

# **Nutrient Correlation Wheels**

**Deficiencies Correlated with Disease Conditions** 

### **Antioxidant Status**

Oxidative imbalance is prevalent in ADHD patients and likely plays a causative role; Deficiency of glutathione common in ADHD.<sup>3,4,5,6</sup>

### **Folate**

Low folate status in pregnancy linked to hyperactivity in children; People with the MTHFR(methyl tetrahydrafolate reductase) gene are predisposed to folate deficiency and more likely to have ADHD. <sup>1,2</sup>

### 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. <sup>7,8,9</sup>

### **Choline**

Precursor to neurotransmitter acetylcholine, which regulates memory focus and muscle control (hyperactivity). <sup>24,25,26</sup>

### **Magnesium**

Deficiency linked to poor function of the neurotransmitters that control emotion, social reactions, hyperactivity and attention; Synergistic effect with Vitamin B6.8.9.10

### **Glutamine**

Precursor for the calming neurotransmitter GABA (gammaaminobutyric acid) that affects mood, focus and hyperactivity; Disruption of the glutamine-containing neurotransmission systems may cause ADHD. <sup>21,22,23</sup>

# 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. 18,19,20

### **Zinc**

Cofactor for dopamine synthesis which affects mood and concentration in ADHD; Low zinc depresses both melatonin and serotonin production which affect information processing and behavior in ADHD. 11,12,13,14

### **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. 15,16.17

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### **Carnitine**

Studies show that carnitine can reduce anxiety and improve feelings of well being.<sup>28,29</sup>

### 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. <sup>24,25,26,27</sup>

### 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. 19,22,23

### Vitamin B6

Cofactor in synthesis of calming neurotransmitters such as GABA (gamma-aminobutyric acid), serotonin and dopamine.<sup>19,20,21</sup>

### Zinc

Reduces anxiety in clinical trials, possibly due to its interaction with NMDA (N-methyl-D- aspartate) receptors in the brain which regulate mood.<sup>16,17,18</sup>

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### **Chromium**

Its effect on serotonin transmission may explain its anxiolytic (anxiety relieving) effect in animal studies.<sup>30,31</sup>

### **Folate**

Aids in production of neurotransmitters such as dopamine and serotonin, which have a calming effect on mood.<sup>19,32,33</sup>

### 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. <sup>1,2</sup>

### **Choline**

Precursor to the neurotransmitter acetylcholine, which affects focus and mood; Low levels of choline linked to anxiety.<sup>3,4</sup>

### **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. 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.<sup>8,9,10</sup>

### 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). 14,15

ANXIETY

### **Magnesium**

Regulates the HPA (hypothalamic-pituitary adrenal) axis which controls physical and psychological reactions to stress; Deficiency can induce anxiety and emotional hyper-reactivity.<sup>11,12,13</sup>

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

**Carnitine** 

Protects the surface of the lungs; Improves pulmonary function in asthmatics; Decreases inflammation in lung tissue. 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.<sup>8,9</sup>

**Zinc** Regulates immune system including allergic response; Deficiency can exacerbate asthma symptoms.<sup>31,32</sup>

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

**Selenium** Part of the enzyme (called glutathione peroxidase) that protects against asthmatic lung tissue damage; Supplementation trials are promising. <sup>27,28,29,30</sup>

ASTHMA

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

### Vitamin A

Prevents exercise-induced asthma; Regulates bronchial responsiveness. 25,26

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

**Vitamin B6** Binds with the chemical that causes airway constriction (histamine) and inactivates it; The common asthma drug theophylline depletes B6.<sup>23,24</sup>

**Vitamin C** Dilates bronchial airways; Inhibits histamine-induced constriction of airways; Needed for production of epinephrine, which mitigates asthma attacks.<sup>21,22</sup>

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

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### 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.<sup>1,2</sup>

### **Vitamin D**

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

### **Carnitine**

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

### 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.<sup>8,9,10</sup>

### **Magnesium**

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

### **Folate**

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

### **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. <sup>28,29,30</sup>

### 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

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# AUTISM

### **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.<sup>21,22,23,24,25</sup>

### Vitamin BI

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

### 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 (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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### **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. 33,34,35,36

### Serine

Regulates brain chemistry; Involved in NMDA receptor function; Acts as a neurotransmitter; Low levels correlate with severity of depression.<sup>31,32</sup>

### **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. <sup>28,29,30</sup>

### **Biotin**

Part of the B-vitamin complex, biotin deficiency has induced depression in animal and human studies. <sup>26,27</sup>

### **Selenium**

Integral part of regulatory proteins (selenoproteins) in the brain; Supplementation trials are promising; May alleviate postpartum depression.<sup>5,6</sup>

### 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. <sup>37,38,39</sup>

### **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.<sup>17,18</sup>

### Inositol

Influences signaling pathways in the brain; Particularly effective in SSRI (selective serotonin reuptake inhibitor) sensitive disorders. <sup>24,25</sup>

DEPRESSION

### **Carnitine**

Increases serotonin and noradrenaline which lift mood; In trials, carnitine alleviates depression with few, if any, side effects.<sup>22,23</sup>

### 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

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### Vitamin B12

Deficiency common in diabetics because metformin depletes B12.<sup>1,2</sup>

### **Chromium**

Helps insulin attach to cell's receptors increasing glucose uptake into cell; Deficiency can cause insulin resistance; Supplementation trials show dose-dependent benefits for type II diabetics. 36,37,38

### **Biotin**

Stimulates glucose-induced insulin secretion in pancreatic B-cells; High dose biotin can improve glycemic control in diabetics. 33,34,35

### **Magnesium**

Deficiency reduces insulin sensitivity; Low magnesium exacerbates foot ulcers in diabetics.<sup>31,32</sup>

### **Zinc**

Needed in the synthesis, storage and secretion of insulin; Protects pancreatic B-cells from damage; Affects the expression of genes linked to diabetes.<sup>29,30</sup>

### **Lipoic Acid**

Enhances glucose uptake in skeletal muscle tissue; Improves glucose tolerance in type 2 diabetics; Very effective treatment for diabetic neuropathy. 26,27,28

### Vitamin B3

Preserves B-cell function in type I diabetics; Part of GTF (glucose tolerance factor) which facilitates insulin binding.<sup>3,4,5</sup>

### **Vitamin D**

Lowers risk of type I and 2 diabetes; Supresses inflammation of pancreatic B-cells; Vitamin D receptor gene linked to diabetes.<sup>6,7,8</sup>

### Vitamin E

Confers protection against diabetes by protecting pancreatic B-cells from oxidative stress induced damage; May prevent progression of type I diabetes.<sup>6,9</sup>

### Vitamin C

Lowers glycolysated hemoglobin (HbA1c) and fasting and post-meal glucose levels and in type 2 diabetics. 10,11,12

### **Inositol**

Evidence suggests that inositol may be effective in treating diabetic neuropathy. 13,14

### **Carnitine**

Reduces and even prevents pain from diabetic neuropathy; Improves insulin sensitivity by increasing glucose uptake and storage. 15,16,17,18

### **Glutamine**

Stimulates a hormone called GLP-I (glucagon-like peptide I) that regulates insulin secretion after meals; Improves insulin signaling and sensitivity. 19,20

### Coenzyme Q10

Protects kidney from diabetes related damage; Improves glycemic control in type 2 diabetics.<sup>21,22</sup>

# DIABETES

# Glutathione & Cysteine

Glutathione-containing enzymes protect B-cells which are particularly sensitive to oxidative stress; Type 2 diabetics have abnormal antioxidant status; Supplementation with the glutathione precursor cysteine restores antioxidant status.<sup>23,24,25</sup>

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### **Manganese**

Cofactor to an antioxidant (superoxide dismutase) that repairs damage to blood vessels caused by oxidized LDL (low density lipoprotein). <sup>1,2</sup>

### **Magnesium**

Deficiency causes proatherogenic (heart-disease causing) changes in lipoprotein metabolism; Protects LDL (low density lipoprotein) from being oxidized. 3.4

### Vitamin C

Protects LDL from oxidation, thus making it less "sticky" and prone to atherosclerosis (clogging of arteries); Prevents white blood cells (monocytes) and oxidized LDL from sticking to blood vessel wall; Lowers Lp(a) in some people. 5,6,7

### Vitamin D

Suppresses foam cell formation thus reducing risk of lipid-related arterial blockages; Deficiency linked to dyslipidemia. 8,9

### Zinc

Suboptimal zinc raises dangerous lipoproteins that promote vascular inflammation and arterial plaque formation; Cellular zinc controls the gene that makes heart-protective HDL (high density lipoprotein). 34,35,36

### **Selenium**

Prevents post-prandial (after a meal) changes in lipoproteins that make them susceptible to oxidation and thus harmful. 32,33

### Copper

Several copper-dependent enzymes affect lipoprotein metabolism; Deficiency contributes to fatty buildup in arteries caused by dyslipidemia. <sup>29,30,31</sup>

### Coenzyme Q10

It is well established that statins, often prescribed for dyslipidemia, deplete CoQ10; Lowers Lp(a) and improves efficacy of some dyslipidemia meds. <sup>27,28</sup>

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# DYSLIPIDEMIA

### **Chromium**

Specifically improves the dyslipidemia that accompanies insulin resistance; May increase HDL; Synergistic effect with niacin (B3) for dyslipidemia. <sup>24,25,26</sup>

### **Choline**

Regulates HDL metabolism; Part of the enzyme lecithincholesterol acyltransferase that has a major impact on lipoprotein metabolism. <sup>22,23</sup>

### **Inositol**

Decreases small, dense LDL especially in patients with metabolic syndrome; Lowers triglycerides. 19,20,21

### Vitamin B3

Niacin (B3) effectively lowers the highly atherogenic Lp(a) by decreasing its rate of synthesis in the liver. [0,1]

### Vitamin B5

Favorably alters low density lipoprotein metabolism and reduces triglycerides; Full benefit of lipid lowering effects may not be seen for up to four months. 12,13

### **Carnitine**

In supplementation trials, carnitine lowers triglycerides, oxidized LDL and the atherogenic Lp(a); This effect is likely due to its role in transporting fatty acids into cells so they can be used as fuel. <sup>14,15,16</sup>

## **Lipoic Acid**

Improves lipid profile by reducing small, dense LDL (dangerous type); Protects vascular lining from oxidized cholesterol. 17,18

Additional nutrients affect lipid metabolism.
This list is non-exhaustive.



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### Cysteine

Prevents oxidation of estrogen into a dangerous form that causes breast cancer. <sup>29,30,31</sup>

### Zinc

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

### **Magnesium**

Cofactor for the enzyme that removes toxic forms of estrogen (catechol-O-methyltransferase); Estrogen alters magnesium levels throughout menstrual cycle. 1,24,25,26

### Selenium

Estrogen levels affect how selenium is distributed to various tissues in the body. <sup>22,23</sup>

### **Calcium**

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

### Vitamin A

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

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### **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. 1,32,33

### **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

### 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.<sup>4,5,6,7</sup>

### 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 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

Estrogen

### Vitamin K

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

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**Carnitine** Transports fatty acids into mitochondria; Decreases both mental and physical fatigue in clinical trials. 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.<sup>8,15,16,26-30</sup>

**Vitamin D** Low levels are seen in patients with chronic fatigue syndrome; Deficiency causes reduced muscle strength.<sup>24,25</sup>

**Vitamin E** Inverse correlation exists between fatigue and vitamin E levels.<sup>23</sup>

# **Vitamin A** When cellular levels of vitamin A are low, mitochondrial respiration and ATP production decreases.<sup>22</sup>

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

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### **Chromium**

Promotes glucose uptake into cells, helping stabilize blood sugar. 16,33

lowers immunity and may cause muscle fatigue; Involved in several reactions for energy metabolism. 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.<sup>1,2,3</sup>

**Biotin** Helps liver utilize glycogen for energy. Animal studies confirm that biotin deficiency causes clinical fatigue.<sup>4</sup>

**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. 5.6.7

# **FATIGUE**

**Serine** Counteracts the overproduction of fatigue-causing stress hormones.<sup>8,9</sup>

causes fatigue due to its role in mitochondrial energy metabolism; therapeutic benefits particularly noticeable in chronic fatigue syndrome. [0,11,12,15]

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. 12,16,18,19,20

### **Magnesium**

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

# Fructose

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

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### **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.<sup>1,2,3,4</sup>

# Vitamin B<sub>6</sub> & B<sub>12</sub>

Both are neededto convert toxic homocysteine to a benign form; Low homocysteine levels linked to a better chance of pregnancy.<sup>5,6,7,8</sup>

### Vitamin C

Increases serum progesterone levels; Induces ovulation in some women; Enhances effect of the fertility drug clomiphene. 9,10,11,12

### **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**. 22,30,31,32

### **Vitamin D**

Higher levels linked to better success rates of IVF (in vitro fertilization); Influences production of the sex hormones estradiol and progesterone. 13,14,15

### **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. <sup>19,22,28,29</sup>

# Female Infertility

### Vitamin E

Protects reproductive cells (follicles); May improve endometrial response (ability of fertilized egg to implant into uterine wall propersly) during IVF. <sup>16,17,18,19</sup>

### **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 .<sup>25,26,27</sup>

### **Glutathione**

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. <sup>22,23,24</sup>

### Selenium

Deficiency implicated in miscarriage and infertility; In one trial, 100% of infertile women achieved pregnancy after supplementation. <sup>20,21</sup>

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### Selenium

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

Coenzyme Q 10
Clinical trials consistently
show that CoQ10 reduces

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. <sup>6,7,8,9</sup>

### **Magnesium**

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

**FIBROMYALGIA** 

### **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

**Zinc** Blood levels of zinc are associated with a number of tender points in fibromyalgic patients.<sup>22</sup>

### **Antioxidants**

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

**Vitamin B I** Thiamin (BI) deficiency mimics fibromyalgia symptoms including serotonin depletion (decreased pain threshold), a decrease in repair enzymes (muscle soreness) and poor energy production (muscle fatigue.) <sup>17,18</sup>

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### 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.

### CoQ10

Aids mitochondrial metabolism; May prevent migraines.

### **Vitamin C**

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

### Vitamin B2

Effective for migraine prevention, aids mitochondrial energy metabolism.

# HEADACHES

### Vitamin B12

Scavenges nitric oxide, which is implicated in migraine pathogenesis.

### Vitamin D & Calcium

Small trials show benefit with combined supplementation.

# 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.

### **Glutathione**

Low levels of glutathione peroxidase implicated in migraine etiology.

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

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

### Copper

Regulates enzymes that keep blood vessels dilating properly; Depletion causes hypertension; Supplementation trials positive.

### **Magnesium**

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

Calcium Optimal calcium status reduces vasconstriction; Particularly effective for saltsensitive 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

Anti-hypertensive effects stem from its role as a potent

### **Lipoic Acid**

Improves vascular tone; Causes vasolidation: Works like calcium channel blocker meds; Recycles vitamins C, E and Cysteine. 18,19

### 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

### Coenzyme Q10

Improves bioenergetics of blood vessel wall; Deficiency highly correlated to hypertension; Benefits of CoQ10 often not seen for several weeks. 9,16,17

> Additional nutrients affect blood pressure. This list is non-exhaustive.

# Hypertension

**Biotin** 

relax. 1,2

Pharmacological doses reduce

activating an enzyme (cGMP)

that causes smooth muscle to

systolic blood pressure by

**Glutathione** 

glutathione deficiency, can

induce hypertension. 39,40

Oxidative stress, which

often manifests as

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### Cysteine

antioxidant; Effective vasolidator. 20,21

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### **Glutathione**

Hypothyroidism decreases efficacy of some antioxidants, such as glutathione peroxidase and superoxide dismutase.<sup>1,2</sup>

### **Choline**

Hypothyroidism negatively affects choline function in the brain, which can affect mood and cognition.<sup>29,30</sup>

### **Lipoic Acid**

Improves endothelial function in people with subclinical hypothyroidism; Protects thyroid cells from oxidative stress; May interfere with T4 therapy.<sup>27,28</sup>

### **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).<sup>3,4,5,6,7</sup>

### Vitamin Cand E

Partially restores thyroid function when liver detoxification ability is compromised.<sup>2,8,9,10,11</sup>

### Vitamin A

Activates gene that regulates TSH (thyroid stimulating hormone). 12,13,14

# **HYPOTHYROIDISM**

### **Carnitine**

Decreased tissue levels of carnitine in both hypo- and hyperthyroidism contribute to muscle fatigue. 24,25,26

### Zinc

Increases thyroid hormone T3 in deficient subjects. 15,16,17,20,21

### **Asparagine**

This amino acid is part of the structure of thyroid stimulating hormone which regulates communication with other hormones.<sup>22,23</sup>

### **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.<sup>18,19,20,21</sup>

**Copper** Low levels seen in experimentally induced hypothyroidism; Indirectly affects thyroid status by its antioxidant role via superoxide dismutase.<sup>17</sup>

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### Selenium

Subclinical deficiency negatively alters genes that regulate the inflammatory response; Deficiency promotes vascular inflammation. <sup>37,38</sup>

### **Manganese**

Cofactor to the powerful antioxidant superoxide dismutase that fights inflammation within cells. <sup>1,2</sup>

### **Magnesium**

Deficiency activates proinflammatory chemicals called cytokines; Deficiency will also kick start a damaging immune response by activating cells called leukocytes and macrophages. 3,4,5

### **Glutathione**

Repairs damage to cells caused by inflammation; Regulates the production of pro-inflammatory cytokines; Recycles vitamins C and E. <sup>6,7</sup>

### **Cysteine**

Low vitamin C linked to inflammation;

Inversely related to C-reactive protein

Vitamin D

cytokine production. 13,14

Vitamin E

related diseases. 15,16

(CRP), a marker for systemic inflammation;

Potent modulator of inflammation; Helps turn off chronic inflammatory

responses; Inhibits pro-inflammatory

Limits destructive cell behavior caused

predisposes a person to inflammation-

by inflammatory enzymes gone wild; Reduces damage from tumor necrosis

factor alpha (TNF- $\alpha$ ); Deficiency

Vitamin C

Increases glutathione. 10,11,12

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

## Copper

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

### **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. <sup>28,29,30</sup>

### Vitamin B2

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

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# INFLAMMATION

## Vitamin B6 Deci

Low B6 status is linked to high levels of CRP and systemic inflammation. <sup>24,25</sup>

### Coenzyme Q10

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

### **Glutamine**

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

### **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. <sup>17,18</sup>

Additional nutrients affect inflammation. This list is non-exhaustive.



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 $Additional\ references\ at\ http://www.spectracell.com/clinicians/clinical-education-center/online-library-mnt-inflammation-abstracts/$ 



### Vitamin BI

(Thiamin) In clinical trials, supplementation of healthy individuals that had marginal B1 deficiency improved their sleep. 1,2,3

### Vitamin B3

(Niacin) Increases REM sleep; Improves both quality and quantity of sleep by converting tryptophan to serotonin.<sup>4,5</sup>

### 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 A Studies

suggest vitamin A deficiency alters brains waves in non-REM sleep causing sleep to be less restorative.<sup>24,25</sup>

INSOMNIA

### Vitamin B12

Normalizes circadian rhythms (sleep-wake cycles); Therapeutic benefits of B12 supplementation, both oral and intravenous, seen in studies. [0,11,12,13]

**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.<sup>21,22,23</sup>

## Zinc & Copper

Both interact with NMDA (N-methyl-Daspartate) 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 B3

Maintains proper methylation of genes that suppress tumor formation and growth.<sup>3,4,5,6</sup>

### Vitamin B6

Cofactor for the enzyme (serine hydroxyl methyl transferase) that transfers methyl units.<sup>7,8</sup>

### 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. 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.<sup>12,13,14</sup>

### Vitamin B2

Helps recycle folate into a usable methyl-donor form; Precursor to FAD (flavin adenine dinucleotide) which assists methylation reactions. 1,2,3

### **Choline**

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

### **Zinc**

Deficiency can lower the ability to use methyl groups from methyl donors such as SAMe, thus causing global hypo-methylation of DNA.<sup>32,33,34</sup>

### **Serine**

Important methyl donor, especially in the case of folate deficiency. 18,19,20

### Glutathione

Deficiency impairs methylation reactions and hinders synthesis of the methyl donor SAMe.<sup>21,22</sup>

### **Selenium**

Inhibits a methylating enzyme (DNA methyltransferase) in cancer genes, effectively turning them off; Selenoproteins protect DNA and metabolize methionine.<sup>30,31</sup>

### **Magnesium**

Its role in the methylation of genes that affect glucose metabolism may explain the link between magnesium deficiency and diabetes.<sup>28,29</sup>

METHYLATION

### Vitamin C

Deficiency alters methylation patterns in cancer cells; Also a cofactor for methylating enzymes.<sup>23,24</sup>

### Copper

Several key enzymes needed for methylation reactions are copper dependent. 25,26,27

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### Cysteine

Reduces pain caused by systemic inflammation due to its potent antioxidant properties.<sup>1,2</sup>

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. 28,29,30,31,32

### **Lipoic Acid**

Very effective treatment for neuropathic pain.<sup>26,27</sup>

**Vitamin D** Deficiency often presents clinically as muscle or bone pain. <sup>23,24,25</sup>

### **Inositol**

PAIN

In animal studies, treatment with inositol induces antinociception (pain reduction).<sup>3,17</sup>

**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.<sup>4,5</sup>

**Carnitine** Deficiency of this amino acid may manifest as muscle weakness, pain (myalgia) or neuropathy. Supplementation reduces several types of chronic pain.<sup>6,7,8</sup>

### **Magnesium**

Lowers pain by blocking NMDA receptors in spinal cord; Effective in reducing post-operative pain. 9,10,11

### 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. 19,20,21,22

**Choline** Activates specific receptors in brain and spine that lower acute pain. <sup>17,18</sup>

**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. 12,13,14,15,16

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### **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

### **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

### **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

### **Glutathione**

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

# **SLEEP APNEA**

### **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. <sup>23,24</sup>

### **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

# Vitamin A Sleep apnea patients

Sleep apnea patients have low retinol (vitamin A); Retinol suppresses the 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. <sup>13,14</sup>

### 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

### Copper Considered a st

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. <sup>21,22</sup>

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



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### **Calcium**

Required cofactor to prevent DNA replication errors.<sup>25</sup>

Folate Influences telomere length via DNA methylation. 1,2,3

**B3** Extends lifespan of human cells in vitro; Slows telomere attrition rate by reducing reactive oxygen species in mitochondria.<sup>4,5</sup>

**B2, B6 and B12** 

Crucial for proper DNA methylation.<sup>6,7</sup>

### **Manganese**

Required cofactor in Mn superoxide dismutase, a deficiency in which decreases telomerase activity.<sup>24</sup>

### Vitamin D

Positively associated with telomere length due to its anti-inflammatory role.<sup>23</sup>

**TELOMERES** 

### **Cysteine**

Stem cell treatment with N-acetyl cysteine corrects DNA damage in telomeres.<sup>8</sup>

**Zinc** Important cofactor for DNA repair enzymes; key role in regulating inflammation.<sup>9</sup>

**Copper** Key cofactor in the potent antioxidant superoxide dismutase that is known to protect telomeres."

**Magnesium** Induced deficiency shortened telomeres in rat livers; Regulates chromosome separation in cell replication.<sup>12</sup>

**Vitamin E** Enhances DNA repair as well as removal of damaged DNA; Shown in vitro to restore telomere length on human cells.<sup>21,22</sup>

# Vitamin C Protects DNA

from oxidation. In vitro studies show it slows down age-related telomere shortening in human skincells. 19,20

### **Glutathione**

Interference of glutathione dependent antioxidant defenses accelerates telomere erosion. 17,18

### Selenium In vitro

supplementation extended telomere length in liver cells; selenoproteins protect DNA. 13,14,15,16

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### Zinc

Deficiency lowers testosterone levels; Inhibits prolactin secretion (testosterone inhibiting hormone); Supplementation increases testosterone depending on baseline levels.<sup>28,29,30,31</sup>

### **Folate**

Deficiency reduces circulating testosterone; Evidence suggests testosterone may regulate folate metabolism.<sup>1,2,3</sup>

### 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

## **Magnesium**

Makes testosterone more biologically active in the body; Raises free and total testosterone levels in men.<sup>25,26,27</sup>

# Vitamin D

Actually a hormone, vitamin D regulates the synthesis of testosterone; Supplementation can significantly increase total, free and bioactive testosterone levels.<sup>8,9,10,11,12</sup>

# **Testosterone**

### Carnitine

Boosts dopamine, which is directly related to testosterone levels; May prevent testosterone decline after intense physical stress.<sup>21,22,23,24</sup>

### Vitamin K

Deficiency reduces testosterone production because the rate-limiting enzyme for testosterone synthesis (Cyp I Ia) is vitamin K dependent. <sup>13,14,15</sup>

### 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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**Zinc** Deficiency of zinc reduces leptin, a beneficial hormone that regulates appetite, which is reversed by zinc repletion. 10,37

### **Asparagine**

This amino acid increases insulin sensitivity which helps the body store energy in muscle instead of storing it as body fat.<sup>1,2</sup>

**Biotin** Boosts metabolism by improving glycemic control (stabilizes blood sugar) and lowering insulin, a hormone that promotes fat formation.<sup>3,4,5</sup>

### **Carnitine**

Carries fatty acids into the cell so they can be burned for fuel; Helps reduce visceral adiposity (belly fat). <sup>6,7</sup>

**Calcium** Inhibits the formation of fat cells; Also helps oxidize (burn) fat cells.<sup>8,9,10</sup>

**Lipoic Acid** Improves glucose uptake into cells, which helps a person burn carbohydrates more efficiently.<sup>11,12,13</sup>

# **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** 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

# WEIGHT MANAGEMENT

### Vitamin K

Poor vitamin K status linked to excess fat tissue;Vitamin K helps metabolize sugars.<sup>35,36</sup>

### 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.<sup>8,33,34</sup>

**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

### 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.<sup>26,27,28</sup>

### **Inositol**

Supplementation may increase adiponectin levels.<sup>25</sup>

### **Cysteine**

Supplementation with this antioxidant reduced body fat in obese patients.<sup>24</sup>

### **Glutamine**

Reduces fat mass by improving glucose uptake into muscle. 22,23

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