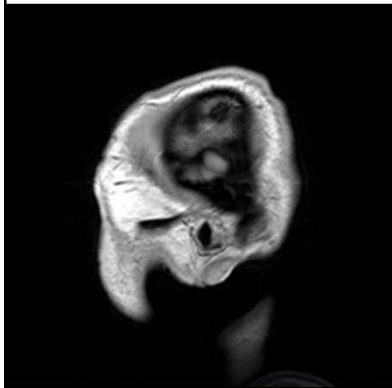


Neurodegenerative and Demyelinating Diseases



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1. Neurodegenerative Disorders

- ▶ A **neurodegenerative** disorder is defined simply as a condition in which **cells of the brain and spinal cord are lost**.
- ▶ Examples include Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis (ALS) and Alcoholic Cerebellar Disease.

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2. Demyelinating Disorders

- ▶ A **demyelinating** disorder is any disease of the nervous system in which the **myelin sheath** of neurons is damaged.
- ▶ Examples include multiple sclerosis, transverse myelitis, Guillian–Barre syndrome and Charcot–Marie–Tooth disease.

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Parkinson's Disease

- ▶ 10 million worldwide live with Parkinson's disease, 1 million in USA, which is more than the combined number of people diagnosed with multiple sclerosis, muscular dystrophy and ALS.



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Parkinson's Disease (PD)

- ▶ Symptoms of Parkinson's disease have been known and treated since medieval times .
- ▶ It was formally recognized and its symptoms documented in 1817 in *An Essay on the Shaking Palsy* by the British physician James Parkinson.
- ▶ It was originally known as paralysis agitans.

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Parkinson's Disease



- ▶ Approximately 60,000 Americans are diagnosed with Parkinson's disease each year, and this number does not reflect the thousands of cases that go undetected.

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Tremor

- ▶ This is the most common and recognized symptom.
- ▶ It is sometimes termed a pill rolling tremor.
- ▶ The tremor is a resting tremor and disappears with movement and sleep.

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Tremor

- ▶ It affects the distal extremity and is usually unilateral at onset
 - This tells you the contralateral basal ganglia is the most affected.
- ▶ It cycles at about 3–6 Hz.
- ▶ Usually the upper limb is affected first, followed by the ipsilateral lower limb within 1 year followed by contralateral limb involvement within 3 years.

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Benign essential tremor vs. Parkinson's

- ▶ Some patients have benign essential tremors that begin later in life and could possibly be confused with PD.
- ▶ Benign essential tremor's will disappear or greatly reduce with alcohol consumption.
- ▶ The tremor of PD will not.
- ▶ This is often the only way to tell the difference between early PD and benign essential tremors.

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Rigidity

- ▶ Affects all somatic muscles but favors flexors.
- ▶ This results in the stooped forward posture characteristic of PD.
- ▶ Passive movement of limbs illustrates the lead pipe rigidity.



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Bradykinesia

- ▶ Often patients report the simple activities require deliberate planning and guided execution.
- ▶ EMG studies show that PD causes a reduction in the initial agonist burst activity for a prime mover.
- ▶ The boost to lower motor neuron activity from the basal ganglia is weak because of decreased supplemental motor area contribution.

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Postural Instability

- ▶ Patients will fall easily from accidental contact.
- ▶ They fall stiffly ('like a telegraph pole' as described by Dr. Parkinson).
- ▶ The problem is with the anticipatory postural response.
 - Because of the slowness of action, stability is lost.

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Other Symptoms

- ▶ Other motor symptoms include:
 - Mask like face
 - Small handwriting
 - Small steps when walking
 - Decreased arm swing
 - “Turning around on a pedestal”
 - Speech and swallowing disturbances

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Main Neurotransmitters in PD

- ▶ The important neurotransmitters to consider are:
 - Glutamate
 - GABA
 - Dopamine

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Glutamate

- ▶ Glutamate is rarely low because of its importance.
- ▶ Over facilitation of glutamate leads to excitotoxic death of neurons.
- ▶ PD patients should be off of all artificial flavors and sweeteners because they over facilitate NMDA receptors in the brain causing further cell death.

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Evidence For Nutrition In Neurodegenerative Diseases

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Treatment – Diet

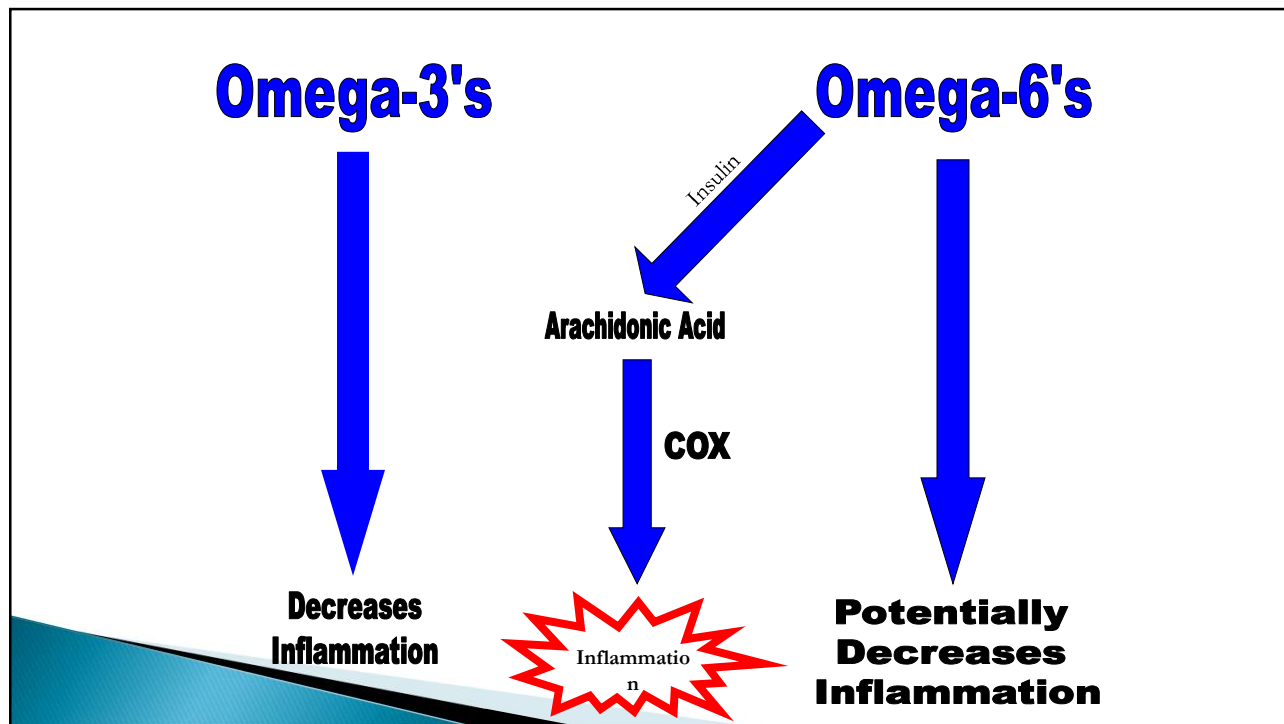
- ▶ Increasingly, PD is being known as a **neuroinflammatory** disease.
- ▶ Therefore, diets designed to reduce inflammation are important.
- ▶ The research also points to a ketogenic diet as beneficial.
- ▶ The key to combining a ketogenic diet and an anti-inflammatory diet is regulating insulin.
- ▶ In both scenarios you want insulin to be extremely low.
- ▶ Low insulin protects the patient from inflammation and also means they are not consuming carbohydrates which leads to ketosis.

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Treatment – Diet cont.

- ▶ The key is to balance omega-3s with the omega-6s.
- ▶ Raise the n-3s and lower the n-6s.
- ▶ Diets that have a favorable ratio of n-3s:n-6s are inherently low carbohydrate because the n-6s are found in high amounts in grain.

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Research – Exercise

- ▶ “Exercise has been shown to be potently neuroprotective in several neurodegenerative models, including 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) model of Parkinson's disease (PD).”

Brain Res. 2010 Jan 29.

20

Research



- ▶ “Combined R-alpha-lipoic acid and acetyl-L-carnitine exerts efficient preventative effects in a cellular model of Parkinson's disease.”

J Cell Mol Med. 2010 Jan;14(1-2):215-25.

21

Research

- ▶ “Studies of in vitro models of neuronal toxicity and animal models of neurodegenerative disorders have demonstrated potential neuroprotective effects of CoQ10.”



Neuropsychiatr Dis Treat. 2009;5:597-610. Epub 2009 Nov 16.

22

Research



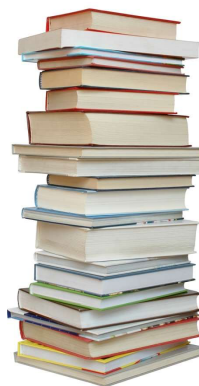
- ▶ “Bioconjugates of curcumin display improved protection against glutathione depletion mediated oxidative stress in a dopaminergic neuronal cell line.”

Bioorg Med Chem. 2010 Apr 1;18(7):2631-8.

23

Research

- ▶ “The modulation of NF- κ B pathway may have therapeutic potential for PD [because NF- κ B plays a key role in regulating neuroinflammation.]”



J Pharmacol Exp Ther. 2010 Jun;333(3):822-33.

24

Research

- ▶ “Dopamine (DA) turnover was increased after omega-3 PUFAs chronic supplementation. Therefore, it is proposed that omega-3 PUFAs action characterizes the adaptation of remaining neuronal activity, altering striatal DA turnover without modifying the estimated neuronal population.”

Neurosci Res. 2010 Mar;66(3):256-64

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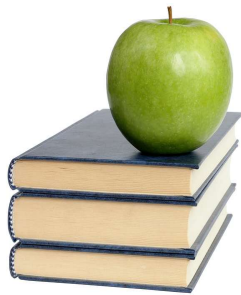
Research

- ▶ “These results reveal that PD patients taking fish oil, with or without antidepressants, presented improvement in depressive symptoms and indicate that the intake of omega-3 can be used with an antidepressant effect or as adjunctive therapy with some other medication.”

J Affect Disord. 2008 Dec;111(2-3):351-9.

26

Research



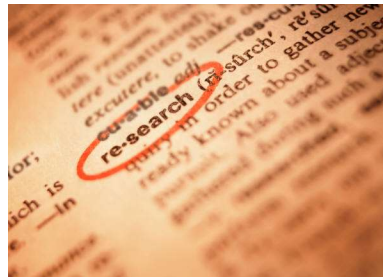
- ▶ “These data suggest that a high n-3 PUFA dietary intake exerts neuroprotective actions in an animal model of Parkinsonism.”

FASEB J. 2008 Apr;22(4):1213-25.

27

Research

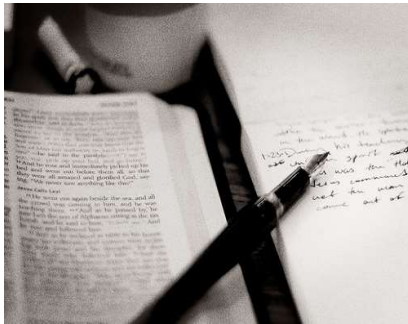
- ▶ “Low intake of vitamin B6 was associated with an increased risk of PD, independent of potential dietary and non-dietary confounders.”



Br J Nutr. 2010 Mar 26:1-8.

28

Research



- ▶ “Higher intake of vitamin E and beta-carotene may be associated with a decreased risk of PD.”

Eur J Neurol. 2010 May 18.

29

PD and heavy metals

- ▶ “Concordant exposures were residential, non-occupational pesticide and heavy metal exposure, each reported by 77.8% (7/9) of couples. Multiple exposures were reported by 88.9% (16/18) of subjects, most often residential agricultural chemical and heavy metal in combination.”
- ▶ (Study conducted on married couples both demonstrating PD symptoms)

Parkinsonism Relat Disord. 2010 Mar;16(3):163-6.

30

PD and heavy metals

- ▶ “Manganese exposure is cytotoxic and alters dopaminergic and GABAergic neurons within the basal ganglia.”



J Neurochem. 2009 Jul;110(1):378-89

31

PD and heavy metals

- ▶ “We found a high prevalence of extrapyramidal signs and symptoms in this group of male dental technicians working in a state technical high school in Rome. We believe that this finding may be due to the presence of toxins in the dental technician's work.”

BMC Neurol. 2007 Aug 8;7:24.

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Elimination of heavy metals

- ▶ If heavy metal overload is suspected it must be eliminated to achieve desired results.
- ▶ The basal ganglia is notorious for heavy metal deposition.
- ▶ The BBB is particularly thin in this area.
- ▶ Wilson's Disease

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PRODUCTS

- ▶ Dopatropic
- ▶ Neuperzine
- ▶ 5 MTHF Plus Forte
- ▶ Acetyl-L-Carnitine
- ▶ Lipoic Acid Plus
- ▶ CoQ Zyme 100 Plus

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Suggested Reading

- ▶ *A Clinician's View of Biotics' Products* by Harry O. Eidenier, Jr.
- ▶ *Functional Neurology for Practitioners of Manual Therapy* by Randy Beck.
- ▶ *The Human Brain* by John Nolte.
- ▶ *Principles of Neural Science 4th ed.* by Kandel, Jessel and Schwartz.
- ▶ *Clinical Neuroanatomy and Neuroscience 5th ed.* By Fitzgerald, Gruener and Mtui.
- ▶ *Neurological Differential Diagnosis 2nd ed.* By John Patten.
- ▶ *Cognitive Neuroscience - The Biology of the Mind 3rd ed.* by Gazzaniga, Ivry, and Mangun.

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2. Demyelinating Diseases

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Multiple Sclerosis



- ▶ MS is the classic demyelinating disease.
- ▶ Demyelination occurs in the spinal cord and brain causing a wide variety of symptoms.

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History

- ▶ The French neurologist Jean-Martin Charcot (1825–1893) was the first person to recognize multiple sclerosis as a distinct disease in 1868.
- ▶ Looking back in history cases that were probably MS have been described as early as 1200 A.D.

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MS Statistics

- ▶ About 1 in 700 people has MS.
- ▶ That's almost 400,000 cases in the US alone.
- ▶ World-wide 2.5 million people are suspected to have MS.
- ▶ Multiple sclerosis affects women twice as much as it affects men.



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MS Statistics



- ▶ MS occurs in most ethnic groups, including African-Americans, Asians and Hispanics/Latinos, but is more common in Caucasians of northern European ancestry.

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Signs and Symptoms

- ▶ MS is most often diagnosed between the ages of 20 and 40 although cases as young as 2 and as old as 75 have been reported.
- ▶ People at northern latitudes are more likely to be diagnosed.
- ▶ Symptoms vary widely and are often transient.

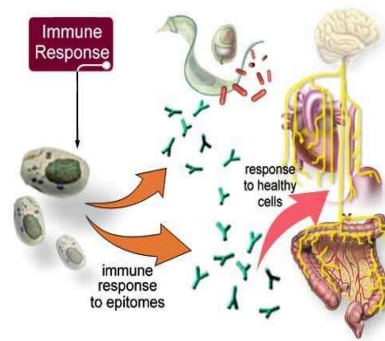
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Traditional Treatment of MS – long term management

- ▶ Interferon beta – 1a (Avonex)
 - Believed to work by counteracting cell surface expression of proinflammatory or pro-adhesion molecules on immune cells.
- ▶ Interferon beta – 1b (Betaseron)
 - Acts similarly to above but may also increase circulating transforming growth factor (TGF) –beta (anti-inflammatory) in serum.

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Pathophysiology of MS



- ▶ Demyelination of the CNS is the cardinal problem in MS.
- ▶ Autoimmunity and inflammation both play a role.

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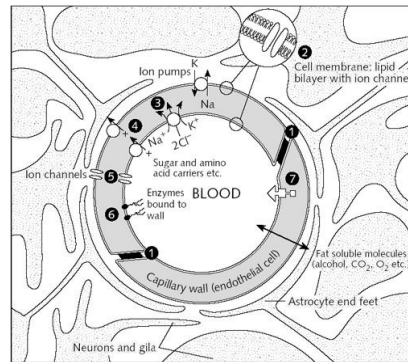
Autoimmune

- ▶ MS is widely considered to be an autoimmune disease first with concomitant inflammatory issues.
- ▶ The autoimmune issue is also complicated by an individual's genetics and environmental factors.

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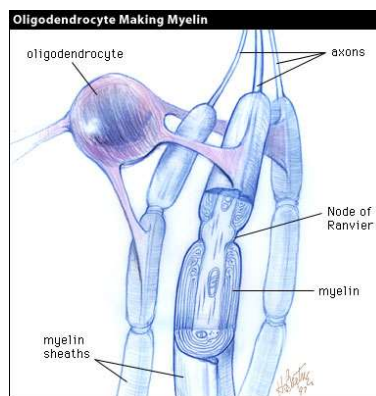
Pathophysiology

- ▶ The earliest event in MS to occur is break down of the blood brain barrier.
- ▶ The loss of tight junctions allows lymphocytes into the brain.



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Pathophysiology



- ▶ Myelin producing oligodendrocytes are destroyed.
- ▶ Tissue edema reaches maximum at about 1 month with sclerosis evolving over the next several months.

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Pathophysiology

- ▶ Immature oligodendrocytes appear and attempt remyelination.
- ▶ Remyelination is incomplete.
- ▶ Eventually axons are destroyed.
- ▶ Activation of inflammatory cytokines also occurs and results in further neuronal degradation.
- ▶ The best term to describe the process of MS is *immune-mediated inflammatory demyelination*.

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MS – Diet and exercise

- ▶ Diet and exercise advice is identical to advice for PD patients.
- ▶ Controlling inflammation and keeping neuromuscular pathways healthy are a must.



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Research

- ▶ “In a 6-month pilot study, 12 subjects taking a regimen of nutritional supplements designed to promote myelin regeneration, improved significantly neurologically as measured by the Kurzke EDSS scale. These were significantly improved ($p=0.002$) compared to 6 control group patients taking multivitamins.”

Metab Brain Dis. 2006 Sep;21(2-3):121-37.

49

Research

B12

- ▶ “We found a significant relationship between MS and vitamin B12 deficiency, and also demonstrated a relationship between vitamin B12 deficiency, VEP and posterior tibial SEP in MS.”

J Clin Neurosci. 2009 Mar;16(3):399-403.

50

Research

- ▶ “Recent studies suggest that vitamin B12, in addition to its known role as a co-factor in myelin formation, has important immunomodulatory and neurotrophic effects.”



J Neurol Sci. 2005 Jun 15;233(1-2):93-7.

51

Research



- ▶ “The antioxidant lipoic acid (LA) treats and prevents the animal model of multiple sclerosis (MS).”

J Neuroimmunol. 2008 Aug 13;199(1-2):46-55.

52

Research in MS and Vitamin D



- ▶ MS research has moved to looking at vitamin D levels and for good reason.
- ▶ The connection is undeniable and research continues to mount that vitamin D is critical for many factors associated with MS.

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KappArest



- ▶ The theme of down regulating inflammatory markers in neurodegenerative and demyelinating diseases cannot be over emphasized.
- ▶ It is also a potent antioxidant.
- ▶ 2-3 capsules twice per day.

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Intenzyme Forte

- ▶ Combine **KappArest** with **Intenzyme Forte** for optimal free radical scavenging.
- ▶ **Intenzyme Forte** combines both animal and plant enzymes to effectively break down any aberrant proteins.
- ▶ Acute Phase or flare ups - 5 tablets 4 times per day on an empty stomach.
- ▶ Maintenance - 3 tablets 3 times per day.



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EFA supplementation

- ▶ An effective dose is two capsules twice per day.
- ▶ The combination of **Optimal EFAs** and **Biomega-3 Liquid** / **Biomega-1000** is essential for patients with poor diets because it balances the fatty acid profile most effectively.



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Free Radical Protection



- ▶ **BioProtect** is a broad spectrum antioxidant.
- ▶ It contains vitamins A, C, E and zinc and selenium as well as CoQ₁₀, glutathione, methionine, taurine and NAC.
- ▶ 2 capsules twice per day.

57

Free Radical Protection

- ▶ **NitroGreens** is a green drink with a very high antioxidant value.
- ▶ It contains grass juices from barley, wheat, oat, alfalfa and kamut (these grasses are gluten free), vegetable sprout concentrates from broccoli, cauliflower and kale, vegetable juices from beet and carrot, acerola berry extract, peppermint leaf and Stevia leaf extract.
- ▶ 1 scoop 1–2 times per day.



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Free Radical Protection



- ▶ Resveratrol is a potent anti-inflammatory and antioxidant.
- ▶ **ResveraSirt HP** is the best resveratrol supplement on the market.
- ▶ It supplies 250 mg of purified Trans Resveratrol with quercetin for its ability to slow the metabolism of resveratrol.
- ▶ 1 capsule twice per day.

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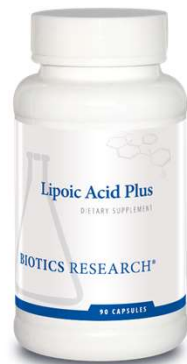
B₁₂-2000

- ▶ **B₁₂-2000** contain 2,000 micrograms of vitamin B₁₂, 800 micrograms of folic acid and 2 mg of phosphorylated vitamin B₆ per lozenge.
- ▶ It contains not only the necessary B₁₂ but also the folate and B₆ needed to reduce homocysteine.
- ▶ It is a dissolvable lozenge.
- ▶ Let 1 tablet dissolve completely twice per day.



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Lipoic Acid



- ▶ **Lipoic Acid** provides 100mg of alpha-lipoic acid per capsule.
- ▶ 1 capsule twice per day

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Vitamin D



- ▶ For adults Bio-D-Mulsion Forte is the most appropriate supplement.
- ▶ With 2,000 IUs per drop it is effective and easily taken.
- ▶ 4-5 drops per day for a total of 8,000-10,000 IUs per day.
- ▶ Monitor serum levels of vitamin D and achieve a level of 55-65ng/ml.
- ▶ Maintenance of this level will require between 2,000 and 4,000 IUs per day.

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