25-50	5		
	50+	5		

29

## Vitamin B5 – Pantothenic Acid: Functions

- Derived from the Greek *pantothen*, meaning "from everywhere"
- Coenzyme A synthesis
  - Starts the Kreb Cycle
- Oxidation of fats
- Carbohydrate metabolism



30

## Vitamin B5 – Pantothenic Acid: Functions

- Involved in synthesis of:
  - Amino acids
  - Fatty acids
  - Cholesterol
  - Phospholipids
  - Steroid hormones
  - Neurotransmitters
  - Antibodies



31

## Vitamin B5 – Pantothenic Acid: Deficiency & Toxicity

- Deficiency extremely rare in humans
- Toxicity very unlikely
  - No Tolerable Upper Level Intake (UL) has been established
  - No reported side effects at 10 grams/day

32

## Vitamin B5 – Pantothenic Acid: Therapeutic Considerations

- Blood lipid imbalances
  - Pantethine (derivative of B5) can lower LDL and triglyceride levels
- Poor cellular energy production or need for cellular energy support
  - Wound healing, adrenal fatigue, autoimmunity, chronic fatigue
- Poor hair growth
- Diabetic neuropathy
  - Studies show that 85% of people treated with alpha-lipoic acid report further improvement with B5

Münchener Medizinische Wochenschrift (Germany), 1997, 109/12 (34-37)

33

## Vitamin B5 – Pantothenic Acid: Food Sources

- Chicken liver
- Avocado
- Sunflower seeds
- Whole grains
- Legumes
- Eggs
- Meat/Salmon
- Yogurt
- Cauliflower/Broccoli



34

<b>Vitamin B6 - Pyridoxine</b>				
RDA	Age	Pyridoxine (B6) mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	.6	20mg-500mg	• 250 to 500 mg long-term may be excessive
	7-10	1		
<b>Males</b>  (SONAs = 25 mg)	15-18	1.3	20mg-500mg	• 250 to 500 mg long-term may be excessive
	19-24	1.3		
	25-50	1.3		
	50+	1.7		
<b>Females</b>  (SONAs = 20 mg)	15-18	1.3	20mg-500mg	• 250 to 500 mg long-term may be excessive
	19-24	1.3		
	25-50	1.3		
	50+	1.5		

35

<b>Vitamin B6 - Pyridoxine</b>	
■ Many forms:	
■ Pyridoxine (most common in supplements)	
■ Pyridoxal	
■ Pyridoxal-5-phosphate (PLP) – metabolically active form (sold as P-5-P)	
■ Pyridoxamine	
■ All forms can be interconverted (theoretically)	
■ Conversion dependent on FMN – need B2	
■ Some people need to be given PLP/P5P	

36

## Vitamin B6 – Pyridoxine: Functions

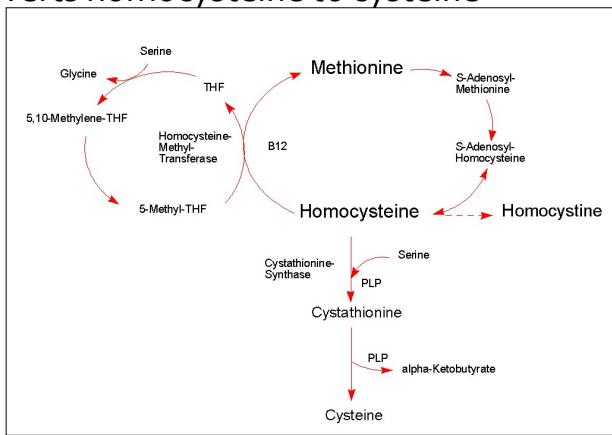
- Active form pyridoxal-5-phosphate (PLP) serves as cofactor in many reactions:
  - Amino acid metabolism
  - Synthesis of neurotransmitters
    - Serotonin, dopamine, epinephrine, norepinephrine, GABA and histamine
  - Glucose metabolism
  - Lipid metabolism
  - Hemoglobin synthesis



37

## Vitamin B6 – Pyridoxine: Functions

- Required for methylation
  - Converts homocysteine to cysteine



38

## Vitamin B6 – Pyridoxine: Functions

- Modulates steroid hormones
  - Can bind to receptor sites for estrogen, testosterone, glucocorticosteroids, etc.
  - Useful for morning sickness, PMS and estrogen-dominant disorders



39

## Vitamin B6 – Pyridoxine: Deficiency

- Seborrhoeic dermatitis-like eruption
- Sore/inflamed tongue
- Angular cheilitis
- Conjunctivitis
- Somnolence
- Confusion
- Neuropathy
- Elevated homocysteine



40

## Vitamin B6 – Pyridoxine: Toxicity

- > 1,000 mg/day can cause neuropathy
  - Pain and numbness in extremities
- Doses over 200 mg not considered safe for pregnancy or lactation



Katan MB (Nov 12, 2005). "[How much vitamin B6 is toxic?]" Ned Tijdschr Geneeskd. 149 (46): 2545–6.

41

## Vitamin B6 – Pyridoxine: Therapeutic Considerations

- Morning sickness during pregnancy
- Neurotransmitter-related disorders
  - Depression, anxiety, ADD, Parkinson's disease
- Carpal tunnel
- PMS
- Elevated homocysteine
  - Take along with Folic acid, B<sub>12</sub> and trimethylglycine (TMG)

42

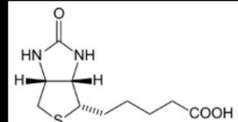
## Vitamin B6 – Pyridoxine: Food Sources

- Avocado
- Brewer's yeast
- Organ meats
- Blackstrap molasses
- Most vegetables/leafy greens
- Eggs
- Beef
- Whole grains
- Nuts
- Bananas



43

## Vitamin B7 - Biotin



RDA	Age	Biotin mcg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	6		
	7-10	12		
<b>Males</b> <small>(SONAs = 75 mcg)</small>	15-18	25	• 300-600 mcg per day	• Up to 10 mg daily for over six months used with no signs of toxicity
	19-24	30		
	25-50	30		
	50+	30		
<b>Females</b> <small>(SONAs = 75 mcg)</small>	15-18	25		
	19-24	30		
	25-50	30		
	50+	30		

44

## Vitamin B<sub>7</sub> – Biotin: Functions

- Metabolism of:
  - Fatty acids
  - Proteins and amino acids
    - Especially isoleucine and valine
  - Carbohydrates
- Helps maintain blood sugar
  - Gluconeogenesis



45

## Vitamin B<sub>7</sub> – Biotin: Deficiency

- Not typical
- Alopecia (hair loss)
- Conjunctivitis
- Scaly dermatitis
  - Especially around eyes, nose, mouth and genitals
- Dry skin, nails
- Depression, lethargy
- Impaired growth



46

## Vitamin B<sub>7</sub> – Biotin: Therapeutic Considerations

- Dermatitis
- Alopecia
- Pregnancy
- Depression
- If consume egg whites (raw) for years



47

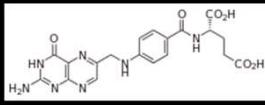
## Vitamin B<sub>7</sub> – Biotin: Food Sources

- Swiss chard
- Leafy greens
- Peanuts
- Raw/runny egg yolk
- Small amount synthesized by gut bacteria



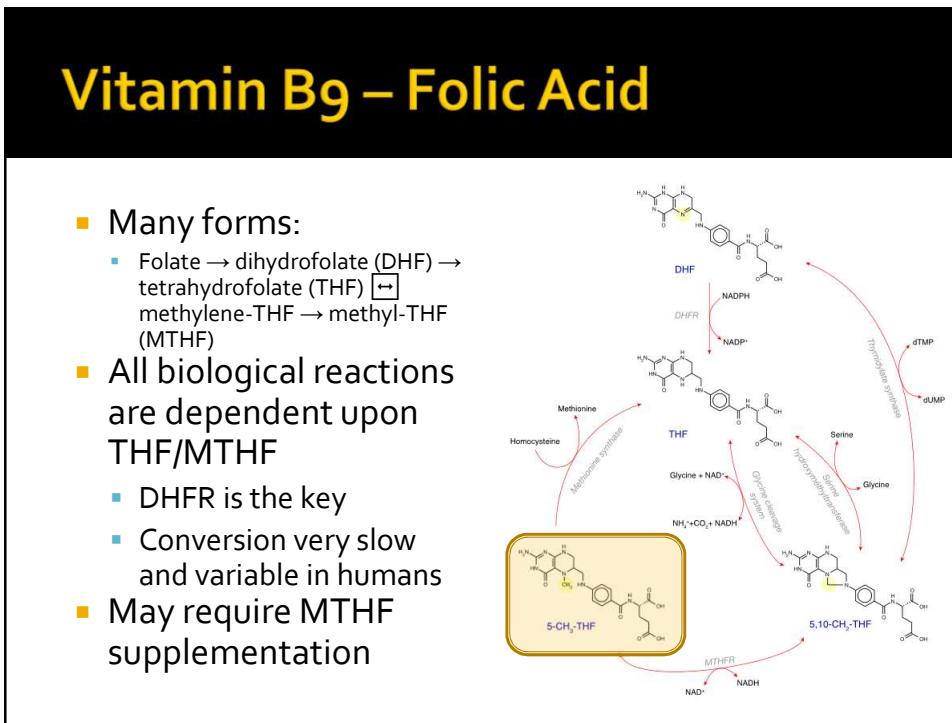
48

## Vitamin B9 – Folic Acid



RDA	Age	Folic Acid mcg	Therapeutic Dosage	Toxic Dosage
Children	4-6	200	• 400 – 1000 mcg	<ul style="list-style-type: none"> <li>&lt;400 mcg if not taking with B12</li> <li>10mg daily for 5 years have been used in adults with no adverse affects</li> </ul>
	7-10	400		
Males	15-18	400	• 400 – 1000 mcg	<ul style="list-style-type: none"> <li>&lt;400 mcg if not taking with B12</li> <li>10mg daily for 5 years have been used in adults with no adverse affects</li> </ul>
	19-24	400		
	25-50	400		
	50+	400		
Females	15-18	400	• 400 – 1000 mcg	<ul style="list-style-type: none"> <li>&lt;400 mcg if not taking with B12</li> <li>10mg daily for 5 years have been used in adults with no adverse affects</li> </ul>
	19-24	400		
	25-50	400		
	50+	400		

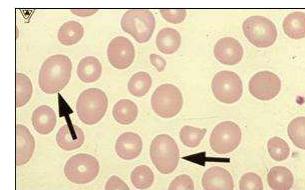
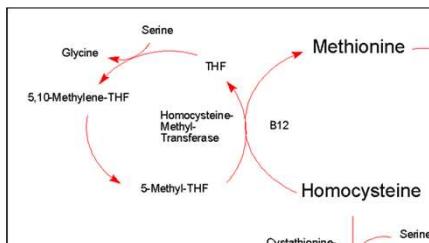
49



50

## Vitamin B9 – Folic Acid: Functions

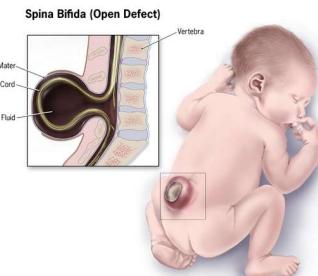
- Cell division, DNA synthesis and repair
  - Very important during pregnancy and infancy
- Red blood cell formation
  - Deficiency results in macrocytic anemia
- Homocysteine metabolism



51

## Vitamin B9 – Folic Acid: Deficiency

- Neural tube defects
  - Spina bifida
- Macrocytic anemia
- Peripheral neuropathy
- Confusion, forgetfulness
- Depression
- Heart palpitations
- Elevated homocysteine
- Rx: Trimethoprim, Pyrimethamine, Methotrexate, Sulfonamides, Valproic acid



52

## Vitamin B9 – Folic Acid: Therapeutic Considerations



- Pregnancy
- Macrocytic anemia – take with B12
- Elevated homocysteine
- Chronic alcohol consumption
- When use/have used:
  - Trimethoprim (Primsol, Trimpex, Proloprim)
  - Pyrimethamine (Daraprim)
  - Methotrexate
  - Sulfonamides (Sulfa drugs, thiazide)
  - Valproic acid (Convulex, Depakote, Epilim, Valparin, Valpro, Vilapro, Stavzor)
- ***Use MTHF/5-MTHF not folic acid/folate***

53

## Vitamin B9 – Folic Acid: Food Sources

- Dark green leafy vegetables
- Avocado
- Brewer's yeast
- Asparagus
- Brussel sprouts
- Legumes/peas
- Poultry and meat
- Eggs
- Whole grains



54

<b>Vitamin B<sub>12</sub> - Cobalamin</b>				
RDA	Age	Cobalamin (B <sub>12</sub> ) mcg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-8	1.2	• Therapeutic doses 1000-5000 mcg daily	No dose recorded
	9-13	1.8		
<b>Males</b>	14-18	2.4	• Therapeutic doses 1000-5000 mcg daily	No dose recorded
	19-30	2.4		
	31-50+	2.4		
<b>Females</b>			• Therapeutic doses 1000-5000 mcg daily	No dose recorded
	19-30	2.4		
	31-50+	2.4		

55

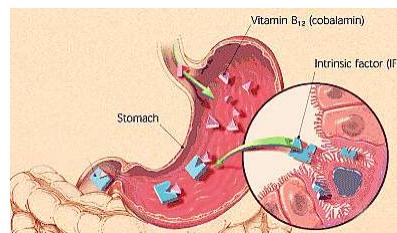
<b>Vitamin B<sub>12</sub> - Cobalamin</b>	
■ Cobalamin may refer to several chemical forms of B <sub>12</sub> :	<ul style="list-style-type: none"> <li>■ Cyanocobalamin (most common; must be converted in the body into active form)</li> <li>■ Hydroxycobalamin</li> <li>■ Methylcobalamin (active form of B<sub>12</sub>)</li> <li>■ Adenosylcobalamin (active form of B<sub>12</sub>)</li> </ul>

56

## Vitamin B<sub>12</sub> - Cobalamin



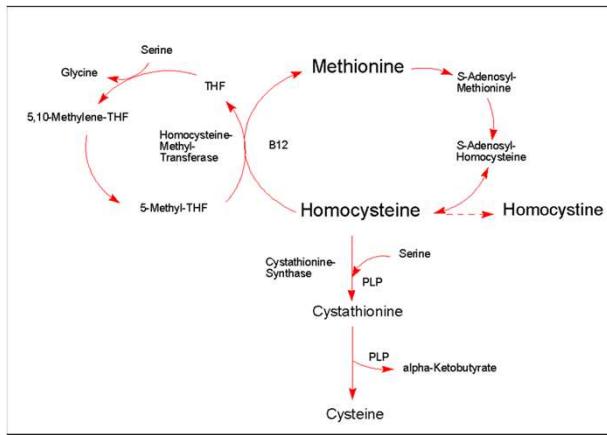
- Need Intrinsic Factor for absorption
  - Parietal cells of stomach secrete HCl and Intrinsic Factor
- Antacids inhibit Intrinsic Factor
  - Pernicious anemia



57

## Vitamin B<sub>12</sub> – Cobalamin: Functions

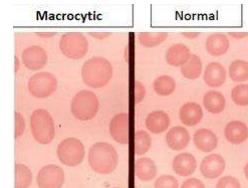
- Homocysteine metabolism



58

## Vitamin B<sub>12</sub> – Cobalamin: Functions

- DNA methylation/repair
  - Helps prevent cancer and autoimmune diseases
- Hemoglobin formation
  - Lack of Intrinsic Factor -> Pernicious anemia
  - Lack of B<sub>12</sub> -> Macrocytic anemia
- Nerve function
  - Needed for myelin production



59

## Vitamin B<sub>12</sub> – Cobalamin: Deficiency

- Macrocytic anemia
- Elevated homocysteine
- Peripheral neuropathy
- Memory loss/cognitive deficits
- Mania (long term)
- Psychosis (long term)

60

## Vitamin B<sub>12</sub> – Cobalamin: Therapeutic Considerations

- Macrocytic anemia
- Elevated homocysteine – use with MTHF
- Peripheral neuropathy
- Memory loss/cognitive deficits
- Elderly
- Long-term antacid use (PPI/H<sub>2</sub> Antagonists)
- Mania (long term)
- Psychosis (long term)
- Cyanide poisoning

61

## Vitamin B<sub>12</sub> – Cobalamin: Food Sources

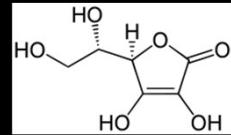


- Meat
- Fish
- Poultry
- Eggs
- Dairy



62

## Vitamin C – Ascorbate



RDA	Age	Vitamin C mg	Therapeutic Dosage	Toxic Dosage
Children	4-8	25		
	9-13	45		
Males	14-18	75	<ul style="list-style-type: none"> <li>• 1000 mg daily</li> <li>• 10-20 grams daily have shown benefits</li> </ul>	
	19-30	90		
	31-50	90		
	51+	90		
	14-18	65		
Females	19-30	75		
	31-50	75		
	51+	75		

63

## Vitamin C – Ascorbate: Functions



- Made internally by almost all organisms
  - Except guinea pigs, most bats, monkeys and HUMANS
- Required in the diet
  - Can only store a small amount
  - Can develop deficiency symptoms in 1-6 months

64

## Vitamin C – Ascorbate: Functions

- Collagen synthesis
- Antioxidant
  - Protects proteins, fats, carbohydrates, DNA & RNA from free radical damage
  - Can regenerate other antioxidants and increase glutathione production



65

## Vitamin C – Ascorbate: Functions



- Immune support
  - Enhances lymphocyte proliferation and phagocytosis
  - Increases natural killer (NK) cell activity up to 10x
  - Helps increase interferon
    - Increases detection/recognition of potential threats
  - Protects against oxidizing agents released by immune cells
  - Enhances iron absorption

66

## Vitamin C – Ascorbate: Deficiency

- Scurvy

- Brown spots on skin (esp. thighs/legs), spongy gums, bleeding from all mucus membranes



67

## Vitamin C – Ascorbate: Deficiency



- Easy bruising
- Impaired wound healing
- Vascular fragility
  - Bleeding hemorrhoids, varicose veins
- Bleeding gums
- Impaired immune function
- Iron deficient anemia



68

## Vitamin C – Ascorbate: Therapeutic Considerations

- Easy bruising
- Impaired wound healing
- Vascular fragility
  - Bleeding hemorrhoids, varicose veins
- Bleeding gums
- Impaired immune function
- Iron deficient anemia
- Detoxification support
- Vitamin C Calibration/Flush

69

## Vitamin C – Ascorbate: Food Sources

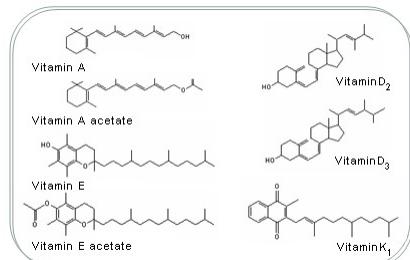
- Cherries
- Plums
- Peppers
- Kiwi
- Broccoli
- Berries
- Papaya
- Citrus
- Pineapple
- Leafy greens...



70

## Fat Soluble Vitamins

- Vitamins A, D, E and K (KADE)
- Soluble in lipids/oil
- Stored in fatty tissues and the liver
- Excessive use may lead to toxic accumulation
- Eliminated slowly from the body



71

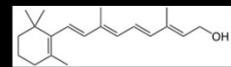
## Vitamin A

Retinyl palmitate -> Retinol, Retinal, Retinoic acid

RDA	Age	Vitamin A mcg RAE	Therapeutic dosage	Toxic Dosage
<b>Children</b>	4-8	400	Convert Vit A as retinol: IU/3.33 = mcg	• 50,000 to 250,000 IU per day up to 5 days is fine
	9-13	600	beta-carotene: IU/1.66 = mcg	• Studies have used 400,000 IU on 6 months olds for 1-2 days with no toxicity effects
<b>Males</b>	14-18	900	alpha-carotene: IU/0.278 = mcg	• 50,000 IU per day for several years is upper limit
	19-30	900		• Nothing over 10,000 IU for pregnant or potentially pregnant females
	31+	900		• Conservative doses if liver disease or taking oral contraceptive
<b>Females</b>	14-18	700	10,000 IU per day = ~3000 mcg retinol OR ~6000 mcg beta-carotene	
	19-30	700	~36 mg alpha-carotene	
	31+	700		

72

## Vitamin A - Retinol



- Vitamin A is a group of compounds
  - Retinol
  - Retinal
  - Retinoic acid
  - Provitamin A carotenoids
    - Alpha-carotene
    - Beta-carotene
    - Gamma-carotene



73

## Vitamin A: Functions

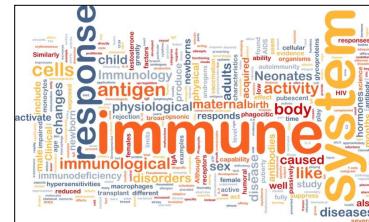


- Vision
  - The retinol is oxidized to its aldehyde, retinal, which complexes with a molecule in the eye called opsin found in the rod cell. When a photon of light hits the complex, the retinal changes from the 11-cis form to the all-trans form, initiating a chain of events which results in the transmission of an impulse up the optic nerve.
  - Vitamin A is important for vision/night vision

74

## Vitamin A: Functions

- Immune function
    - Reduces infections
    - Maintains mucosal surface integrity (respiratory and GI tracts) which act as natural barrier to pathogens
    - Improves antibody response
    - Increases WBC proliferation



75

## Vitamin A: Functions



- Skin and cellular health
    - Maintains normal skin health by switching on genes and differentiating keratinocytes (immature skin cells) into mature epidermal cells

Fuchs E, Green H (1981). "Regulation of terminal differentiation of cultured human keratinocytes by vitamin A". *Cell* 25 (3): 617-25.

76

## Vitamin A: Functions

- Growth
  - Regulates genetic growth hormone expression
- Fetal Development
  - Promotes proper cellular differentiation and development of the limbs, heart, eyes and ears



Mol pharmacol 1993 Nov;44(5):997-1002. Growth hormone and vitamin A induce P450<sub>2C7</sub> mRNA expression in primary rat hepatocytes. Westin S, Mode A, Murray M  
Food and Nutrition Board, Institute of Medicine, National Academies. (2003) "Dietary Reference Intakes".

77

## Vitamin A: Functions

- Gene expression
- Bone metabolism
- Blood cell formation (hematopoiesis)
- Antioxidant



78

## Vitamin A: Deficiency



- Dry eyes
- Impaired vision
- Night blindness
- Impaired immunity
  - Ear infections, UTIs
- Hyperkeratosis (white lumps at hair follicles)



79

## Vitamin A: Toxicity

- Acute toxicity > 25,000 IU/kg of body weight
- Chronic toxicity > 4000 IU/kg daily for 6-15 months
- Liver toxicity can occur as low as 15,000 IU/day
- People with kidney failure: 4000 IU/day
- Children can reach toxic levels at 1500 IU/kg body weight

80

## Vitamin A: Toxicity

- Toxicity only occurs with preformed (retinoid) vitamin A, NOT carotenoid forms
- Nausea, irritability, reduced appetite, vomiting, blurry vision, headache, hair loss, diarrhea, fatigue, hair loss, dry skin, bone fractures, osteoporosis, systemic itchy skin
- Pregnancy: doses used for acne treatment have been shown to disrupt normal fetal development



81

## Vitamin A: Therapeutic Considerations

- Early weaning from breastmilk
- Removal of gall bladder/impaired bile production or release
- Chronic alcohol use
- Low-fat diets

82

## Vitamin A: Therapeutic Considerations

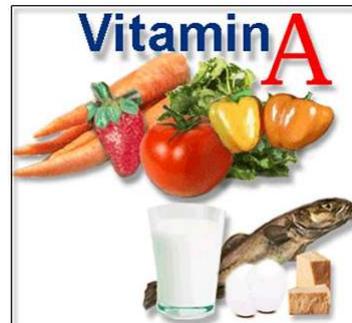
- Oral contraceptive use
  - Oral contraceptives can significantly increase vitamin A plasma levels. Oral contraceptives that contain estrogen and progestin increase retinol binding protein (RBP) synthesis by the liver, increasing the export of RBP-retinol complex in the blood. Whether this increases the dietary requirement of vitamin A is not known.



83

## Vitamin A: Food Sources

- Cod liver oil
- Liver
- Sweet potato/pumpkin/squash
- Carrot
- Broccoli
- Butter/cheese
- Kale/spinach/collards



84

## Vitamin D3

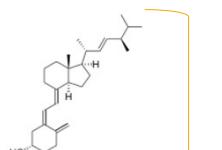
RDA	Age	Vitamin D IU	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	600	IU to mcg: IU/40 = mcg  <b>400 – 10,000 IU = 10 – 250 mcg</b>	<ul style="list-style-type: none"> <li>• Children</li> <li>• 2500 – 6000 IU daily for 4 months upper limit</li> </ul>
	7-10	600		
<b>Males</b>	15-18	600		<ul style="list-style-type: none"> <li>• Adults</li> <li>• 5000 – 10,000 daily for 6 months upper limit</li> <li>• Consider sunlight exposure</li> </ul>
	19-24	600		
	25-50	600		
	50+	600		
<b>Females</b>	15-18	600		
	19-24	600		
	25-50	600		
	50+	600		

85

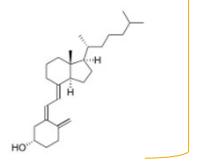
## Vitamin D – Calciferol

### Two Major Forms

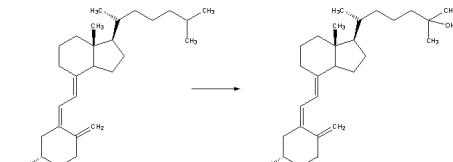
Vitamin D2:  
Ergocalciferol



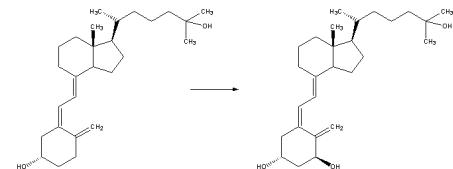
Vitamin D3:  
Cholecalciferol



Liver hydroxylation of cholecalciferol to calcidiol



Kidney hydroxylation of calcidiol to calcitriol



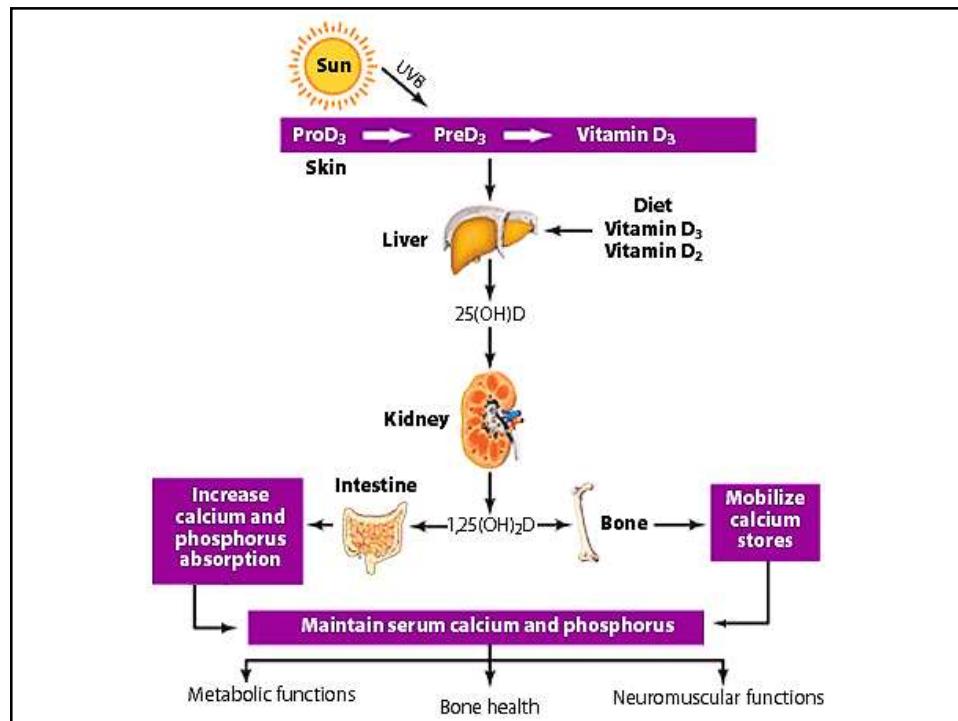
86

## Vitamin D: Sources

- Hormone-like in action
- D<sub>3</sub> results from
  - UV irradiation (sunlight) of 7-dehydrocholesterol, which is then converted in the liver and kidneys to active form
    - 10 minutes of sun exposure to face and hands = 400 IU
  - Supplementation with D<sub>3</sub>



87



88

## Sun Exposure Not Enough

- Researchers at University of Wisconsin investigated vitamin D status of healthy males living in Hawaii
  - Mean of 11.1 hours/week of total body sun exposure with no sunscreen
  - 51% had low vitamin D levels
- Ability to convert vitamin D in the skin becomes significantly diminished with age

Binkley N, Novotny R, Krueger D, et al. Low vitamin D status despite abundant sun exposure. *J Clin Endocrinol Metab.* 2007 Jun;92(6):2130-35.

89

## Vitamin D: Functions

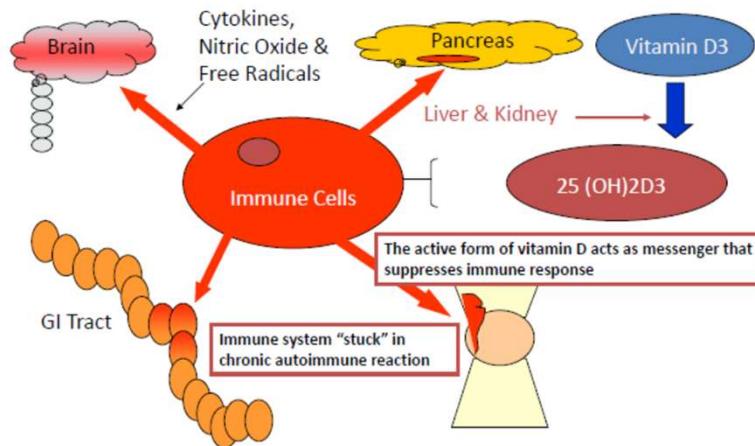
- Bone health
  - Helps with calcium absorption from small intestine in ileum
- Immune Function
  - Regulates proteins that up- and down-regulate immune functions
  - Anti-Inflammatory:  $\geq 80 \text{ ng/ml}$

American Journal of Clinical Nutrition, Vol 51, 290-300  
Vitamin D: its role and uses in immunology The FASEB Journal. Hector F. DeLuca and Margherita T. Cantorna 2001;15:2579-2585

90

## Vitamin D: Functions

Vitamin D Inhibits Inflammatory Cytokines & Acts as an Immune System Brake



In general, Vitamin D<sub>3</sub> activates the innate and dampens the adaptive immune systems

91

## Vitamin D: Functions

Vitamin D Plays Direct Role in Balancing Inflammation Cascade

MINIREVIEW

Mounting Evidence for Vitamin D as an Environmental Factor Affecting Autoimmune Disease Prevalence

MARGHERITA T. CANTOFINA<sup>1</sup> AND BRETT D. MAHON<sup>2</sup>

"This review discusses the increasing evidence pointing to a link between Vitamin D and autoimmunity. Increased vitamin D intakes might decrease the incidence and severity of autoimmune diseases"

Exp Biol Med 2004; 229: 1136-42

Autoimmune diseases are characterized by the targeted destruction of self-tissue by the immune system. More than

This work was supported in part by Children's and Family Foundation of Alberta Research Council, Alberta, Canada, and the Canadian Institutes of Health Research, Institute of Neurological Diseases and Stroke (Grant MOP-14090).

<sup>1</sup>On this correspondence should be addressed to Department of Pathobiology, University of Alberta, Edmonton, AB, T6G 2R3, Canada.

<sup>2</sup>Correspondence to: Brett D. Mahon, Department of Pathobiology, University of Alberta, Edmonton, AB, T6G 2R3, Canada.

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0888-8785/04/229-1136-07\$15.00/0

Autoimmune diseases are characterized by the targeted destruction of self-tissue by the immune system. More than 80 different diseases have been linked to the immune system attacking normal tissue. These diseases include multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and type 1 diabetes. The exact cause of these diseases is unknown, but genetic factors and environmental factors such as viruses and bacteria may play a role. Vitamin D is a steroid hormone that is important for bone health. It has also been shown to have anti-inflammatory properties. Recent studies have shown that low levels of vitamin D are associated with increased risk of developing certain cancers, heart disease, and stroke. The recommended intake levels for vitamin D are too low to support these health benefits. New evidence from animal, cell, and *in vitro* mechanistic experiments suggest that vitamin D may play a role in the etiology of autoimmunity.

9136

92

## Vitamin D: Functions

### Vitamin D Status Implicated in Multiple Conditions Related to Inflammation

*Lead Article*

November 2006; 479–490

#### Vitamin D Status and the Metabolic Syndrome

Liaia A. Martin, PhD, and Richard J. Wood, PhD

##### ABSTRACT

The expression of vitamin D receptor in different tissues suggests a widespread role for vitamin D in maintaining homeostasis and promoting mineral metabolism. Recently, the importance of vitamin D in the development of metabolic syndrome has been the focus of several studies.

**Key words:** hypertension, insulin resistance, obesity, vitamin D deficiency

The metabolic conversion in the body of the pre-hormone 25-hydroxyvitamin D to the active hormonal form, 1,25-dihydroxyvitamin D<sub>3</sub>, is mediated by the enzyme 25-hydroxyvitamin D<sub>3</sub> hydroxylase (CYP27B1), which is found mainly in the kidney but also in the liver, heart, brain, mammary gland, and immune cells, colon cells, placenta, breast, prostate, and bone. The concentrations of 1,25-dihydroxyvitamin D<sub>3</sub> concentrations are 1000 times greater than that of the inactive precursor 25-hydroxyvitamin D in the circulation. Vitamin D is involved in the regulation of blood pressure, insulin sensitivity, and lipid metabolism.

"Recently, the importance of vitamin D status as a risk factor in the development of metabolic syndrome has been the focus of several studies".

*Nutrition Reviews* 2006; 64: 479

doi:10.1111/j.1753-4881.2006.tb00011.x

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© 2006 Blackwell Publishing Ltd, *Nutrition Reviews* 64: 479–490  
Received 10 July 2006; accepted 10 September 2006  
Published online 1 November 2006 in Wiley InterScience (www3.interscience.wiley.com). DOI: 10.1111/j.1753-4881.2006.tb00011.x

479

93

## Vitamin D: Functions

- May be involved in:
  - Depression and mood
  - Cognition and dementia
  - Pregnancy – deficiency associated with:
    - Gestational diabetes, pre-eclampsia and small birth weight
  - Testosterone production
  - Improving body composition
  - Decreasing VAT
  - Better overall health and mortality

94

## Vitamin D: Deficiency

- Rickets

- Impeded growth and soft, weak deformed long bones that bend and bow

- Osteomalacia

- Softening of bones
  - Bending of spine, bowing of legs
  - Bone fragility
  - Increased risk of fractures
  - 25-OH Vit D  $\leq$  10 ng/ml



95

## Vitamin D: Deficiency

- Compromised Immune Function

- Auto-immune disorders
    - MS, Diabetes, Lupus, RA, IBD, etc.
  - Frequent upper respiratory infections
    - Cold/flu
  - Cancer
- Inflammation
  - Cardiovascular disease, fibromyalgia, chronic pain

96

## Vitamin D: Toxicity

- Rare without high-dose supplementation
- Hypercalcemia
- Anorexia, nausea, vomiting
- Increased urination and thirst
- Weakness, insomnia
- Kidney damage (chronic)

97

## Vitamin D: Therapeutic Considerations



- Ideal levels: 50-65 ng/ml
- Autoimmunity/Inflammation: 80-90 ng/ml
- SAD/Depression
- Fractures, Osteoporosis/Osteopenia
- Dark skin
  - Research shows that dark-skinned people living in temperate climates have lower vitamin D levels
    - Melanin hinders vitamin D synthesis
- Sunscreen – blocks vitamin D synthesis

98

## How Much Vitamin D Do You Need?

- Have blood tested: 25-hydroxyvitamin D
    - Optimal levels 50-80 ng/ml
- | Daily Vitamin D Dose | Increases blood levels by: |
|----------------------|----------------------------|
| 1,000 IU = 25 mcg    | 11.6 ng/ml                 |
| 10,000 IU = 250 mcg  | 58.5 ng/ml                 |
| 50,000 IU = 1250 mcg | 257.6 ng/ml                |
- BMI important – larger people need more D
  - Example: target 60 ng/ml
    - 154 lb person, baseline level: 20 ng/ml
    - Need ~5,000 IU/day (125 mcg/day)

Barger-Lux MJ, Heaney RP, Dowell S, Chen TC, Holick MF. Vitamin D and its major metabolites: serum levels after graded oral dosing in healthy men. *Osteoporos Int.* 1998;8(3):222-30.

99

## Vitamin D: Food Sources

- Liver, cod liver oil
  - 3 Tbsp cod liver oil provides ~ 4000 IU
- Fatty fish – salmon, mackerel, tuna, sardines
- Butter
- Supplements
- Sunshine
  - 10 minutes of sun exposure to face and hands = 400 IU



100

## Vitamin E

RDA	Age	Vitamin E mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-8	7	<u>dl-alpha tocopherol:</u> IU * 0.9 = mg	<ul style="list-style-type: none"> <li>&gt;800 IU for extended periods of time can interfere with blood clotting, and can elevate blood pressure in hypertensive individuals</li> <li>&gt;1500 IU for extended periods of time can result in diarrhea, nausea, flatulence</li> </ul>
	9-13	11		
<b>Males</b>	14-18	15	<u>d-alpha tocopherol:</u> IU * 0.67 = mg  <b>200 IU-800 IU = 180-720 mg</b> <b>dl-alpha = 134-536 mg</b> <b>d-alpha</b>	<ul style="list-style-type: none"> <li>&gt;800 IU for extended periods of time can interfere with blood clotting, and can elevate blood pressure in hypertensive individuals</li> <li>&gt;1500 IU for extended periods of time can result in diarrhea, nausea, flatulence</li> </ul>
	19-30	15		
	31-50+	15		
<b>Females</b>				
	19-30	15		
	31-50+	15		

101

## Vitamin E

- Tocopherols
  - $\alpha$ -tocopherol
  - $\beta$ -tocopherol
  - $\gamma$ -tocopherol
  - $\delta$ -tocopherol
  - $\epsilon$ -tocopherol
- $d\alpha$ -tocopherol most biologically active
- “dl” forms are synthetically derived
- Tocotrienols
  - $\alpha$ -tocotrienol
  - $\beta$ -tocotrienol
  - $\gamma$ -tocotrienol
  - $\delta$ -tocotrienol
  - $\epsilon$ -tocotrienol

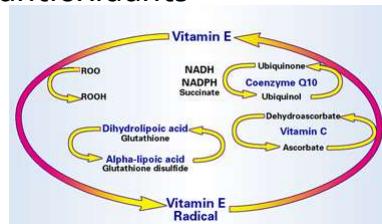
102

## Vitamin E: Functions



### ■ Antioxidant

- Protects cell membranes from oxidation
  - Inhibits lipid peroxidation
- Reduces inflammation
  - Inhibits cyclooxygenase (COX) enzymes
- Can be recycled by other antioxidants
  - Vitamin C, vitamin A
  - Alpha-Lipoic-acid
  - CoQ10



103

## Vitamin E: Functions

### ■ Cardiovascular disease

- Gene expression
  - Down-regulates CD36 scavenger receptor gene
    - Inhibits atherogenetic plaque formation
  - Up-regulates CTGF gene
    - Helps repair and regenerate tissue damaged during atherosclerosis
  - Inhibits platelet aggregation



Devaraj S, Hugon I, Jialal I, Hugon J, Jialal (2003). "Tocopherol decreases CD36 expression in human monocyte-derived macrophages". *J Lipid Res* 44 (4): 521–526.

Muller DP, Stocker R (2000). "Vitamin E: non-antioxidant roles". *Prog Lipid Res* 39 (3): 231–255.

Villacorta L, Graca-Souza AV, Ricciarelli R, Zingg JM, Azzi AJ, Graca-Souza, Ricciarelli; Zingg, Azzi (2003). "α-Tocopherol induces expression of connective tissue growth factor and antagonizes tumor necrosis factor- $\alpha$ -mediated downregulation in human smooth muscle cells". *Circ Res* 93 (3): 104–110.

Muller DP (2000). "Vitamin E and neurological function. Review". *Mol Nutr Food Res* 44 (5): 710–718.

Davies P, Zheng ZB, Zheng (1995). "On the mechanism of the anticoagulant action of vitamin E quinone". *Proc Natl Acad Sci U S A* 92 (18): 8172–8175.

Brigelus-Flöhé R, Davies KJ, Davies (2007). "Is vitamin E an antioxidant, a regulator of signal transduction and gene expression, or a 'junk' food? Comments on the two accompanying papers: 'Molecular mechanism of alpha-tocopherol action' by A. Azzi and 'Vitamin E, antioxidant and nothing more' by M. Traber and J. Atkinson". *Free radical biology & medicine* 43 (3): 2–3.

Atkinson J, Eason RF, Eason RM, Eason (2000). "Tocopherols and tocotrienols in membranes: a critical review". *Free radical biology & medicine* 28 (3): 739–746.

104

## Vitamin E: Deficiency

- Neuromuscular problems
  - Spinocerebellar ataxia
  - Myopathies
- Neurological problems
  - Dysarthria
  - Loss of deep tendon reflexes
- Male infertility
- Retinopathy
- Impairment of immune response

105

## Vitamin E: Toxicity

- Toxicity is rare
- Can act as anticoagulant
  - Increased risk of bleeding
  - Caution/monitor when use with aspirin, anti-coagulants (Warfarin, Coumadin) or surgery

106

## Vitamin E: Therapeutic Considerations

- Male infertility
- Cardiovascular disease
- Fat malabsorption – often have greasy stools
  - Gastric bypass
  - IBD (Crohn's disease, Ulcerative colitis)
  - Liver disease
  - Pancreatic insufficiency

107

## Vitamin E: Food Sources

- Wheat germ oil
- Sunflower oil/seeds
- Almonds/Almond oil
- Flax oil
- Pecans and walnuts
- Avocado
- Dark leafy greens



108

## Vitamin K

RDA	Age	Vitamin K mcg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	50	1mg-5 mg	<ul style="list-style-type: none"> <li>• 1000 mcg daily has been used in studies for osteoporosis with no toxic side effects</li> </ul>
	7-10	50		
<b>Males</b>	15-18	120	1mg-5 mg	<ul style="list-style-type: none"> <li>• No interaction with vitamin K and anti-coagulant drugs at 60-120 mcg daily</li> </ul>
	19-24	120		
	25-50	120		
	50+	120		
<b>Females</b>	15-18	90	1mg-5 mg	<ul style="list-style-type: none"> <li>• No interaction with vitamin K and anti-coagulant drugs at 60-120 mcg daily</li> </ul>
	19-24	90		
	25-50	90		
	50+	90		

109

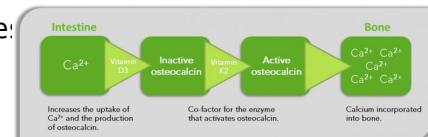
## Vitamin K

- Vitamin K1
  - Phylloquinone
  - Synthesized by plants
  - Found in green leafy vegetables
  - Can be converted to K2 in the body
    - Bacteria in colon
- Vitamin K2
  - Main storage in animals
  - Several subtypes
    - Menaquinones
    - "MK-n"
  - MK-4 most common in animals/humans
    - Can be made from K1

110

## Vitamin K: Functions

- “K” is for “Koagulation”
- Protein Formation
  - Blood coagulation
    - 7 vitamin K-dependent clotting factors in the coagulation cascade
    - Prothrombin and other factors/proteins
  - Bone metabolism
    - Osteocalcin and bone matrix proteins
    - Helps bind calcium in the bone:



111

## Vitamin K: Deficiency

- Anemia
- Bruising
- Bleeding gums/nose
- Heavy menses
- Osteoporosis (K<sub>2</sub>)
- Coronary heart disease (K<sub>2</sub>)
- Aortic calcification (MK-7)

112

## Vitamin K: Toxicity

- No known toxicity – no UL set
- Studies done at 45 mcg – 135 mcg/day of K<sub>2</sub> (MK-4) show no increase risk of blood clotting
- Doses as high as 250 mcg/kg body weight in rats did not alter blood clot formation
- Unlike safe natural forms of vitamin K<sub>1</sub> and K<sub>2</sub>, a synthetic form – Vitamin K<sub>3</sub> (menadione) – can be toxic

113

## Vitamin K: Therapeutic Considerations

- Those at risk of deficiency:
  - Liver damage/disease (alcoholics)
  - IBD (Crohn's, UC, Celiac)
  - Bulimics
  - Anticoagulant meds
  - Long-term aspirin use
- Hemorrhagic disease
  - Newborns, spontaneous nose bleeds
- Osteoporosis/fractures
- CVD & elevated diastolic blood pressure
- Kidney stones (calcium based)

114

## Vitamin K: Food Sources

### ■ Vitamin K<sub>1</sub>

- Dark leafy greens
- Broccoli
- Brussel sprouts
- Cabbage
- Parsley



### ■ Vitamin K<sub>2</sub>

- Natto
- Fermented/aged cheese
- Eggs, chicken, beef
- Liver/organ meats
- Sauerkraut
- Kefir



115

## Vitamins: Questions??



116

## Minerals

Major Minerals	Trace Minerals	Metals
<ul style="list-style-type: none"> <li>– Calcium</li> <li>– Phosphorus</li> <li>– Magnesium</li> <li>– Potassium</li> <li>– Sodium</li> </ul>	<ul style="list-style-type: none"> <li>– Chromium</li> <li>– Copper</li> <li>– Cobalt</li> <li>– Iodine</li> <li>– Iron</li> <li>– Manganese</li> <li>– Molybdenum</li> <li>– Selenium</li> <li>– Vanadium</li> <li>– Zinc</li> </ul>	<ul style="list-style-type: none"> <li>– Boron</li> <li>– Lithium</li> <li>– Nickel</li> <li>– Silicon</li> <li>– Strontium</li> <li>– Tin</li> </ul>

117

## Minerals – Why So Important?

- Act as co-enzymes
- Regulate fluid balance
- Help muscle function
  - Muscle contraction
- Help nerve function – alter electrical currents
  - Nerve conduction
  - Transport channels
- Keep bones healthy

118

## Mineral Facts



- Can be stored in the body
- Are NOT affected by cooking or light
- Absorption rates vary
  - Digestive enzymes and HCl production
  - Age – less absorbed as we age
  - GI imbalance
  - Mineral type/salt
- Minerals must be chelated to an amino acid to pass through the gut wall

119

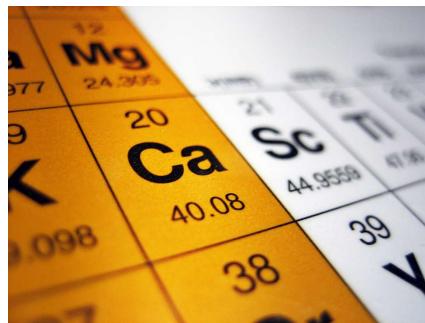
## Calcium

RDA	Age	Calcium mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-8	1000		
	9-13	1300		
<b>Males</b>	14-18	1300	<ul style="list-style-type: none"> <li>• MCHC 3000 mg daily</li> <li>• 400 mg supplemental calcium</li> </ul>	
	19-30	1000		
	31-50	1000		
	51+	1000		
<b>Females</b>				
	19-30	1000		
	31-50	1000		
	51+	1200		

120

## Calcium

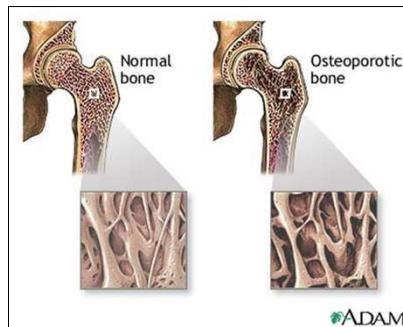
- Most abundant mineral in the body
- 95-99% in bones and teeth
- 1-5% in nerves, blood, muscles



121

## Calcium: Functions

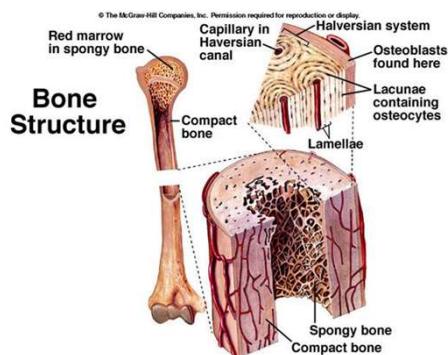
- Bone health
  - Need for optimal bone density and strength
    - Other nutrients also involved
  - Slows rate of bone loss
  - Can be leeched from bone to buffer acidic conditions in blood resulting from diet
    - Sugar, soda, caffeine, alcohol, fried foods, excessive protein



122

## What is comprehensive bone nourishment?

- Bones are formed of a composite structure. They consist of fibrous organic factors which serve as a foundation onto which the bone matrix forms
- This matrix consists of:
  - Calcium
  - Phosphorus
  - Sodium
  - Magnesium
  - Zinc
  - And other minerals



123

## MCHC provides Complete Bone Food

Active Ingredients	ORGANIC MCHC	Bone Ash/ Bone Meal	INORGANIC Hydroxyapatite Crystals	Other Calcium (carbonates, chelates)
<b>Mineral Complex</b>	✓	✓	none	none
Hydroxyapatite	✓	✓	✓	✓
• Calcium	✓	✓	✓	✓
• Phosphorus	✓	✓	✓	none
Trace Minerals	✓	✓	none	none
• Magnesium, Zinc, Sodium, Boron, Manganese, Copper	✓	✓	none	none
<b>Protein</b>	✓	TRACE	none	none
<b>Biologically Active Growth Factors</b>	✓	none	none	none
• IGF I & II	✓	none	none	none
• TGFβ I & II	✓	none	none	none
• Calcitonin	✓	none	none	none
Type I Collagen	✓	TRACE	none	none
Bone Amino Acids	✓	TRACE	none	none
Chondroitin Sulfate	✓	none	none	none

124

## Comprehensive Bone Nourishment, cont.

- Comprehensive bone nourishment provides a broad range of essential nutrients needed to build and maintain strong bones.
- Derived from whole bone extract, the calcium-rich supplement microcrystalline hydroxyapatite concentrate (MCHC) provides many minerals found in bone, in the correct proportions, along with proteins and other organic factors.

125

## Study on Effects of MCHC

Study of 64 postmenopausal women with primary biliary cirrhosis were assigned to 3 groups to see how supplementation affects bone density:

1. No mineral supplementation
2. MCHC supplementation at 8 grams/day
3. Calcium gluconate supplementation

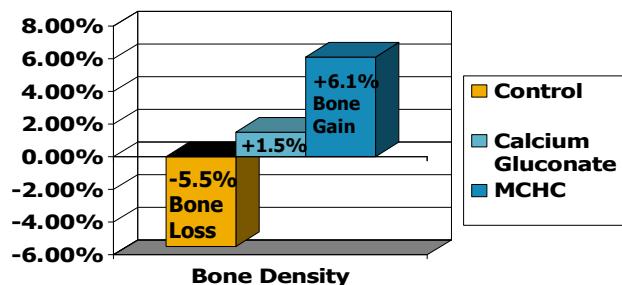
All subjects received Vitamin D supplementation

126

## MCHC Effects: cont.

- Results: After 14 months, there was no significant change in serum calcium or inorganic phosphate

But, there were significant differences in bone density.



American Journal of Clinical Nutrition. September, 1982; 42:6-430.

127

## Calcium Types and Absorption



Type	Advantages	Disadvantages
ASPARTATE (10% Ca)	<ul style="list-style-type: none"> <li>Well Absorbed</li> </ul>	Expensive
ASCORBATE (10% Ca)	<ul style="list-style-type: none"> <li>Well Absorbed</li> <li>Non-acidic Vitamin C</li> </ul>	Expensive
LACTATE (18% Ca)	<ul style="list-style-type: none"> <li>Well Absorbed</li> </ul>	May contain allergens
AMINO ACID CHELATE (20% Ca)	<ul style="list-style-type: none"> <li>Well Absorbed</li> </ul>	<ul style="list-style-type: none"> <li>Soy Sensitivity</li> <li>Often incorrectly made</li> <li>Sometimes not a true chelate</li> </ul>
PHOSPHATE (29% Ca)	<ul style="list-style-type: none"> <li>Inexpensive</li> <li>Antacid</li> </ul>	<ul style="list-style-type: none"> <li>Fair absorption</li> <li>Possible lead contamination</li> </ul>
CALCIUM CARBONATE (40% Ca)	<ul style="list-style-type: none"> <li>Inexpensive</li> <li>Antacid</li> </ul>	Poorly absorbed

128

## Calcium Types and Absorption



Type	Advantages	Disadvantages
CITRATE (22% Ca)	<ul style="list-style-type: none"> <li>• Very well absorbed</li> <li>• Reduces risk to kidney stones</li> <li>• Absorbed by those with poor digestion</li> </ul>	Doesn't provide all the building blocks necessary for bone formation
MCHC (24% Ca)	<ul style="list-style-type: none"> <li>• Best absorbed calcium source</li> <li>• Increases cortico bone density</li> <li>• Arrests trabecular bone loss</li> <li>• Absorbed by malabsorbers</li> <li>• Proven scientific studies on humans</li> </ul>	None known

129

## MCHC is MCHC, right?

- All MCHC products are not the same! The source of the bone extract as well as the processing procedure determine the quality of MCHC.
- Some sources may contain high levels of lead and other contaminants
- High heat processing and excessive grinding can destroy the matrix leading to a simple bone meal product
  - Key marker is Type I collagen; should be 17-21%
  - Bone meal is less than 1% Type I collagen

130

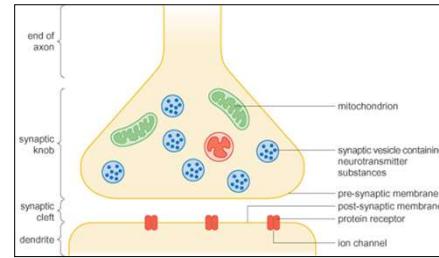
## Osteoporosis & Osteopenia

- Bone Health:
  - Weight bearing exercise – 3 or more sessions/week; at least 30 min/session
  - Sunshine and calcium rich foods
  - Avoid extremely acidic foods/habits
- Bone maintenance:
  - [Cal Apatite Bone Builder Forte \(~3000 mg MCHC\)](#) – 1 tablet BID w/ food
- Osteopenia:
  - [Cal Apatite Bone Builder Prime](#) – 1 tablet TID w/ food
    - 1500 mg MCHC + Ipriflavone + Vit D
- Osteoporosis:
  - [Cal Apatite Bone Builder Prime](#) – 2 tablets TID w/ food OR
    - 3000 mg MCHC + Ipriflavone + Vit D
- Functional Testing – [Bone Resorption Assessment](#) (Genova Diagnostics)

131

## Calcium: Functions

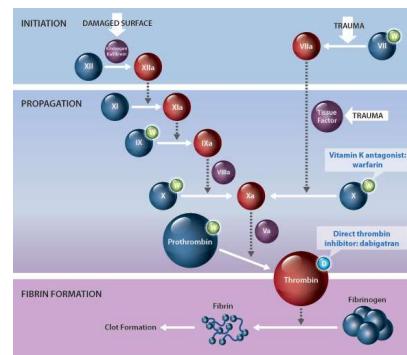
- Nerve conduction
  - Muscle, heart and GI tract (peristalsis)
  - Neurotransmission
    - Opening of calcium ion channels for an influx of calcium ions is necessary for transmitting an impulse through the synaptic cleft



132

## Calcium: Functions

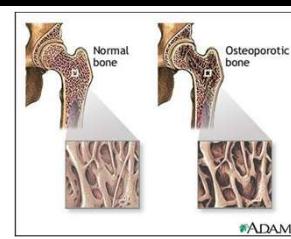
- Cardiovascular support
  - Supports synthesis and function of RBCs
  - Required for blood clotting
    - Necessary for prothrombinase complexes to function
    - Required at several points in coagulation cascade



133

## Calcium: Deficiency

- Rickets
- Osteoporosis
- Poor blood clotting
- Increased risk of bone fractures
- Muscle cramping/twitching
- Headache
- Dizziness



134

## Calcium: Toxicity

- Toxicity rare
- Kidney stones
- Overconsumption of calcium carbonate/antacids over weeks/months can lead to Milk-alkali syndrome
  - Dizziness, poor appetite, headache, confusion
  - Kidney failure and death possible



135

## Calcium: Therapeutic Considerations

- Likely deficient if:
  - Regular caffeine use
  - Long-term steroid use
  - Drink soda or alcohol regularly
- Can diminish absorption of thyroxine
  - Take 4-6 hours apart



136

## Calcium: Food Sources

Food	mg Calcium	Food	mg Calcium
Hijiki*	1400	Sunflower seeds	175
Wakame*	1300	Watercress	150
Kelp*	1100	Garbanzo beans	150
Kombu*	800	White beans (dried)	145
Wheat/barley grass	515	Quinoa	140
Sardines	445	Mustard greens	140
Agar agar*	400	Black beans	135
Nori*	260	Pinto beans (dried)	135
Sesame seeds (hulled)	200-300	Broccoli	130
Amaranth	220	Yogurt	120
Canned salmon (w/ bones)	200-250	Milk	120
Hazelnuts	210	Beet greens	120
Parsley	200	Tofu	115
Turnip greens	190	Spinach (cooked)	105
Collard greens	190	Walnuts	85
Brazil nuts	185	Eggs	55
Dandelion greens	185	Brown rice	35
Kale	185	Halibut	15

Based on 3.5 oz. portions

137

## Phosphorus

RDA	Age	Phosphorus mg	Therapeutic Dosage	Toxic Dosage
Children	4-8	500	• 1400 mg as portion of MCHC	• No toxic levels have been reported
	9-13	1250		
Males	14-18	1250		
	19-30	700		
	31-50+	700		
Females	19-30	700		
	31-50+	700		

138

## Phosphorus

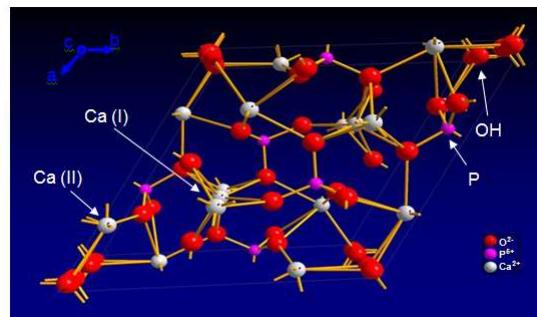
- 2<sup>nd</sup> most abundant mineral in the body
- 85-90% in bones and teeth
  - As hydroxyapatite
- 10-15% in soft tissues and extracellular fluid



139

## Phosphorus: Functions

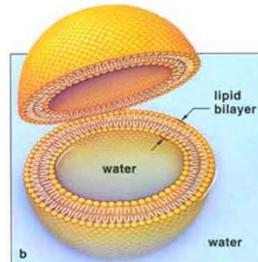
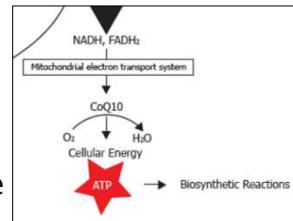
- Bone and teeth enamel
  - Hydroxyapatite main component of bone and tooth enamel



140

## Phosphorus: Functions

- Required for all known forms of life
  - Energy production
    - Transport cellular energy as adenosine triphosphate (ATP)
  - Part of RNA and DNA structural framework
  - Phospholipids are main structural components of all cellular membranes



141

## Phosphorus: Deficiency

- Muscle dysfunction
  - Muscle weakness, double vision, low cardiac output
- Neurological dysfunction
  - May range from irritability to gross confusion/dementia
- Instability of cell membranes (due to low ATP)
  - Rhabdomyolysis with increased CPK

142

## Phosphorus: Therapeutic Considerations

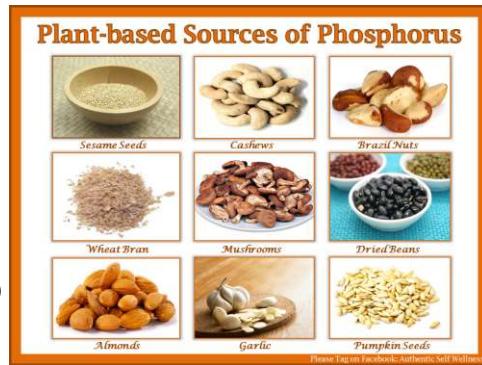
- Consider if:
  - Chronic alcohol use
  - Chronic antacid use
  - Malabsorption
    - IBD, low HCl



143

## Phosphorus: Food Sources

- Meat, poultry, fish
- Dairy products
- Soy
- Brewer's yeast
- Nuts and seeds
- Soda & fast food
  - Not recommended ☺



144

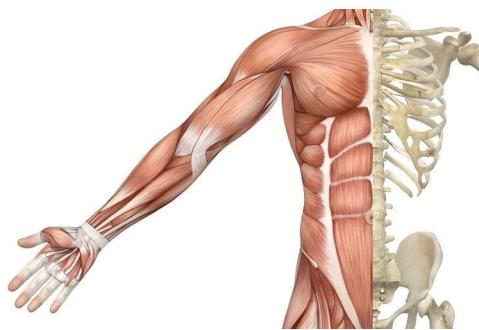
## Magnesium

RDA	Age	Magnesium mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-8	130	100mg-1000mg	<ul style="list-style-type: none"> <li>•600 mg daily long periods of time with no adverse effects</li> <li>•Diarrhea can occur at dosages &gt;600 mg/day</li> </ul>
	9-13	240		
<b>Males</b>	14-18	410	100mg-1000mg	<ul style="list-style-type: none"> <li>•600 mg daily long periods of time with no adverse effects</li> <li>•Diarrhea can occur at dosages &gt;600 mg/day</li> </ul>
	19-30	400		
	31-50	420		
	51+	420		
<b>Females</b>	14-18	360	100mg-1000mg	<ul style="list-style-type: none"> <li>•600 mg daily long periods of time with no adverse effects</li> <li>•Diarrhea can occur at dosages &gt;600 mg/day</li> </ul>
	19-30	310		
	31-50	320		
	51+	320		

145

## Magnesium

- 60% in bones
- 39% intracellular
  - 20% in skeletal muscle
- 1% extracellular

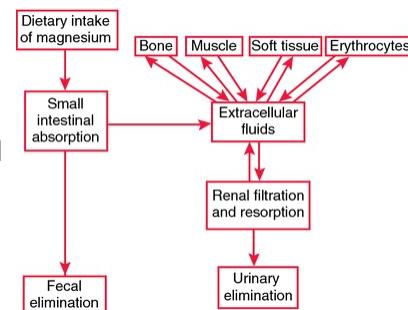


146

## Magnesium: Functions

### ■ Co-enzyme

- Involved in over 300 enzymatic reactions
  - Glycolysis, creatine phosphate formation (via creatine kinase), nucleic acid synthesis, amino acid activation (protein synthesis), cardiac and smooth muscle contractility, cyclic AMP formation
  - Improves function of insulin receptors
  - Energy production



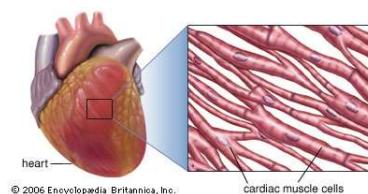
147

## Magnesium: Functions



### ■ Neuromuscular function

- Relaxes skeletal muscle
  - Relieves cramping
- Regulates heart contractibility
  - Heart has 20x greater Mg concentration than skeletal muscle
  - Blocks calcium uptake into heart muscle
- Relaxes smooth muscle
  - Bronchioles, arterioles, relaxes uterine muscles

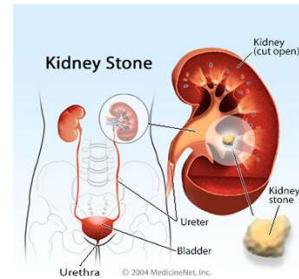


148

## Magnesium: Functions



- Calcium regulation
  - Helps excrete excess calcium
    - Helpful for kidney stones
  - Necessary for strong teeth and bones



149

## Magnesium: Functions



- Bowel function
  - Promotes bowel movements at higher doses
    - Magnesium citrate – 400-1000 mg/day
  - Osmotic agent
    - Unabsorbed magnesium pulls water into the colon to stimulate motility
  - Non-addictive, non-irritating



150

## Magnesium: Deficiency

- Mg deficiency is common: 2.5-15% of population
  - Intracellular Mg can be deficient with normal serum levels
- Muscle twitches/cramps
  - Especially calves, feet and toes
- Weakness/fatigue
- Heart irregularities
- Hypertension
- Headaches



Ayuk J., Gittoes N.J. (Mar 2014). "Contemporary view of the clinical relevance of magnesium homeostasis" Ann. Clin. Biochem. 51 (2): 179-88.

151

## Magnesium: Therapeutic Considerations

- Primary causes of Mg deficiency:
  - Insufficient dietary intake – only 32% of US population meet RDA
  - PPI/antacid use
  - Alcoholism
  - Malabsorption/increased excretion
    - Diarrhea, IBD, chronic laxative use
- Supplementation
  - Citrate best for constipation
  - Glycinate and/or amino acid chelate best for muscle pain, bone, spasm, relaxation

152

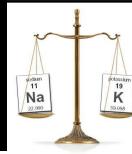
## Magnesium: Food Sources

- Legumes and nuts
- Green vegetables
- Whole grains



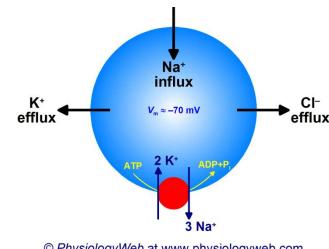
153

## Potassium & Sodium



	RDA	Therapeutic Dosage	Toxic Dosage
Sodium	<2,300 mg		
Potassium	4,500 mg	100mg-300mg daily	3,900mg regarded as safe

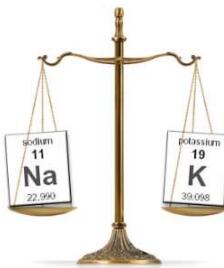
- Regulate fluid balance
  - Blood volume, blood pressure, pH



154

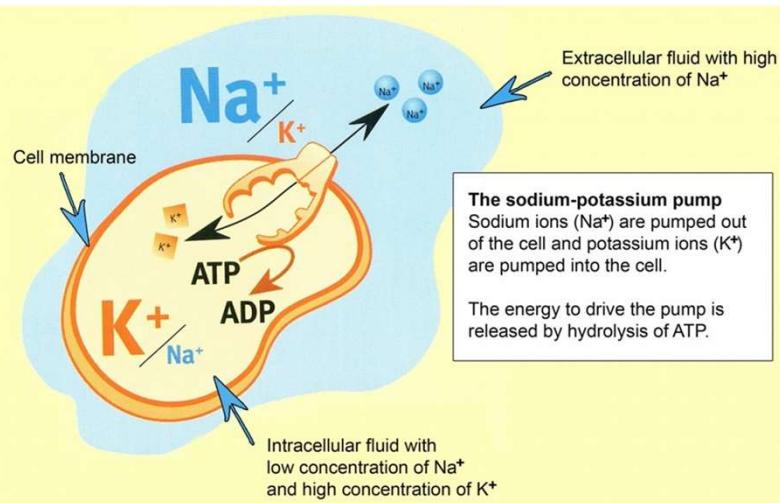
## Potassium & Sodium

Extracellular water	Intracellular water
<ul style="list-style-type: none"> <li>Cells bathed in</li> <li>1/3 of total body water</li> <li>Major solutes, sodium and chloride</li> </ul>	<ul style="list-style-type: none"> <li>Inside the cell</li> <li>2/3 of total body water</li> <li>Major solute, potassium</li> </ul>



155

## Potassium, Sodium and Chloride



156

## Potassium: Functions

- Neurological function
  - Nerve impulse transmission
- Muscle relaxation
  - Cardiac, smooth muscle and skeletal muscle
- Kidney stones
- Cardiovascular health
  - Hypertension
    - Especially if due to low K, high Na and Africa American
  - Decreased risk of stroke

157

## Potassium: Deficiency & Therapeutic Considerations

- Results from vomiting, diarrhea or increased urination (diuretics), or renal disease
- Symptoms: muscle weakness, abnormal heart beat/arrhythmia, decreased reflex response
- Hypertension can result from low K
- Monitor and use cautiously with kidney disease

158

## Sodium: Functions

- Usually concerned with excess vs. deficiency
- Regulates blood volume, blood pressure, water balance (ICW vs. ECW) and pH
  - Important for hypertension



159

## Sodium: Deficiency

- Hyponatremia
  - Very rarely due to low sodium in the diet
  - Can occur with congestive heart failure, liver failure, kidney failure and pneumonia
  - Most common in endurance athletes (marathon, Ironman, etc.)
  - Symptoms include nausea/vomiting, confusion, lethargy/fatigue, loss of appetite, irritability, muscle weakness, spasms/cramps, seizures
  - IV saline often needed



160

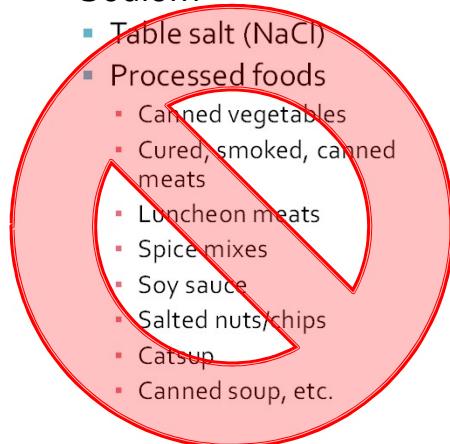
## Potassium and Sodium: Food Sources

### Potassium

- Avocado
- Sweet potato
- Tomato pate
- Orange juice
- Beet greens/spinach
- White beans
- Potatoes
- Bananas

### Sodium

- Table salt (NaCl)
- Processed foods
  - Canned vegetables
  - Cured, smoked, canned meats
  - Luncheon meats
  - Spice mixes
  - Soy sauce
  - Salted nuts/chips
  - Catsup
  - Canned soup, etc.



161

## Minerals

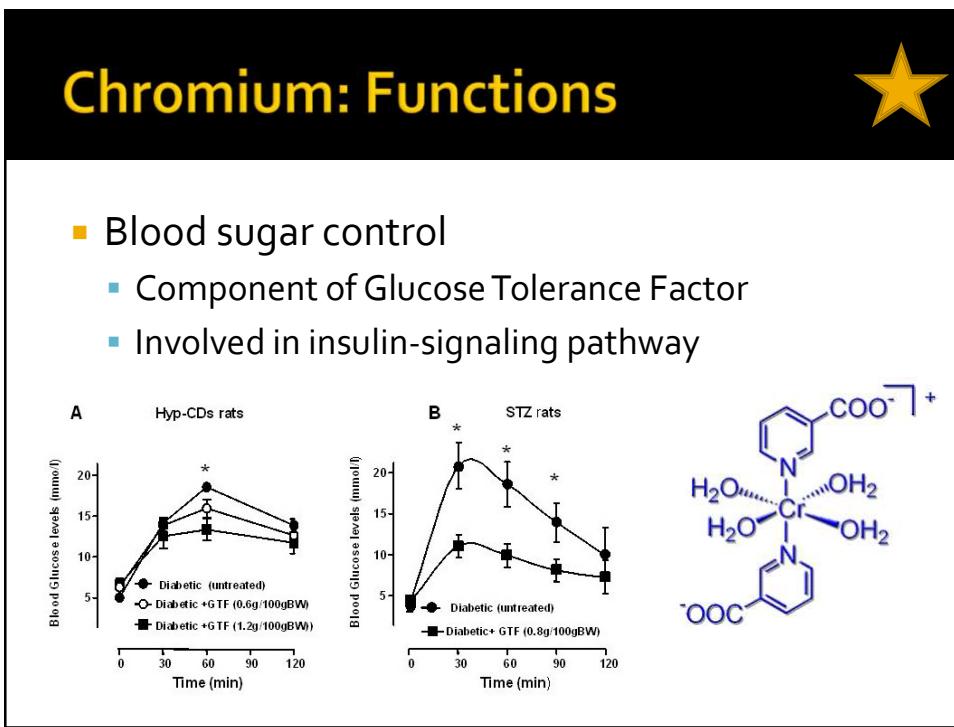
Major Minerals	Trace Minerals	Metals
<ul style="list-style-type: none"> <li>– Calcium</li> <li>– Phosphorus</li> <li>– Magnesium</li> <li>– Potassium</li> <li>– Sodium</li> </ul>	<ul style="list-style-type: none"> <li>– Chromium</li> <li>– Copper</li> <li>– Cobalt</li> <li>– Iodine</li> <li>– Iron</li> <li>– Manganese</li> <li>– Molybdenum</li> <li>– Selenium</li> <li>– Vanadium</li> <li>– Zinc</li> </ul>	<ul style="list-style-type: none"> <li>– Boron</li> <li>– Lithium</li> <li>– Nickel</li> <li>– Silicon</li> <li>– Strontium</li> <li>– Tin</li> </ul>

162



RDA	Age	Chromium mcg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-6	11	1000mcg-3000mcg	<ul style="list-style-type: none"> <li>• 3000 mcg long term with no adverse effects</li> <li>• Acute oral toxicity ranges between 1.5 and 3.3 mg/kg</li> </ul>
	7-10	15		
<b>Males</b>	15-18	25		
	19-24	35		
	25-50	35		
	50+	30		
<b>Females</b>	15-18	21		
	19-24	25		
	25-50	25		
	50+	20		

163



164

## Chromium: Deficiency and Therapeutic Considerations

### ■ Deficiency

- Elevated blood sugar and/or elevated insulin
- Glucose intolerance
- Insulin resistance



165

## Chromium: Sources

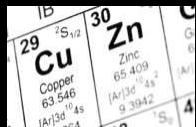
### ■ Chromium content in foods varies widely due to differences in soil mineral content, growing season, plant cultivation methods and contamination during processing

- Very little chromium is absorbed from food

### ■ Supplements

- Chromium picolinate, nicotinate and glycinate are all absorbed well (~98%)

166



## Copper

RDA	Age	Copper mcg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-8	440	• 2 mg	<ul style="list-style-type: none"> <li>• &gt; 5 mg/kg body weight</li> <li>• &gt;60 mg emetic</li> <li>• &gt;3.5 grams lethal</li> </ul>
	9-13	700		
<b>Males</b>	14-18	890	• 2 mg	<ul style="list-style-type: none"> <li>• &gt; 5 mg/kg body weight</li> <li>• &gt;60 mg emetic</li> <li>• &gt;3.5 grams lethal</li> </ul>
	19-30	900		
	31-50+	900		
<b>Females</b>			• 2 mg	<ul style="list-style-type: none"> <li>• &gt; 5 mg/kg body weight</li> <li>• &gt;60 mg emetic</li> <li>• &gt;3.5 grams lethal</li> </ul>
	19-30	900		
	31-50+	900		

167

## Copper: Functions

<ul style="list-style-type: none"> <li>■ Necessary for proper growth, development and maintenance of bone, connective tissue, brain, heart and other organs</li> <li>■ Involved in formation of red blood cells &amp; absorption of iron</li> <li>■ Metabolism of cholesterol and glucose</li> <li>■ Supports immune health and health</li> </ul>
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168

## Copper: Deficiency

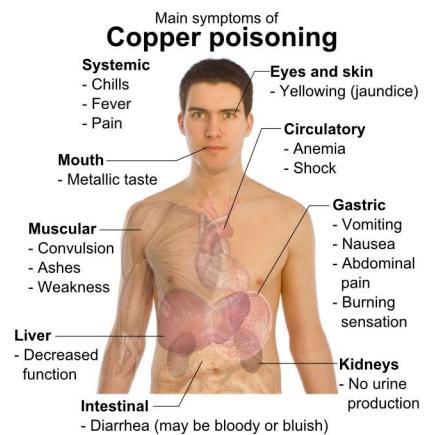
- Elevated zinc and/or cadmium
- High intakes of phytates (grains) and simple sugars and inhibit absorption
- Symptoms:
  - Anemia, poor wound healing, bone and joint problems, CNS impairment
  - Osteoporosis, osteoarthritis, rheumatoid arthritis
  - Connective tissue disorders

copper 29 <b>Cu</b> 63.546	zinc 30 <b>Zn</b> 65.39
silver 47 <b>Ag</b> 107.87	cadmium 48 <b>Cd</b> 112.41

169

## Copper: Toxicity

- Stomach upset, nausea, diarrhea, tissue injury and disease
- Tachycardia, difficulty breathing, hemolytic anemia, easy bruising, GI bleeding
- Oxidative damage
- Alzheimer's disease



170

## Copper: Sources

### ■ Food Sources

- Seafood (shellfish), mushrooms, spinach, leafy greens, seeds, raw nuts (esp. cashews and walnuts), tempeh, barley

### ■ Supplements

- Best absorbed: gluconate, acetate and sulfate
- Usually in multi or trace mineral products
- Generally, aim for a 10:1 zinc:copper ratio

171

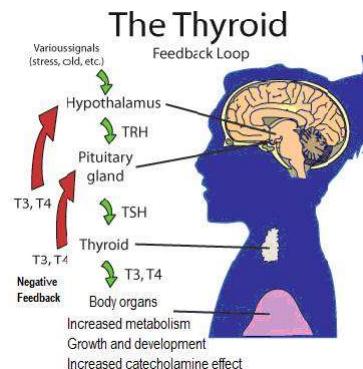
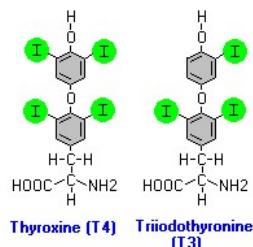
## Iodine

RDA	Age	Iodine mcg	Therapeutic Dosage	Toxic Dosage
Children	4-6	90	• 300mcg-600mcg	<ul style="list-style-type: none"> <li>• 6 grams per day for several years without toxic effect in those diagnosed as iodine deficient</li> </ul>
	7-10	120		
Males	15-18	150	• 300mcg-600mcg	<ul style="list-style-type: none"> <li>• 6 grams per day for several years without toxic effect in those diagnosed as iodine deficient</li> </ul>
	19-24	150		
	25-50	150		
	50+	150		
	15-18	150		
Females	19-24	150	• 300mcg-600mcg	<ul style="list-style-type: none"> <li>• 6 grams per day for several years without toxic effect in those diagnosed as iodine deficient</li> </ul>
	25-50	150		
	50+	150		

172

## Iodine: Functions

- Thyroid function
  - Necessary for formation of thyroxine (T<sub>4</sub>) and triiodothyronine
    - Regulates basal metabolic rate

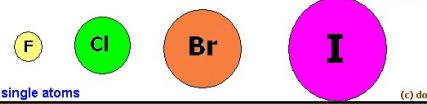


173

## Iodine: Deficiency & Therapeutic Considerations

- Hypothyroid, goiters
  - Fatigue, constipation, dry skin, intolerant to cold, low basal temperature, depression, mental slowing, weight gain, thinning hair
  - Can be displaced by chlorine and fluorine
    - Avoid tap water if hypothyroid
    - May need to avoid swimming pools that use Cl

with increase in electron shells, more electrons, bigger atom or molecule

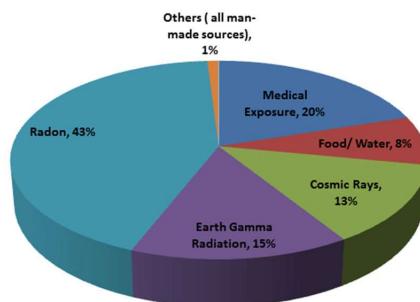


9	19.0
F	Fluorine
17	35.5
Cl	Chlorine
35	79.9
Br	Bromine
53	126.9
I	Iodine
85	210
At	Astetine

174

## Iodine: Deficiency & Therapeutic Considerations

- Breast cancer/fibrocystic breasts
- Stomach cancer
- Radiation exposure
  - Potassium iodide can prevent radioactive iodine uptake



175

## Iodine: Toxicity

- Safe up to 30 mg/kg
  - Extremely safe
- More cytotoxic in the presence of selenium-deficiency
- Hypersensitivity possible (both orally and topically)
- Prolonged use of excess iodine can cause:
  - Thyroid gland hyperplasia, goiter and severe hypothyroidism

176

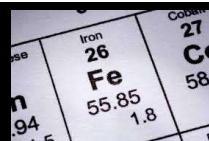
## Iodine: Sources

- Iodine-rich foods
  - Kelp, sea vegetables, seafood, eggs, dairy products
  - Iodized salt
- Supplements
  - Potassium iodide (reduced form)
  - Iodine (oxidized form) – typically topical solutions
  - Kelp



177

## Iron

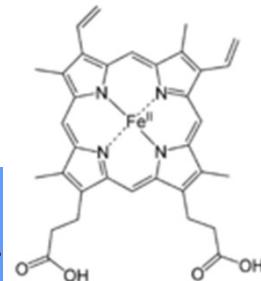
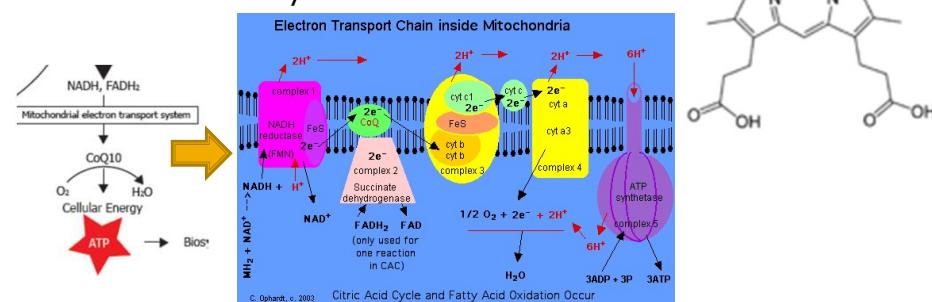


RDA	Age	Iron Mg	Therapeutic Dosage	Toxic Dosage
Children	4-8	10	• 30-60 mg	<ul style="list-style-type: none"> <li>• &gt; 20mg/kg</li> <li>• &gt; 60 mg/kg lethal</li> </ul>
	9-13	8		
Males	14-18	11	• 30-60 mg	<ul style="list-style-type: none"> <li>• &gt; 20mg/kg</li> <li>• &gt; 60 mg/kg lethal</li> </ul>
	19-30	8		
	31-50	8		
	50+	8		
	14-18	15		
Females	19-30	18		
	31-50	18		
	50+	8		

178

## Iron: Functions

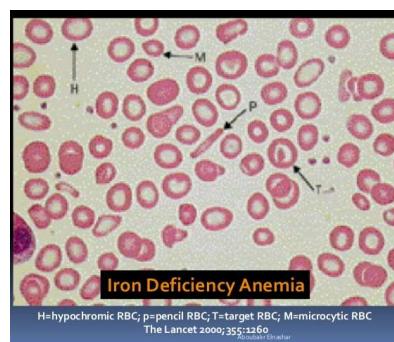
- Hemoglobin and myoglobin synthesis
  - Oxygen transport
- Cellular energy production
  - Redox enzymes



179

## Iron: Deficiency

- Anemia
  - Hypochromic/microcytic
  - Decreased hemoglobin (or RBC)
  - Fatigue, weakness, shortness of breath, light-headed, poor stamina, confusion, increased thirst
  - Significant anemia necessary before a person becomes noticeable pale



180

## Iron: Therapeutic Considerations

- Poor absorption
  - IBD, post-surgical resection of bowel, low HCl
- High intake of cow's milk
- Inflammation
- Pregnancy
- Elderly
- Vegetarian/vegan
- Excessive bleeding

181

## Iron: Toxicity

- Poorly excreted/easily accumulated
- Can cause free radical damage & inflammation
  - Can damage heart, liver and joints
- Only supplement iron when labs indicate need
- Keep iron supplements away from children

182

## Iron: Sources

### ■ Food

- Heme sources (animals) best absorbed (15-35%)
  - Red meat, poultry, fish, eggs
- Non-heme sources (plants) less absorbed (2-20%)
  - Dark leafy greens, legumes, blackstrap molasses

### ■ Supplements

- Best absorbed (non-constipating): gluconate, (bis)glycinate, amino-acid chelate
- Poorly absorbed: sulfate, fumarate
- Absorption enhanced with ascorbate (Vit C)

183

## Manganese

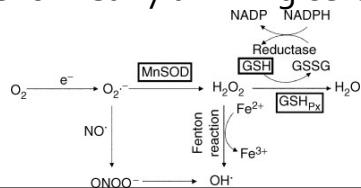


RDA	Age	Manganese Mg	Therapeutic Dosage	Toxic Dosage
<b>Children</b>	4-8	1.5	• 1-3 mg	• > 12 mg/day
	9-13	1.9		
<b>Males</b>	14-18	2.2		
	19-30	2.3		
	31-50	2.3		
	50+	2.3		
	14-18	1.6		
<b>Females</b>	19-30	1.8		
	31-50	1.8		
	50+	1.8		

184

## Manganese: Functions

- Cofactor for many enzymes
  - Energy production, carbohydrate metabolism, bone development, collagen synthesis, protein and fatty acid synthesis
- Antioxidant protection
  - Superoxide dismutase (SOD)
  - Defense for nearly all living cells



185

## Manganese: Deficiency, Toxicity and Therapeutic Considerations

- Deficiency rare
- Consider if widespread symptoms, including
  - Impaired growth, poor carbohydrate and fat metabolism, loss of hair color, decreased hair/nail growth, fatigue, premature aging
- Toxicity
  - Estimated at >12 mg/day
  - Kidney and/or liver dysfunction

186

## Manganese: Sources

### Food sources

- Pecans and most nuts, whole grains, dark leafy greens/spinach, carrots, broccoli, eggs

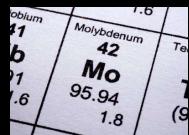


### Supplements

- Citrate, sulfate, aspartate, glycinate, gluconate, amino acid chelate

187

## Molybdenum



RDA	Age	Molybdenum mcg	Therapeutic Dosage	Toxic Dosage
Children	4-6	22	• 1.2 mg	• > 10 mg/day
	7-10	34		
Males	15-18	43		
	19-24	45		
	25-50	45		
	50+	45		
	15-18	43		
Females	19-24	45		
	25-50	45		
	50+	45		

188

## Molybdenum: Functions

- Involved in many enzymes that affect
  - Protein synthesis, metabolism, growth, detoxification, purine metabolism, alcohol detoxification, dental health

189

## Molybdenum: Deficiency, Toxicity & Therapeutic Considerations

- Consider if:
  - Fatigue, joint pain, tachycardia, headache, disorientation (sulfite toxicity)
  - Sensitivity to sulfites in foods
- Toxicity
  - > 10 mg/day
  - Can cause gout ( $\uparrow$  production of uric acid)

190

## Molybdenum: Sources

- Food sources:
  - Pork, beef, lamb, liver, peas, green beans, eggs, sunflower seeds, lentils, cucumber, whole grains
  
- Supplements
  - Amino acid chelate or aspartate best
  - Usually used in 'multi-mineral' products

191

## Selenium

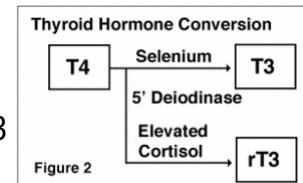


RDA	Age	Selenium mcg	Therapeutic Dosage	Toxic Dosage
Children	4-8	30	100-400 mcg	<ul style="list-style-type: none"> <li>• Should not supplement &gt;400 mcg daily</li> <li>• &gt;900 mcg is toxic</li> </ul>
	9-13	40		
Males	14-18	55	100-400 mcg	<ul style="list-style-type: none"> <li>• Should not supplement &gt;400 mcg daily</li> <li>• &gt;900 mcg is toxic</li> </ul>
	19-30	55		
	31-50+	55		
Females	19-30	55	100-400 mcg	<ul style="list-style-type: none"> <li>• Should not supplement &gt;400 mcg daily</li> <li>• &gt;900 mcg is toxic</li> </ul>
	31-50+	55		

192

## Selenium: Functions

- Antioxidant protection
  - Cofactor for reduction of antioxidant enzymes
    - Glutathione peroxidases
$$2 \text{ GSH} + \text{H}_2\text{O}_2 \longrightarrow \text{GSSG} + 2 \text{ H}_2\text{O}$$
- Protection against mercury toxicity
  - Binds with methyl mercury
- Thyroid hormone production
  - Activate and deactivates T<sub>4</sub> & T<sub>3</sub>



193

## Selenium: Deficiency, Toxicity & Therapeutic Considerations

- Consider if:
  - Hashimoto's disease
    - 21% reduction in TPO AB with 0.2 mg/day
  - Mercury toxicity/exposure
  - Antioxidant need
    - Immune support, inflammatory conditions, detoxification
- Toxicity
  - Garlic breath, hair loss, fatigue, irritability, cirrhosis

194

## Selenium: Sources

■ Food sources:

- Brazil nuts, kidney, tuna, crab, lobster, nuts, whole grains, meat, eggs

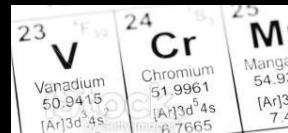


■ Supplements

- Selenomethionine, amino acid chelate, aspartate

195

## Vanadium



RDA	Age	Vanadium mcg	Therapeutic Dosage	Toxic Dosage
Children	4-6	N/A	• 50mcg -1.5 mg daily	<ul style="list-style-type: none"> <li>UL: 1.8 mg/day</li> <li>&gt;20 mg is toxic</li> </ul> <p>(daily for 5 months – cramps, fatigue)</p>
	7-10	N/A		
Males	15-18	N/A		
	19-24	N/A		
	25-50	N/A		
	50+	N/A		
Females	15-18	N/A	<ul style="list-style-type: none"> <li>UL: 1.8 mg/day</li> <li>&gt;20 mg is toxic</li> </ul> <p>(daily for 5 months – cramps, fatigue)</p>	
	19-24	N/A		
	25-50	N/A		
	50+	N/A		

196

## Vanadium: Functions



- Blood sugar control
  - May be able to mimic the actions of insulin
    - Activates insulin receptor
    - Stimulates glucose oxidation & transport
    - Inhibits lipolysis in adipose tissue
    - Stimulates glycogen synthesis in the liver & muscles
    - Increases glucose uptake & utilization

Harland BF, Harden-Williams BA. Is vanadium of human nutritional importance yet? J Am Diet Assoc 39(6,pt 1):821-4.  
 Malabu UH, Dryden S, McCarthy HD, et al. Effects of chronic vanadate administration in the STZ-induced diabetic rat. Diabetes 1991;42:9-15.  
 Aharon Y, Mevorach M, Shamoon H. Vanadyl sulfate does not enhance insulin action in patients with type 1 diabetes. Diabetes Care 1998;21:2194-5.  
 Goldwaser I, Li J, Gershonov E, et al. L-Glutamic acid gamma-monohydroxamate. A potentiator of vanadium-evoked glucose metabolism in vitro and in vivo. J Biol Chem 1999;274:26617-24.



197

## Vanadium: Deficiency, Toxicity & Therapeutic Considerations

- Only recently considered an essential nutrient
- Deficiency rare
- Consider if:
  - Type 1 or Type 2 Diabetes or insulin resistant
- Poorly absorbed (~5%)
- Toxicity
  - GI: abdominal discomfort, diarrhea, nausea, gas
  - Kidney dysfunction/stones

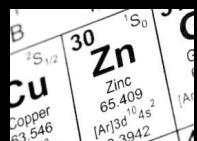
198

## Vanadium: Sources

- Food sources
  - Mushrooms, shellfish, black pepper, parsley, dill, whole grains, beer and wine
  
- Supplements
  - Vanadyl sulfate (100 mg = 31 mg elemental vanadium)

199

## Zinc



RDA	Age	Zinc mg	Therapeutic Dosage	Toxic Dosage
Children	4-8	5	• 15 mg daily	• >100 mg can be toxic
	9-13	8		
Males	14-18	11	• 15 mg daily	• >100 mg can be toxic
	19-30	11		
	31-50	11		
	51+	11		
Females	14-18	9	• 15 mg daily	• >100 mg can be toxic
	19-30	8		
	31-50	8		
	51+	8		

200

## Zinc: Functions

- Found in over 300 enzymes
  - Only metal which appears on all enzyme classes
  - Metabolism of carbohydrates, proteins and lipids
  - Protein and DNA synthesis
  - Anti-oxidant (component of Cu-Zn SOD)
  - Plays a role in taste, smell, hormone production, immune health, prostate and reproductive organ health, GI health, detoxification, eye health, learning, neurotransmission, gene expression, programmed cell death, etc...

201

## Zinc: Functions

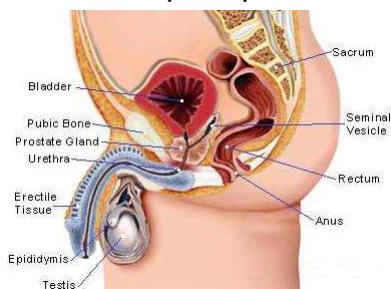
- Immune health
  - Zinc found in all WBC and is necessary for proper function
  - Antioxidant (Cu-Zn SOD)
    - Combats free radical damage in all tissues
  - Speeds up healing process after injury
  - Shown to shorten the duration of colds
    - 80-100 mg/day



202

## Zinc: Functions

- Prostate and reproductive organ health
  - Highest concentration of zinc found in prostate
  - High levels of Zn also found in testes
  - Evidence that Zn may preferentially kill prostate cancer cells



203

## Zinc: Deficiency

- In children
  - Growth retardation, delayed sexual maturation, infection susceptibility and diarrhea
- Decreased immunity / Poor wound healing
- Alopecia, impaired appetite, impaired digestion, reproductive issues
- Depression
- Eye and skin lesions, macular degeneration

204

## Zinc: Toxicity

- Copper and/or iron deficiency
  - Displaces copper and causes decreased absorption
  - Anemia (can be microcytic, normocytic or macrocytic), neutropenia, peripheral neuropathy, color/vision loss
- Ataxia, lethargy

205

## Zinc: Therapeutic Considerations

- Failed zinc tally test
- White spots on fingernails
- Prostate health
  - BPH, prostatitis, cancer
- Infertility, especially male
- Low testosterone
- Immune/healing support
- Depression
- Poor sense of smell/taste
- Chronic alcohol use



206

# Zinc: Sources

- Food
    - Oysters, pumpkin seeds, beans, sea vegetables, nuts, seeds, peas, seafood, meat
    - High in whole grains but poorly absorbed
      - Bound to phytic acid



- Supplements
    - Best: gluconate, picolinate and citrate
    - Lozenges can help with sore throat & colds
    - Zinc carnosine: effective for H. pylori



207

# Minerals

Major Minerals	Trace Minerals	Metals
<ul style="list-style-type: none"> <li>– Calcium</li> <li>– Phosphorus</li> <li>– Magnesium</li> <li>– Potassium</li> <li>– Sodium</li> </ul>	<ul style="list-style-type: none"> <li>– Chromium</li> <li>– Copper</li> <li>– Cobalt</li> <li>– Iodine</li> <li>– Iron</li> <li>– Manganese</li> <li>– Molybdenum</li> <li>– Selenium</li> <li>– Vanadium</li> <li>– Zinc</li> </ul>	<ul style="list-style-type: none"> <li>– <i>Boron</i></li> <li>– <i>Lithium</i></li> <li>– <i>Nickel</i></li> <li>– <i>Silicon</i></li> <li>– <i>Strontium</i></li> <li>– <i>Tin</i></li> </ul>

208

## Other Trace Minerals & Metals

Element	RDA	Functions	Deficiency	Toxicity	Food Sources
Cobalt	N/A	Required for synthesis of B <sub>12</sub>	Rare; pernicious anemia	Rare	
Boron	2.1 mg	Reduces calcium excretion; activates Vitamin D	Unknown	Rare	N/A
Lithium	1 mg	Mood stabilization	Bi-polar disorder	Kidney failure	N/A
Silicon	5 mg	Connective tissue formation	Wrinkles, thinning hair, brittle nails	Rare	Grains, nuts, seeds
Strontium		Calcium uptake into bone	Osteoporosis, bone fracture	Rare	N/A

209

## Summary of mineral effects on body systems



Immune System .....	Cu, Zn, Fe, Se
Energy Production.....	Mg, P, Mn
Hormone System .....	Fe, Mn, Zn, Cu, Mg, K
Vitamin Production.....	Co
Blood Production.....	Cu, Fe
Enzyme Systems .....	Zn, Cu, K, Mn, Mg, Fe, Ca, Mo
Skeletal System .....	Ca, Mg, Zn, Mn, B, P
Reproduction .....	P, Cu, K, Mn, Zn, Mg

210

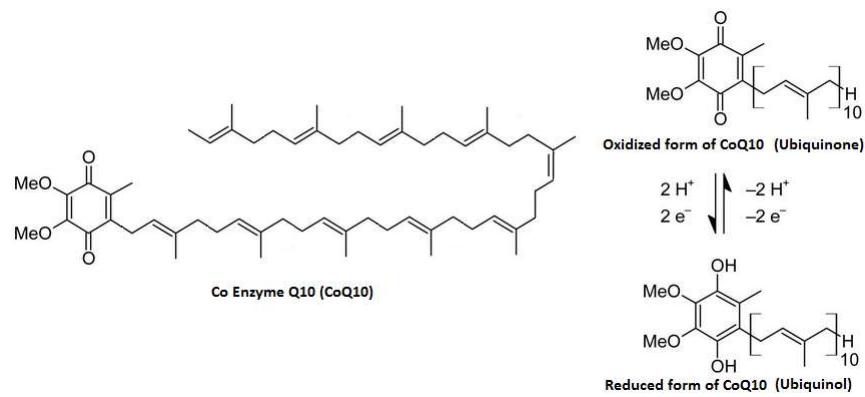
## Conditionally Essential Nutrients

- May become essential under certain conditions:
  - Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>)
  - Alpha lipoic acid
  - Amino acids
    - Acetyl-L-carnitine
    - L-arginine
    - L-lysine
    - L-glutamine
    - N-acetyl-cysteine
    - 5-hydroxytryptophan (5-HTP)

211

## Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>)

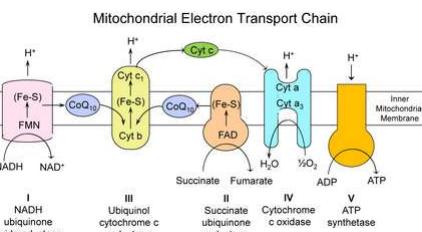
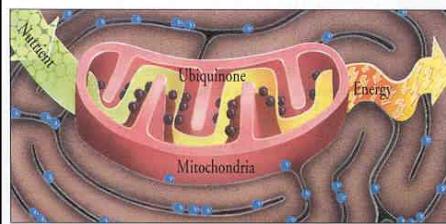
- Three redox states



212

## CoQ<sub>10</sub>: Functions

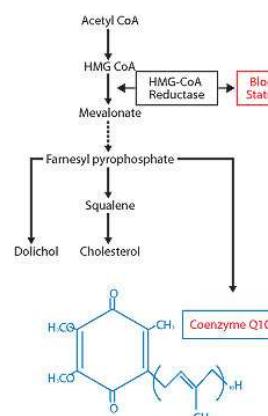
- Vital for energy production
  - Component of electron transport chain
    - Generates ATP
    - 95% of the human body's energy is generated this way
    - Very important for heart, liver, kidney, brain and muscle function



213

## CoQ<sub>10</sub>: Therapeutic Considerations ★

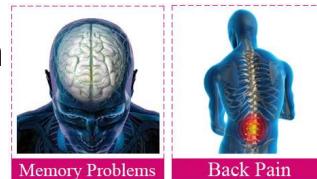
- Statin and beta-blocker use
  - CoQ<sub>10</sub> shares a biosynthetic pathway with cholesterol
  - Statin use can reduce serum CoQ<sub>10</sub> levels by 40%
  - Can lead to heart attack, severe muscle pain, memory issues, fatigue



214

## CoQ10: Therapeutic Considerations

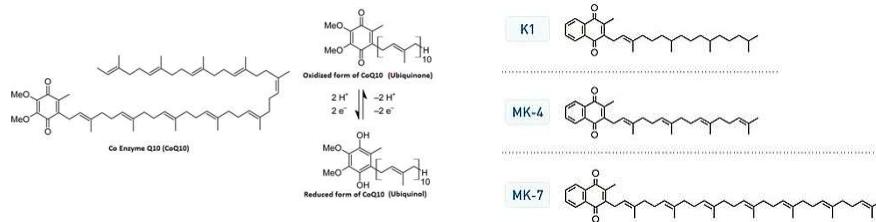
- Inflammation & Chronic Pain
- Diabetes, Cancer
- Brain health
  - Dementia, Parkinson's disease, concussions
- Cardiovascular disease
  - CHF, hypertension, MI
- Migraine headaches
- Fatigue issues
  - Chronic fatigue, fibromyalgia
- Mitochondrial dysfunction



215

## CoQ10: Therapeutic Considerations

- Has the potential to inhibit effects of warfarin (Coumadin) by reducing INR
  - CoQ10 very similar structure to vitamin K1
    - Competes with and counteracts warfarin's anticoagulation effects



216

## CoQ<sub>10</sub>: Food Sources

- Meat and fish
- Organ meats
- Avocado



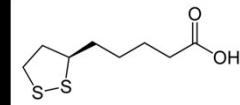
217

## CoQ<sub>10</sub>: Dosing & Toxicity

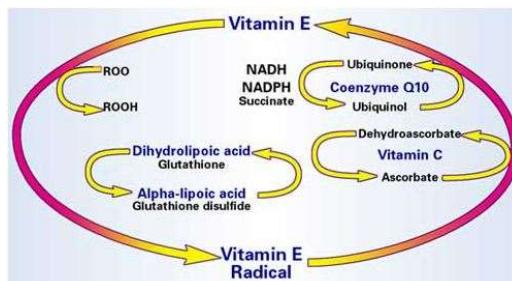
- Toxicity not observed
  - Studies done at 3600 mg/day tolerated well
- Supplementation
  - Oil emulsion
  - Typical dosing: 100-400 mg/day
  - Statin/beta-blocker use: 200+ mg/day
  - Migraines: 100 mg TID for 3 months
  - Chronic disease: 200-3200 mg/day

218

## Alpha-lipoic acid (ALA)



- Potent antioxidant
  - ALA and metabolite DHLA both antioxidants
  - Increases production of glutathione
  - Water *and* fat soluble
  - Can also regenerate other antioxidants



219

## ALA: Functions

- Carbohydrate metabolism
  - Improves glucose uptake and fasting blood sugar
  - Improves insulin sensitivity
  - Decreases postprandial glucose levels
- Modulates inflammatory response
  - May suppress vascular inflammation
  - Inhibits NF KB
- Enhances detoxification

Konrad T, Vicini P, Kusterer K, et al. Alpha-lipoic acid treatment decreases serum lactate and pyruvate concentrations and improves glucose effectiveness in lean and obese patients with Type 2 diabetes. *Diabetes Care* 1999;22:280-7.  
 Jacob S, Henriksen EJ, Tritschler HJ, et al. Improvement of insulin-stimulated glucose-disposal in type 2 diabetes after repeated parenteral administration of thiolic acid. *Exp Clin Endocrinol Diabet* 1996;104:284-8.  
 Jacob S, Henriksen EJ, Schiessl A, et al. Enhancement of glucose disposal in patients with type 2 diabetes by alpha-lipoic acid. *Arzneimittelforschung* 1995;45:872-4.  
 Jacob S, Ruus P, Hermann R, et al. Oral administration of RAC-alpha-lipoic acid modulates insulin sensitivity in patients with type-2 diabetes mellitus: a placebo-controlled, pilot trial. *Free Rad Biol Med* 1999;27:309-14.  
 Porasuphatana S, Suddee S, Narthampong A, Konsil J, Harnwong B, Santaweesuk A. Glycemic and oxidative status of patients with type 2 diabetes mellitus following oral administration of alpha-lipoic acid: a randomized double-blinded placebo-controlled study. *Asia Pac J Clin Nutr* 2012;21(3):12-21.

220

## ALA: Therapeutic Considerations

- Diabetes/Insulin Resistance
- Peripheral neuropathy
- Weight loss
- Chronic alcohol use/liver disease
- Detoxification/chelation
- Brain health/injury
- Inflammatory disorders
- Cardiovascular disease
- Ischemia (cerebral)/brain injury

221

## ALA: Toxicity and Dosing

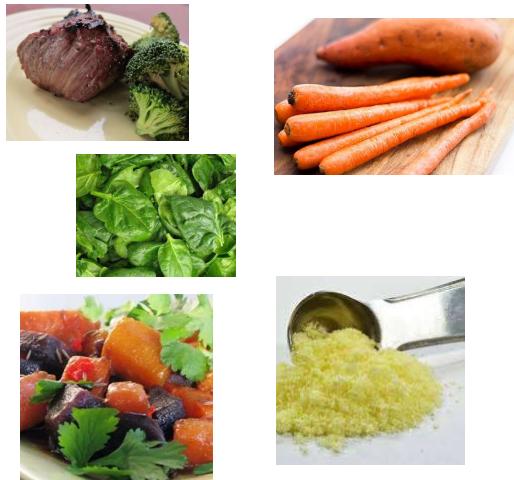
- Toxicity rare; more likely if thiamine deficient
  - Alcoholics – supplement with thiamine
- Supplementation
  - Diabetes and peripheral neuropathy: 600-1200mg/day
  - Peripheral arterial disease: 300 mg BID

222

## ALA: Sources

- Food Sources

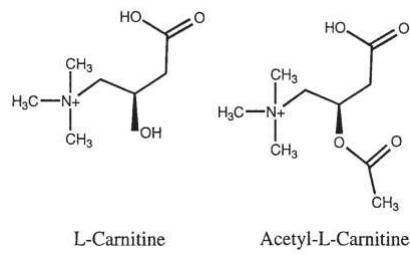
- Red meat
- Organ meats
- Spinach
- Broccoli
- Potatoes
- Yams
- Carrots
- Beets
- Nutritional yeast



223

## L-carnitine

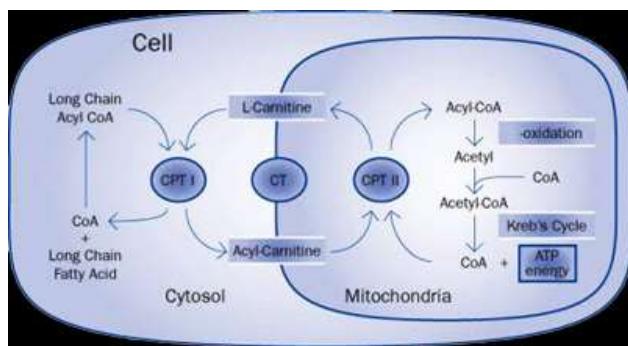
- Body can synthesize from lysine and methionine
- Most found in cardiac and skeletal muscle



224

## L-carnitine: Functions

- Key role in cellular energy production
  - Essential for beta-oxidation of long-chain fatty acids in mitochondria to make ATP



225

## L-carnitine: Therapeutic Considerations

- Hyperthyroidism
  - Blocks entry of thyroid hormones into cell nuclei
  - Can significantly improve symptoms
  - Can reduce ALT, AST, GGT and ferritin
- Angina/heart attack
- Diabetes
  - Can improve insulin sensitivity
- Male infertility- increases sperm motility
- Hyperlipidemia – can ↓ Lp(a), LDL and trigs
- Fatty liver

226

## L-Carnitine: Sources

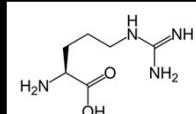
- Food Sources:
  - Grass fed red meat
    - ~ 56-162 mg per serving



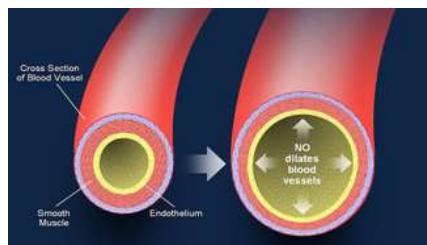
- Supplementation
  - Typically, 2-6 grams/day in divided doses
  - No more than 2 grams at one dose

227

## L-Arginine



- Can be synthesized from citrulline
  - Often not sufficient; must be consumed
- Precursor for nitric oxide (NO) synthesis
  - Causes vasodilation
- Can improve
  - Hypertension
  - Erectile dysfunction
  - Inflammation



228

## L-Arginine: Functions

- Collagen formation and wound healing
- Secretion of growth hormone
- Pregnancy
  - Can reduce blood pressure and lengthen pregnancy for women with gestational diabetes and/or pre-eclampsia

229

## L-Arginine: Therapeutic Considerations

- Hypertension, CHF
- Sickle cell anemia
- Pulmonary hypertension
  - Helps produce NO – reduces blood pressure
  - Decreases endothelin-1 (a vasoconstrictor)
- Erectile dysfunction
- Injury – bone or soft tissue
  - Improves repair and reduces healing time

Hughes NT, Tavak JA. Oral arginine reduces systemic blood pressure in type 2 diabetes: its potential role in nitric oxide generation. *J Am Coll Nutr* 2003;22:422-7.  
Morris CR, Morris SM Jr, Hager W, et al. Arginine therapy: a new treatment for pulmonary hypertension in sickle cell disease? *Am J Respir Crit Care Med* 2003;168:63-9.  
Stechmiller JK, Childress B, Cowan L (Feb 2005). "Arginine supplementation and wound healing". (review). *Nutrition in Clinical Practice* 20 (1): 52-61.  
Witte MB, Barbul A (2003). "Arginine physiology and its implication for wound healing". (review). *Wound Repair and Regeneration* 11 (6): 419-33.

230

## L-Arginine: Sources

- Food sources:

- Red meat, poultry, fish/seafood, dairy products
  - Wheat germ, oatmeal, nuts & seeds, chickpeas

- Supplementation

- Typically, 2-6 grams/day in divided doses
  - Post workout or injury: 1-3 grams
  - To increase NO production: start with 1.5-6 grams with 200-400 mg magnesium glycinate

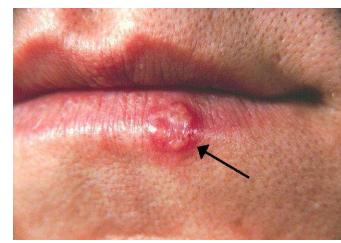
231

## L-Lysine

- Essential amino acid for everyone

- Needs increase with viral infections

- Herpes simplex
  - Epstein Barr
  - Suppresses viral replication



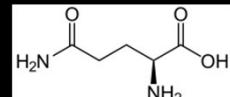
232

## L-Lysine: Therapeutic Considerations

- Cold/canker sores
- Acute and chronic viral infections
- Supplementation
  - Oral: typically 1-6 grams/day
    - 1000 mg TID for 3 weeks, then 500 mg BID ongoing
  - Topically: for herpes simplex, a specific combination of lysine plus zinc oxide (Super Lysine Plus+) – applied every 2 hrs PRN

233

## L-Glutamine



- Most abundant amino acid in the body
- Produced primarily in skeletal muscle
- Many tissues require glutamine
  - Immune system
  - GI tract
  - Kidneys
  - Liver
  - Muscles
- Additional glutamine needed in times of stress, injury and/or illness



234

## L-Glutamine: Functions

- Immune support
  - Can enhance function of immune cells
    - Increase lymphocyte proliferation, bacterial killing by neutrophils and phagocytic activities of macrophages
    - In cancer patients, show to restore NK cells function and improve protein metabolism



235

## L-Glutamine: Therapeutic Considerations



- Following surgery or injury
- Compromised immunity and/or illness
- Severe acute and/or chronic stress
- Gastrointestinal disorders/imbalance
  - Enterocytes need glutamine to rebuild and repair
  - GI tract one of the largest utilizers of glutamine
- Cancer
  - Muscle wasting
  - Prevent chemo/radiation induced GI toxicity
- Athletes

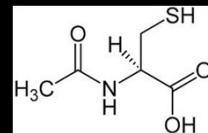
236

## L-Glutamine: Supplementation

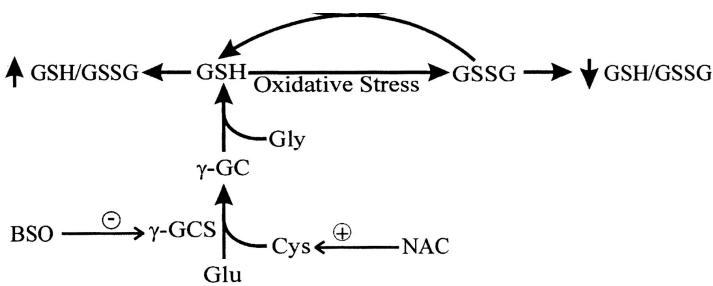
- Significant side effects not reported
- Typically: 3-6 grams powder TID
  - Up to 40 grams/day have been used
  - Often used in combination with other supportive nutrients (aloe, DGL, slippery elm, marshmallow root, etc.) for GI function
  - Athletes: 5-10 grams 15-30 minutes after workout and before bed to stimulate muscle repair
- Ideally, take before meals and/or on an empty stomach

237

## N-acetyl cysteine (NAC)

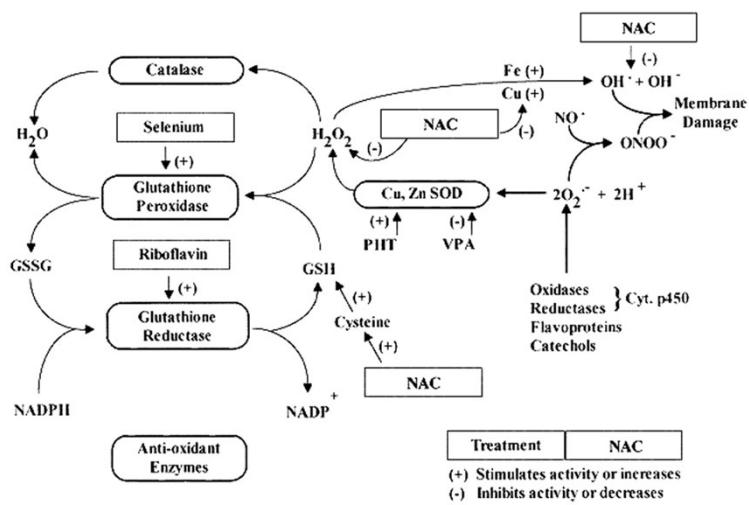


- Antioxidant protection
  - Precursor of glutathione
  - Also acts as an antioxidant itself
- Support for detoxification and toxicity



238

## NAC: Functions



239

## NAC: Functions

- Decrease inflammation
  - Reduces cellular production of TNF- $\alpha$  and IL-1
- Neurotransmitter function
  - Increase uptake of cystine, which increases glutamate in the synapse
  - This inhibits further release of glutamate, which can improve compulsive behaviors and addiction

240

## NAC: Therapeutic Considerations

- Acetaminophen poisoning
- Inflammatory disorders
  - RA, OA, chronic pain, GI disorders
- Compulsive behaviors
  - OCD, trichotillomania, addiction
- Lung and heart disorders
  - Reduces mucus viscosity
  - Anti-inflammatory and antioxidant
- Allergies/upper respiratory congestion

241

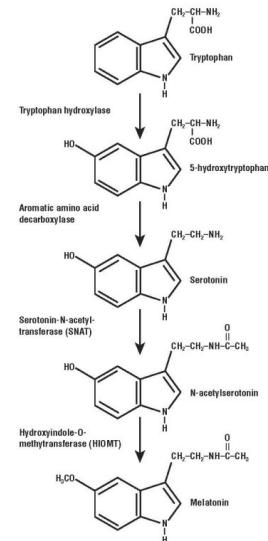
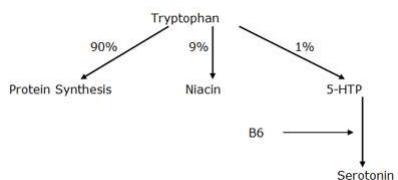
## NAC: Therapeutic Considerations

- Supplementation
  - Acetaminophen overdose
    - Oral loading dose of 140 mg/kg of a 5% solution should be administered (through a straw)
    - Seventeen additional doses of 70 mg/kg as a 5% solution should be given every 4 hours, for a total dose of 1330 mg/kg over 72 hours
  - Other conditions – 600-1000 mg BID/TID

242

## 5-Hydroxytryptophan (5-HTP)

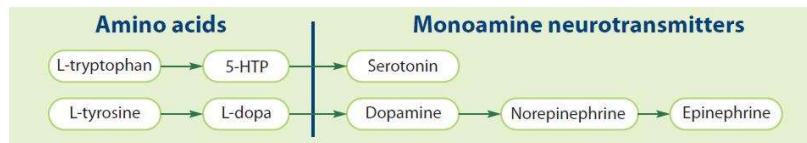
- Precursor to serotonin & melatonin
- Cannot be shunted to niacin like tryptophan
- Easily crosses the BBB
- From Griffonia simplicifolia



243

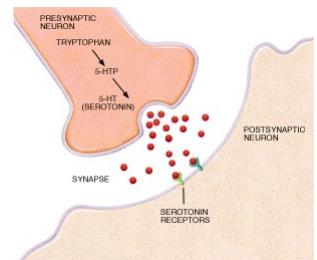
## 5-HTP: Functions

- Serotonin production



- Optimal results when balanced with catecholamine precursors
  - L-tyrosine and/or L-dopa

[www.amino-acid-therapy.com](http://www.amino-acid-therapy.com)



244

## 5-HTP: Therapeutic Considerations

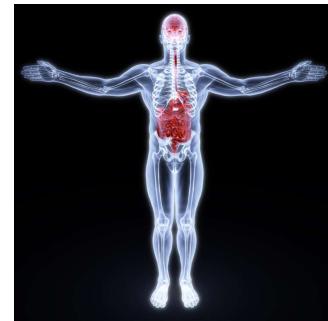
- Depression
- Appetite suppression
- Sleep aid/Insomnia
- Fibromyalgia
- Chronic pain
- Migraines



245

## 5-HTP: Therapeutic Considerations

- Side effects
  - Nausea/GI upset upon starting
    - Severe serotonin deficiency
    - Need to start more slowly so body can adjust
  - Nausea/GI upset after onset
    - Imbalance between serotonin and dopamine
    - Carbohydrate intolerance



246

## 5-HTP: Therapeutic Considerations

### ■ Supplementation

- Typically 100-300 mg 5-HTP daily in divided doses balanced with 10x L-tyrosine
  - i.e., 150 mg of 5-HTP + 1500 mg L-tyrosine BID
- Can potentiate effectiveness and side effects of SSRI medications
- Use with caution with MAOi medications
- Learn more at: [www.amino-acid-therapy.com](http://www.amino-acid-therapy.com)

247

## Phytonutrients

- “phyto” means “plant” in Greek
- Responsible for color and smell of many foods
- Have biological significance but are not established as essential nutrients
  - i.e., carotenoids and flavonoids
- ~4,000 phytonutrients

248

## Red phytonutrients

Phytonutrient	Benefits	Found in
<b>Lycopene*</b>	Reduces the risk of prostate, breast, and skin cancer; reduces the risk of heart attacks	Tomato-based products (tomato juice, spaghetti sauce, tomato soup, tomato paste), watermelon, pink grapefruit, fresh tomato, guava
<b>Anthocyanins*</b>	Reduce the risk of cancer; powerful antioxidants; help control high blood pressure; reduce the risk of diabetes complications; reduce the risk of heart attacks, reduce the risk of Alzheimer's disease	Red raspberries, sweet cherries, strawberries, cranberries, beets, red apples (with skin), red cabbage, red onion, kidney beans, red beans
<b>Astaxanthin</b>	Potent antioxidant, particularly for the liver; Gastroprotective effects; Immune stimulant; Chemoprotectant.	Microalgae, yeast, salmon, trout, krill, shrimp, crayfish, crustaceans,

\*Provided by the National Cancer Institute, [www.cancer.gov](http://www.cancer.gov)

249

## Vegetables

- Beets
- Red potatoes
- Radishes
- Rhubarb
- Red apples
- Red cabbage
- Red peppers

## Fruits

- Cherries
- Cranberries
- Pink grapefruit
- Red grapes
- Pomegranates
- Raspberries
- Strawberries
- Tomatoes
- Watermelon

250

## Orange phytonutrients

Phytonutrient	Benefits	Found in
<b>Beta-carotene*</b>	Powerful antioxidant; boosts immunity; reduces risk for cancer; reduces risk of heart attacks; helps maintain good vision.	Carrots, sweet potatoes, pumpkin, butternut squash, cantaloupe, mangos, apricots, peaches
<b>Bioflavonoids*</b>	Powerful antioxidants; Works with vitamin C to reduce the risk of heart attacks, reduce the risk of cancer, and to help maintain strong bones/teeth, healthy skin, and good vision.	Oranges, grapefruit, lemons, tangerines, clementines, peaches, papaya, apricots, nectarines, pears, pineapple, yellow raisins, yellow pepper

\*Provided by the National Cancer Institute, [www.cancer.gov](http://www.cancer.gov)

251

### Vegetables

- Butternut squash
- Carrots
- Pumpkin
- Rutabaga
- Sweet corn
- Sweet potatoes
- Yellow peppers
- Yellow tomatoes
- Yellow summer or winter squash

### Fruits

- Yellow apples
- Apricots
- Cantaloupe
- Grapefruit
- Lemons
- Mangoes
- Nectarines
- Oranges
- Papayas
- Peaches
- Pears
- Persimmons
- Pineapple
- Tangerines
- Yellow watermelon

252

## Yellow-green phytonutrients

Phytonutrient	Benefits	Found in
<b>Lutein*</b> <b>/Zeaxanthin</b>	Helps maintain good vision; reduces the risk of cataracts or macular degeneration.	Kale, spinach, leafy greens (turnip, collard, mustard), romaine lettuce, broccoli, green peas, kiwifruit, honeydew melon
<b>Indoles*</b>	Reduce the risk of cancer (particularly breast and prostate cancers); reduce the risk of tumor growth in cancer patients.	Broccoli, cabbage, brussels sprouts, bok choy, arugula, Swiss chard, turnips, rutabaga, watercress, cauliflower, kale
<b>Chlorophyll</b>	Powerful antioxidant	All green vegetables
<b>Folate</b>	Methylation; cell growth.	Leafy greens

\*Provided by the National Cancer Institute, [www.cancer.gov](http://www.cancer.gov)




253

### Vegetables

- Artichokes
- Asparagus
- Green beans
- Broccoli
- Brussels sprouts
- Green cabbage
- Cucumbers
- Lettuce
- Green onions
- Peas
- Green pepper
- Spinach
- Zucchini

### Fruits

- Avocados
- Green apples
- Green grapes
- Honeydew melon
- Kiwi
- Limes

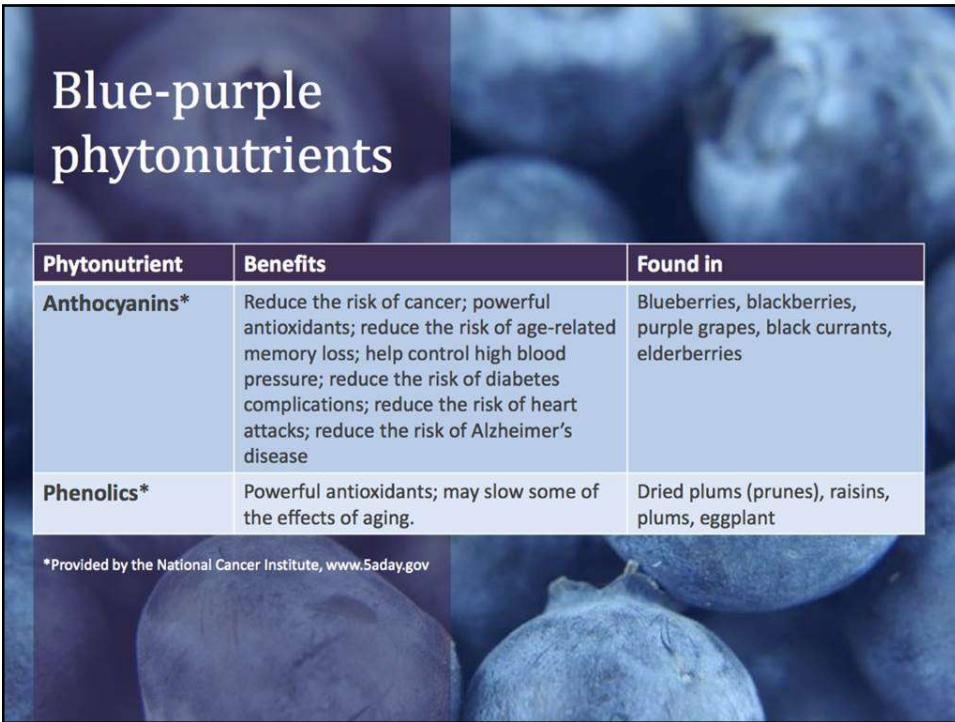


254

## Blue-purple phytonutrients

Phytonutrient	Benefits	Found in
<b>Anthocyanins*</b>	Reduce the risk of cancer; powerful antioxidants; reduce the risk of age-related memory loss; help control high blood pressure; reduce the risk of diabetes complications; reduce the risk of heart attacks; reduce the risk of Alzheimer's disease	Blueberries, blackberries, purple grapes, black currants, elderberries
<b>Phenolics*</b>	Powerful antioxidants; may slow some of the effects of aging.	Dried plums (prunes), raisins, plums, eggplant

\*Provided by the National Cancer Institute, [www.cancer.gov](http://www.cancer.gov)



255



**Vegetables**

- Purple kale
- Purple cabbage
- Purple potatoes
- Eggplant

**Fruit**

- Purple grapes
- Blueberries
- Blackberries
- Boysenberries
- Marionberries
- Raisins
- Figs
- Plums

256

## White,Brown, Black phytonutrients

Phytonutrient	Benefits	Found in
Allicin*	Boosts immunity; helps lower high cholesterol; helps control high blood pressure; reduces the risk of heart attacks; reduces the risk for spread of cancer (particularly stomach and colon cancer)	Garlic, onions, leeks, scallions, chives,
<b>Other Plants</b>		
Vegetables & fungi	mushrooms, cauliflower, seaweed, jicama	
Fruits	Apples and pears (white on the inside) Coconut	

\*Provided by the National Cancer Institute,  
[www.5aday.gov](http://www.5aday.gov)

257

## Phytonutrients

- Eat as many deep colored foods as possible daily

White	Orange	Red	Purple	Green
Mushrooms	Lemons	Pink Grapefruit	Blueberries	Spinach
Horseradish	Passion Fruit	Guava	Boysenberries	Green Peppers
White Kidney Beans	Oranges	Pomegranate	Red Cabbage	Watercress
Parsnips	Cantaloupe	Radishes	Black Currants	Lettuce
Garlic	Carrots	Raspberries	Eggplant	Zucchini
Cauliflower	Apricots	Strawberries	Purple Potato	Broccoli
Black-Eyed Peas	Sweet Potatoes	Acerola Cherries	Black Beans	Brussels Sprout
Pears	Tangerines	Tomatoes	Plums	Green Beans
Turnips	Squash	Red Apples	Beets	Soybeans
Onions	Papaya	Cranberries	Blackberries	Green Tea
	Corn	Watermelon	Figs	Kale
	Pineapple		Grapes	Collard Greens

258

## Phytonutrients: Therapeutic Considerations

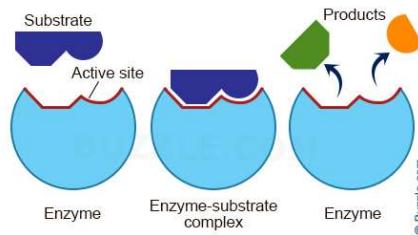
- Can be degraded by processing/cooking
  - Exception is lycopene and some carotenoids
    - Increases with cooking
      - Tomatoes, broccoli, Brussel sprouts, kale, collard greens
- Cell wall must be broken to release
  - Chewing and/or blending



259

## Enzymes

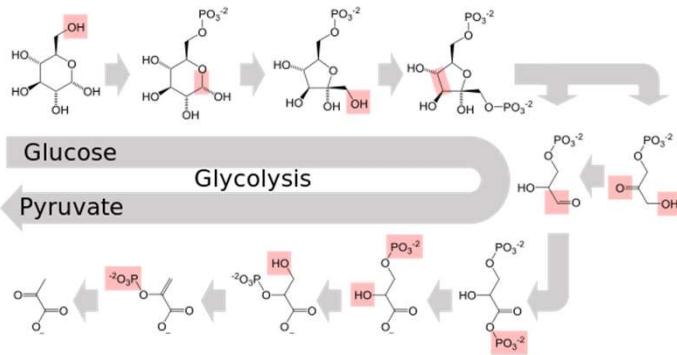
- Accelerate (catalyze) chemical reactions
- Necessary for almost all metabolic processes in the cell in order to sustain life
- Most are proteins
- Two main types
  - Metabolic
  - Digestive



260

## Metabolic Enzymes

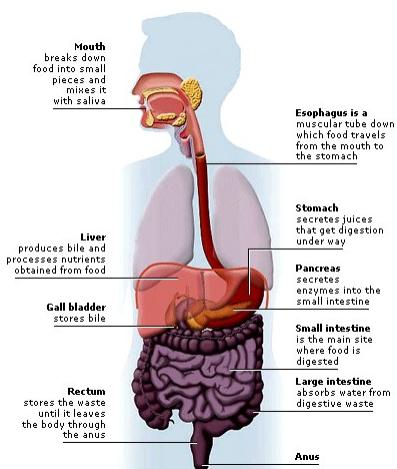
- Speed up or slow down reactions
- Often require cofactors (vitamins and/or minerals) to work properly



261

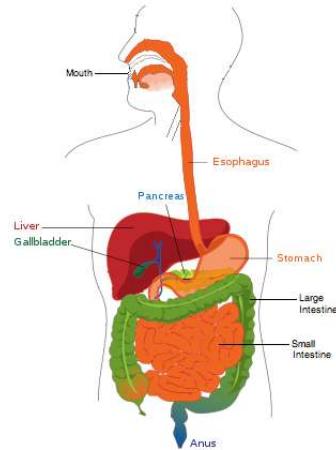
## Digestive Enzymes

- Break down food into smaller building blocks to facilitate absorption by the body
- Found in saliva, stomach, pancreas & intestines



262

## Digestive Enzymes

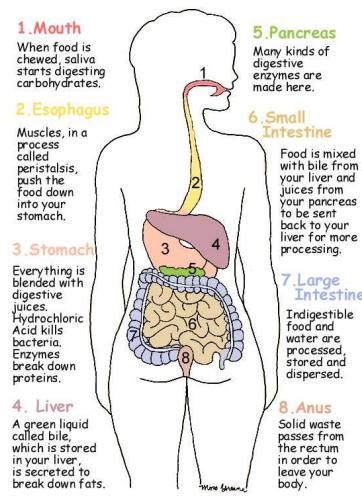


- Proteases/Proteolytic enzymes
  - Break down proteins into small peptides and amino acids
  - Stomach: pepsin
  - Pancreas: trypsin & chymotrypsin
- Lipases
  - Split fat into fatty acids and glycerol
  - Saliva: lingual lipase
  - Gastric and pancreatic lipases
- Amylases
  - Split carbohydrates into simple sugars
  - Saliva: amylase (ptyalin)
  - Pancreas and small intestine
- Nucleases
  - Split nucleic acids into nucleotides

263

## Digestion and Enzymes

- Digestion begin in the mouth (fats and carbs)
- Stomach
  - Protein & fat digestion
    - Pepsin and HCl; lipase
  - Kill foreign invaders
- Liver
  - Fat digestion (bile)
- Small intestine
  - Pancreatic juice
  - Brush border enzymes
- Large intestine
  - Absorption & waste removal



264

Major Digestive Enzymes			
Enzyme	Produced In	Site of Release	pH Level
<b>Carbohydrate Digestion:</b>			
Salivary amylase	Salivary Glands	Mouth	Neutral
Pancreatic amylase	Pancreas	Small Intestine	Basic
Maltase	Small intestine	Small intestine	Basic
<b>Protein Digestion:</b>			
Pepsin	Gastric glands	Stomach	Acidic
Trypsin	Pancreas	Small intestine	Basic
Peptidases	Small Intestine	Small intestine	Basic
<b>Nucleic Acid Digestion:</b>			
Nuclease	Pancreas	Small intestine	Basic
Nucleosidases	Pancreas	Small intestine	Basic
<b>Fat Digestion:</b>			
Lipase	Pancreas	Small intestine	Basic

265

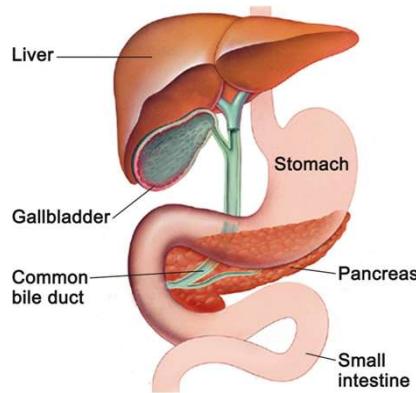
## Digestive Enzymes

ENZYMES	SOURCES	ACTIVITY UNITS & ASSAY METHOD	FOOD TYPES DIGESTED
Protease	<i>Aspergillus oryzae</i> , <i>A. melleus</i> , <i>A. niger</i>	USP (pH 7.5) PC, FCC (pH 7.0) HUT; FCC (pH 4.7)	Proteins and polypeptides from animals & plants (meat, fish, eggs, dairy, wheat, legumes, vegetables, etc.), proline dipeptides from gluten, casein
Amylase	<i>A. oryzae</i>	USP (pH 6.8) DU; FCC (pH 4.8)	Starches, complex carbohydrates, polysaccharides
Lipase	<i>Rhizopus oryzae</i> , <i>A. niger</i>	FIP (pH 7.0) LU; FCC (pH 6.5)	Fats, oils, triglycerides from animals and plants
Cellulase	<i>A. niger</i>	CU; FCC (pH 4.5)	Dietary fiber, cellulose, hemicellulose
Lactase	<i>A. oryzae</i>	ALU; FCC (pH 4.5)	Lactose
Sucrase	<i>Saccharomyces sp.</i>	INVU; FCC (pH 4.6)	Sucrose
Maltase	Malt barley ( <i>Hordeum vulgare</i> )	DP <sup>1</sup> ; FCC (pH 4.6)	Maltose, starch, polysaccharides
Phytase	<i>A. niger</i>	PU; FCC (pH 6.0)	Dietary phytate, phytic acid, pectin, cellulose
Alpha-Galactosidase	<i>A. niger</i>	GalU; FCC (pH 5.5)	Indigestible oligosaccharides and sugars, in beans, legumes, vegetables, grains, e.g. stachyose, raffinose

266

## Pancreatic Enzymes

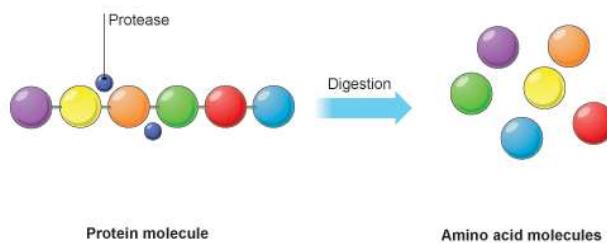
- Pancreatic juice contains:
  - Proteases
    - Trypsin
    - Chymotrypsin
    - Elastases
    - Carboxypeptidase
  - Amylase
  - Lipase



267

## Proteases/Proteolytic Enzymes

- Pepsin
- Trypsin
- Chymotrypsin
- Carboxypeptidase
- Bromelain
- Papain



268

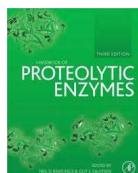
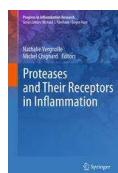
## Proteolytic Enzymes

- Taken with food – will digest proteins/food
- Taken on an empty stomach, can:
  - Greatly reduce inflammation
  - Break down scar tissue
  - Improve immunity
  - Speed healing

269

## Modulation of the Inflammatory Process

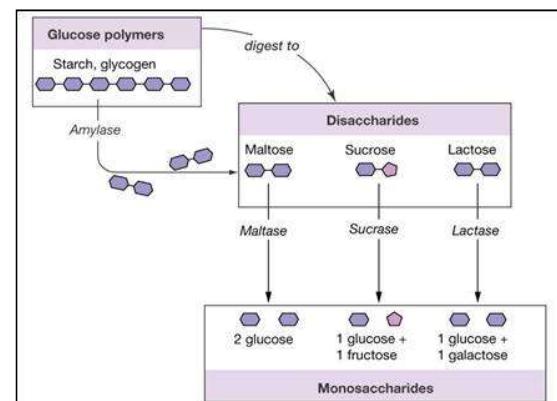
- Proteolytic enzymes
  - Bromelain (pineapple), papain (papaya), proteases, trypsin, chymotrypsin, pancreatic  
    - Reduce pain and inflammation and promote recovery
    - Inhibit pro-inflammatory compounds, remove wastes and improve circulation to speed healing
    - Significantly reduce pain and inflammation
    - Also very good for acute pain/trauma



270

## Amylases

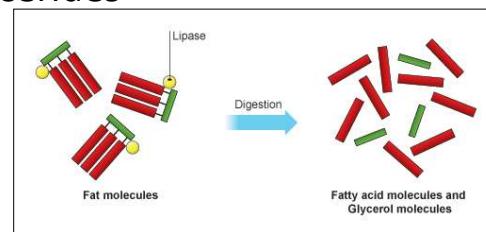
- Break down complex carbohydrates into smaller chains or simple sugars
  - Amylase/ptyalin
  - Maltase
  - Lactase
  - Sucrase



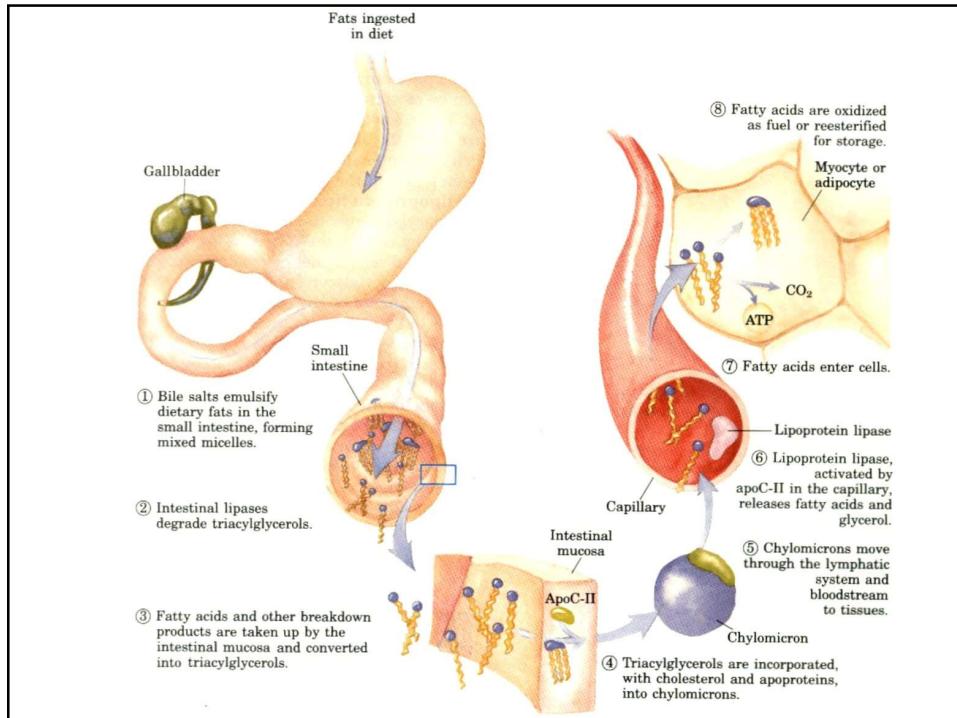
271

## Lipases

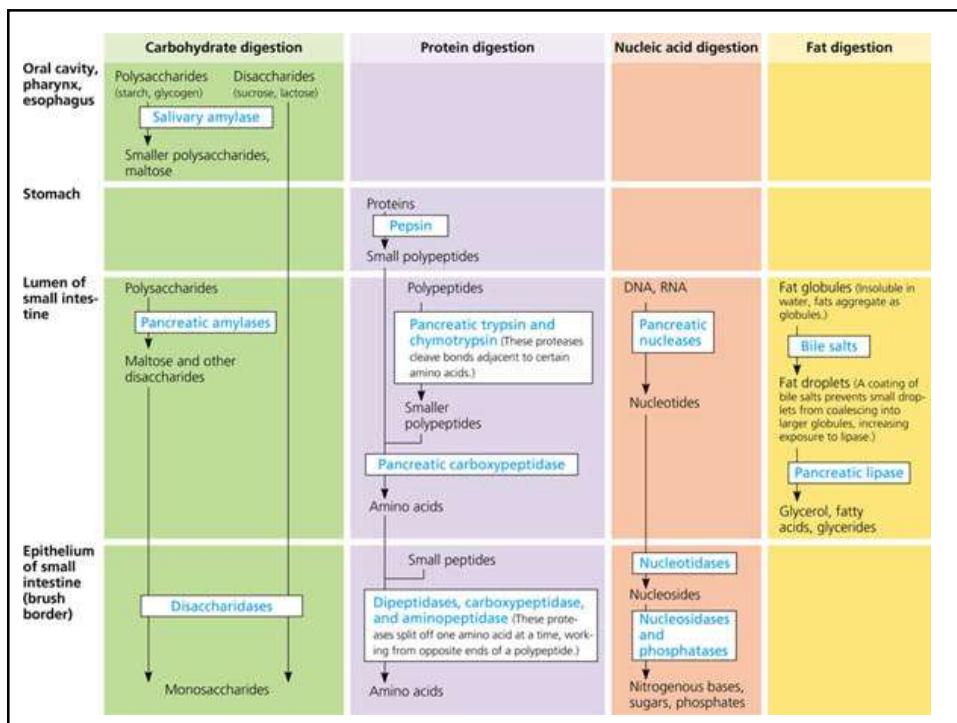
- Degrade fats/triglycerides into fatty acids and glycerol
  - Acidic lipases
    - Lingual lipase
    - Gastric lipase
    - Do not require bile to work
    - Make up ~30% of fat digestion
  - Alkaline lipases
    - Pancreatic lipase



272



273



274

## Digestive Enzyme Formulas

- Pancreatic Digestive Enzyme Formula
  - Use with normal HCl production
  - Serving size: 1 tablet

	Amount Per Serving Value	% Daily
Protease	104,000 USP units	
Amylase	104USP units	
Lipase	16,640 USP units	

275

## Digestive Enzyme Formulas

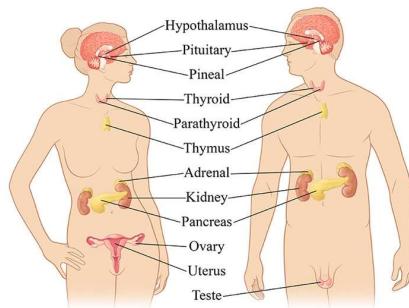
- Non-animal Derived Digestive Formula
  - Use when suboptimal HCl
    - Work over a larger pH range than animal-based enzymes
  - Serving size: 2 tablets

	Amount Per Serving
Protease I	20,000 PC
Protease II	200,000 USP
Protease III	40,000 HUT
Amylase	20,000 DU
Lipase	2,000 LU
Cellulase	2,000 CU
Peptidase	600 UNITS
Maltase	600 DP
Lactase	400 LAC U
Invertase	400 SUMNER
Amia Fruit (Phyllanthus emblica)	40 mg

276

## Glandulars

- Based on the theory that “like heals like”
  - Consuming a glandular/tissue extract can provide the necessary nutrients needed for healing/repair
  - Thought to help carry nutrients to target tissues
- Most common sources
  - Cow (bovine), Pig (porcine) & Sheep (ovine)
- Frequently used for:
  - Thyroid, adrenal, thymus, reproductive organs



277

## Glandulars - Pros

- Tissue specific
  - Demonstrated through radioactive isotope tracing
  - Contain nutrients necessary for organ/tissue healing
    - Do NOT contain hormones; can contain hormone precursors
- Restorative
  - Support biochemical balance of both underactive and overactive conditions
- Overdosing not noted

Andrew Muir, Endocrinology and Metabolism Clinicalopathology in North America, Vol.21, No.2, 1992, pp.199-219; David Stipp, The Wall Street Journal, 2 Dec. 1994, p.B1.  
iv Michael T. Murray, N.D., Glandular Extracts, New Canaan: Keats Publishing, 1994, pp.7-8; DicQie Fuller, Ph.D., Health Freedom News, Vol.13, No.5, May 1994, p.43; David Williams, Alternatives, Vol.4, No.7, Nov. 1992, pp.129-130.  
v Howard Weiner, et al., Science, Vol.259, 26 Feb. 1993, pp.1321-1324; Hikoaki Fukaura, et al., Journal of Clinical Investigation, Vol.98, No.1, July 1996, pp.70-77; Caroline Whitacre, et al., Oral Tolerance: Mechanisms and Therapeutic Potential, Vol.775, Annals NY Academy of Sciences, 1996, pp.217-227; Nejma Javed, The Journal of Immunology, Vol.155, 1995, pp.1599-1605; Caroline Whitacre, et al., Clinical Immunology and Immunopathology, Vol.80, No.3, Sept. 1996, pp.531-539; Lisa Seachrist, Science News, Vol.146, 2 Sept. 1995, pp.158-159; David Williams, Alternatives, Vol.6, No.20, Feb. 1997, pp.156-159; David Stipp, The Wall Street Journal, 2 Dec. 1994, p.B1.  
Robert Santoto, Alfred Weyhrer, Journal of Applied Nutrition, Vol.45, No.2, February 1993.

278

## Glandulars - Cons

- May be contaminated
  - Antibiotics, steroid hormones, pesticide residues, drugs, chemicals, and other toxins
- Difficult to regulate quality batch-to-batch
- Possibility of virus/prion contamination
  - Theoretical, no data to support
  - FDA regulates that bovine ingredients may be obtained ONLY from animals raised in countries free of BSE

Gerald Collee, Ray Bradley, The Lancet, Vol.349, Nos.9052 & 9053, 1 & 8 March 1997, pp.636-641, 715-721.  
Stuart Nightingale, JAMA, Vol.277, No.5, 5 Feb 1997, p.370; American Health, Vol.XV, No.7, Sept. 1996, p.92; Nutrition Week, Vol.XXVII, No.3, 17 Jan. 1997, p.3.

279

## Questions???

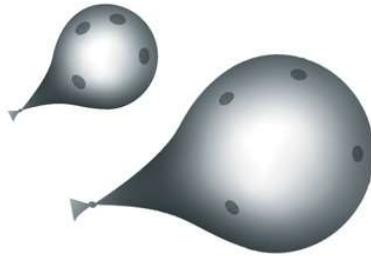


280

## Review

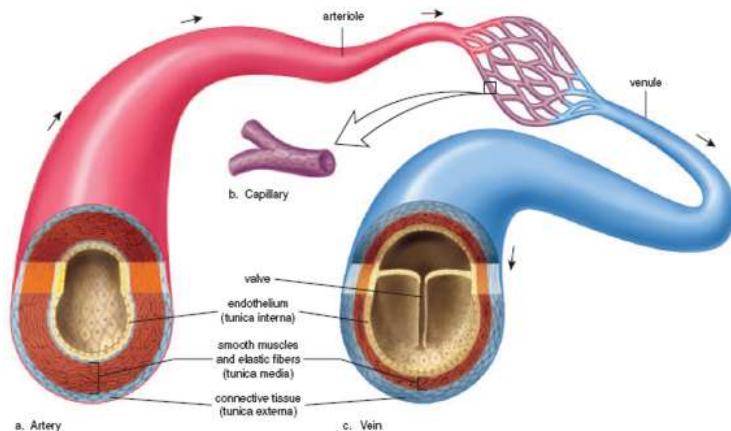
281

## Salt and Blood Pressure



282

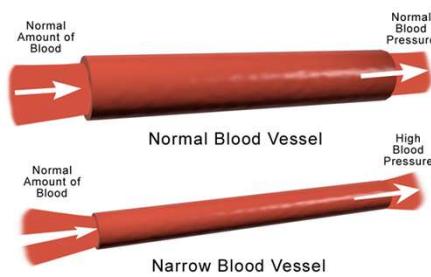
## Salt and Blood Pressure



283

## Salt and Blood Pressure

- Sodium intake stresses the system
  - Stimulates adrenalin production
  - Adrenalin causes blood vessel constriction



### Blood Pressure Blood Flow

Journal of Hypertension: <http://www.foodnavigator-usa.com/R-D/Salt-increases-blood-pressure-by-adrenalin-not-volume-expansion>

284

## Tips to Reduce Salt/Sodium

- Buy fresh or frozen “no salt added” vegetables
- Use fresh poultry, fish and lean meat rather than canned, smoked or processed.
- Limit
  - Cured foods (bacon & ham)
  - Foods packed in brine (pickles, pickled vegetables, olives & sauerkraut)
  - Condiments (MSG, mustard, catsup, barbecue sauce, soy sauce, teriyaki sauce)
- Use spices/herbs instead of salt
- Rinse canned foods (tuna, legumes) to remove sodium

285