Nutrient Correlation Wheels

Deficiencies Correlated with Disease Conditions
**ADHD**

**Antioxidant Status**
Oxidative imbalance is prevalent in ADHD patients and is likely a causative factor. Deficiency of glutathione is common in ADHD.

**Choline**
Precursor to neurotransmitter acetylcholine, which regulates memory, focus, and muscle control (hyperactivity).

**Glutamine**
Precursor for the calming neurotransmitter GABA (gamma-aminobutyric acid) that affects mood, focus, and hyperactivity. Disruption of the glutamine-containing neurotransmission systems may cause ADHD.

**Folate**
Low folate status in pregnancy linked to hyperactivity in children. People with the MTHFR (methyltetrahydrofolate reductase) gene are predisposed to folate deficiency and more likely to have ADHD.

**Serine**
Administration of phosphatidylserine with omega 3 fatty acids improved ADHD symptoms (attention scores) significantly better than omega 3 fatty acids alone, suggesting a synergistic effect. Phosphatidylserine increases dopamine levels.

**Carnitine**
Reduces hyperactivity and improves social behavior in people with ADHD due to its role in fatty acid metabolism; some consider it a safe alternative to stimulant drugs.

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**Vitamin B6**
Evidence suggests high dose supplementation of B6 is as effective as Ritalin for ADHD, probably due to its role in raising serotonin levels.

**Magnesium**
Deficiency linked to poor function of the neurotransmitters that control emotion, social reactions, hyperactivity, and attention. Synergistic effect with Vitamin B6.

**Zinc**
Cofactor for dopamine synthesis which affects mood and concentration in ADHD. Low zinc depresses both melatonin and serotonin production affecting information processing and behavior in ADHD.

**Folate**
Low folate status in pregnancy linked to hyperactivity in children; People with the MTHFR (methyltetrahydrofolate reductase) gene are predisposed to folate deficiency and more likely to have ADHD.

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Additional references at http://www.spectracell.com/online-library-mnt-adhd-abstracts/
Vitamins D and E
Low vitamin D status is linked to anxiety; Animal studies confirm the role of vitamins D and E in reducing anxiety-related behavior.\cite{24,25,26,27}

Vitamin B3
One of the symptoms of severe B3 deficiency (pellagra) is anxiety; Pharmacological doses of B3 may enhance the calming effects of GABA in the brain; Converts tryptophan to serotonin.\cite{19,22,23}

Vitamin B6
Cofactor in synthesis of calming neurotransmitters such as GABA (gamma-aminobutyric acid), serotonin and dopamine.\cite{19,20,21}

Carnitine
Studies show that carnitine can reduce anxiety and improve feelings of well-being.\cite{28,29}

Chromium
Its effect on serotonin transmission may explain its anxiolytic (anxiety relieving) effect in animal studies.\cite{30,31}

Folate
Aids in production of neurotransmitters such as dopamine and serotonin, which have a calming effect on mood.\cite{19,32,33}

Inositol
A neurochemical messenger in the brain, inositol (vitamin B8) affects dopamine and serotonin receptors; Trials confirm it is very effective in reducing panic attacks.\cite{1,2}

Choline
Precursor to the neurotransmitter acetylcholine, which affects focus and mood; Low levels of choline linked to anxiety.\cite{3,4}

Serine
Exerts a calming effect by buffering the adrenal response to physical or emotional stress; Lowered anxiety scores of patients with post traumatic stress disorder.\cite{5,6,7}

Copper
Integral part of certain chemicals in the brain (such as endorphins) that calm anxious feelings; Anxiety-like behavior may be exacerbated with copper deficiency.\cite{8,9,10}

Selenium
Repletion of selenium to normal levels reduced anxiety scores in clinical trials; Some suggest the mechanism of action is due to its role in key regulatory proteins (selenoproteins).\cite{14,15}

Magnesium
Regulates the HPA (hypothalamic-pituitary-adrenal) axis which controls physical and psychological reactions to stress; Deficiency can induce anxiety and emotional hyper-reactivity.\cite{11,12,13}

Zinc
Reduces anxiety in clinical trials, possibly due to its interaction with NMDA (N-methyl-D-aspartate) receptors in the brain which regulate mood.\cite{16,17,18}

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Zinc Regulates immune system including allergic response; Deficiency can exacerbate asthma symptoms.\textsuperscript{31,32}

Selenium Part of the enzyme (called glutathione peroxidase) that protects against asthmatic lung tissue damage; Supplementation trials are promising.\textsuperscript{27,28,29,30}

Vitamin A Prevents exercise-induced asthma; Regulates bronchial responsiveness.\textsuperscript{25,26}

Vitamin B6 Binds with the chemical that causes airway constriction (histamine) and inactivates it; The common asthma drug theophylline depletes B6.\textsuperscript{23,24}

Vitamin C Dilates bronchial airways; Inhibits histamine-induced constriction of airways; Needed for production of epinephrine, which mitigates asthma attacks.\textsuperscript{21,22}

Vitamin D Higher levels increase lung capacity in asthmatics; Deficiency increases severity of asthma attacks.\textsuperscript{18,19,20}

Magnesium Promotes relaxation of bronchial smooth muscle; Inhibits histamine release; Reduces tendency to develop anaphylaxis; Low intracellular levels linked to asthma severity.\textsuperscript{1,2,3,4}

Carnitine Protects the surface of the lungs; Improves pulmonary function in asthmatics; Decreases inflammation in lung tissue.\textsuperscript{5,6,7}

Coenzyme Q10 Steroid medications for asthma cause damage to mitochondria (site of cellular energy production); CoQ10 repairs this damage and may reduce corticosteroid dosage in asthmatics.\textsuperscript{8,9}

Vitamin E In pulmonary epithelial tissue (inside surface of lungs), vitamin E fights inflammatory enzymes that cause asthmatic symptoms.\textsuperscript{10,11,12,13}

Choline Animal and human studies show that taking choline strongly suppresses oxidative stress in lung tissue caused by asthma.\textsuperscript{14,15}

Folate Plays a key role in cellular immunity; Low folate status linked to severity of an allergic response.\textsuperscript{16,17}

Vitamin E In pulmonary epithelial tissue (inside surface of lungs), vitamin E fights inflammatory enzymes that cause asthmatic symptoms.\textsuperscript{10,11,12,13}

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Additional references at http://www.spectracecell.com/online-library-mnt-asthma-abstract/
Vitamin A
One cause of autism may be a defect in a retinoid receptor protein (G-alpha protein) which is critical for language processing, attention and sensory perception; Evidence suggests natural vitamin A fixes this protein defect in autistics.1,2

Vitamin D
High dose vitamin D therapy reversed autistic behaviors in severely deficient children; Maternal vitamin D deficiency may predispose children to autism.3,4,5

Carnitine
Transports fatty acids into cells; Low carnitine (common in autism) impairs the ability to use fatty acids for learning and social development.6,7

Zinc
Eliminates toxic mercury from brain tissue; Zinc/ copper ratio is particularly low in autistic kids; Low zinc impairs the protein (called metallothionein) that removes heavy metals from the body.8,9,10

Magnesium
Cofactor for the neurotransmitters that affect social reactions and emotion; Autistics have low levels; Improves effectiveness of B6 therapy.11,12,13

Vitamin B6
Cofactor the neurotransmitters serotonin and dopamine; Conversion of B6 to its active form is compromised in many autistics; Supplementation trials with B6 resulted in better eye contact, speech and fewer self-stimulatory behavior in autistics; Some consider B6 in combination with magnesium to be a breakthrough treatment for autism.14,15

Vitamin B12
Low B12 impairs methylation processes; Low zinc impairs the protein (called metallothionein) that removes heavy metals from the body.8,9,10

Vitamin C
Improved symptom severity and sensory motor scores in autistic patients possibly due to interaction with dopamine synthesis; Vitamin C also has a strong sparing effect on glutathione.26,27

Folate
Oral folate therapy can resolve symptoms of autism in some cases, particularly in autistics with genes that impair folate dependent enzymes.31,32,33

Glutamine
Blood levels of this amino acid which acts as a neurotransmitter are particularly low in autistics. Glutamine also helps prevent leaky gut syndrome, which can exacerbate autistic symptoms.28,29,30

Glutathione & Cysteine
Commonly deficient in autistic patients, lack of these antioxidants impair detoxification and methylation processes; Low levels linked to neurological symptoms in autism which is often considered an oxidative stress disorder.21,22,23,24,25

Vitamin B1
Deficiency linked to delayed language development; Supplementation may benefit autistic patients.19,20

Vitamin B12
Low B12 impairs methylation (detoxification) which causes the neurological damage responsible for many autistic symptoms; Deficiency of B12 can cause optic neuropathy and vision loss in autistics; B12 raises cysteine and glutathione levels.16,17,18

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DEPRESSION

Magnesium
Deficiency damages NMDA (N-methyl-D-aspartate) receptors in the brain, which regulate mood; Well-documented anti-depressant effects.\(^1\),\(^2\),\(^3\),\(^4\)

Zinc
Improves efficacy of antidepressant drugs; Particularly useful for treatment resistant patients; Regulates neurotransmitters.\(^23\),\(^34\),\(^35\),\(^36\)

Serine
Regulates brain chemistry; Involved in NMDA receptor function; Acts as a neurotransmitter; Low levels correlate with severity of depression.\(^31\),\(^32\)

Antioxidants
Oxidative stress in the brain alters neurotransmitter function; Antioxidants protect our brain, which is very sensitive to oxidation; Several antioxidants – Vitamins A, C and E, Lipoic Acid, CoQ10, Glutathione and Cysteine – play a key role in prevention and treatment of depression.\(^28\),\(^29\),\(^30\)

Selenium
Integral part of regulatory proteins (selenoproteins) in the brain; Supplementation trials are promising; May alleviate postpartum depression.\(^5\),\(^6\)

Chromium
Elevates serotonin (feel-good neurotransmitter) levels in the brain; May be particularly effective on eating symptoms of depression such as carbohydrate craving and increased appetite, due to its effect on blood sugar regulation.\(^37\),\(^38\),\(^39\)

Selenium
Integral part of regulatory proteins (selenoproteins) in the brain; Supplementation trials are promising; May alleviate postpartum depression.\(^5\),\(^6\)

Folate
Building block for many “feel-good” neurotransmitters such as serotonin, dopamine and norepinephrine; Low folate causes poor response to anti-depressant meds; The lower the folate, the more severe the depression.\(^7\),\(^8\),\(^9\),\(^10\)

Vitamin B12
Depression may be a manifestation of B12 deficiency; Repletion of B12 to adequate levels can improve treatment response; B12 deficiency common in psychiatric disorders.\(^11\),\(^12\),\(^13\)

Vitamin B6
Cofactor for serotonin and dopamine production (feel good chemicals); Studies indicate that low levels may predispose people to depression.\(^14\),\(^15\),\(^16\)

Vitamin B2
Low B2 has been implicated in depression due to its role in methylation reactions in the brain.\(^17\),\(^18\)

Vitamin B2
Low B2 has been implicated in depression due to its role in methylation reactions in the brain.\(^17\),\(^18\)

Vitamin B6
Cofactor for serotonin and dopamine production (feel good chemicals); Studies indicate that low levels may predispose people to depression.\(^14\),\(^15\),\(^16\)

Vitamin D
Clinical trials suggest increasing blood levels of vitamin D, which is actually a hormone precursor, may improve symptoms of depression.\(^19\),\(^20\),\(^21\)

Inositol
Influences signaling pathways in the brain; Particularly effective in SSRI (selective serotonin reuptake inhibitor) sensitive disorders.\(^24\),\(^25\)

Carnitine
Increases serotonin and noradrenaline which lift mood; In trials, carnitine alleviates depression with few, if any, side effects.\(^22\),\(^23\)

Biotin
Part of the B-vitamin complex, biotin deficiency has induced depression in animal and human studies.\(^26\),\(^27\)

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Estrogen

Cysteine
Prevents oxidation of estrogen into a dangerous form that causes breast cancer. 29,30,31

Choline
Estrogen stimulates the breakdown of phosphatidylcholine (cell membrane) so those with low estrogen (postmenopausal women) require more choline; Detoxifies excess estrogen via methylation pathway. 1,2,3

Folate
Deficiency reduces estrogen levels; Excess folate is linked to some types of estrogen-related breast cancer; Detoxifies excess estrogen via methylation pathway; Regulates estrogen's effect on genes. 1,2,3

Zinc
Estrogen lowers risk of zinc deficiency; Zinc dependent proteins metabolize estrogen. 26,27,28

Magnesium
Cofactor for the enzyme that removes toxic forms of estrogen (catechol-O-methyltransferase); Estrogen alters magnesium levels throughout menstrual cycle. 1,2,25,26

Selenium
Estrogen levels affect how selenium is distributed to various tissues in the body. 22,23

Calcium
Calcium-D-glucarate lowers estradiol levels; Helps breakdown estrogen in the liver and convert it to a less toxic form. 1,20,21

Vitamin A
Helps metabolize the biologically active estrogen (estradiol) to an inactive form (estrone). 18,19

Vitamin E
Deficiency impairs estrogen detoxification pathway; Some forms of vitamin E inhibit estrogen action, especially in breast tissue; Low levels linked to higher estrogen. 1,16,17

Vitamin B6
Protects genes from estrogen-induced damage thus lowering risk of hormone related cancers; Detoxifies excess estrogen via methylation pathway; Estrogen-based oral contraceptives cause B6 deficiency. 4,5,6,7

Vitamin D
Regulates synthesis of estradiol and estrone; Enhances estrogen's protective effect on bones. 8,9,10

Vitamin C
Increases the most potent estrogen (estradiol) in women on hormone therapy; Lowers aromatase (enzyme that converts testosterone to estrogen) in ovaries. 11,12,13

Vitamin K
Inhibits estrogen activity by binding to estrogen receptors; Lowers the ratio of estradiol (strong estrogen) to estrone (weaker estrogen). 14,15

Vitamin B6

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Carnitine Transports fatty acids into mitochondria; Decreases both mental and physical fatigue in clinical trials.\textsuperscript{15,31,32}

B Vitamins Necessary for converting food into energy; Cofactors in the mitochondrial respiratory chain include B1, B2, B3, B5, B6, B12 and Folate.\textsuperscript{8,15,16,26-30}

Vitamin D Low levels are seen in patients with chronic fatigue syndrome; Deficiency causes reduced muscle strength.\textsuperscript{24,25}

Vitamin E Inverse correlation exists between fatigue and vitamin E levels.\textsuperscript{23}

Vitamin A When cellular levels of vitamin A are low, mitochondrial respiration and ATP production decreases.\textsuperscript{22}

Vitamin C Assists iron uptake and transport; Precursor to carnitine and several hormones that affect energy levels. Supplementation reduced fatigue in various trials.\textsuperscript{15,16,21}

Antioxidants Several studies confirm that oxidative stress exacerbates clinical symptoms of fatigue. Mitochondrial dysfunction (inefficient energy metabolism) can be treated therapeutically with antioxidants such as Selenium, Cysteine, a-Lipoic acid and Glutathione, of which unusually low levels are seen in chronic fatigue patients.\textsuperscript{12,16,18,19,20}

Chromium Promotes glucose uptake into cells, helping stabilize blood sugar.\textsuperscript{16,33}

Zinc Deficiency lowers immunity and may cause muscle fatigue; Involved in several reactions for energy metabolism.\textsuperscript{15,34,35}

Asparagine Supplementation of this amino acid delayed fatigue during exercise by decreasing the rate at which glycogen was used up; needed for gluconeogenesis, a process that allows glucose to be made from protein to prevent blood sugar from getting too low.\textsuperscript{1,2,3}

Biotin Helps liver utilize glycogen for energy. Animal studies confirm that biotin deficiency causes clinical fatigue.\textsuperscript{4}

Glutamine Mental and physical fatigue coincides with reduced levels of this amino acid in various tissues. Supplementation makes muscle more sensitive to insulin, increasing energy levels.\textsuperscript{5,6,7}

Serine Counteracts the overproduction of fatigue-causing stress hormones.\textsuperscript{8,9}

CoQ10 Deficiency causes fatigue due to its role in mitochondrial energy metabolism; therapeutic benefits particularly noticeable in chronic fatigue syndrome.\textsuperscript{10,11,12,15}

Fructose Intolerance Fatigue (and hypoglycemia) are classic symptoms of this condition, since it depletes the main form of cellular energy, ATP.\textsuperscript{13,14}

Magnesium Required to store energy molecule ATP; Repletion of magnesium in chronic fatigue patients shows clinical improvement in energy levels.\textsuperscript{15,16,17}

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For more references, go to [http://www.spectracell.com/online-library-mnt-fatigue-abstracts/](http://www.spectracell.com/online-library-mnt-fatigue-abstracts/)
Female Infertility

Minerals
Several enzymes needed to protect a woman’s reproductive organs (such as superoxide dismutase) are dependent on the trace elements zinc, copper and magnesium.

Cysteine
N-acetyl cysteine can improve ovulation and pregnancy rates in women with infertility due to PCOS (polycystic ovary syndrome) that do not respond to fertility drugs; Improves viability of endometrial cells in vitro; Precurso to glutathione.

Vitamin B₆ & B₁₂
Both are needed to convert toxic homocysteine to a benign form; Low homocysteine levels linked to a better chance of pregnancy.

Vitamin C
Increases serum progesterone levels; Induces ovulation in some women; Enhances effect of the fertility drug clomiphene.

Vitamin D
Higher levels linked to better success rates of IVF (in vitro fertilization); Influences production of the sex hormones estradiol and progesterone.

Vitamin E
Protects reproductive cells (follicles); May improve endometrial response (ability of fertilized egg to implant into uterine wall properly) during IVF.

Vitamin C
Protects eggs (fertilized or not) from damage by reactive oxygen species; Protective action of follicle stimulating hormone on embryonic development is due largely to glutathione synthesis.

Selenium
Deficiency implicated in miscarriage and infertility; In one trial, 100% of infertile women achieved pregnancy after supplementation.

Antioxidant Status
Reproductive cells, including embryos, are very susceptible to damage from oxidative stress due to the rapid rate of growth; Low antioxidant status can cause infertility or miscarriage.

Folate
Protects genes during rapid cell division which increases likelihood of a healthy embryo (via methylation of DNA); Deficiency raises homocysteine which damages reproductive cells.

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FIBROMYALGIA

Selenium
Deficiency is linked to fibromyalgia; In one trial, symptoms improved in 95% of patients supplemented with selenium for at least 4 weeks.25,26,27

Magnesium
Involved in pain perception pathways and muscle contraction; Treatment with magnesium can improve tenderness and pain.23,24,25

Zinc
Blood levels of zinc are associated with a number of tender points in fibromyalgic patients.22

Antioxidants
Low antioxidant status increases pain in fibromyalgia, which is often considered an oxidative stress disorder.19,20,21

Coenzyme Q10
Clinical trials consistently show that CoQ10 reduces fibromyalgia symptoms such as pain and fatigue.1,2,3,4

Carnitine
Deficiency causes muscle pain due to inefficient cellular energy metabolism (mitochondrial myopathy) which presents as fibromyalgia.4,5

Choline & Inositol
Altered levels of both nutrients seen in fibromyalgia; Choline & inositol are involved in pain perception.6,7,8,9

Serine
Blood levels of this amino acid are much lower in fibromyalgia patients.10,11

Vitamin D
Low levels impair neuromuscular function and cause muscle pain; Deficiency is common in fibromyalgia patients.12,13,14,15,16

Vitamin B1
Thiamin (B1) deficiency mimics fibromyalgia symptoms including serotonin depletion (decreased pain threshold), a decrease in repair enzymes (muscle soreness) and poor energy production (muscle fatigue.)17,18
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Additional references at http://www.spectracell.com/online-library-mnt-fibromyalgia-abstract/
CoQ10
Aids mitochondrial metabolism; May prevent migraines.

Vitamin B3
Dilates blood vessels; Increases serotonin.

Carnitine
Implicated in migraine pathophysiology due to its role in mitochondrial energy metabolism.

Lipoic Acid
Enhances mitochondrial energy metabolism.

Vitamin D & Calcium
Small trials show benefit with combined supplementation.

Vitamin B2
Effective for migraine prevention, aids mitochondrial energy metabolism.

Vitamin B12
Scavenges nitric oxide, which is implicated in migraine pathogenesis.

Vitamin C
Newly discovered role in neural tissue may explain its clinical benefit in a double blind trial on headache frequency.

Glutathione
Low levels of glutathione peroxidase implicated in migraine etiology.

Magnesium
Efficacious for migraine prevention in several trials; Magnesium deficiency can cause arterial spasm and its role in neurotransmission may explain the migraine-magnesium depletion link.

Folate
MTHFR gene linked to migraines. This gene raises folate requirements.


For additional references, go to http://www.spectracell.com/online-library-
Hypertension

**Zinc**
Regulates angiotensin and endothelin, two enzymes that directly affect blood pressure; Deficiency causes blood vessels to constrict. 37,38

**Magnesium**
Promotes dilation of blood vessels; Low intracellular levels are a well established cause of hypertension. 31,32,33

**Calcium**
Optimal calcium status reduces vasoconstriction; Particularly effective for salt-sensitive hypertension as it increases sodium excretion. 9,29,30

**Folate**
Lowers blood pressure by improving endothelial function, or the ability of blood vessels to properly dilate. 27,28

**Carnitine**
Lowers blood pressure in the same way as ACE inhibitors, a common hypertension drug which reduces angiotensin, a substance that causes arteries to constrict; Its role in fat metabolism explains this effect. 25,26

**Oleic Acid**
The benefits of olive oil for blood pressure are largely due to its high oleic acid content, which protects endothelial cells (inner lining of blood vessels) from inflammation. 22,23,24

**Biotin**
Pharmacological doses reduce systolic blood pressure by activating an enzyme (cGMP) that causes smooth muscle to relax. 1,2

**Glutathione**
Oxidative stress, which often manifests as glutathione deficiency, can induce hypertension. 39,40

**Vitamin A**
Suppresses the growth of vascular smooth muscle, thus keeping blood vessels (lumen) clear and wide. 3,4

**Vitamin B2**
People with a certain gene (called MTHFR type TT) tend to respond well to B2 therapy for lowering blood pressure. 5,6

**Vitamin B6**
Lowers homocysteine, a toxin that makes arteries stiff and raises blood pressure; Low B6 is strongly linked to hypertension. 6,7,8,9

**Vitamin C**
Improves the ability of blood vessels to react appropriately to relaxation signals; Increases nitric oxide, a powerful vasodilator. 9,10,11

**Vitamin D**
Low vitamin D is strongly linked to hypertension, possibly due to its role in calcium transport; Augments blood pressure lowering effect of calcium; Keeps blood vessels smooth and healthy. 9,12,13

**Vitamin E**
Increases nitric oxide synthase, an enzyme that causes blood vessels to dilate; Protects blood vessels from damage. 14,15

**Vitamin B6, B2, C**
Additional nutrients affect blood pressure. This list is non-exhaustive.

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Choline
Hypothyroidism negatively affects choline function in the brain, which can affect mood and cognition.

Carnitine
Decreased tissue levels of carnitine in both hypo- and hyperthyroidism contribute to muscle fatigue.

Selenium
Converts thyroid hormones T4 (thyroxine) into T3 (triiodothyronine); Deficiency reduces T3 levels causing classic hypothyroidism symptoms such as fatigue, depression and/or weight gain.

B Vitamins
A deficiency in B6, B12 or B9 (folate) can cause elevated homocysteine, which is linked with hypothyroidism. Folic acid levels have been linked to levels of thyroid stimulating hormone (TSH).

Glutathione
Hypothyroidism decreases efficacy of some antioxidants, such as glutathione peroxidase and superoxide dismutase.

Lipoic Acid
Improves endothelial function in people with subclinical hypothyroidism; Protects thyroid cells from oxidative stress; May interfere with T4 therapy.

Vitamin C and E
Partially restores thyroid function when liver detoxification ability is compromised.

Asparagine
This amino acid is part of the structure of thyroid stimulating hormone which regulates communication with other hormones.

Vitamin A
Activates gene that regulates TSH (thyroid stimulating hormone).

Copper
Low levels seen in experimentally induced hypothyroidism; Indirectly affects thyroid status by its antioxidant role via superoxide dismutase.

Zinc
Increases thyroid hormone T3 in deficient subjects.

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INFLAMMATION

Selenium
Subclinical deficiency negatively alters genes that regulate the inflammatory response; Deficiency promotes vascular inflammation. 37,38

Copper
Deficiency lowers enzyme activity (such as superoxide dismutase) that fights inflammation; Lowers damaging isoprostanes, a by-product of inflammation. 34,35,36

Zinc
Inflammation raises demand for zinc; Pro-inflammatory chemicals (cytokines) dose dependently decrease in response to zinc repletion. 31,32,33

Vitamin A
Regulates the cellular immune response to inflammatory signals; Deficiency increases the severity of chronic inflammation; Zinc depletion lowers vitamin A status. 28,29,30

Vitamin E
Limits destructive cell behavior caused by inflammation; Deficiency will also kick start a damaging immune response by activating cells called leukocytes and macrophages. 34,5

Glutathione
Recycles vitamins C and E. 6,7

Vitamin C
Low vitamin C linked to inflammation; Inversely related to C-reactive protein (CRP), a marker for systemic inflammation; Increases glutathione. 10,11,12

Vitamin D
Regulates the production of pro-inflammatory cytokines; Repairs damage to cells caused by inflammation; Stimulates vitamin A production. 13,14

Cysteine
Protects organs such as blood vessels, brain and liver from inflammatory damage; Precursor to glutathione production; Supplementation with N-acetyl cysteine raises glutathione. 8,9

Vitamin B2
Riboflavin (B2) helps minimize pain associated with inflammation; Detoxifies homocysteine, an amino acid that indirectly causes inflammation in various tissues. 26,27

Vitamin B6
Decreases several inflammatory markers (CRP and IL-6) in supplementation trials; Affects genes that control response to inflammatory stress. 21,22,23

Coenzyme Q10
Decreases cytokine production; Invokes anti-inflammatory response; Precursor to glutathione. 19,20

Glutamine
Neutralizes free radicals caused by uncontrolled inflammation in both water and lipid phases of the cell; Protects endothelial cells from inflammation; Regenerates other antioxidants such as vitamin E, C and glutathione. 17,18

Lipoic Acid
Neutralizes free radicals caused by uncontrolled inflammation in both water and lipid phases of the cell; Protects endothelial cells from inflammation; Regenerates other antioxidants such as vitamin E, C and glutathione. 17,18

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Additional nutrients affect inflammation. This list is non-exhaustive.
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Vitamin A Studies suggest vitamin A deficiency alters brain waves in non-REM sleep causing sleep to be less restorative.24,25

Vitamin B1 (Thiamin) In clinical trials, supplementation of healthy individuals that had marginal B1 deficiency improved their sleep.12,23

Vitamin B3 (Niacin) Increases REM sleep; Improves both quality and quantity of sleep by converting tryptophan to serotonin.4,5

Folate & Vitamin B6 Both are cofactors for several neurotransmitters in the brain such as serotonin and dopamine, many of which regulate sleep patterns.4,6,7,8,9

Vitamin B12 Normalizes circadian rhythms (sleep-wake cycles); Therapeutic benefits of B12 supplementation, both oral and intravenous, seen in studies.10,11,12,13

Oleic Acid This fatty acid is a precursor of oleamide, which regulates our drive for sleep and tends to accumulate in the spinal fluid of sleep-deprived animals. Oleic acid also facilitates the absorption of vitamin A.21,22,23

Zinc & Copper Both interact with NMDA (N-methyl-D-aspartate) receptors in the brain that regulate sleep; A higher Zn/Cu ratio is linked to longer sleep duration.15,19,20

Magnesium Improving magnesium status is associated with better quality sleep; Mimics the action of melatonin; Also alleviates insomnia due to restless leg syndrome.14,15,16,17,18
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Vitamin B2
Helps recycle folate into a usable methyl-donor form; Precursor to FAD (flavin adenine dinucleotide) which assists methylation reactions.\textsuperscript{1,2,3}

Vitamin B6
Cofactor for the enzyme (serine hydroxyl methyl transferase) that transfers methyl units.\textsuperscript{7,8}

Vitamin B12
B12 is a key enzyme needed in the synthesis of S-adenosylmethionine (SAMe), the body’s most important methyl donor. Methionine synthase, an enzyme that catalyzes the methylation cycle is B12 dependent.\textsuperscript{9,10,11}

Folate
Methyl donor for many reactions in the body, including neurotransmitter synthesis and conversion of homocysteine to methionine; Precursor to SAMe; Required for proper DNA synthesis.\textsuperscript{12,13,14}

Choline
A major source of methyl groups (methyl donor); Deficiency linked to DNA damage.\textsuperscript{15,16,17}

Serine
Important methyl donor, especially in the case of folate deficiency.\textsuperscript{18,19,20}

Glutathione
Deficiency impairs methylation reactions and hinders synthesis of the methyl donor SAMe.\textsuperscript{21,22}

Vitamin C
Deficiency alters methylation patterns in cancer cells; Also a cofactor for methylating enzymes.\textsuperscript{23,24}

Zinc
Deficiency can lower the ability to use methyl groups from methyl donors such as SAMe, thus causing global hypo-methylation of DNA.\textsuperscript{25,26,27}

Vitamin B3
Maintains proper methylation of genes that suppress tumor formation and growth.\textsuperscript{3,4,5,6}

Selenium
Inhibits a methylating enzyme (DNA methyltransferase) in cancer genes, effectively turning them off; Selenoproteins protect DNA and metabolize methionine.\textsuperscript{30,31}

Magnesium
Its role in the methylation of genes that affect glucose metabolism may explain the link between magnesium deficiency and diabetes.\textsuperscript{28,29}

Copper
Several key enzymes needed for methylation reactions are copper dependent.\textsuperscript{25,26,27}
Antioxidants Clinical trials show antioxidant therapy is an effective treatment for chronic pain; Vitamin E reduces neuropathic pain; Vitamin C can lower morphine consumption after surgery; Coenzyme Q10 relieves statin-induced myopathy.

Vitamin D Deficiency often presents clinically as muscle or bone pain.

Lipoic Acid Very effective treatment for neuropathic pain.

Cysteine Reduces pain caused by systemic inflammation due to its potent antioxidant properties.

Inositol In animal studies, treatment with inositol induces antinociception (pain reduction).

Oleic Acid This fatty acid is a precursor of oleamide, an analgesic that affects neurotransmitters such as dopamine, serotonin, acetylcholine and GABA (gamma amino butyric acid), all of which play a role in pain signaling.

Carnitine Deficiency of this amino acid may manifest as muscle weakness, pain (myalgia) or neuropathy. Supplementation reduces several types of chronic pain.

Magnesium Lowers pain by blocking NMDA receptors in spinal cord; Effective in reducing post-operative pain.

Vitamin B1, B2, B6, B12 These produce a dose dependent decrease in various kinds of pain (heat, pressure, chemical); Increases sensitivity to pain meds; Their effect is likely mediated through serotonergic neurotransmitters.

Choline Activates specific receptors in brain and spine that lower acute pain.

Minerals is a cofactor for the potent antioxidant superoxide dismutase, which fights free radicals, a known source of pain. Copper supplementation can relieve arthritic pain. Treatment with Selenium improves muscle pain in deficient patients. Research suggests both Zinc and Calcium play a role in the transmission of pain signals through nerves.
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Minerals
The trace minerals zinc, copper, magnesium, manganese and selenium are critical cofactors for the major antioxidant enzymes, which are important in repairing cellular damage caused by hypoxia (lack of oxygen) in sleep apnea. 23,24

Copper
Considered a strong predictor of oxidative stress in sleep apnea patients; Copper’s role as a key cofactor in the powerful antioxidant superoxide dismutase (SOD) explains this; SOD is very low in apnea patients. 21,22

Selenium
In one case report, selenium supplementation completely stopped snoring caused by non-obesity sleep apnea; Selenium’s role as a potent antioxidant may reduce the oxidative stress seen in sleep apnea patients. 18,19,20

Glutathione
Low levels linked to sleep apnea; This powerful antioxidant helps repair liver damage caused by sleep apnea. 25,26,27

Vitamin D
People with sleep apnea have a high prevalence of vitamin D deficiency; The worse the apnea, the more severe the deficiency; Evidence suggests low vitamin D worsens sleep apnea’s negative effect on heart disease risk. 15,16,17

Cysteine
Oral supplementation with cysteine, the precursor to glutathione, has therapeutic potential for sleep apnea. Snore time and duration were significantly reduced for patients treated with N-acetyl cysteine compared to untreated sleep apnea patients. 1,2,3,4

Vitamin A
Sleep apnea patients have low retinol growth of vascular smooth muscle, a process that causes blood vessels to clog, linking low vitamin A levels to the cardiovascular complications seen in sleep apnea patients. 13,14

Vitamin E
Mitigates the oxidative stress seen in sleep apnea patients; Works synergistically with vitamin C. 5,11,12

Vitamin C
Improves endothelial function (blood vessel health) in sleep apnea patients to levels seen in people without sleep apnea. 9,10,11

Vitamin E
Mitigates the oxidative stress seen in sleep apnea patients; Works synergistically with vitamin C. 5,11,12

Antioxidant Status
It is well documented that sleep apnea patients have both reduced antioxidant capacity and higher levels of oxidative stress than controls. 5,6,7,8

Selenium
In one case report, selenium supplementation completely stopped snoring caused by non-obesity sleep apnea; An antioxidant may reduce the oxidative stress seen in sleep apnea patients. 18,19,20

Additional nutrients affect sleep apnea. This list is non-exhaustive.
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Testosterone

**Zinc**
Deficiency lowers testosterone levels; Inhibits prolactin secretion (testosterone inhibiting hormone); Supplementation increases testosterone depending on baseline levels.\(^{20,29,30,31}\)

**Magnesium**
Makes testosterone more biologically active in the body; Raises free and total testosterone levels in men.\(^{25,26,27}\)

**Carnitine**
Boosts dopamine, which is directly related to testosterone levels; May prevent testosterone decline after intense physical stress.\(^{21,22,23,24}\)

**Folate**
Deficiency reduces circulating testosterone; Evidence suggests testosterone may regulate folate metabolism.\(^{1,2,3}\)

**Vitamin B6**
Regulates sex hormones; Vitamin B6 reduces prolactin which stimulates hypothalamus to increase testosterone; B6 also a cofactor for dopamine synthesis which influences testosterone levels.\(^{4,5,6,7}\)

**Vitamin D**
Actually a hormone, vitamin D regulates the synthesis of testosterone; Supplementation can significantly increase total, free and bioactive testosterone levels.\(^{8,9,10,11,12}\)

**Vitamin K**
Deficiency reduces testosterone production because the rate-limiting enzyme for testosterone synthesis (Cyp11a) is vitamin K dependent.\(^{13,14,15}\)

**Vitamin C**
Studies suggest it protects prostate from testosterone induced tumors.\(^{18,19,20}\)

**Vitamin E**
Long term administration of some forms of vitamin E may reduce testosterone levels.\(^{16,17}\)
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Weight Management

**Asparagine**
- Deficiency of zinc reduces leptin, a beneficial hormone that regulates appetite, which is reversed by zinc repletion.\(^{1,2}\)

**Biotin**
- Boosts metabolism by improving glycemic control (stabilizes blood sugar) and lowering insulin, a hormone that promotes fat formation.\(^{3,4,5}\)

**Carotene**
- Carries fatty acids into the cell so they can be burned for fuel; Helps reduce visceral adiposity (belly fat).\(^{6,7}\)

**Calcium**
- Inhibits the formation of fat cells; Also helps oxidize (burn) fat cells.\(^{8,9,10}\)

**Lipoic Acid**
- Improves glucose uptake into cells, which helps a person burn carbohydrates more efficiently.\(^{11,12,13}\)

**Chromium**
- Makes the body more sensitive to insulin, helping to reduce body fat and increase lean muscle.\(^{14,15,16,27,28,4}\)

**Vitamin B5 (Niacin)**
- Taking B5 lowers body weight by activating lipoprotein lipase, an enzyme that burns fat cells. One study linked B5 supplementation to less hunger when dieting.\(^{17,18}\)

**Magnesium**
- Low magnesium in cells impairs a person's ability to use glucose for fuel, instead storing it as fat; Correcting a magnesium deficiency stimulates metabolism by increasing insulin sensitivity. Magnesium may also inhibit fat absorption.\(^{19,20,21}\)

**Vitamin B3 (Niacin)**
- Treatment with B3 increases adiponectin, a weight-loss hormone secreted by fat cells; Niacin-bound chromium supplements helped reduced body weight in clinical trials.\(^{26,27,28}\)

**Carnitine**
- Carries fatty acids into the cell so they can be burned for fuel; Helps reduce visceral adiposity (belly fat).\(^{6,7}\)

**Vitamin K**
- Poor vitamin K status linked to excess fat tissue; Vitamin K helps metabolize sugars.\(^{35,36}\)

**Biotin**
- Boosts metabolism by improving glycemic control (stabilizes blood sugar) and lowering insulin, a hormone that promotes fat formation.\(^{3,4,5}\)

**Inositol**
- Supplementation may increase adiponectin levels.\(^{25}\)

**Cysteine**
- Supplementation with this antioxidant reduced body fat in obese patients.\(^{24}\)

**Glutamine**
- Reduces fat mass by improving glucose uptake into muscle.\(^{22,23}\)

**Vitamin D**
- Deficiency strongly linked to poor metabolism of carbohydrates; Genes that are regulated by vitamin D may alter the way fat cells form in some people.\(^{8,33,34}\)

**Vitamin E**
- Inhibits pre-fat cells from changing into mature fat cells, thus reducing body fat.\(^{10,31,32}\)

**Vitamin A**
- Enhances expression of genes that reduce a person's tendency to store food as fat; Reduces the size of fat cells.\(^{10,29,30}\)

**Zinc**
- Deficiency of zinc reduces leptin, a beneficial hormone that regulates appetite, which is reversed by zinc repletion.\(^{10,37}\)

**Calcium**
- Inhibits the formation of fat cells; Also helps oxidize (burn) fat cells.\(^{8,9,10}\)

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