Film 8

Energy Production and Hypoxia

Personalising Nutrition

Nutritional intervention effect on muscle 'less than expected': Review

By Will Chu, 14-Mar-2017
Last updated on 14-Mar-2017 at 13:24 GMT

Post a comment

Sarcopenia has been defined as a progressive and general loss of muscle mass and muscle function with advancing age. iStock

Related tags: Elderly, Nutrition, Creatine, HMB, Diet, Sarcopenia, Muscle, Function, Mass, Size, Healthy

The effect of dietary supplementation on muscle function in the elderly appears limited, as a review describes the combined benefits of exercise and nutrition intervention were 'less than expected.'

Medscape Medical News

Life Expectancy Nears 90 Years in Some Countries, but US Falls Short

Diana Phillips

February 22, 2017

14 comments Print Email

Following top-ranked South Korea, female life expectancy in France, Japan, and Spain have overlapping distributions, making them similarly likely to occupy any of the next three positions in rank. For men, South Korea, Australia, and Switzerland occupy the top three ranks, with overlapping distributions of projected life expectancy.

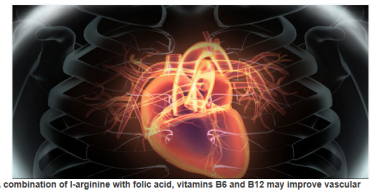
Average life expectancies in developed countries are predicted to increase through 2030, and female life expectancy in some countries may break the 90-year barrier, according to a study published online February 21 in the *Lancet*.

The United States, however, emerges as a relative poor performer compared to other high-income countries, given its already shorter life expectancy at birth and smaller projected gains.

Unlike most current mortality and life expectancy projections that rely on a single model, the current projections are derived from an ensemble of forecasting models "to more completely capture the uncertainty about future trends," write Vasilis Kontis, PhD, of the Department of Epidemiology and Biostatistics in the School of Public Health, Imperial College London, United Kingdom, and colleagues.

L-Arginine-B vitamin combination effective for blood pressure improvements: Study

By Stephen Daniells, 22-Feb-2017
Last updated on 22-Feb-2017 at 18:13 GMT



A combination of l-arginine with folic acid, vitamins B6 and B12 may improve vascular function and help reduce blood pressure, says a new study from Germany.

Participants aged between 40 and 65 were randomly assigned to receive a combination of L-arginine and B vitamins (2.4 g l-arginine, 3 mg vitamin B6, 0.4 mg folic acid, 2 micrograms vitamin B12) or placebo for three months. The participants were followed for a further three months without supplementation.

Harper's Biochemistry, 29th Edition. R. Murray et al

Porphyyria, 3rd Edition. S. Rochlitz

The Magnificent Biochemical Architecture of the Human Body. 1st Edition. Inci Ozden

Role of Nutrition in Health and Disease. 1st Edition. W.E.Cornatzer

Functional Medicine Update. Jeffery Bland

Minerals for the Genetic Code. Updated Edition. Charles Walters

Nutrition and Pain Control. 1st Edition. David Seaman

Oxidology. 2nd Edition. Robert Bradford

Causes of aging

1. Excess Free radicals (ROS)
2. Chronic Inflammation
3. Decreased immune system
4. Cell apoptosis – programmed cell death

Any or all leading to-

1. Degradation of "cellular timekeepers", known as telomeres.
2. Progressive death over time to the cellular main "power source", the mitochondria.
3. Oxidative damage to Lipids, Amino acids, DNA and Glycosylation(i.e. the "rusting" of the body's cells).

So any remedy(s) should address each / all of these issues.

Diagnostic Entry Points

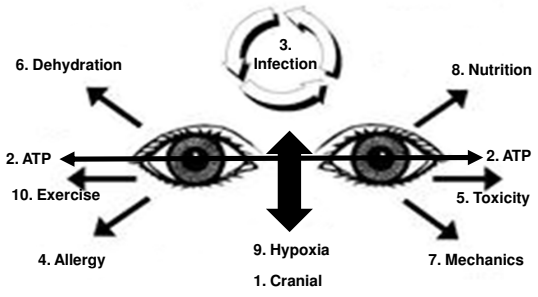
- Body Type Acetates
- Meridian points – Biophoton acetates
- Hormones
- Therapy localisation
- Biomarkers
- Weak muscle(s)
- Eyes into Distortion
- Food allergens
- Phonocardiograph

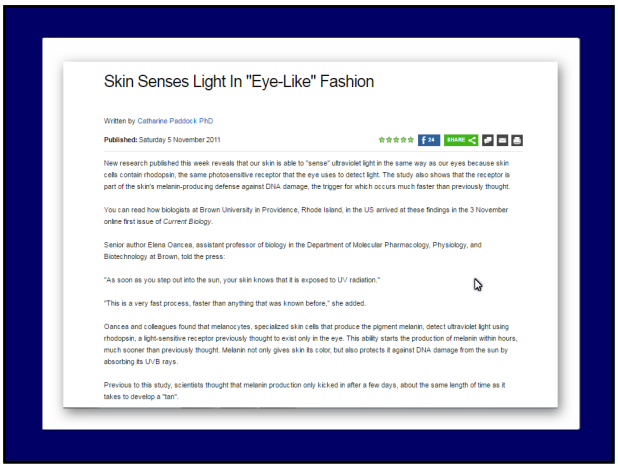
The 5 R Program

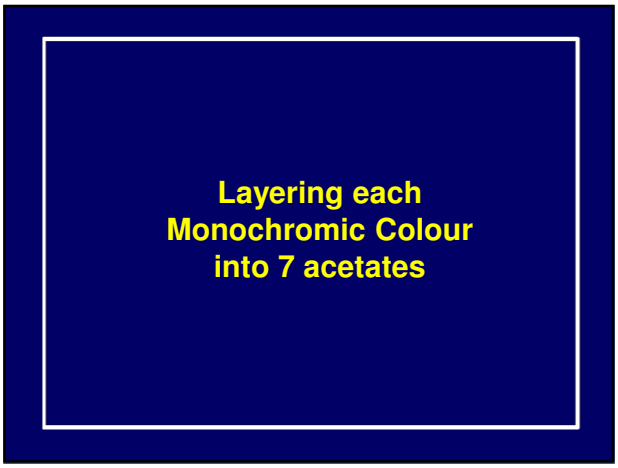
1. Remove – Allergens, Toxins, Infections
2. Replace – Nutrients, Digestive enzymes
3. Re-inoculate - Probiotics
4. Repair – High or Low
5. Regeneration – High or Low

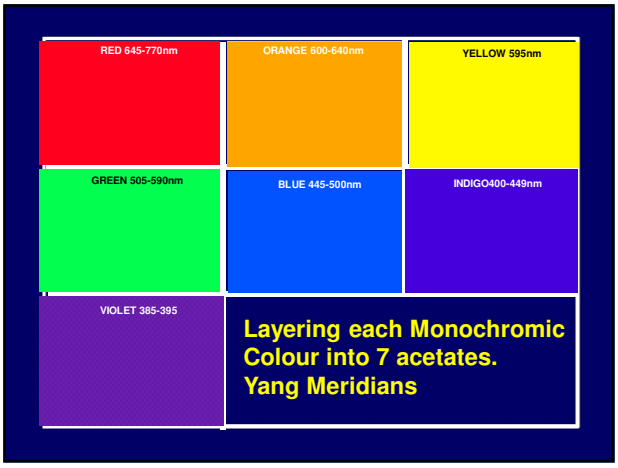
Functional Medicine Update 2010. Jeffery Bland

Eyes into Distortion (EID)

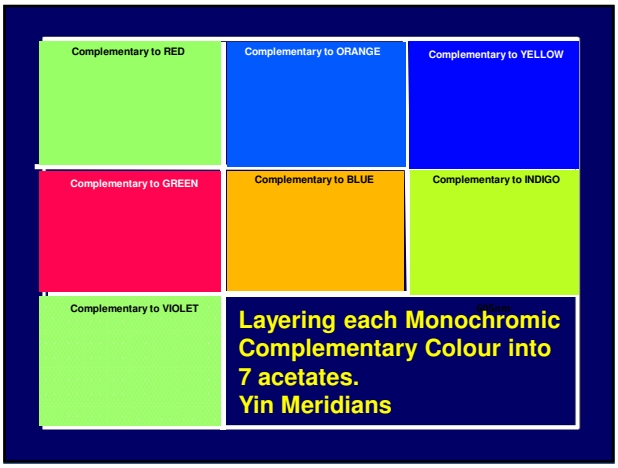


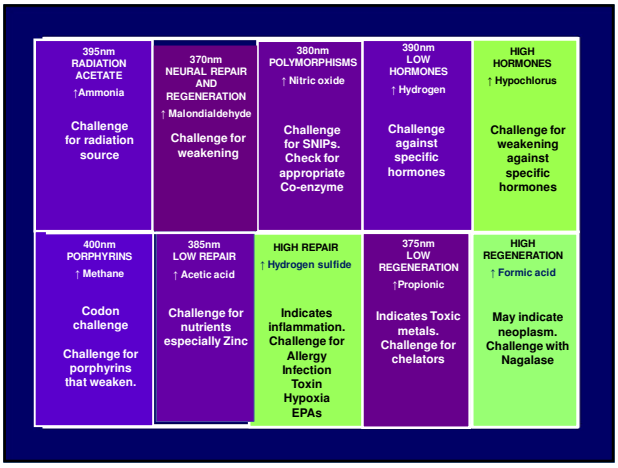

Skin Senses Light In "Eye-Like" Fashion
Written by Catharine Paddock PhD
Published: Saturday 5 November 2011
New research published this week reveals that our skin is able to "sense" ultraviolet light in the same way as our eyes because skin cells contain rhodopsin, the same photosensitive receptor that the eye uses to detect light. The study also shows that the receptor is part of the skin's melanin-producing defense against DNA damage, the trigger for which occurs much faster than previously thought.
You can read how biologists at Brown University in Providence, Rhode Island, in the US arrived at these findings in the 3 November online first issue of Current Biology.
Senior author Elena Oancea, assistant professor of biology in the Department of Molecular Pharmacology, Physiology, and Biotechnology at Brown, told the press:
"As soon as you step out into the sun, your skin knows that it is exposed to UV radiation."
"This is a very fast process, faster than anything that was known before," she added.
Oancea and colleagues found that melanocytes, specialized skin cells that produce the pigment melanin, detect ultraviolet light using rhodopsin, a light-sensitive receptor previously thought to exist only in the eye. This ability starts the production of melanin within hours, much sooner than previously thought. Melanin not only gives skin its color, but also protects it against DNA damage from the sun by absorbing its UVB rays.
Previous to this study, scientists thought that melanin production only kicked in after a few days, about the same length of time as it takes to develop a "tan".


Layering each Monochromic Colour into 7 acetates


RED 645-770nm
ORANGE 600-640nm
YELLOW 595nm
GREEN 505-590nm
BLUE 445-500nm
INDIGO400-449nm
VIOLET 385-395
Layering each Monochromic Colour into 7 acetates. Yang Meridians

Layering each Monochromic Complementary Colour into 7 acetates





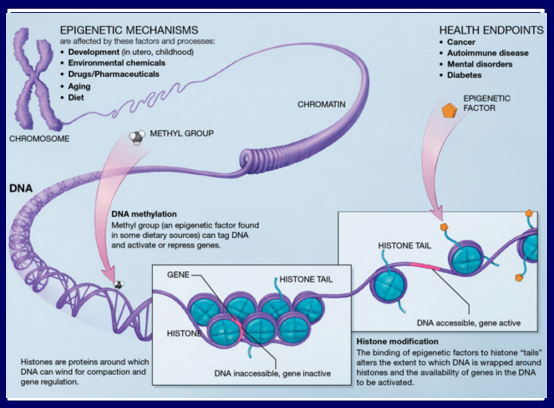
360nm ATP Challenge for weakening to ADP	365nm Water

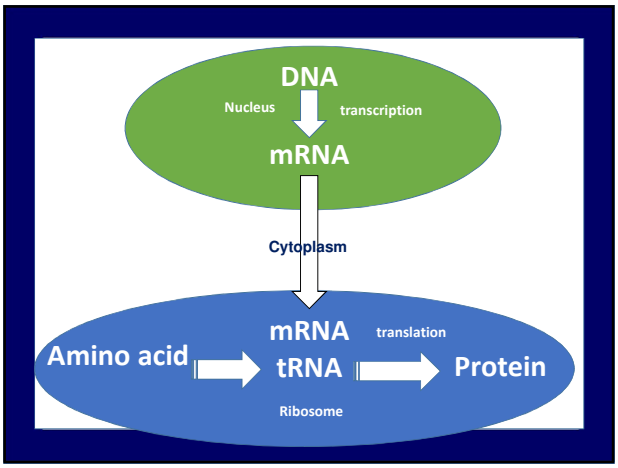
Diagnostic acetate challenge
Place acetate over both eyes and test a strong muscle for weakening

Genetics

1. Damage to the DNA – DNA polymerase enzyme - Zn
2. Single nucleotide polymorphisms SNIPs – need for extra co-enzyme
3. Histones - (De)Methylation and (De)Acetylation
4. Malfunctioning codons – need for specific amino acid, mineral, probiotic

Minerals for the Genetic Code. Updated Edition. Charles Walters





Genotype (Definitive or Constitutional meridian) is the sum total of the genes transmitted from parents to the offspring.

Phenotype (Gene expression) is the appearance of an organism resulting from the interaction of the genotype and the environment.

Phenotype-
Scale of Gene Expression
On a Scale of 1 to 100 the percentage of your gene expression with 100 being absolutely perfect is …….

2. Environment

1. Infections – Bacteria, Viruses, Fungus, Parasites
2. Chemicals – Endogenous and Exogenous
3. Toxic metals
4. Radiation – Ionizing and Non-Ionizing
5. Allergy
6. Hypoxia

All caused by Nutritional Deficiency or Toxicity

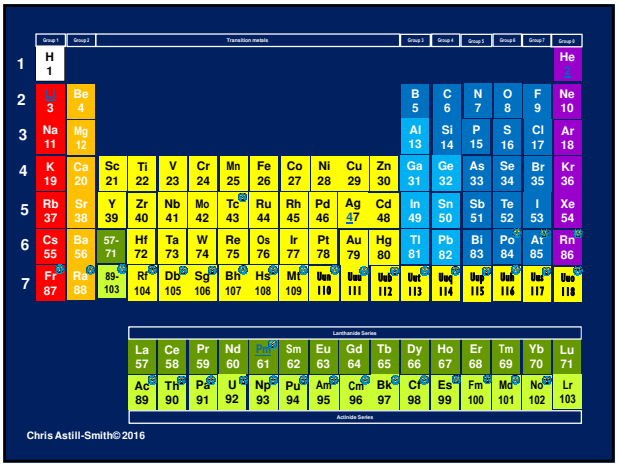
Essential minerals

Boron
Calcium
Copper ↑↓
Chromium ↑↓
Indium
Iodine
Iron ↑↓
Magnesium
Manganese ↑↓
Molybdenum
Platinum
Potassium
Selenium
Silica
Silver
Sulphur
Zinc

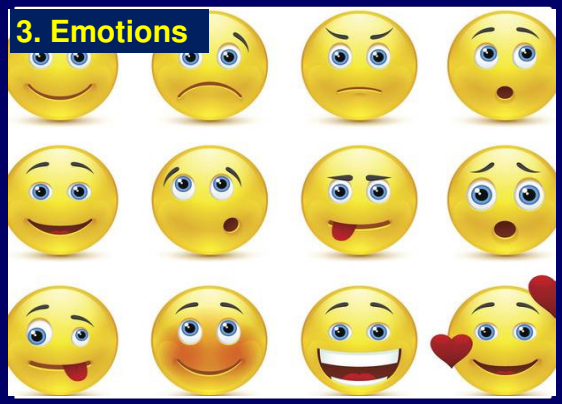
Toxic minerals

Aluminium
Antimony
Arsenic*
Beryllium*
Bismuth
Bromine
Cadmium*
Caesium
Chlorine
Cobalt
Fluorine
Lead
Lithium
Mercury
Nickel*
Palladium
Promethium*
Radium
Radon*
Thallium
Thorium
Uranium

* Known to be Carcinogenic



3. Emotions

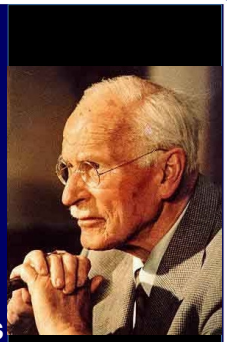


The consciousness mind is your awareness at the present moment. You are aware of something on the outside as well as some specific mental functions happening on the inside. For example, you are aware of this lecture room, the person next to you, or me talking.

The subconscious mind consists of accessible information. You can become aware of this information once your direct your attention to it. Think of this as memory recall. You drove from your house without consciously needing to be alert to your surroundings. Acquired input through 5 senses.

The unconscious mind, consists of the primitive, instinctual wishes and the information that we cannot access. We don't have easy access to the information stored in the unconscious mind. Inherent within us as beliefs, patterns, subjective maps of reality that drive our behaviours. Carl Jung's dark shadow.

In Jungian psychology, the "dark shadow" may refer to
(1) an unconscious aspect of the personality which the conscious ego does not identify in itself.



Carl Gustav Jung
1875-1961

Because one tends to reject or remain ignorant of the least desirable aspects of one's personality, the shadow is largely negative.
or (2) the entirety of the unconscious, i.e., everything of which a person is not fully conscious.

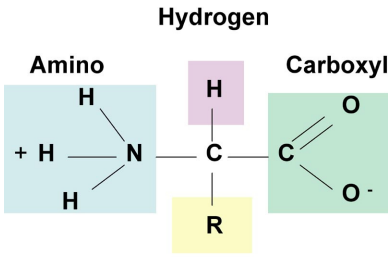
LIFE and HEALTH
ARE DEPENDANT
UPON
ADEQUATE NUTRITIONAL
INTAKE

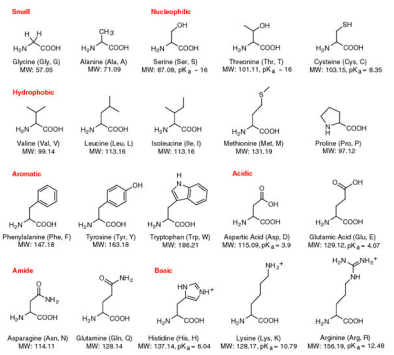
AMINO ACIDS

1. BUILD TISSUES
2. TRANSPORT MOLECULES
3. FORM ANTIBODIES
4. FORM ENZYMES
5. BUILD CHEMICAL MESSENGERS i.e. HORMONES AND NEUROTRANSMITTERS

Amino acids are biologically important organic compounds composed of amine (-NH_2) and carboxylic acid (-COOH) functional groups, along with a side-chain specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen.

Amino Acid Structure



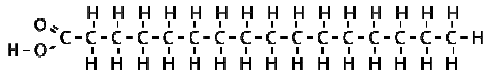


Essential			Nonessential		
Histidine	N 90%,	Hydrophobic	Alanine	N	Hydrophobic
Isoleucine	N	Hydrophobic	Arginine	+ve	Hydrophilic
Leucine	N	Hydrophobic	Asparagine	N	Hydrophilic
Lysine	+ve	Hydrophilic	Aspartic acid	–ve	Hydrophilic
Methionine	N	Hydrophobic	Cysteine	N	Hydrophobic
Phenylalanine	N	Hydrophobic	Glutamic acid	–ve	Hydrophilic
Threonine	N	Hydrophilic	Glutamine	N	Hydrophilic
Tryptophan	N	Hydrophobic	Glycine	N	Hydrophobic
Valine	N	Hydrophobic	Ornithine		
Left brain weakness give hydrophilic Right brain weakness give hydrophobic			Proline	N	Hydrophobic
			Selenocysteine		
			Serine	N	Hydrophilic
			Tyrosine	N	Hydrophilic

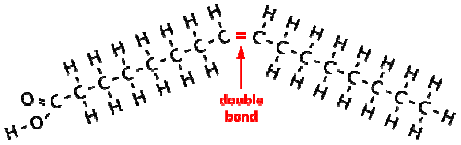
FATTY ACIDS

1. FORM CELL MEMBRANES
2. ARE SOURCES OF ENERGY
3. ARE STORES OF ENERGY
4. PROTECT ORGANS
5. ACT AS ELECTRICAL AND THERMAL INSULATORS
6. BUILD STEROID HORMONES

saturated fatty acid



unsaturated fatty acid



Alzheimer's linked to fat metabolism malfunction, research notes

By Will Chu, 24-Mar-2017
Last updated on 24-Mar-2017 at 13:56 GMT

Post a comment

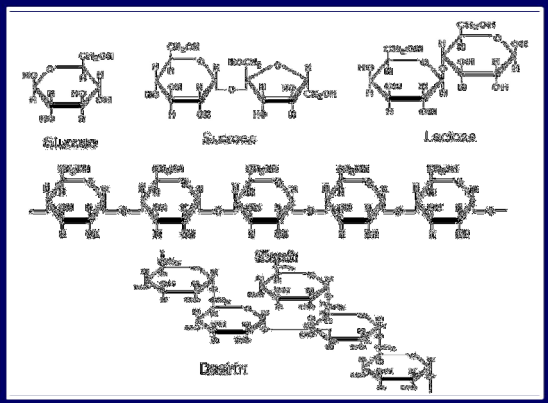
Alzheimer's disease accounts for between 60% and 80% of total dementia cases worldwide and represents a major cause of global morbidity and mortality. ©iStock/

Related tags: Eicosapentaenoic, Arachidonic, Alzheimers, Tau, DHA, EPA, Docosahexaenoic, Amyloid, Oleic, Linoleic, Linolenic

The metabolism of omega-3 and omega-6 unsaturated fatty acids in the brain may be linked with the progression of Alzheimer's disease.

CARBOHYDRATES

1. Are a source of energy
2. Link with amino acids to form glycoproteins
3. Link with fatty acids to form glycolipids.

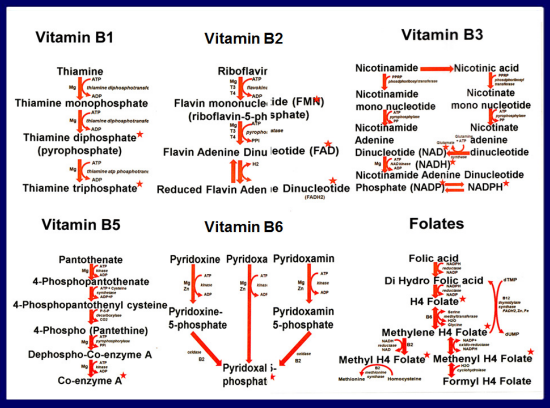


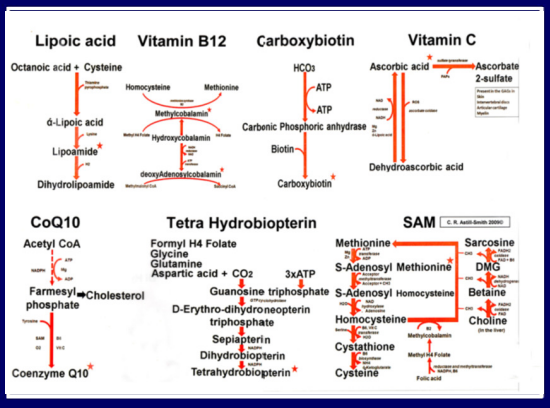
VITAMINS

1. CO-ENZYMES PRECURSORS IN SPECIFIC ENZYME PATHWAYS
   e.g. B1, B2, B3, B5, B6, Folates, B12, Biotin
2. ACT AS ANTIOXIDANTS
   e.g. Vitamin A, Carotenoids, Vitamin C, Vitamin E
3. INVOLVED WITH BLOOD CLOTTING e.g. Vitamin K
4. PART OF CELL MEMBRANES
   e.g. Choline, Inositol

Co-Enzymes

Thiamine pyrophosphate	Methylene H4 Folate
Thiamine triphosphate	Methyl H4 Folate
FMN – FMN H	H4 Biopterins
FAD - FADH2	Adenosylcobalamin
NAD – NADH	Methylcobalamin
NADP – NADPH	Biotin
CoA	Vitamin C
Pyridoxal-5-phosphate	Alpha Lipoic acid
H4Folate	SAM
Methenyl H4 Folate	CoQ10





MINERALS ACT TO

1. Supply major elements and trace elements that may be lacking in the diet.
2. Act as catalysts, thus playing a major role in metabolism and cell building.
3. Regulate the permeability of cell membranes.
4. Maintain water balance and osmotic pressure between the inside and outside environment.
5. Influence the contractility of muscles.
6. Regulate the response of nerves to stimuli.

LIFE
DEPENDS UPON IONIC BALANCE TO MAINTAIN HOMEOSTASIS

IONIC BALANCE DEPEND UPON ADEQUATE NUTRIENT UPTAKE FROM IONIZED MINERALS

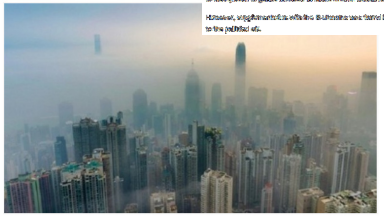
Optimising human performance depends upon optimal ATP mitochondrial production requiring

1. Optimal nutritional
2. Optimal oxygen delivery
3. Absence of toxins
4. Absence of infections
5. Positive emotional state

Vitamins and Co-Enzymes

Certain B vitamins could protect against air pollution risk

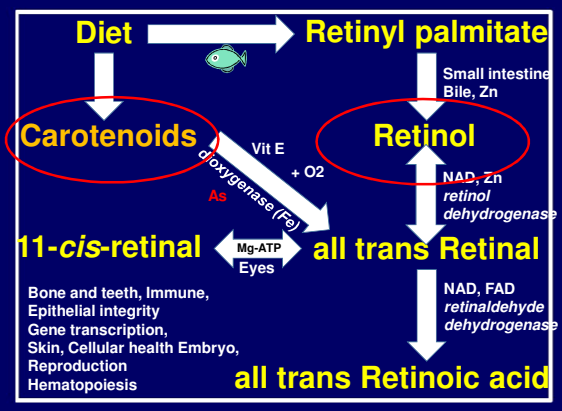
By Nathan Gray+
15-Mar-2017



Related tags: Air pollution, Air quality, Pollution, Vitamins, Vitamin B, Folic acid, B vitamins, Epigenetics

Dietary intake of B vitamins might play a role in reducing the impact of air pollution on the epigenome, say researchers.

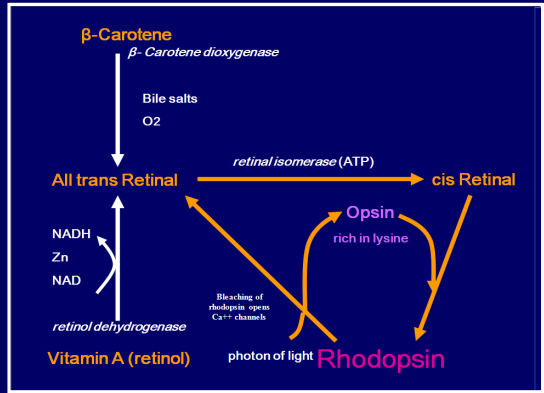
Vitamin A



Vitamin A (retinol) is a fat-soluble compound. It is a generic term referring to all substances from animal sources (retinol, retinal and retinoic acid) that exhibit the biological activity of vitamin A. Only retinol has full activity of vitamin A;
the others fulfil some, but not all, vitamin A functions.

It is stored mainly in the liver as an ester bound to intracellular lipoproteins. Outside the liver, vitamin A is bound and stored by a cellular retinol-binding protein. The term **"retinoids"** is used to describe both the natural forms and synthetic analogues of retinol.

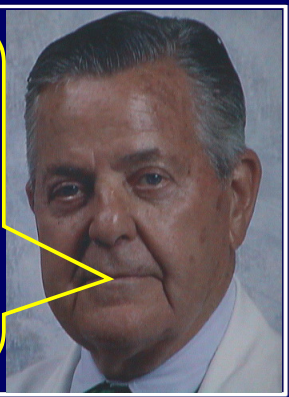
Vitamin A supports vision, especially **dim vision,** growth, reproductive function, the body's defence system and maintenance of skin and mucous membranes.



New findings have become available on the effects of thoroughly selected doses of Vitamin A in the prevention of cardiovascular conditions. Vitamin A is present exclusively in animal foods, especially fish liver oils and animal livers (e.g. Chicken pate).

May need pancreatic enzymes to aid the absorption of Vitamin A. Good for thick heavy calluses. Check for need in sinusitis.

Dr Goodheart says take 1500 IU Vitamin A every 15 minutes when hay fever attacks the eyes + HCl)



Patient may have daytime frequency, not night time.

Rough skin on the extensor surface of the arm or lower legs.

Can be used locally in cases of epistaxis.

RDA

UK	USA
2664 IU	5000 IU

RDA

UK	USA
1.4mg	1.5mg

Carotenoids

Lycopene
Astaxanthine
Beta carotene
Zeaxanthine*
Lutein*

Mixed carotenoids

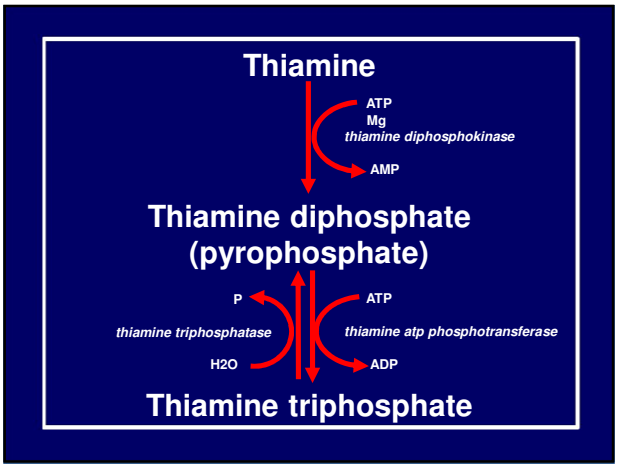
*Both macular pigments are required for optimal eye health. Beta carotene is a direct precursor to retinal and thus to rhodopsin.

Lutein absorbs in the 415-435nm range
Zeaxanthine absorbs in the 425-435nm range
β-Carotene absorbs in the 440-465nm range
Lycopene absorbs in the 470-515nm range
Thus making them all photo-sensitive in the blue spectrum.

Anthocyanidins
Most frequently occurring in nature are the glycosides
of cyanidin, delphinidin, malvidin, pelargonidin (rich in strawberries), peonidin,
and petunidin.
Present in Bilberry, Blueberry, Cranberry, Blackberry, Blackcurrant, Raspberry, Red grapes.

Anthocyanins can be used as pH indicators because their colour changes with pH; they are pink in acidic solutions (pH < 7), purple in neutral solutions (pH ~ 7), greenish-yellow in alkaline solutions (pH > 7), and colourless in very alkaline solutions, where the pigment is completely reduced.

Vitamin B1
Thiamine



Function

Thiamine pyrophosphate TPP

1. **Pyruvate dehydrogenase**
   converts pyruvate to acetyl CoA
2. **α-Ketoglutarate dehydrogenase**
   converts a-Ketoglutarate to Succinyl CoA
3. **Oxidative decarboxylation**
   can be an alternative to pyridoxal-5-phosphate
4. **2-Oxo acid dehydrogenase**
   oxidative decarboxylation of branched, short-chain alpha-ketoacids

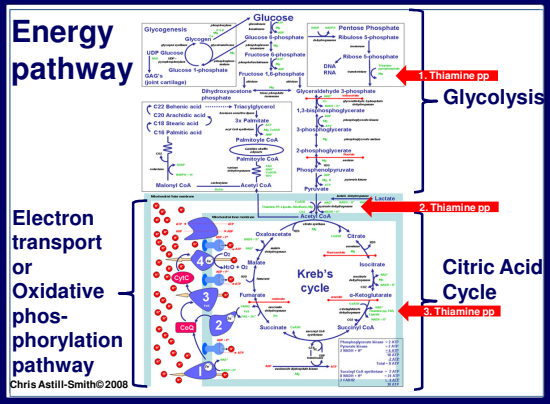
Maple syrup urine disease. Defect in leucine, valine and isoleucine metabolism

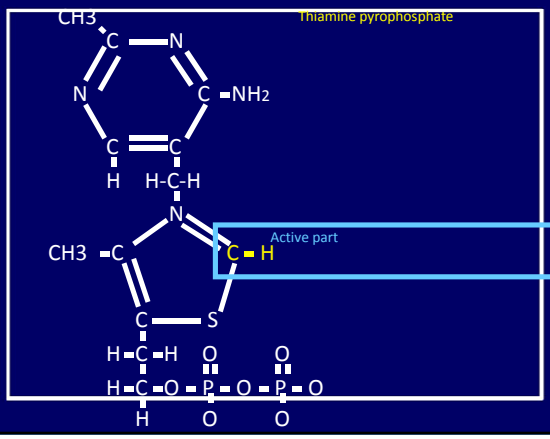
5. Xylulose-5-phosphate transketolase
Pentose phosphate shunt

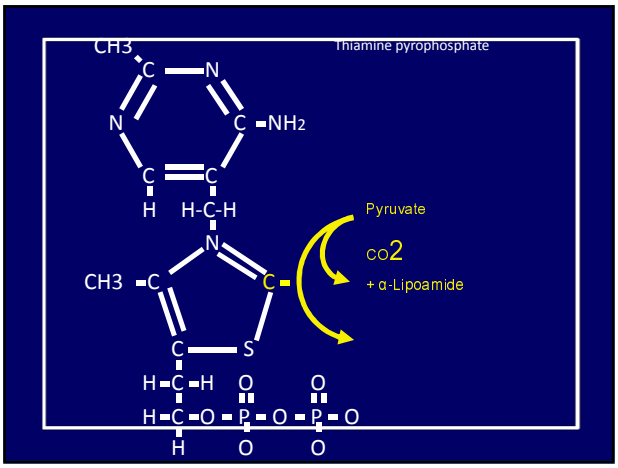
6. Transketolase
Pentose phosphate shunt

7. Thiamine pyrophosphate-ATP phosphoryltransferase
synthesises thiamine triphosphate

Energy pathway



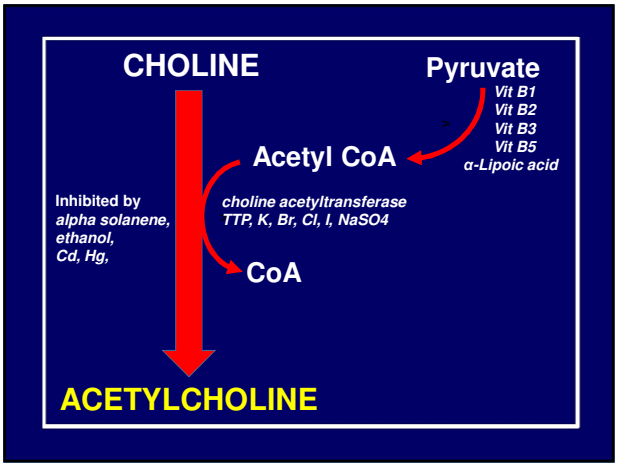




Function

Thiamine triphosphate TTP

Acetyltransferase in the synthesis of acetylcholine



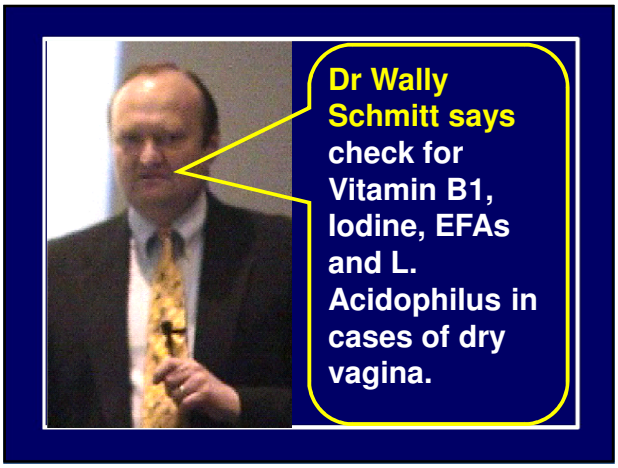
Deficiency symptoms

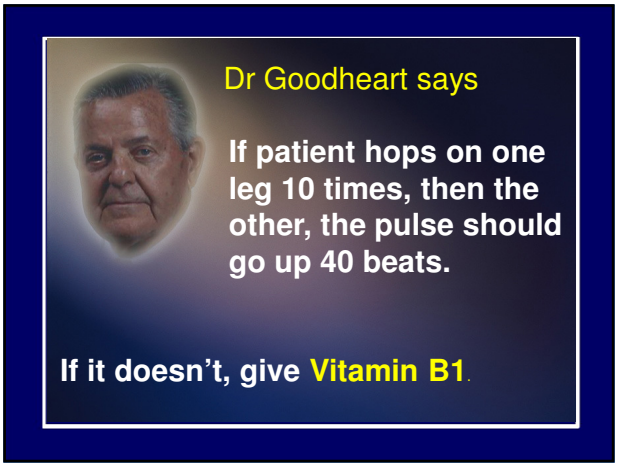
Yawning, Fatigue, muscle pains, parasthesia, atrophy, foot drop, weight loss, anorexia, megaloblastic anemia, hyperkinetic myopathy. Behaviour changes, enuresis, memory loss. Skin rashes, respiratory symptoms

Patient has a variety of complaints. "I have this skin trouble. It breaks out all over. It starts out with this one little patch. I haven't changed my diet any. It itches. I was in the car and I get sleepy.

Then when I go to bed I have this trouble falling asleep."
The tension usually goes to the skin and they don't tell you about the sleepiness because they have got used to it.


Dr Goodheart says patients who yawn a lot while talking need Vitamin B1


Dr Wally Schmitt says check for Vitamin B1, Iodine, EFAs and L. Acidophilus in cases of dry vagina.


Dr Goodheart says
If patient hops on one leg 10 times, then the other, the pulse should go up 40 beats.
If it doesn't, give Vitamin B1.

Sources

Highest in seeds and nuts

Yeast	Brown rice
Liver	Wheat germ and bran

Foods that have anti-thiamine activity

Blueberries	Blackcurrant
Red chicory	Sprouts
Red cabbage	Coffee
Tea (green and black)	Betal nut
Cotton seed	Baking soda

Raw carp, herring, shellfish, freshwater fish contain thiaminase

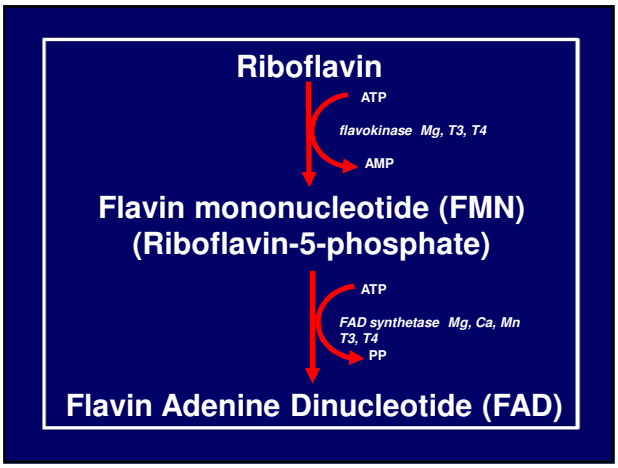
RDA

EEC 1.4mg USA 1.5mg

Dr Goodheart says use branched chain amino acids 1 hour before aerobic exercise. 3mg per Kg body weight.

Cortisol peaks at 7am and 9pm. Do not exercise at these times without branched chain amino acid support.

Vitamin B2
Riboflavin



In order to become their component,vitamin B2 has to be converted into active forms – flavin mononucleotide (FMN otherwise known as Riboflavin-5-phospgate) or flavin adenine dinucleotide (FAD and its reduced form – FADH2).

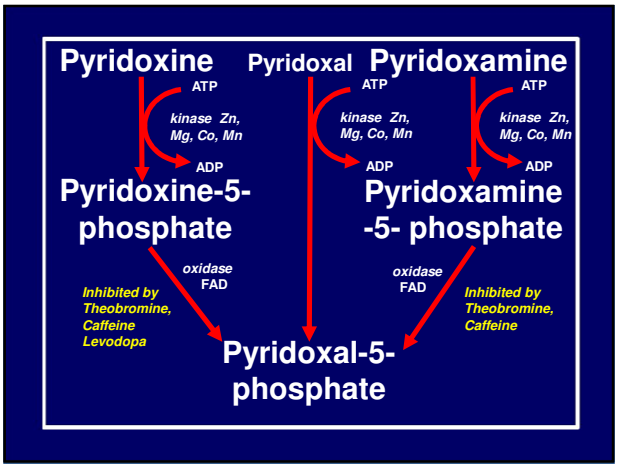
It is an orange-coloure fluorescent substance that is relatively heat-stable but decomposes under visible or ultraviolet light.

The riboflavin-dependent enzymes are known as flavo enzymes or flavo-proteins.

Many **flavo-enzymes** also contain one or more metals, for example, molybdenum, iron and / or copper, and are therefore named metallo-flavoproteins.

They are widespread and important for **amino acid deamination,** detoxifying aldehydes, sulfites, breaking down purines, fatty acids, for the functioning of the Krebs cycle and electron transport in the mitochondria.

They also function as components of glutathione reductase (providing reduced glutathione, a potent antioxidant and detoxifier) and of the enzyme producing an activated form of vitamin B6 in the liver.



Some medicines like adrenocorticotropic hormone – ACTH, chlorpromazine (a sedative) inhibit the conversion of riboflavin to its activated forms.

Early symptoms of riboflavin deficiency are: angular stomatitis (inflammation at sides of the mouth), cheilosis (fissures at corners of the mouth) and glossitis (inflamed tongue).

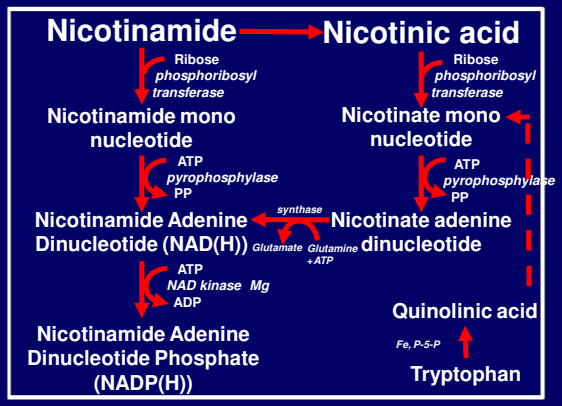
Deficiency of vitamin B2 may also occur in phototherapy and in intensive sun tanning.

Patients complain of "I have this pain in my legs, so I stop walking and it goes away".

RDA

UK	USA
1.6mg	1.7mg

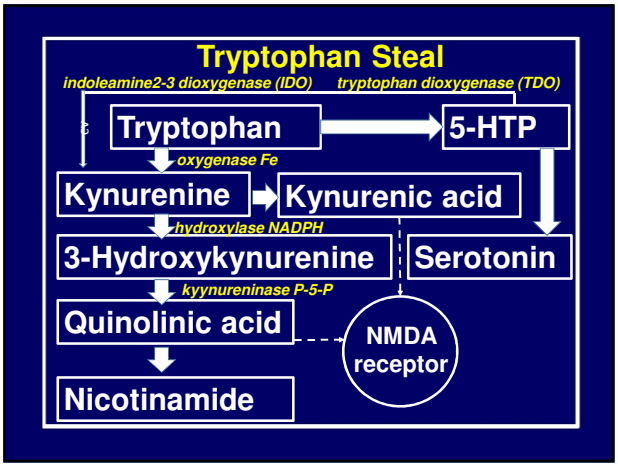
Vitamin B3
Niacin



Niacin is the generic name for **nicotinic acid and nicotinamide,** either of which may act as a source of the vitamin in the diet. It is a for the functioning of a wide range of enzymes catalysing redoxreaction, the oxidoreductases.

In order to become their coenzyme component, vitamin B3 has to be converted into active forms – nicotinamide adenine dinucleotide (NAD^+) or nicotinamide adenine dinucleotide phosphate ($NADP^+$). For this, niacin should be present in the cell in the form of nicotinic acid.

Besides the dietary entry, nicotinic acid has been well known to be obtained from the amino acid tryptophan. However, this pathway is inefficient: as much as 60 mg tryptophan is needed to make 1 mg of niacin. The process requires vitamins B1, B2 and B6, and occurs only after the needs of protein synthesis are met.



NAD-and NADP-linked oxidoreductases act in many metabolic pathways regulating the turnover of carbohydrates, lipids and amino acids. NAD-dependent enzymes catalyse oxidation pathways while those depending on NADP are often active in the reductive syntheses (like synthesis of fatty acids or steroids).

Besides redox reactions, NAD is also required for the repair of **ultraviolet light-damaged DNA.**

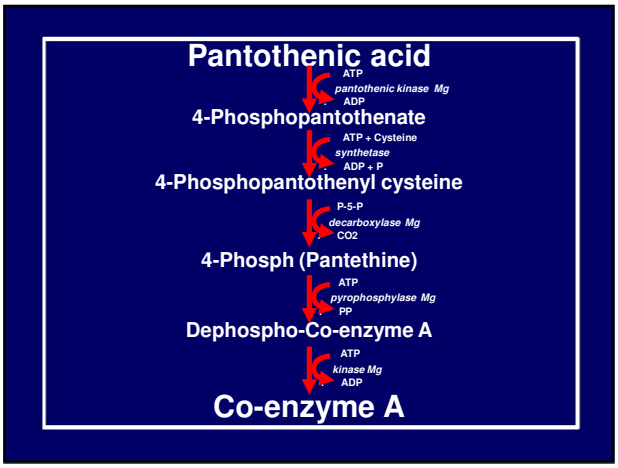
Major dietary sources of niacin are whole grain cereals, meat and fish.

Vitamin B3

Pellagra

1. Diarrhea
2. Dermatitis
3. Dementia

Vitamin B5
Pantothenic acid



Enzymes requiring Coenzyme A

1. Pyruvate dehydrogenase
2. α-ketoglutarate dehydrogenase
3. Carnitine acyltransferase
4. Acyl-CoA dehydrogenase in the mitochondria
5. Choline acetyltransferase

6. Acetyl-CoA Glucosamine-6-phosphate transferase
7. Acetyl-CoA-Sphingosine phosphorylcholine transferase (making sphingosine)
8. Acetyl-CoA-Sphingosine transferase (ceramides to cerebrosides and gangliosides

Acetylation of phase 2 reactive intermediates derived from

1. Petroleum
2. Newspaper print
3. Isoniazide

Deficiency symptoms

Burning foot syndrome, anorexia, indigestion, abdominal pain, respiratory infections, neuritis, cramps, tenderness of the heel, insomnia, fatigue, depression, psychoses, headaches, tachycardia and hypotension.

Sources

Yeast, liver, nuts, soy flour, eggs, meat, oat flakes, peas

GUT bacteria

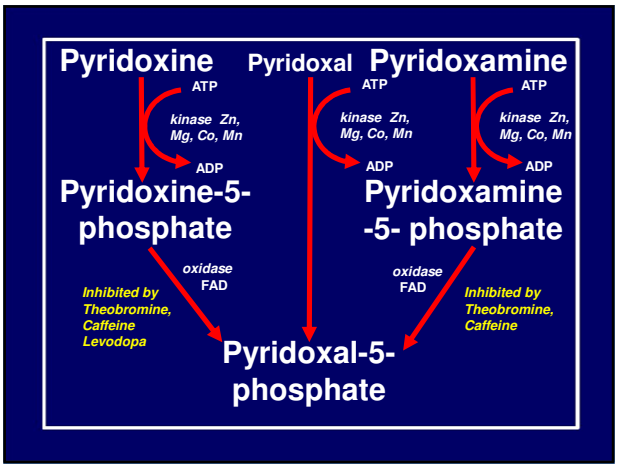
RDAs

UK 6mg USA 10mg

Functional test for Acetyl CoA

1. Strong muscle weakens to pyruvate.
2. Weakness negated by Acetyl CoA.

Vitamin B6
Pyridoxine



Pyridoxal-5-phosphate (P5P)

Major form present in the plasma. It is distributed to all tissues.

Other forms are Pyridoxine-5-Phosphate and Pyridoxamine-5-Phosphate

Functions

1. Transamination
2. Decarboxylation
3. Neurotransmitter synthesis
4. Transulfation
5. Protoporphyrin synthesis

6. Niacin synthesis

7. Polyamines synthesis (Growth factors, inhibition of some enzymes, stimulation of DNA / RNA synthesis, stabilization of membranes and DNA)

There are 76 enzymes involved with amine metabolism that require P5P.

Transamination

1.Aspartate aminotransferase (Glutamate oxaloacetate transaminase – GOT)
Glutamic acid + Oxaloacetic acid = Aspartic acid + alpha-ketoglutaric acid

↑ in liver disease, coronary heart disease and muscular diseases.

Glutamic acid + Oxaloacetic acid

↓ *Aspartate aminotransferase (Glutamate oxaloacetate transaminase – GOT)*

P5P

Aspartic acid

+

alpha-ketoglutaric acid

2. *Alanine aminotransferase (glutamate pyruvate transaminase – GPT)*

Glutamic acid + Pyruvic acid = alpha-ketoglutaric acid + Alanine

↑ in liver diseases such as hepatitis, cirrhosis, biliary disease and alcoholism.

Glutamic acid + Pyruvic acid

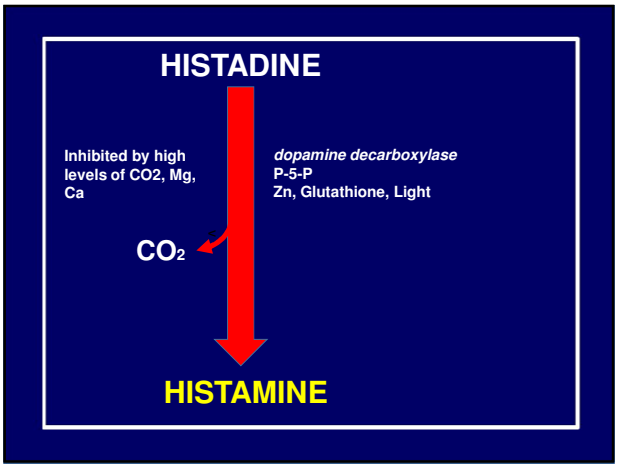
↓ Alanine aminotransferase (glutamate pyruvate transaminase – GPT)

P5P

alpha-ketoglutaric acid + Alanine

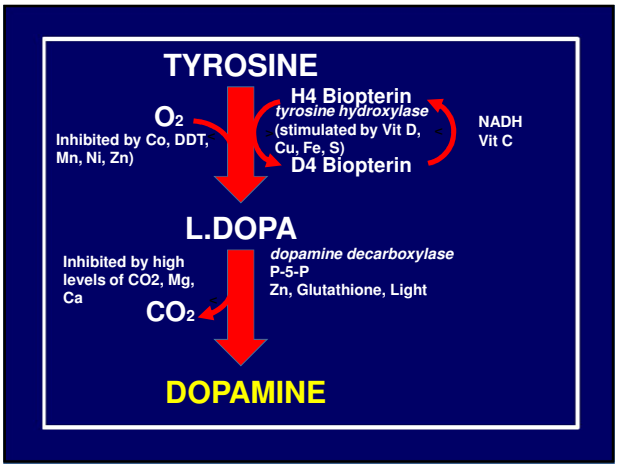
Decarboxylation

1. ***Histidine decarboxylase*** found in the mast cells of the skin, parietal cells of the stomach and other tissues. Stimulated by gastrin.

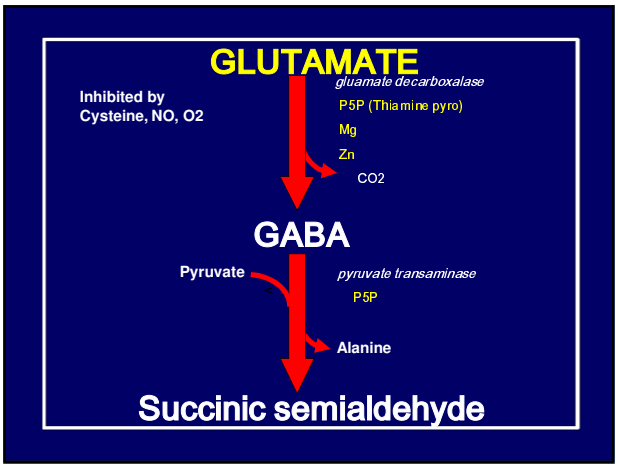


Low stomach acid (hypochlorrhydria) causes the morning nausea and sickness often associated with pregnancy

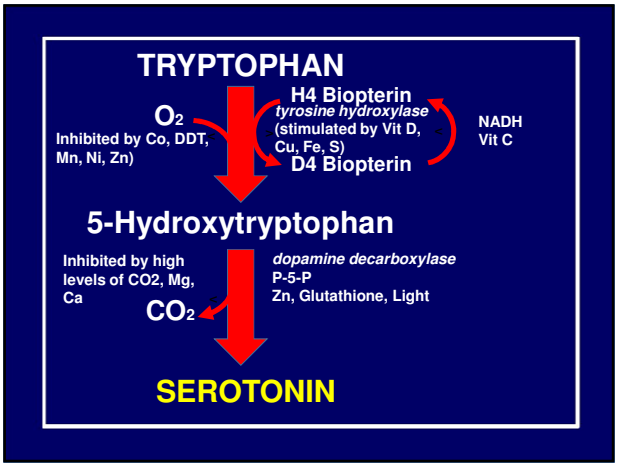
2. *DOPA decarboxylase*
converts L.DOPA to dopamine. Found mainly in the adrenal medulla, brain and sympathetic nerve endings.



3. *Glutamate decarboxylase*
catalyzes the conversion of glutamate to the inhibitory neurotransmitter - GABA.



4. *5-Hydroxytryptophan* decarboxylase
catalyzes the conversion of 5-hydroxytryptophan to serotonin. It is found in the pineal gland, CNS, argentaffin cells of the intestine, blood platelets and mast cells.

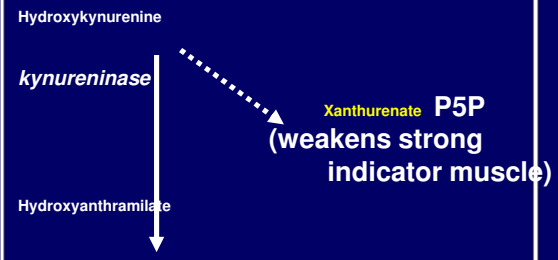


Kynureninase **is involved with the conversion of tryptophan via 3-hydroxykynurenine to niacin (Vit B3)**

High urinary levels of kynurenates are diagnostic of P5P deficiency.

Functional test

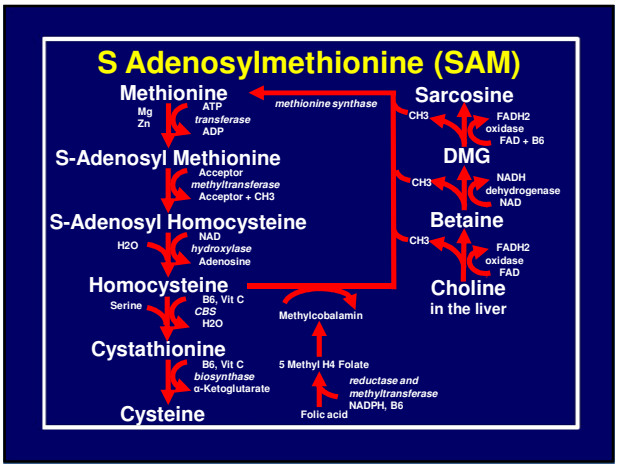
Tryptophan Metabolism



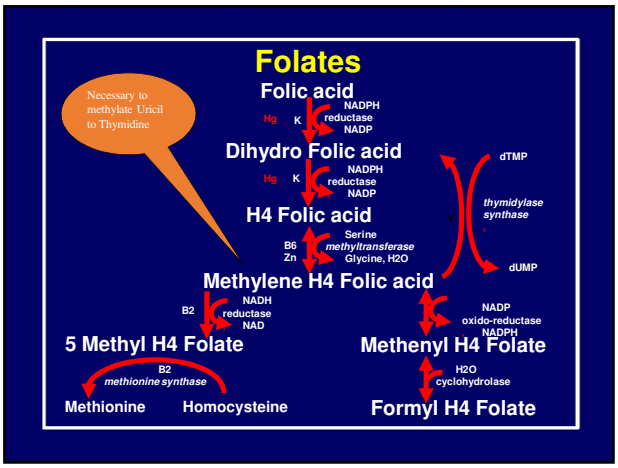
Cystathione β transferase **catalyzes the conversion of homocysteine to cystathione.**

Cysteine biosynthase **catalyzes the conversion of cystathione to cysteine.**

Cystathionuria is an inborn error of metabolism resulting in mental retardation and slow development.



Methyltransferase catalyzes the conversion of tetrahydrofolate to methylene tetrahydrofolate which is necessary to methylate uracil to thymidine.



P5P deficiency affects the metabolism of alpha linolenic acid to docosahexaenoic acid (DHA). DHA and DPA are necessary in the growth and development of the CNS.

Deficiency can lead to attention deficit hyperactivity disorder (ADHD) and failure of proper development of the visual system.

Deficiency symptoms

Dry rough skin, cracking lips, flaking nails, retarded healing, mouth ulcers, gastric and varicose ulcers. Anaemia.

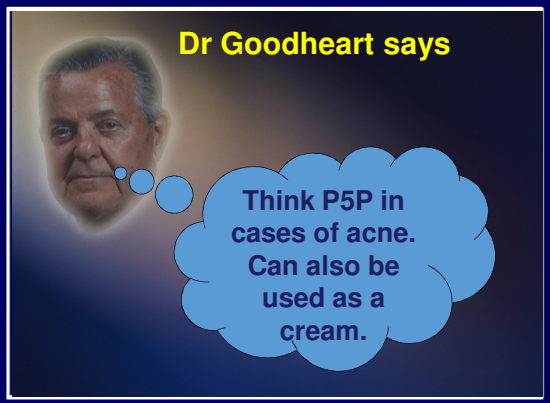
Depression, PMS, menopausal symptoms.

Kidney stones.

High homocysteine levels inhibit lysyloxidase enzyme needed to synthesise collagen. This may lead to aneurysms, (Campell de Morgan spots) CVA's, coronary infarction.

Methylation defects may lead to cancer formation.

Patients may complain of "this snapping finger" which is **stenosing tenosynovitis** of the flexor or extensor tendon. It is usually palpable.



Sources

Yeast, wheat bran, wheat germ, oats, sunflower seeds, liver, soy, bananas.

RDAs

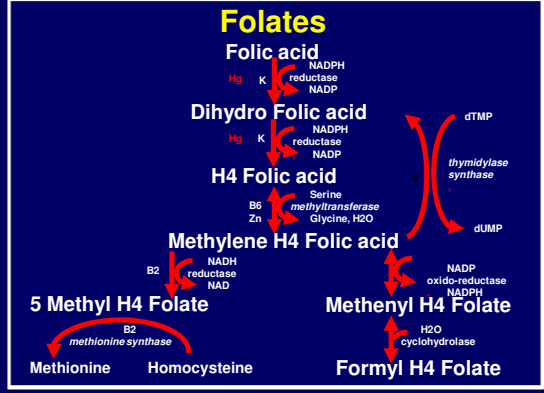
UK 2mg USA 2mg

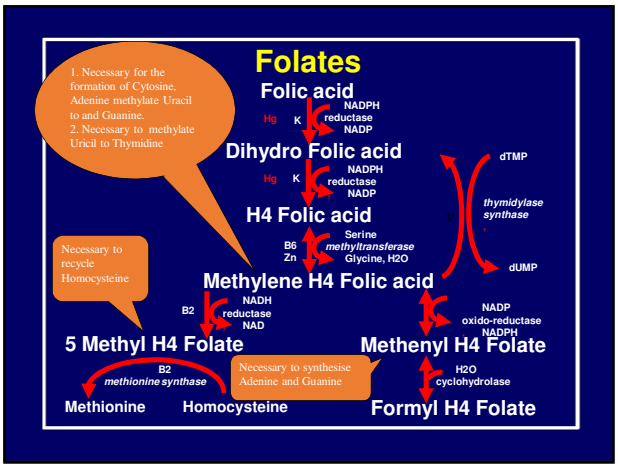
Functional tests

Strong muscle weakens to
1. Homocysteine
2. Xanthurenate
3. alpha Linolenic acid

The Folates

Folates



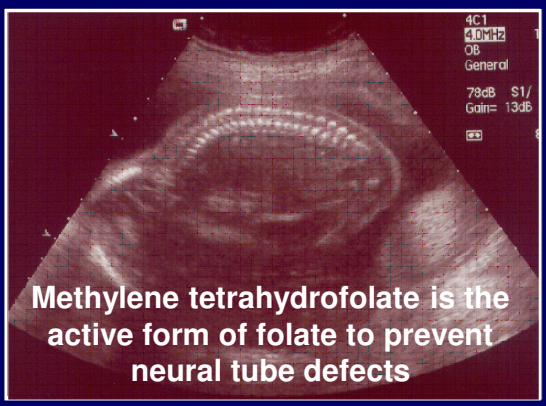


The intestine cell has on the surface of the brush border a **specific folic acid binding protein.** It transfers folic acid to the inside of the cell. Here dihydrofolate reductase twice reduces the folic acid to **tetrahydrofolate.**

Methylation then occurs either directly or indirectly via the formation of N10 formyltetrahydrofolate to N5, N10 methyltetrahydrofolate.

It is used in the synthesis of the **purines adenine and guanine** found in the RNA and DNA of intestinal cells. The average half-life of the intestinal cell is 3 days.

Most folate in the serum is in the methyltetrahydrofolate form. Serum folic acid levels decrease in pregnancy reaching their lowest level at full term. Look out for post-pregnant **cervical dysplasia and gum dysplasia.**



Methylene tetrahydrofolate is the active form of folate to prevent neural tube defects

Function

One carbon group transfer

- Nucleotide synthesis
- Glycine synthesis
- Homocysteine recycling

Folate deficiency limits cell division, erythropoiesis, production of red blood cells, is hindered and leads to megaloblastic anemia, which is characterized by large immature red blood cells.

This pathology results from persistently thwarted attempts at **normal DNA replication**, DNA repair, and cell division, and produces abnormally large red cells called megaloblasts with abundant cytoplasm capable of RNA and protein synthesis, but with clumping and fragmentation of nuclear chromatin.

Folic acid is itself not biologically active, but its biological importance is due to tetrahydrofolate and other derivatives after its conversion to dihydrofolic acid in the liver.

H4Folate Tetrahydrofolate
CHH4Folate Methenyl tetrahydro folate
CH2H4Folate Methylene tetrahydro folate
CH3H4Folate Methyl tetrahydro folate

Deficiency symptoms

Birth defects
Retarded growth
Scaling dermatitis
Alopecia
Megaloblastic anaemia
Cervical dysplasia
Mouth ulcers
Depression

Dr Goodheart says in cases of a bad haematoma use pancreatic enzymes and folic acid.

Sources

Leafy green vegetables, Yeast, Soya flour, Wheatgerm, Wheatbran, Nuts, Liver, Pulses, Oatflakes, Citrus fruit, Eggs, Berries, Beans, Asparagus, Cucumber.

RDAs

UK 200mcg USA 400mcg

90% of folates are lost by steaming vegetables. Hence the importance of drinking the vegetable water.

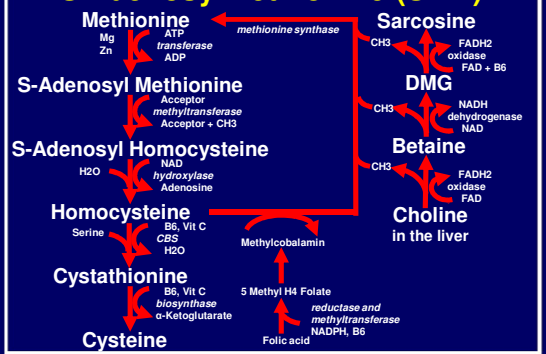
70-90% lost by frying in an open pan.

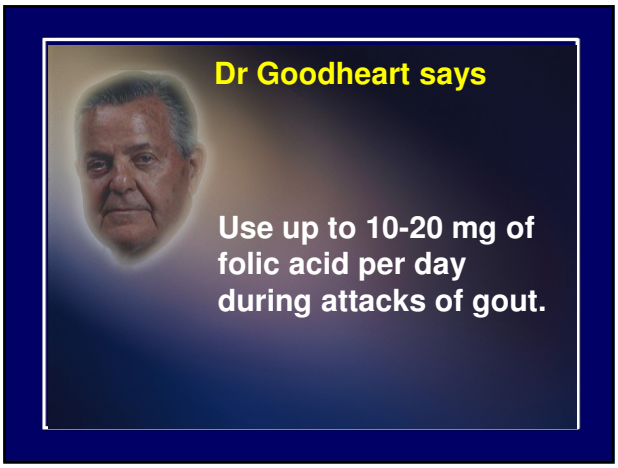
Dr Wally Schmitt says a yellow tongue is a need for folic acid.

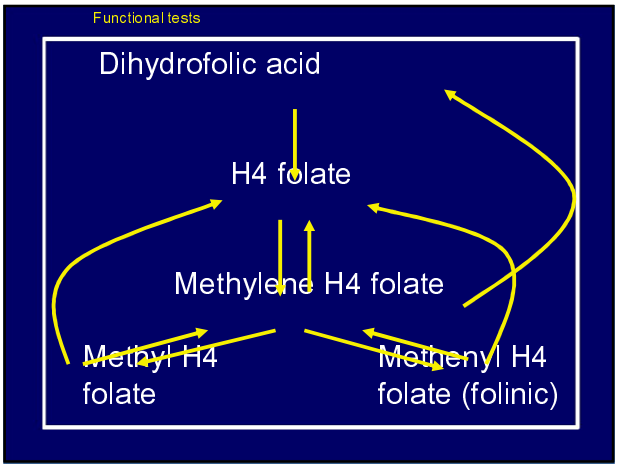
In pernicious anemia, there is a rise in serum levels of methyltetrahydrofolate and there is an increase excretion of formiminoglutamic acid (Figlu).

Check this especially in MS patients.

S Adenosylmethionine (SAM)







Folate deficiency clinical expression times

Homocysteinemia	10days
Low serum folate	22days
High urine FIGLU	95days
Low RBC folate	123days
Megaloblastic marrow	134days
Anemia	137days

So **homocysteinemia** is the best functional marker for folate deficiency.

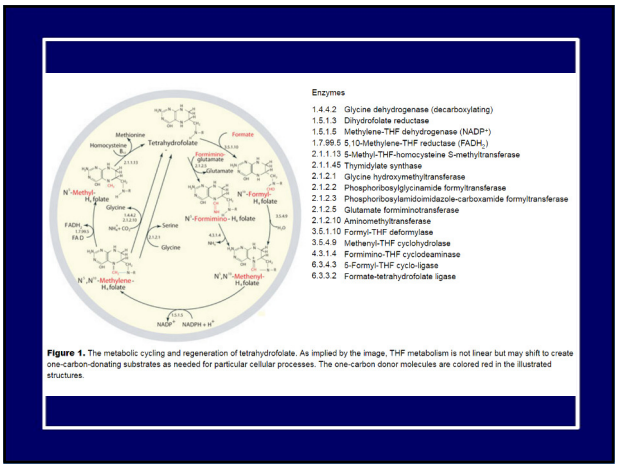
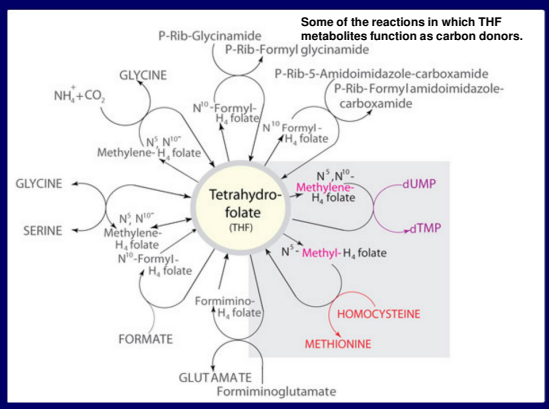
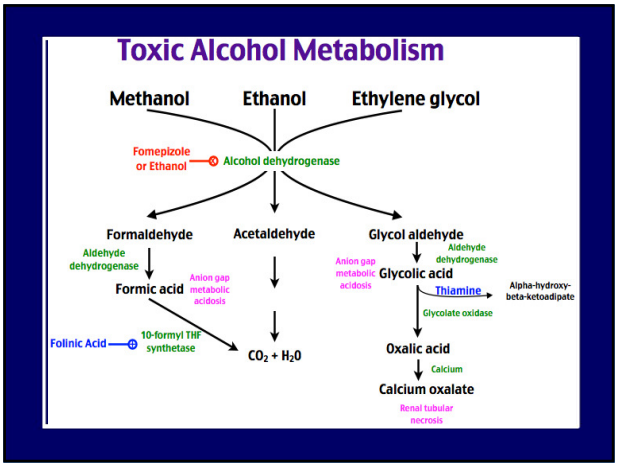


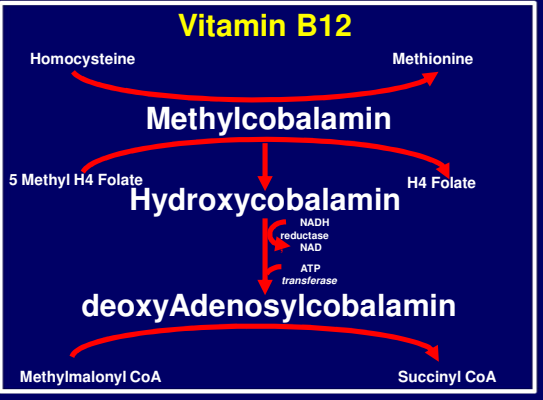
Figure 1. The metabolic cycling and regeneration of tetrahydrofolate. As implied by the image, THF metabolism is not linear but may shift to create one-carbon-donating substrates as needed for particular cellular processes. The one-carbon donor molecules are colored red in the illustrated structures.





Vitamin B12
Cobalamin

Vitamin B12



Produced by bacteria in the guts of ruminants and plant micro-organisms.

Similar structure to heme but contains cobalt instead of iron.

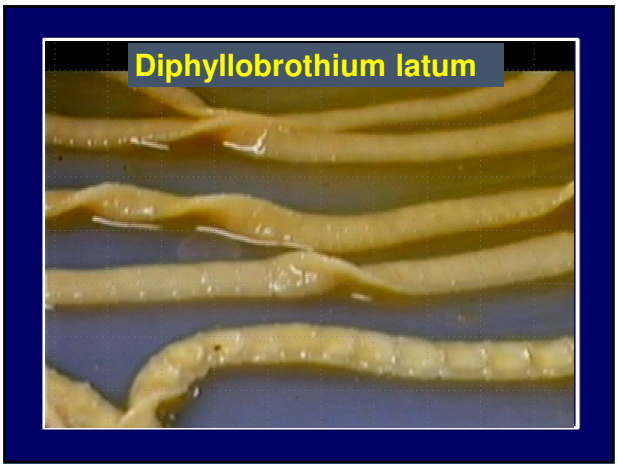
Intrinsic Factor

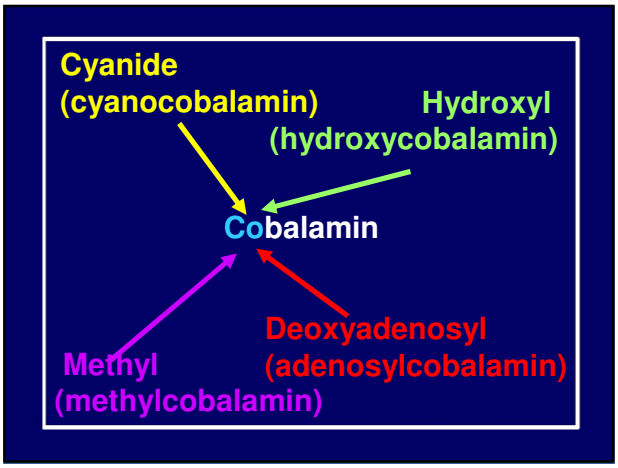
Intrinsic Factor is a protein secreted by the parietal cells (which also secretes HCl) and binds with B12. The reaction forms a B12 / Intrinsic factor complex in the stomach.

Specialised cells in the distal part of the ileum recognise this complex and absorb the B12. Intrinsic factor requires P-5-P for its activation.

So often hypochlorhydria is associated with a B12 deficiency.

People with intestinal parasites especially cestodes such as Diphyllobrothium latum, may develop B12 deficiency as the worms live in the lower part of the ileum and compete for the B12.





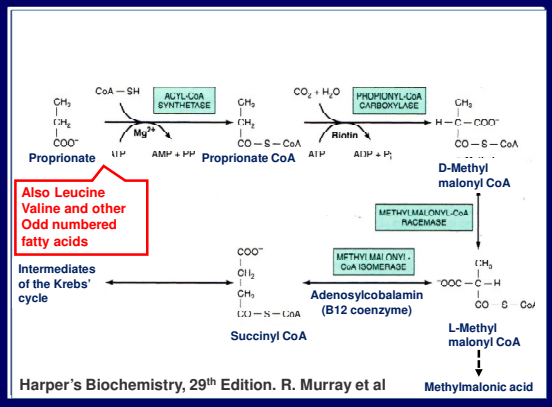
Function test

deoxyAdenosylcobalamin

Conversion of proprionates to succinates.

Functional test

Strong muscle weakens to Methylmalonic acid



Deficiency of Adenosylcobalamin results in the accumulation of proprionate and subsequent build up of odd numbered fatty acids.

Bacteria in the gut of ruminants produce large amounts of proprionate, which is absorbed and enters the metabolism.

Consequently, intake of animal and dairy products results in higher levels of odd numbered fatty acids.
A similar process occurs in humans who suffer from gut dysbiosis.

The association between B12 and abnormal fatty acid synthesis provides a rationale for the neuropathy of B12 deficiency.

Odd chained fatty acids build up in the CVN lipid membranes with B12 deficiency resulting in altered myelin integrity and demyelination.

Functional test

Methylcobalamin
Recycling of homocysteine.

Strong muscle weakens to homocysteine

Cobalamin

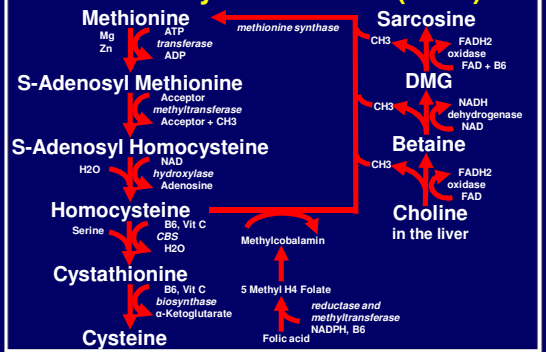
methyltetrahydrofolate homocysteine methyltransferase

Methyl H4 folate

H4 folate

Methylcobalamin

S Adenosylmethionine (SAM)



Deficiency symptoms
deoxyAdenosylcobalamin
Hypoxia, fatigue, dementia.

Methylcobalamin
Pernicious anaemia
CV diseases.

Sources

Animal products
Meat, liver, fish, eggs, cheese, milk.
Spirulina?
Legume nodules of root vegetable-must not wash soil off

Bacterial synthesis of B12
occurs in the human colon, but little is absorbed!

RDAs

UK 1mcg **USA 6mcg**

Dr Goodheart says don't forget to give the patient B12 with fascial agglutination problems.

Tetrahydrobiopterin
H4Biopterin

Folinic acid + Glycine + Glutamine + Aspartic acid + CO_2 + 3x ATP

Guanosine triphosphate (GTP)

↓ *GTP cyclohydrolase I*

7,8-Dihydroneopterin triphosphate

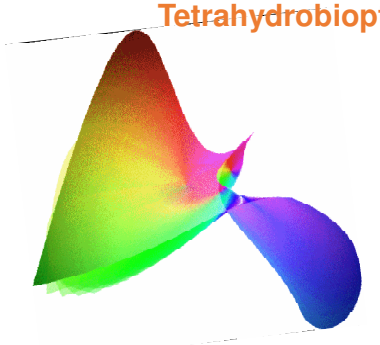
↓ NADPH, Mg
6-pyruvoyltetrahydropterin synthase

6-Pyruvoyl-tetrahydropterin

↓ NADP
sepiapterin-reductase

Tetrahydrobiopterin

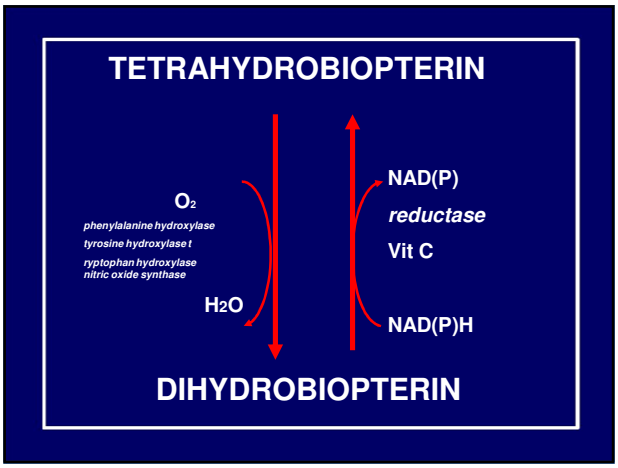
Tetrahydrobiopterin

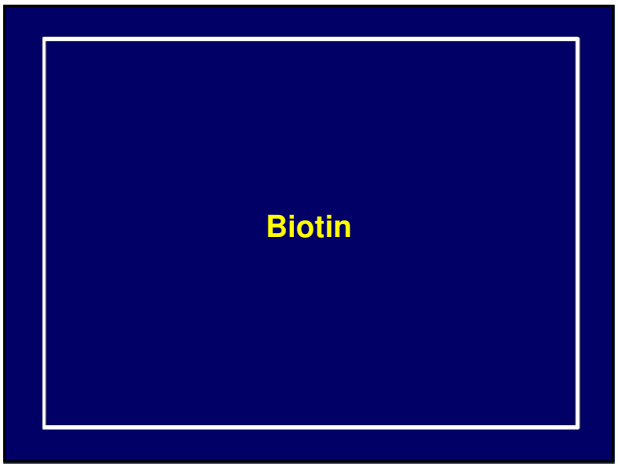


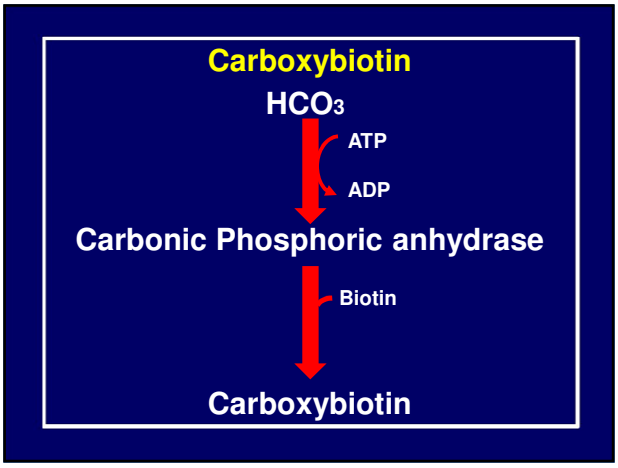
First identified in 1954 in butterfly wings

This co-enzyme functions as a hydrogen donor to 4 hydroxylase enzymes.

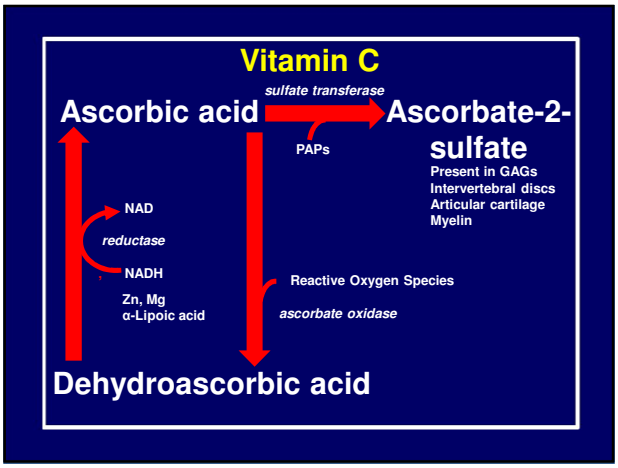
1. Phenylalanine hydroxylase
2. Tyrosine hydroxylase
3. Tryptophan hydroxylase
4. Nitric oxide synthase


TETRAHYDROBIOPTERIN
O2
phenylalanine hydroxylase
tyrosine hydroxylase t
ryptophan hydroxylase
nitric oxide synthase
H2O
NAD(P)
reductase
Vit C
NAD(P)H
DIHYDROBIOPTERIN


Biotin


Carboxybiotin
HCO3
ATP
ADP
Carbonic Phosphoric anhydrase
Biotin
Carboxybiotin

Vitamin C
Ascorbic acid

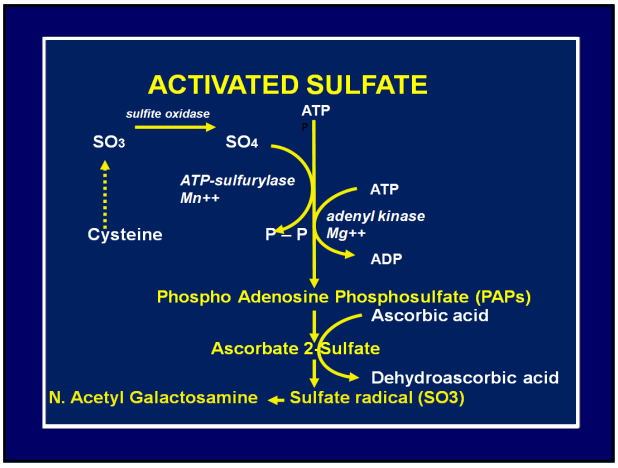


The highest concentration of Vitamin C is in the **adrenal glands and the pituitary gland.** Decreasing then are the eye lens, liver, brain, spleen, pancreas, kidney, lungs, heart and testes.

Vitamin C has a half life of 16 days with a turn over of 1mg / kilogram of body weight / day. (70mg)

There is a body pool of 22mg of Vitamin C per kilogram of body weight. **(1540mg)**

Following a oral dose, the peak of plasma occurs in **3 hours.**



Function

Collagen synthesis
Degradation of Tyrosine
Synthesis of Noradrenalin
Bile acid formation
Adrenal cortex
Absorption of iron
Antioxidant

Vitamin C is necessary for the formation of **hydroxyproline and hydroxylysine** found in collagen. Hydroxylysine is necessary for the cross-linkage which gives the tensile strength to collagen.

Deficiency of Vitamin C, most of the pathological changes are associated with defective collagen in **blood vessels and intracellular cement** substances.

Vitamin C is required in the biosynthesis of carnitine, a compound that transports the long chain fatty acids across the mitochondrial membrane.

Thus without adequate Vitamin C, mitochondria cannot oxidise fatty acids.

So Vitamin C may have a role in weight control and heart disease.

Deficiency symptoms

Lassitude, weakness, irritability, muscle and joint pains, loss of weight, bleeding gums, gingivitis, loosening of teeth. Petechial and other haemorrhages.

Recurrent infections

Men generally need more Vitamin C than women.

Dr Goodheart says 2gm for men, 1gm for women.

Men have a higher risk of heart attacks.

Dr Goodheart says

Challenge patients who bruise easily against Vitamin C, Bioflavonoids and Vitamin K.

Also Pyridoxal-5-phosphate.

Sources

Rosehips, blackcurrants, guavas, parsley, kale, horseradish, broccoli, peppers, tomato puree, sprouts.

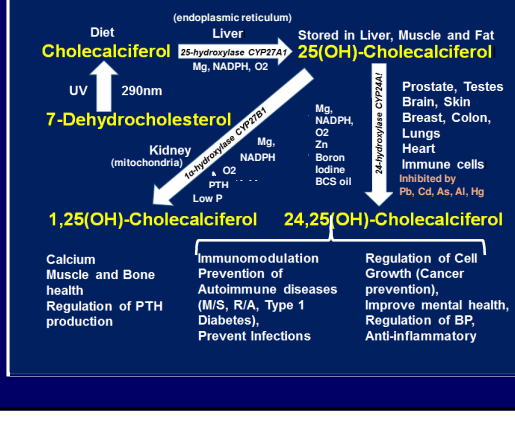
RDAs

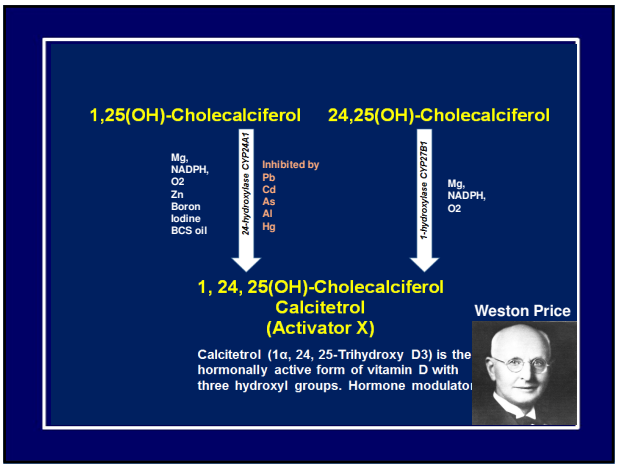
UK 60mg USA 120mg?

Functional test for Vitamin C

1. Strong muscle weakens to either proline or lysine
2. Weakness negated either hydroxyproline or hydroxylysine respectively
3. Weakness negates with Vitamin C

Vitamin D
Cholecalciferol





Applied Kinesiology Challenges

From a weakness for strengthening

1. Challenge with Cholecalciferol
2. Challenge with 25 (OH) Vit D3
3. Challenge with 1.25 (OH) Vit D3
4. Challenge with 24.25 (OH) Vit D3
5. Challenge with 1.24.25 (OH) Vit D3

Precursor, where applicable will weaken a strong muscle if enzyme inhibited.

1. Cholecalciferol give Cholecalciferol in oil such as Hempseed
2. 25 (OH) Cholecalciferol give Cholecalciferol in Black cumin seed oil
3. 1.25 (OH) Cholecalciferol give Cholecalciferol in Black cumin seed oil

4. 24.25 (OH) Cholecalciferol give Cholecalciferol in Black cumin seed oil

5. 1.24.25 (OH) Cholecalciferol give Cholecalciferol in Black cumin seed oil + Vitamin K2

Consider probiotics to regenerate enzymes

Heme dependant enzymes

Hemoglobin – Carries Oxygen in red blood cells
Myoglobin – Stores Oxygen in muscle fibres
Catalase - Reduces H_2O_2 to water
Cyclo-oxygenase – Synthesizes PgE1, PgE2 and PgE3
Cystathionine synthase – Converts Homocysteine to Cysteine
Cytochrome C – Transfers electroms from Complex III to Complex IV
Cytochrome C oxidase – Tansfers electrons in Complex IV to Oxygen
Cytochrome p450 - Detoxifies endogenous and exogenous chemicals
Myeloperoxidase – Synthesises Hypochlorite from H_2O_2
Nitric oxide synthase – Synthesises Nitric oxide from Arginine
Peroxidases – Reduce H_2O_2 to water
Sulfite oxidase – Synthesises Sulfate from Cysteine sulphite

Low Heme synthesis

↓

Low 24 hydroxylase CYP 24A1 expression

↓

Low synthesis of 24, 25 (OH) Vitamin D3

↓

Low synthesis of 1, 24, 25 (OH) Vitamin D3

Vitamin D is not really a vitamin since it can be synthesised in the skin but more of a steroid hormone, and under most conditions that is the major source of the vitamin.

Only when sunlight exposure is inadequate is a dietary source required.

In humans, the most important compounds are **vitamin D_3** (also known as cholecalciferol) and vitamin D_2 (ergocalciferol)

Its main function is in the regulation of **calcium, magnesium, iron, phosphate and zinc** absorption and homeostasis, NOT JUST CALCIUM. Most of its actions are mediated by of nuclear receptors that regulate gene expression.

In the liver, cholecalciferol (vitamin D_3) is converted to calcidiol, which is also known as 25-hydroxycholecalciferol, or 25-hydroxyvitamin D_3 — abbreviated.$25(OH)D_3$. Ergocalciferol (vitamin D_2) is converted in the liver to 25-hydroxyvitamin D_2 — abbreviated $25(OH)D_2$.

These two specific vitamin D metabolites are measured in serum to determine a person's vitamin D status.

Part of the Calcidiol ($25(OH)D_3$) is converted by the kidneys to Calcitriol ($1.25(OH)D_3$) one of the biologically active form of vitamin D.

Calcitriol (1.25 OH D3) circulates as a hormone in the blood, regulating the concentration of calcium and phosphate in the bloodstream and promoting the healthy growth and remodeling of bone.
Calcitriol (1.25 OH D3) also affects neuromuscular and immune function.

Sun exposure
1. 1 MED (Minimal Erythermal Dose) enough sun time to give a slight pinkness to the skin.
2. Up to 20,000IU often within 30 minutes depending on skin tone.
3. No lotion. SPF 15 blocks 95%, SPF 30 and above blocks 99%.
4. Aim for 20mins of 40% skin exposure per day.

September 21st to March 21st no UVA so no Vit D produced. Solely reliant upon summer production and dietary intake.
Vitamin D slowly released from fat stores over the winter.
Sunshine Vitamin D half life is 6 weeks.

Darker skin. More melanin = less Vitamin D production
Obesity – Vitamin D stored in adipose tissue (up to 40% more Vitamin D required)
Elderly – Partly less sun exposure and reduced skin ability to synthesise Vitamin D.

Optimal levels
2.5 nmol/l = 1ng/ml

<25nmol/L (10ng/ml) Deficient

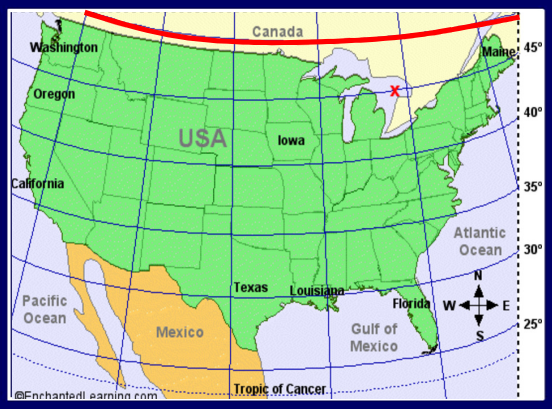
50-87.4 nmol/L (20-35ng/ml) Insufficient

125-250nmol/L (50-100ng/ml) Optimal

45 year olds across the UK (latitude 52.4º) between 2002-2004 Using <75nmol/L as reference range.

Nearly 90% of subjects deficient in the winter.

60% of subjects deficient all year.



Common Clinical Symptoms

- Low back pain
- Diffuse body aches and pains
- Growing pains
- Tender bones on palpation
- Shin pain
- Depression
- Fatigue
- Steroid hormone imbalances

How does deficiency cause symptoms.

1. Less calcium absorbed
   - i) Increased PTH
   - ii) Release of calcium from bone
   - iii) Unable to mineralise collagen matrix
   - iv) Hydrates and expands periosteal coverings

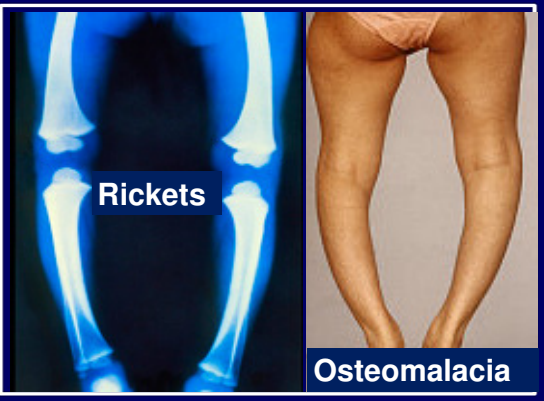
How does deficiency cause symptoms.

2. Central hypersensitivity
   - i) Nociceptors express Vitamin D receptors
   - ii) Deficiency leads to hyper-innervation of skeletal muscle leading to muscle hypersensitivity and pain.

How does deficiency cause symptoms.

3. Pro-inflammatory state
   - i) Deficiency shown to create higher scores on Severity Scale for Somatic Symptoms (SSS)
   - ii) Vitamin D shown to reduce hs-CRP levels

Rickets, a childhood disease, is characterized by impeded growth and soft, weak, deformed long bones that bend and bow under their weight as children start to walk. This condition is characterized by bow legs, which can be caused by calcium or phosphorus deficiency, as well as a lack of vitamin D.



Osteomalacia is a disease in adults that results from vitamin D deficiency. Characteristics of this disease are softening of the bones, leading to bending of the spine, bowing of the legs, proximal muscle weakness, bone fragility, and increased risk for fractures.

Osteomalacia reduces calcium absorption and increases calcium loss from bone, which increases the risk for bone fractures. Osteomalacia is usually present when 25-hydroxyvitamin D levels are less than about **10 ng/mL**. The effects of osteomalacia are thought to contribute to chronic musculoskeletal pain.

Vitamin D toxicity is rare. The threshold for vitamin D toxicity has not been established. Vitamin D toxicity is not caused by sunlight exposure (self regulating), but can be caused by supplementing with very high doses of vitamin D.

In healthy adults, sustained intake of more than 1250 µg/day (50,000 IU) can produce overt toxicity after several months and can increase serum 25-hydroxyvitamin D levels to **150 ng/ml** and greater.

Hypercalcemia is a strong indication of vitamin D toxicity, noted with an increase in urination and thirst. If hypercalcemia is not treated, it results in excess deposits of calcium in soft tissues and organs such as the kidneys, liver, and heart, resulting in pain and organ damage. Test with **calcium phosphate.**

Exposure to sunlight for extended periods of time does not normally cause vitamin D toxicity. Within about 20 minutes of ultraviolet exposure in light-skinned individuals the concentrations of vitamin D precursors produced in the skin reach an equilibrium, and any further vitamin D produced is degraded.

Vitamin D_3 (cholecalciferol) is produced through the action of ultraviolet irradiation (270-300nm) on it's precurser **7-dehydrocholesterol.** This molecule occurs naturally in the skin of animals and in milk.

Vitamin D_3 can also be made by exposing milk directly to UV (one commercial method).

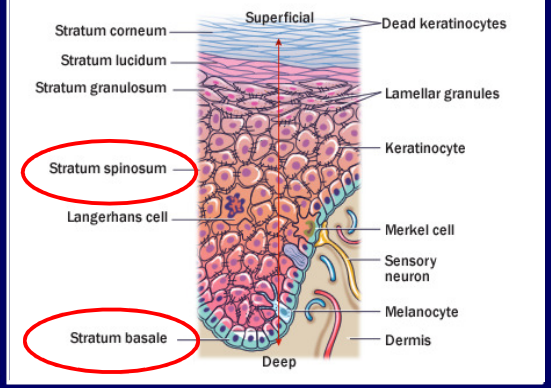
Vitamin D_3 is also found in oily fish, cod liver oil, hempseed oil and coco husks.

Vitamin D_2 is a derivative of ergosterol, which is produced by some kinds higher fungi such as mushrooms. The vitamin ergocalciferol (D_2) is produced from ergosterol, in response to UV irradiation.

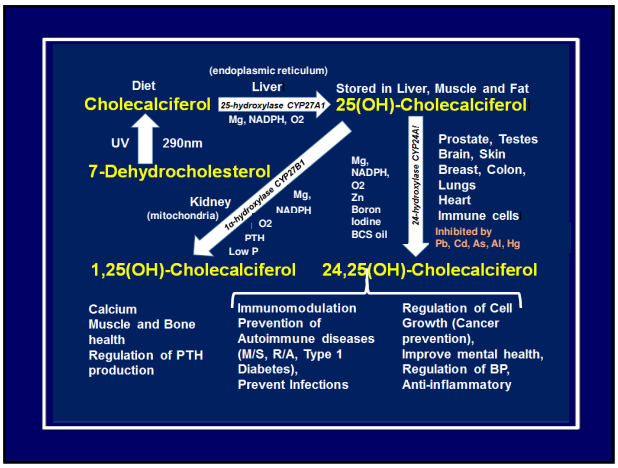
The biological fate for producing 25(OH)D from vitamin D_2 is expected to be the same as for 25(OH)D_3, although some controversy exists over whether or not D_2 can fully substitute for vitamin D_3 in the human diet.

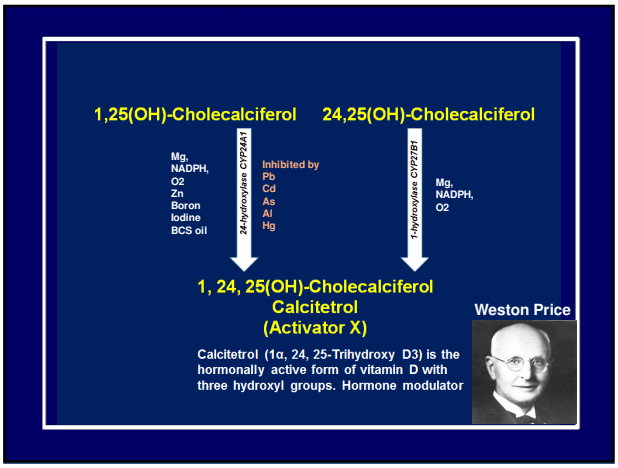
Exposure to light through **windows** is insufficient because glass almost completely blocks UVB light.

In the epidermal strata of the skin, production is greatest in the stratum basal and stratum spinosum.



Activation of Vitamin D

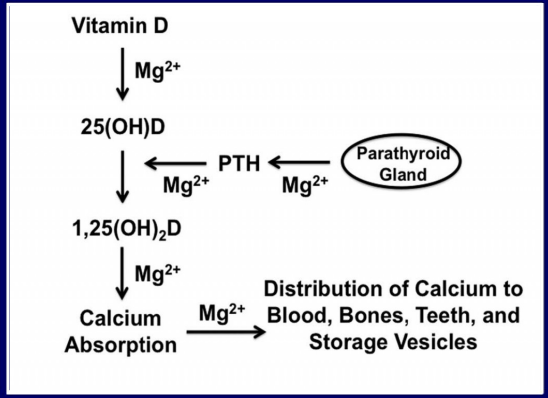




Vitamin D 25-hydroxylase **is a member of the cytochrome P450 superfamily of enzymes. An inherited mutation in the *CYP27A1* gene which eliminates the enzyme activity and is associated with low circulating levels of 25-hydroxyvitamin D and classic symptoms of vitamin D deficiency.**

Calcidiol is transported to the proximal tubules of the kidneys, where it is hydroxylated at the 1-α position to form **calcitriol** (1,25-dihydroxycholecalciferol and abbreviated to $1,25(OH)_2D$). This product is a potent ligand of the vitamin D receptor, which mediates some of the physiological actions of the vitamin.

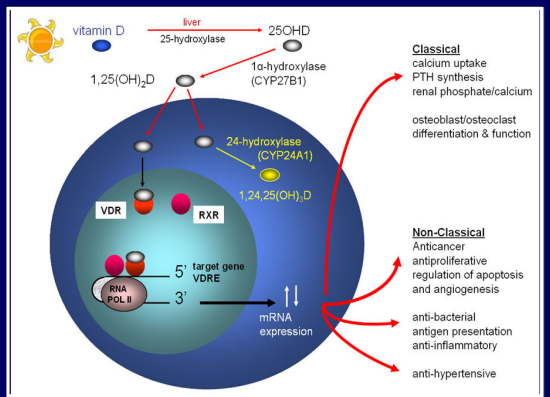
The conversion of 25 OH D3 to 1.25 OH D3 is catalyzed by the enzyme ***25-hydroxyvitamin D_3 1-alpha-hydroxylase***, the levels of which are increased by parathyroid hormone (and additionally by low calcium or phosphate) and modulated by magnesium.



25-Hydroxyvitamin D_3 1-alpha-hydroxylase **is also known as cytochrome p450 (CYP27B1). is located in the proximal tubule of the kidney and a variety of other tissues, including skin (keratinocytes), immune cells, and bone (osteoblasts).**

Calcidiol + NADPH + H_+ + O2 = Calcitriol + NADP + H2O

The active vitamin D metabolite calcitriol mediates its biological effects by binding to the vitamin D receptor (VDR), which is principally located in the nuclei of target cells.



The binding of calcitriol to the VDR allows the VDR to act as a **transcription factor** that modulates the gene expression of transport proteins, which are involved in calcium absorption in the intestine.

The Vitamin D receptor belongs to the nuclear receptor superfamily of steroid / thyroid hormone receptors, and VDRs are expressed by cells in most organs, including the brain, heart, skin, gonads, prostate, and breast.

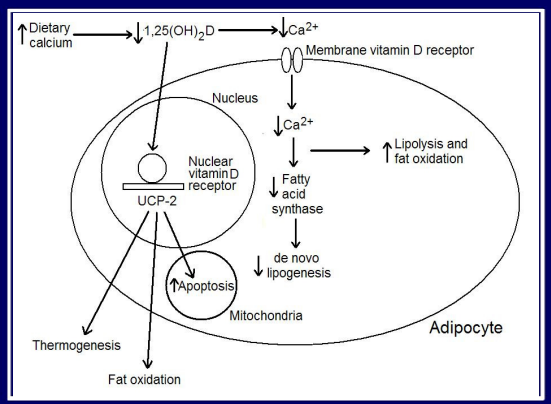
VDR activation in the intestine, bone, kidney, and parathyroid gland cells leads to the maintenance of calcium and phosphorus levels in the blood (with the assistance of **parathyroid hormone and calcitonin**) and to the maintenance of bone content.

Osteoclasts reabsorb bone

Stimulated by	Inhibited by
Vitamin A	Calcitonin
Parathyroid hormone	Estrogens
1,25 OH D3	TGF-β
IL1 and IL6	INFα
TNF	PgE2
TGF-α	

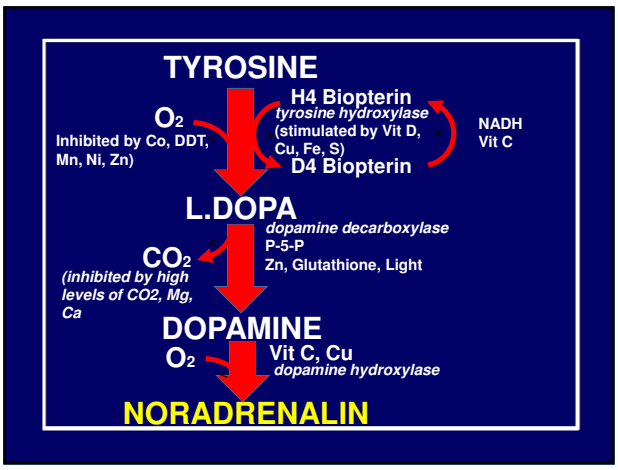
Osteoblasts form bone.

Stimulated by	Inhibited by
Parathyroid hormone	Corticosteroids
1,25-OH D3	
T3 and T4	
hGF and IGF-1	
PgE2	
TGF-β	
Progesterone	
DHEA	
Testosterone	
Dihydrotestosterone in women	



Thus, although it may initially appear paradoxical, Vitamin D is also critical for bone re-modeling through its role as a potent stimulator of bone resorption.
The VDR is known to be involved in cell proliferation and differentiation.

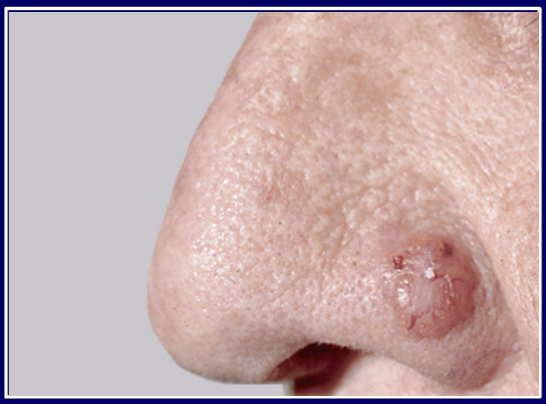
Vitamin D also affects the immune system, and VDRs are expressed in several white blood cells, including monocytes, macrophages and activated T and B cells.
Vitamin D increases expression of the *tyrosine hydroxylase* gene in adrenal medullary cells.



It also is involved in the biosynthesis of
1. Neurotrophic factors
2. Synthesis of nitric oxide synthase
3. Increased glutathione levels.

An alternative action is its role as a natural inhibitor of signal transduction by hedgehog (a hormone involved in morphogenesis).

The Hedgehog signaling pathway is a signaling pathway that transmits information to embryonic cells required for proper development. The pathway has roles in the adult. Diseases associated with the malfunction of this pathway include basal cell carcinoma.



Basal-cell carcinoma or basal cell cancer (BCC), a skin cancer, is the most common cancer. It rarely metastasizes or kills.

Daily dosage

Age	Minimum	Maximum
0-1 year	5mcg 200IU	25mcg 1000IU
1-18 years	5mcg 200IU	100mcg 4000IU
19-50 years	5mcg 200IU	100mcg 4000IU
51-70 years	10mcg 400IU	100mcg 4000IU
70 + years	15mcg 600IU	100mcg 4000IU
Pregnancy / Lactation	45mcg 600IU	100mcg 4000IU

Hearney and Holick contend the human physiology is fine-tuned to an intake of 4,000–12,000 IU/day from sun exposure with concomitant serum 25-hydroxyvitamin D levels of 40 to 80 ng/ml (100-200 nmol/l) and this is required for optimal health.

(1 ng/ml = 2.5 nmol/l)

A serum 25-hydroxyvitamin D level of 20-50 ng/ml (150 nmol/l) is desirable for bone and overall health.

The risk of **cardiovascular disease** is lower when vitamin D ranged from 8-24 ng/ml (20 to 60 nmol/l).

Health benefits
Cancer
Cardiovascular disease
Hypertension
Diabetes
Mortality
Bone health
Multiple sclerosis
Immune system
Muscle function. Inflammatory response

Sources
Vitamin D2 – Mushrooms exposed to UV
Alfalfa
Cocao husks
Hemp seed
Vitamin D3 –Fish liver oil
Oily fish
Whole egg
Beef liver

Serum concentration of **25(OH)D** is the best indicator of vitamin D status. It reflects vitamin D produced cutaneously and that obtained from food and supplements and has a fairly long circulating **half-life of 15 days.**

25(OH)D functions as a biomarker of exposure, but it is not clear to what extent 25(OH)D levels also serve as a biomarker of effect (i.e., relating to health status or outcomes).
Serum 25(OH)D levels do not indicate the amount of vitamin D stored in body tissues.

In contrast to 25(OH)D, circulating $1,25(OH)_2D$ is generally not a good indicator of Vitamin D status because it has a short half-life of 15 hours and serum concentrations are closely regulated by parathyroid hormone, calcium, and phosphate. Levels of $1,25(OH)_2D$ do not typically decrease until Vitamin D deficiency is severe.

Enzymes that are induced by Vitamin D

Enzymes that are induced by Vitamin D

Tyrosine hydroxylase
Tryptophan hydroxylase
Cholesterol to pregnenalone
Nitric oxide synthase
Increases Glutathione levels

Enzymes that are induced by Vitamin D

Tyrosine hydroxylase
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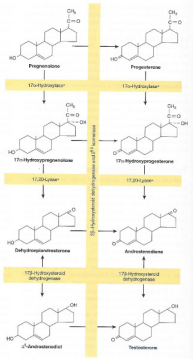
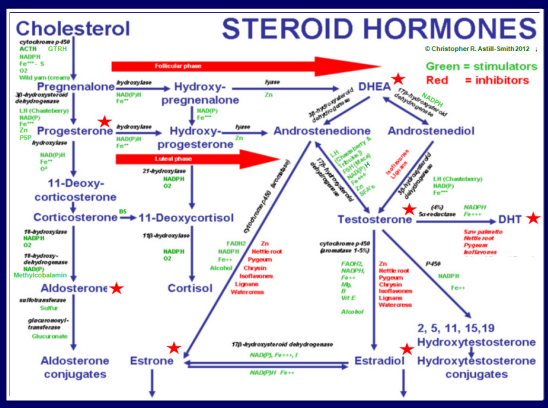
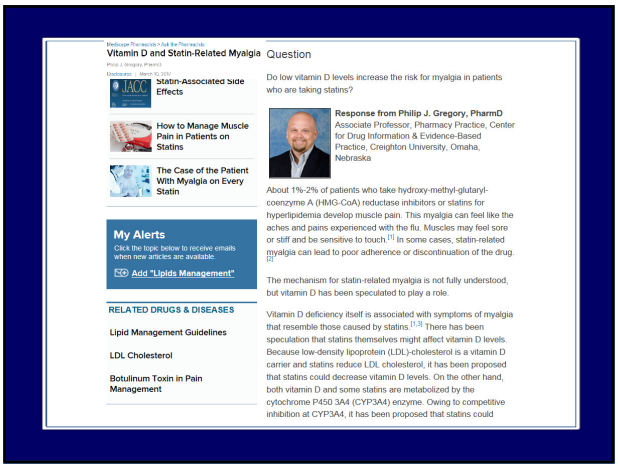
Cholesterol to pregnenalone
Nitric oxide synthase
Increases Glutathione





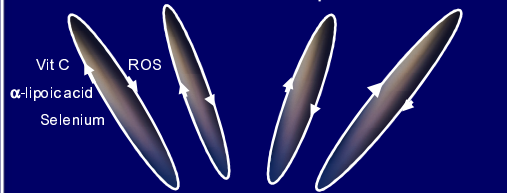


Vitamin E
Tocopherols and Tocotrienols

Vitamin E

Mixed Tocopherols

Alpha Tocopherol | Beta Tocopherol | Gamma Tocopherol | Delta Tocopherol



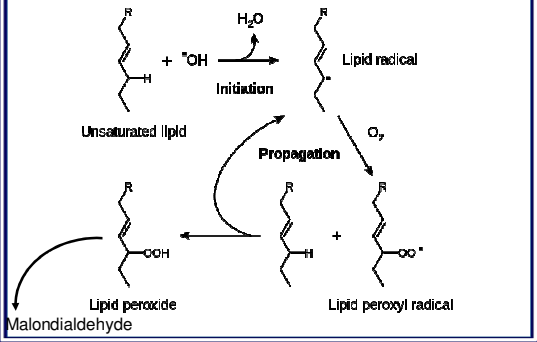
TOCOPHEROL RADICAL

Vitamin E refers to a group of compounds that include both tocopherols and tocotrienols. Of the many different forms of vitamin E, γ-tocopherol is the most common form found in the diet. γ-Tocopherol can be found in corn oil, soybean oil, margarine, and dressings.

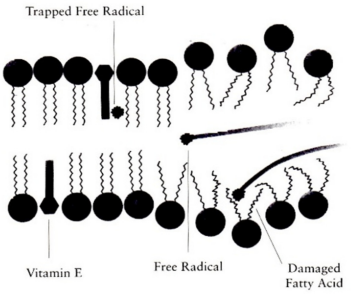
α-tocopherol, the most biologically active form of vitamin E, is the second-most common form of vitamin E in the diet. This can be found most abundantly in wheat germ oil, sunflower, and safflower oils.

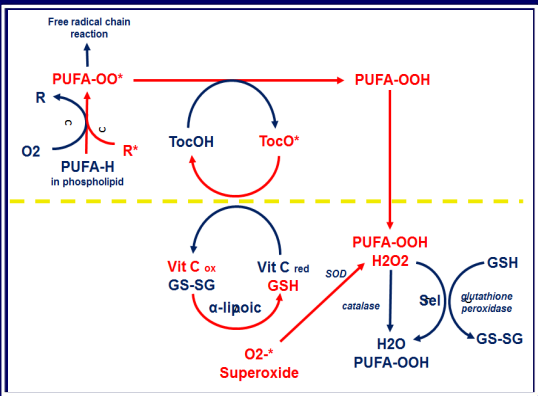
As a fat-soluble antioxidant, it interrupts the propagation of reactive oxygen species (ROS) that spread through biological membranes or through a fat when its lipid content undergoes oxidation by reacting with more-reactive lipid radicals to form more stable products.

RANCID FATS



Vitamin E Activity in Cell membrane



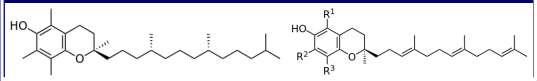


Vitamin E
the phospholipids of the mitochondria, endoplasmic reticulum and the plasma membranes possess affinities for tocopherols and the vitamin appears to concentrate predominantly at these sites.

Tocotrienols are members of the vitamin E family. The body contains four tocotrienols (alpha, beta, gamma, delta) and four tocopherols (alpha, beta, gamma, delta). However these have different antioxidant activities when measured in human plasma

The critical difference between tocotrienols and tocopherols is in that tocopherols have saturated side chains, whereas tocotreinols have unsaturated isoprenoid side chains (farnesyl isoprenoid tails) with three double bonds.

Tocopherol structure | Tocotrienol structure



Tocotrienols are compounds naturally occurring at higher levels in select vegetable oils, including palm oil, rice bran oil wheat germ, barley, saw palmetto, evening primrose, and certain other types of seeds, nuts, grains, and the oils derived from them.

High levels of up to 70% occur in palm oil. This vitamin E analogue typically only occurs at very low levels in the human body but different isomers function well as a physical antioxidant.

Vitamin E, nuclear receptors and xenobiotic metabolism ☆
Maret G Traber
Show more
Abstract
Supplemental vitamin E (α-tocopherol) is taken daily by more than 35 million people in the US. Following absorption and liver uptake, the fate of vitamin E is largely unknown. Of potential importance are recent clinical studies that have reported adverse effects of vitamin E that may be directly related to its hepatic metabolism. In an in vitro system, both vitamin E and rifampicin, a known stimulator of xenobiotic metabolism, activated the pregnane X receptor (PXR), an orphan nuclear receptor. PXR as a heterodimer with the retinoid X receptor (RXR), binds to specific *cis*-elements in the promoter regions of genes. PXR/RXR regulates a constellation of genes involved in xenobiotic detoxification, including oxidation, conjugation, and transporters. Importantly, PXR/RXR regulates the cytochrome P450 (CYP), CYP3A, involved in the hepatic detoxification of more than 50% of prescription drugs. Vitamin E acting as a PXR ligand could alter these PXR-mediated reactions. Unfortunately, the extent to which pharmacologic doses of vitamin E modulate these pathways in vivo has not been determined.

Vitamin K 1 and K2 Menaquinone

Menadione (K3)
(water soluble, most potent form but not found naturally)

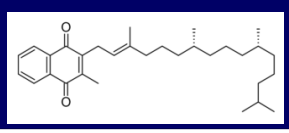
Menaquinone- 4, 7 (K2)
(fat soluble, from animal tissue and synthesised by intestinal bacteria)

MK4- Synthesized in artery walls, pancreas and testes.

MK7 -By bacterial fermentation in the colon by B. Subtilis.

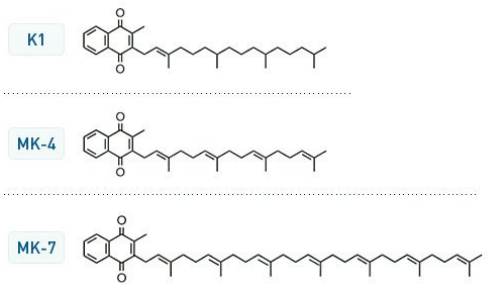
Phyloquinone (K1)
(fat soluble from plant tissue)

Phyloquinone (K1)
(fat soluble from plant tissue)



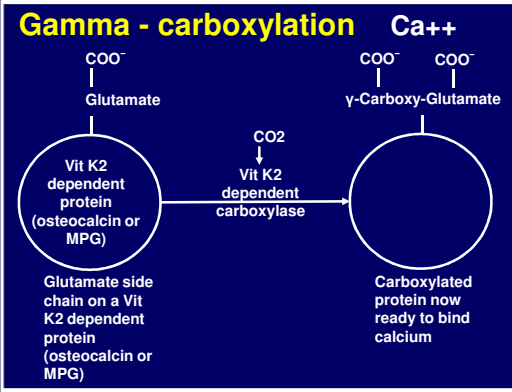
The best-known function of vitamin K in animals is as a cofactor in the formation of coagulation factors II (prothrombin), VII, IX, and X by the liver. It is also required for the formation of anticoagulant factors protein C and S. It is commonly used to treat warfarin toxicity.

Menaquinone- 4, 7 (K2)
(fat soluble, from animal tissue and synthesised by intestinal bacteria)



Vitamin K_2 or menaquinone has nine related compounds, generally subdivided into the short-chain menaquinones (with MK-4 as the most important member) and the long-chain menaquinones, of which MK-7, MK-8 and MK-9 are nutritionally the most recognized.

Gamma - carboxylation



Function of K2

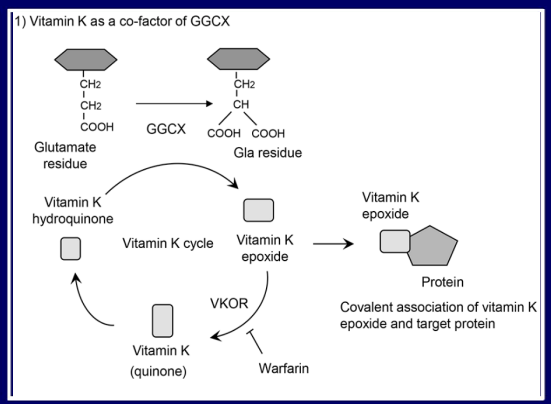
- Regulation of calcium
- Moves calcium into bones
- Removes calcium from arteries
- Fights osteoporosis
- Fights Coronary Heart Disease

K2 dependent enzymes

- K2 activates a protein called Osteocalcin, which attracts calcium into bones and teeth
- K2 activates a protein called matrix gla protein (MGP) which removes calcium from soft tissue like arteries and veins

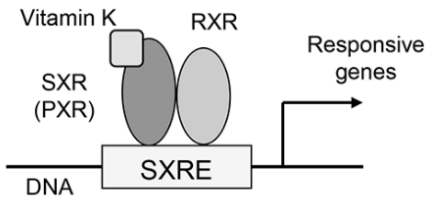
K2 dependent enzymes

- K2 is the cofactor for an enzyme called vitamin K dependent carboxylase
- This enzyme when activated by K2 alters the structure of osteocalcin and MGP to allow those proteins to bind calcium

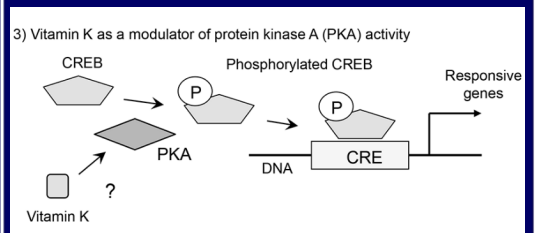


Multiple mechanisms of vitamin K actions. (1) GGCX catalyzes conversion of glutamate residues into Gla residues by incorporating an additional carboxyl group to glutamate. This reaction requires cyclic use of vitamin K. Vitamin K epoxide reductase (VKOR) is required for recycling vitamin K which is oxidized during γ-glutamyl carboxylation. Warfarin inhibits VKOR and vitamin K recycling, thereby suppressing GGCX activity. . Covalent binding of vitamin K epoxide and a target protein is also proposed as a novel mode of vitamin K action which is dependent on GGCX activity.

2) Vitamin K as a ligand of SXR/PXR



(2) On the other hand, we discovered GGCX-independent mode of vitamin K function mediated by transcriptional regulation [3] as compared to posttranscriptional modifications explained above. Vitamin K was found to be one of the ligands of the nuclear receptor, SXR, and its murine ortholog, PXR. This receptor is also called NR1I2 according to standardized nomenclature designated by the nuclear receptor committee. In 1998, SXR/PXR was cloned as a novel nuclear receptor that is mainly expressed in the liver and intestine [6]. At first, its functions were characterized as a ligand-dependent transcription factor which is activated by various pharmaceutical agents and xenobiotic compounds [7]. It was originally classified as an orphan receptor since the endogenous ligand was not known when it was cloned. It was later shown that some kinds of secondary bile acids (such as lithocholic acid) could be endogenous ligands for this receptor [8, 9]. It forms a heterodimer with 9-cis-retinoid acid receptor (RXR) on ligand stimulation. This complex then binds to SXR-responsive elements (SXRE) in the promoter or enhancer regions of target genes (Figure 1). Some of its target genes are the drug-metabolizing enzyme, such as *CYP3A4*, and the ABC (ATP-binding cassette) family transporter, *MDR1*. Because of that, a function of SXR/PXR is considered as a xenobiotic sensor-inducing genes involved in detoxification and drug excretion [10] and named as such. The discovery of novel vitamin K function as a ligand for SXR/PXR indicated that physiological and pathological processes mediated by PXR/SXR would be affected by vitamin K.



(3) Vitamin K also activates protein kinase A (PKA) with unknown mechanism. This action was suppressed by PKA inhibitor but not affected by stimulation with SXR agonist or knocking down of GGCX. Typical substrate of PKA is CREB (cyclic AMP-responsive element binding protein) and it binds to CRE (cyclic AMP-responsive element) within the promoter or enhancer regions of target genes when CREB is phosphorylated.

Lipoic acid
Thioctic acid

Lipoic acid

Octanoic acid + Cysteine

↓ Thiamine pyrophosphate

α-Lipoic acid

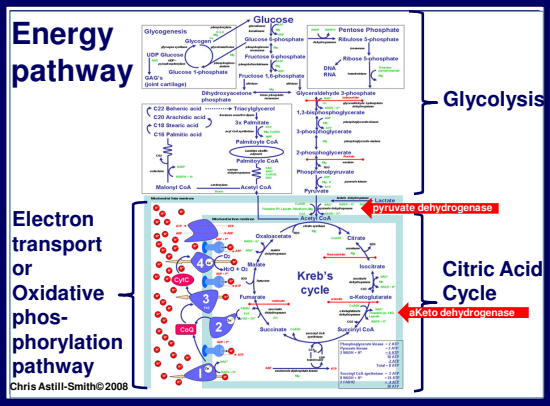
↓ Lysine

Lipoamide

↓ H_2

Dihydrolipoamide

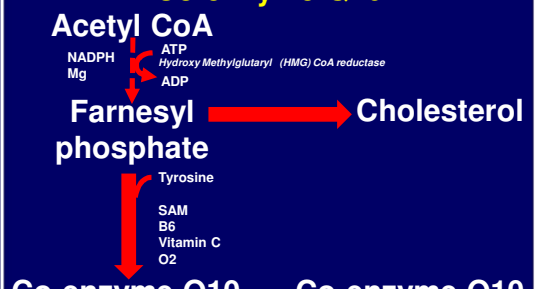
Lipoic acid (LA), also known as α-lipoic acid or thioctic acid is an organosulfur compound derived from octanoic acid. It is made in animals normally, and is essential
For aerobic metabolism.
As an antioxidant.
Toxic metal chelator.
Blood glucose modulator.



Gastrointestinal absorption is variable and decreases with the use of food. It is therefore recommended that dietary LA be taken 30-60 minutes before or at least 120 minutes after a meal. Maximum blood levels of LA are achieved 30-60 minutes after dietary supplementation.

Co-Enzyme Q10
Ubiquinone - Ubiquinol

Co-enzyme Q10



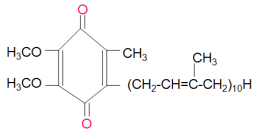
This fat-soluble substance, which resembles a vitamin, is present in most eukaryotic cells, primarily in the mitochondria. It is a component of the electron transport chain and participates in aerobic cellular respiration, which generates energy in the form of ATP.

Ninety-five percent of the human body's energy is generated this way. Therefore, those organs with the highest energy requirements—such as the heart, liver, and kidney—have the highest CoQ_{10}concentrations.

There are three redox states of CoQ_{10}: fully oxidized (ubiquinone), semiquinone (ubisemiquinone), and fully reduced (ubiquinol). The capacity of this molecule to act as a two-electron carrier (moving between the quinone and quinol form) and-

a one-electron carrier (moving between the semiquinone and one of these other forms) is central to its role in the electron transport chain due to the iron–sulfur clusters that can only accept one electron at a time, and as a free radical-scavenging antioxidant.

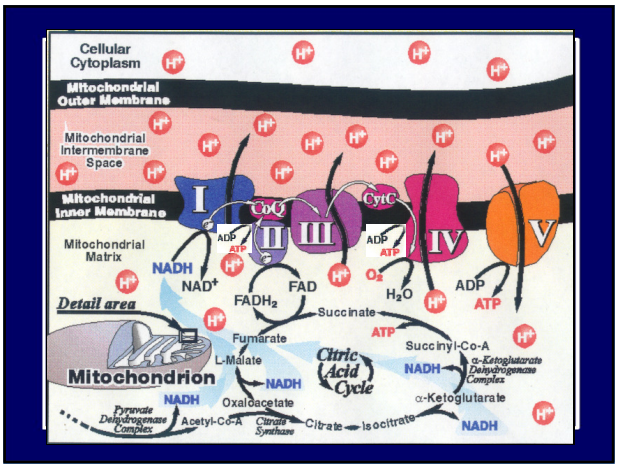
Ubiquinone (Coenzyme Q10)



(2,3-dimethoxy, 5-methyl,
6- polyisoprene parabenzoquinone)

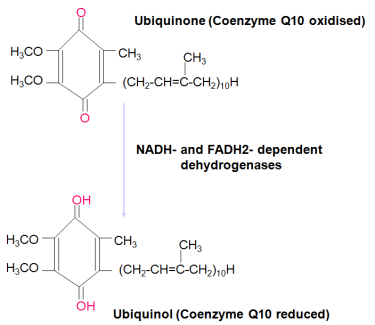
Functions of CoQ10

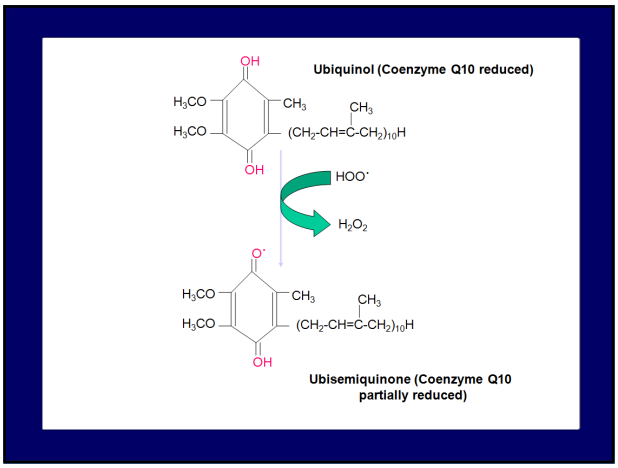
- Mitochondrial energy coupling
- Antioxidant
- Generation of intracellular signals
- Control of membrane structure and phospholipid composition

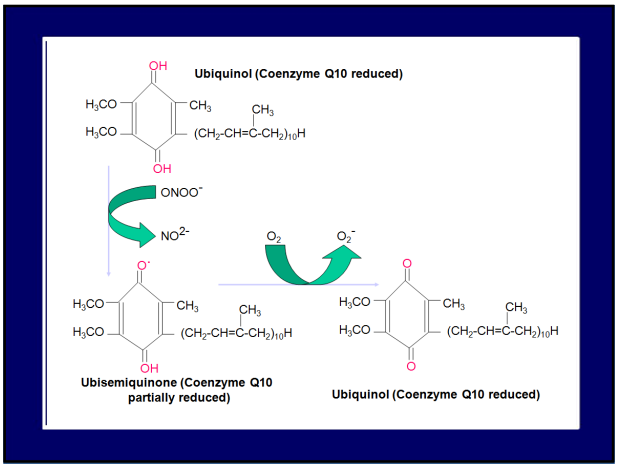


CoQ deficiency in humans

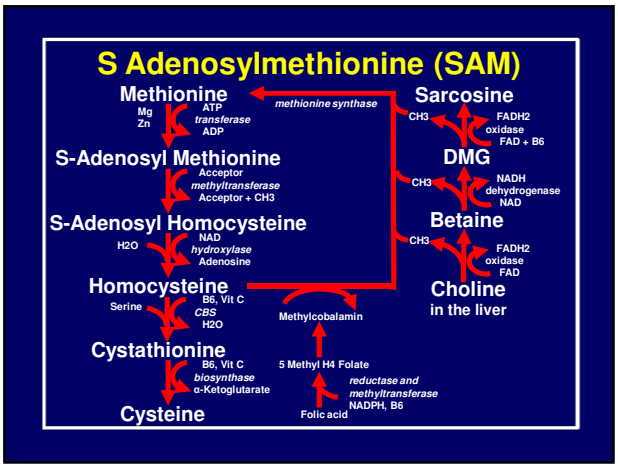
Basis	Tissue	% decrease
Age	Myocardium	72
Age	Heart	58
Age	Pancreas	83
Age	Adrenal	50
Age	Kidney	45
Age	Epidermis	75
Age	Liver	17
Statins	Serum	20-30
Diabetes	Serum	65







S. Adenosyl Methionine
SAMe



SAMe is a common co-substrate involved in methyl group transfers, transsulfuration, and aminopropylation. Although these anabolic reactions occur throughout the body, most SAM-e is produced and consumed in the liver.

More than 40 methyl transfers from SAM-e are known, to various substrates such as nucleic acids, proteins, lipids and second ary metabolites. It is made from adenosine triphosphate (ATP) and methionine by methionine adenosyltransferase.