

<b>Final Report Date:</b>	12-14-2020 13:30	<b>Specimen Collected:</b>	12-13-2020
<b>Accession ID:</b>	2012130014	<b>Specimen Received:</b>	12-13-2020 14:52

LAST NAME	FIRST NAME	GENDER	DATE OF BIRTH	ACCESSION ID	DATE OF SERVICE
DOE	JOH	MALE	1999-03-11	2012130014	12-13-2020

## PATIENT

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 Date of Birth: 1999-03-11  
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 Age: 21

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Fasting: UNKNOWN  
 EMR #: 2012130014

## PROVIDER

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LAST NAME	FIRST NAME	GENDER	DATE OF BIRTH	ACCESSION ID	DATE OF SERVICE
DOE	JOH	MALE	1999-03-11	2012130014	12-13-2020

## Whole Blood Nutrient Profile Test Results:

### Vitamins

Test Name	Current	Previous ( )	Ref. Range
Vitamin A (mcg/dL)	5.0 ↓		40.0~90.0
Vitamin B1 (nmol/L)	5.0 ↓		70.0~180.0
Vitamin B2 (mcg/L)	5.0 ↓		137.0~290.0
Vitamin B3 (ng/mL)	5.0		5.0~80.0
Vitamin B6 (ng/mL)	5.0		4.0~83.0
Vitamin B5 (mcg/L)	5.0 ↓		20.0~360.0
Vitamin C (mg/dL)	5.0 ↑		0.5~4.0
Vitamin D3 (mcg/mL)	5.0		1.1~5.2
Vitamin E (mg/L)	5.0		5.0~30.0
Vitamin K1 (ng/mL)	5.00		0.10~5.00
Vitamin K2 (ng/mL)	5.00		1.00~8.00
Folate (ng/mL)	5.0 ↓		≥498.0

### Minerals

Test Name	Current	Previous ( )	Ref. Range
Calcium (mg/dL)	5.0 ↓		15.0~30.0
Manganese (ng/mL)	5.0 ↓		8.0~19.0
Zinc (mcg/mL)	5.0		4.4~8.6
Copper (mcg/mL)	5.0 ↑		0.5~1.5
Chromium (ng/mL)	5.00 ↑		0.10~1.20
Iron (mg/dL)	5.0 ↓		88.0~117.0
Magnesium (mg/dL)	5.0		3.6~7.7
Copper to Zinc Ratio	5.00 ↑		0.15~0.41

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## Metabolites

Test Name	Current	Previous	Ref. Range
Choline (nmol/mL)	5.0 ↓	()	10.0~35.0
Inositol (nmol/mL)	5.0 ↓		40.0~85.0
Carnitine (nmol/mL)	5.0 ↓		20.0~75.0
MMA (nmol/mL)	5.0 ↓		6.0~14.9

## Amino Acids

Test Name	Current	Previous	Ref. Range
Asparagine (nmol/mL)	5.0 ↓		90.0~160.0
Glutamine (nmol/mL)	5.0 ↓		450.0~817.0
Serine (nmol/mL)	5.0 ↓		184.0~280.0
Arginine (nmol/mL)	<25.0 ↓		85.0~250.0
Citrulline (nmol/mL)	<9.8 ↓		40.0~85.0
Isoleucine (nmol/mL)	<10.0 ↓		53.0~124.0
Valine (nmol/mL)	<37.0 ↓		195.0~370.0
Leucine (nmol/mL)	<23.2 ↓		121.0~249.0

## Antioxidants

Test Name	Current	Previous	Ref. Range
Coenzyme Q10 (mcg/mL)	5.00 ↑		1.10~4.89
Cysteine (nmol/mL)	5.0 ↓		10.0~37.0
Glutathione (mcg/mL)	5.0 ↓		176.0~323.0
Selenium (ng/mL)	<8.7 ↓		120.0~200.0

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## Whole Blood Omega Fatty Acids

Test Name	Current	Previous	Ref. Range
Docosahexaenoic acid (DHA) (%)	5.00		2.42~10.52
Eicosapentaenoic acid (EPA) (%)	5.00 ↑		0.15~2.26
Docosapentaenoic acid (DPA) (%)	5.00 ↑		0.45~1.80
Total Omega-3 (%)	5.00		3.25~13.99
Arachidonic acid (AA) (%)	5.00 ↓		5.50~19.01
Linoleic acid (LA) (%)	5.00		3.22~10.49
Total Omega-6 (%)	5.00 ↓		11.03~34.96
Omega-3 Index (%)	5.00 ↓		8.00~12.66
AA/EPA	1.00 ↓		1.40~52.70
Omega-6/Omega-3	1.00 ↓		2.30~14.50

## VITAMINS

### Physiological Function

- Vitamin A is a group of fat-soluble vitamins which includes retinol, retinal, retinoic acid, and several provitamin A carotenoids, among which beta-carotene is the most important.
- Vitamin A has multiple functions including: growth and development in infants, children and adolescents, maintenance of the immune system, and healthy vision.
- Vitamin A is needed by the retina of the eye for both low-light and color vision.
- Vitamin A also functions as retinoic acid, an important hormone-like growth factor for epithelial and other cells.
- Other important roles that vitamin A plays in the body include: gene transcription, haematopoiesis, and antioxidant activity.

### How it gets depleted

Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, and use of laxatives.

### Clinical Manifestations of Depletion

Vitamin A deficiency may result in night blindness, impaired immunity, impaired healing, increased risk of infection, thyroid disorders, leukoplakia or keratosis.

Assess zinc status to assess if zinc deficiency has led to secondary functional deficiency of vitamin A release from liver stores.

### Food Sources

Food sources of vitamin A include: cod liver oil, liver (turkey, beef, pork, fish and chicken), dandelion greens, fortified cereals and milk, butter, eggs, sweet potato, pumpkin, carrot, cantaloupe, mango, spinach, broccoli leaf (broccoli florets have much less), kale, and butternut

### Supplement Options

- The RDA for vitamin A is 700mcg RAE/day for women and 900 mcg RAE/day for men. This is the amount needed to prevent chronic deficiency, but more may be needed for optimal health.
- These measurements are the equivalent of 2500 IU/day for women and 3000 IU/day for men of pre-formed vitamin A sources (animal sources).
- The upper intake level (UL) for vitamin A in adults is set at 3,000 µg RAE/day.
- Vitamin A toxicity can occur from taking pre-formed vitamin A from sources other than plant sources.

### Physiological Function

Vitamin B1 aids in energy transformation and production of ATP. It acts a coenzyme in the breakdown of carbohydrates, fats and proteins to produce energy.

### How it gets depleted

Thiamin can become depleted or deficient from frequent consumption of thiaminases present in higher amounts in raw fish and tannins/tannic acid (tea and coffee).

Thiamin is vulnerable to loss during cooking. Can be depleted with excessive or chronic alcohol intake. There may be higher risk of depletion with gastric bypass surgery.

### Clinical Manifestations of Depletion

Thiamin deficiency can lead to nervous system and cardiac abnormalities.

The most severe form of thiamin deficiency is called beri beri, a condition commonly resulting in weakness, fatigue, confusion, irritability, weight loss, muscle wasting, and peripheral neuropathy.

### Food Sources

Food sources of thiamin include: pork, organ meats, legumes, sweet potato, brown rice, brewer's yeast, pine nuts, sunflower seeds, enriched grains\*

### Supplement Options

- The RDA for thiamin is 1.0 mg/day for females and 1.2 mg/day for males.
- The RDA for thiamin during pregnancy/lactation is 1.4 mg/day.
- Therapeutic intake of thiamin is commonly 25-100mg/day.
- No UL for thiamin has been set.
- Thiamin is commonly found in multi-B vitamin products.

### Physiological Function

Two very important coenzymes involved in energy metabolism are derived from riboflavin to participate in oxidation/reduction reactions.

Riboflavin is also essential for NOS enzyme (nitric oxide synthase) and glutathione reductase which regenerates glutathione, and which is very important for antioxidation/detoxification.

### How it gets depleted

Riboflavin is commonly depleted by excessive or chronic alcohol consumption. Need for riboflavin is increased in the elderly.



### Clinical Manifestations of Depletion

Frank deficiency of riboflavin is rare, however, marginal deficiency is common.

Deficiency of riboflavin is associated with fatigue/weakness.

### Food Sources

Food sources high in riboflavin include: organ meats, dairy foods, eggs, leafy greens (spinach), broccoli, and liver.

\*Enriched grains include riboflavin

### Supplement Options

- The RDA for riboflavin is 1.7 mg/day.
- Common levels of therapeutic intake of riboflavin are 25-50 mg/day.
- No UL for riboflavin has been set.

### Physiological Function

Vitamin B5 is part of the structural component of coenzyme A. It is also important for synthesis of red blood cells, sex hormones, adrenal hormones, and vitamin D. Another significant function of B5 is to work with carnitine and CoQ10 for fatty acid oxidation/metabolism.

### How it gets depleted

It is possible to block absorption of B5 in the intestines by taking high doses of supplemental biotin.



### Clinical Manifestations of Depletion

Deficiency of B5 is very rare, however, in a diet that is high in biotin, or if high dose biotin supplementation occurs, B5 may become conditionally deficient due to competition for the same uptake receptor in the intestine.

### Food Sources

Food sources of B5 include: beef, pork, chicken, fish, egg yolks, whole grains, legumes, lentils.

### Supplement Options

There is currently no RDA established for B5.

The AI for B5 is 5 mg/day in adults, 6 mg/day during pregnancy, and 7 mg/day during lactation.

Because breakdown of B5 is metabolically slow, and deficiency is rare, there is probably no need for supplementation.

## Physiological Function

Vitamin C has a major function of being an antioxidant. It boosts immunity through increasing white blood cells, in addition to supporting regeneration of vitamin E. Vitamin C can also reduce atherosclerosis, stroke and high blood pressure, and inflammation.

Because of its role in the generation of connective tissue, it is necessary for optimal collagen production. Vitamin C is also an important component of l-carnitine, which is necessary for breakdown of fats into energy.

## How it gets depleted

Vitamin C is most commonly depleted in the absence of sufficient dietary intake.

Vitamin C levels can be depleted during times of severe oxidative stress.



## Clinical Manifestations of Depletion

- Low levels of vitamin C have been associated with reduced bone density.
- Signs of deficiency include: bleeding gums, easy bruising, anemia, fatigue, weakness and joint pain. These symptoms are the result of weakened or deficient connective tissues throughout the body.
- Severe cases of vitamin C deficiency are called scurvy.

## Food Sources

Food sources of vitamin C include: oysters, tropical fruits such as guava, papaya, pineapple, oranges, kiwi, and cantaloupe; leafy greens such as kale and spinach; cruciferous vegetables such as broccoli, brussel sprouts, cauliflower, and cabbage; berries, such as strawberries, raspberries, blueberries, blackberries, bell peppers, and amaranth.

## Supplement Options

- The RDA for vitamin C is 75 mg/day for women and 90 mg/day for men. 120 mg/day is recommended during pregnancy and lactation.
- The half-life of vitamin C in circulation after supplementation is about 30 minutes, therefore, large singular doses of vitamin C may not be as therapeutic as smaller, more frequent doses of vitamin C.
- In addition to taking supplemental vitamin C,  $\alpha$ -Lipoic acid helps restore vitamin C levels when depleted.

### Physiological Function

Folate is the naturally occurring form found in foods; folic acid is the supplement/synthetic form. Folate is more bioavailable.

Once in circulation, folate gets methylated.

Methyl-tetrahydrofolate is the most abundant folate in circulation and it functions with vitamin B12 in methylation reactions to reduce homocysteine, but is also involved in DNA synthesis, and red blood cell synthesis.

### How it gets depleted

Folate can be depleted by use of methotrexate, anticonvulsants, antacids, and oral contraceptives.



### Clinical Manifestations of Depletion

- Deficiency of folate can manifest as anemia. Megoblastic anemia will also involve vitamin B12.
- Often folate deficiency is secondary to vitamin B12 deficiency because conversion to 5-methyl folate is B12 dependent.
- Symptoms of B12 deficiency can include: elevated homocysteine (hyperhomocysteinemia), neural tube defects if mother is deficient during pregnancy, mood disorders such as anxiety and depression, particularly in the elderly, and fatigue, impaired immune function, and cardiovascular disease.

### Food Sources

Food sources of folate include: green leafy vegetables, legumes (especially black-eyed peas) and lentils, brewer's yeast, and brown rice. Folate is easily destroyed by cooking.

\*Enriched grains are a supplemental source of folate

### Supplement Options

- The RDA for folate is 400 mcg/day for adults and 600 mcg/day in pregnant women.
- Consider MTHFR mutations before supplementing. Even in the presence of MTHFR mutations, individuals can be either under- or over-methylated, and supplementation should include a thorough review of levels of other co-factors and nutrients involved in methylation cycles.
- Doses of folate ranging from 400 mcg to 10 mg have been used clinically. A more common therapeutic range is 400 to 1000 mcg per day.
- Supplemental doses have been recommended not to exceed 400 mcg/day, because folic acid supplementation may mask the symptoms of B12 deficiency.

## MINERALS

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### Clinical Manifestations of Excess/ Risk for Toxicity

Symptoms and conditions that are associated with excess calcium include: Calcification of soft tissues (including heart and arteries); parathyroid disorders; kidney stones.

Causes of excess calcium in the blood include: low levels of PTH; high or excess intake of vitamin D2 or D3 supplements (unlikely with D2, however); hyperparathyroidism; reduced conversion of 25-OHD to 1,25-OHD in the kidneys; renal failure; parathyroid cancer.

Caution with excess calcium Supplements:

Calcium supplements may cause an excess of calcium in the blood if one has parathyroid dysfunction or renal failure. It is not recommended to take calcium supplements if those conditions exist, unless under the direction of a doctor.

Calcium supplementation should almost always be accompanied with supplementation of Vitamin D and possibly Vitamin K2 to ensure calcium is assimilated into bone and not ectopically deposited into soft tissue.

### Physiological Function

Calcium is a mineral that is a major component of bones and teeth, is required for muscle contraction, nerve transmission, cellular metabolism, and aids in blood clotting.

### How it gets depleted

Calcium stores in the blood are not depleted metabolically, however, calcium stores elsewhere in the body may become depleted, conditionally, due to increased demand.

Low dietary intake of calcium during times of growth or stress may result in low stores of calcium. Evaluate vitamin D and magnesium levels alongside calcium status.

Iron supplementation may interfere with calcium absorption, and it is recommended to take iron supplements at least 2 hours apart from a meal containing calcium-rich foods.

### Clinical Manifestations of Depletion

A deficiency of calcium causes osteoporosis. Some research connects low calcium intake to increased risks of high blood pressure, colon cancer and preeclampsia (high blood pressure and excess protein in the urine of a woman more than 20 weeks pregnant).

### Food Sources

Good sources of calcium are: dairy foods, salmon, turnip greens, \*Chinese cabbage, kale, bok choy and broccoli. Sardines and other canned fish with bones are additional sources. Some foods such as orange juice and bread are fortified with calcium.

\*Chinese cabbage, kale and turnip greens contain absorbable calcium. Spinach and some other vegetables contain calcium that is poorly absorbed.

### Supplement Options

- The AI for adults aged 19 to 50 is 1000 mg/day. Because calcium is so critical to preventing bone disease later in life, the AI is higher for adolescents.
- The AI for males and females aged nine to 18 is 1300 mg/day. For those aged 51 and older, the AI is 1200mg/day.
- The UL for calcium is 2,500 milligrams. Excess calcium may cause mineral imbalances because it interferes with the absorption of iron, magnesium, zinc and other minerals.
- Forms of calcium supplementation available include calcium carbonate, calcium citrate, calcium citrate malate, calcium gluconate, and calcium lactate.
- Calcium citrate is the preferred form of calcium for individuals with hypo- or achlorhydria (low or insufficient stomach acid).
- In order to maximize absorption of calcium supplements, limit doses to no more than 500mg/dose.
- Supplementation of calcium should be accompanied by concurrent adequate vitamin D supplementation due to insufficient vitamin D levels impairing cellular calcium absorption, which can lead to atopic calcium deposits in epidermal tissue.
- Iron supplementation may interfere with calcium absorption, and it is recommended to take iron supplements at least 2 hours apart from a meal containing calcium-rich foods.



## Physiological Function

Manganese is important in many enzyme-mediated chemical reactions including enzymes involved in antioxidant actions in mitochondria and enzymes involved in the synthesis of cartilage in skin and bone.

Manganese also activates enzymes that participate in metabolism of carbohydrates, amino acids, and cholesterol.

In addition, enzymes that incorporate manganese convert the neuro-excitatory glutamate to glutamine.

## How it gets depleted

- Iron supplementation may decrease absorption of dietary manganese.
- Intestinal absorption of manganese is reduced when iron stores (ferritin levels) are higher, and tends to be lower in men than women.
- Magnesium supplementation has been shown to decrease manganese levels through reduced intestinal absorption or increased urinary excretion.

## Clinical Manifestations of Depletion

- Manganese deficiency is rare.
- Symptoms of manganese deficiency are impaired growth, particularly skeletal abnormalities, and possibly glucose tolerance abnormalities.
- Toxicity is also uncommon and is most frequently the result of exposure to airborne manganese dust.
- Symptoms of toxicity include multiple neurological problems that resemble Parkinson's disease. In children, exposure to elevated levels of manganese in drinking water has been associated with increased rates of attention deficit hyperactivity disorder, cognitive decline, and behavioral problems.
- Individuals with liver failure are at risk for manganese toxicity-associated neurological symptoms.

## Food Sources

Tea and coffee are significant sources of manganese in the American diet. Additional sources are nuts, whole grains, legumes and some fruits and vegetables, such as leafy greens.

## Supplement Options

- The AI for manganese is 1.8 mg/day.
- The UL for manganese is 11 mg per day.
- Supplementation of manganese is not generally necessary, and may result in toxicity.



## Physiological Function

- Copper assists with the transport of iron, supports energy production within cells, supports methylation and gene transcription that affects cellular detoxification mechanisms, neurotransmitter generation, supports the myelin sheath around nerves, and aids in connective tissue development.
- Copper is important for redox reactions and is a potent antioxidant for this reason.
- Copper also supports melanin production in the cells of hair, skin, and nails.
- Most serum copper is found in ceruloplasmin and elevated levels may be an indicator of increase inflammation and oxidative stress, rather than specifically excess copper in the blood.

## How it gets depleted

Deficiencies or excesses of copper are rare in healthy people, however, copper deficiency can occur in the following populations: infants or children fed only cow's milk formula; premature infants and infants or children with recurring diarrhea; individuals with malabsorption syndromes such as celiac disease, bowel resections, Crohn's disease, and ulcerative colitis; individuals with cystic fibrosis; individuals with high supplemental zinc intake for prolonged periods of time.

Consider testing for the presence of celiac disease or neurological indications of demyelination to assess if copper deficiency may be associated.



## Clinical Manifestations of Depletion

- Copper may become deficient or depleted in the presence of supplemental zinc intake at or above 60mg/day for prolonged periods of time.
- Because copper is critical to iron metabolism and red blood cell formation and function, anemia can be a clinical sign of copper deficiency, as iron becomes trapped in the liver without adequate copper to facilitate transport.
- Copper depletion is rare, but can be seen in Wilson's disease, in which dietary copper intake does not affect copper status. Severe copper deficiency may also lead to cardiovascular abnormalities and cardiomyopathy, however, some epidemiological studies suggest that elevated levels of copper may also be associated with increased atherosclerosis.
- Low levels of neutrophils may be seen in individuals with copper deficiency, as well as anemias that do not respond to iron supplementation.
- In children, copper deficiency may lead to impaired growth, neurological problems, and loss of skin pigmentation.

## Food Sources

Rich sources of copper include liver, shellfish, cashews, hazelnuts, almonds, peanut butter, lentils, mushrooms, and sunflower seeds.

## Supplement Options

- The RDA for copper in adults is 900 µg/day.
- The UL for copper is 10 mg/day, which has been shown not to produce liver damage in healthy individuals.
- Copper supplementation of 2 mg/day is usually sufficient to correct deficiencies of copper.
- Copper is most commonly available in the following supplemental forms: cupric oxide, copper gluconate, copper sulfate, copper amino acid chelates.
- Some research suggests elevated blood levels of free unbound copper, which depletes zinc levels, may have an association with the onset of Alzheimer's disease, and supplementation of copper in this population is not recommended if zinc deficiency is suspected.

### Clinical Manifestations of Excess/ Risk for Toxicity

Chromium occurs in primarily two states, trivalent chromium (chromium 3) typically found in foods and hexavalent chromium (chromium 6) typically found in industrial sources and pollutants. Chromium 3 is much less toxic than chromium 6. The body can detoxify some amount of chromium 6 to chromium 3 using glutathione, hydrogen peroxide, glutathione reductase, and ascorbic acid. Few serious adverse effects have been linked to high intakes of chromium 3, so no UL has been established for chromium 3. Overexposure to chromium 6 can occur in welders and other workers in the metallurgical industry, use of chromium-containing paints and primers, individuals with metallic surgical implants, individuals who ingest chromium salts. Chromium toxicity, depending upon route of exposure, can cause nausea, vomiting, diarrhea, muscle cramps, skin lesions, sinus, nasal and lung cancer, renal failure, liver damage, circulatory collapse, coma and death.

### Physiological Function

Chromium is an essential nutrient used in trace amounts in humans that acts as a cofactor for chromodulin, a peptide that enhances the effect of insulin on target tissues, which aids in regulation of blood sugar and lipid metabolism.

### How it gets depleted

Deficiency is very rare, but can occur in patients receiving IV parenteral nutrition, without supplemental chromium added, and individuals who regularly participate in endurance exercise.

### Clinical Manifestations of Depletion

Chromium deficiency can contribute to the development of diabetes and metabolic syndrome. Even mild deficiencies of chromium can produce problems in blood sugar metabolism, and contribute to other symptoms such as anxiety or fatigue.

### Food Sources

Food sources of chromium include: brewer's yeast, especially beer, broccoli, grape juice, meat and whole-grain products. Some fruits, vegetables, and spices provide chromium. Romaine lettuce, raw onions and ripe tomatoes are all good sources.

### Supplement Options

- The AI for chromium is 35 µg/day for men and 25 µg/day for women.
- Increased needs may be present during pregnancy and lactation.
- Supplemental chromium is generally not needed as dietary consumption easily meets physiological needs.
- Supplementation is poorly studied and insufficient evidence exists to provide recommendations, but chromium picolinate is a form commonly used in treatment of insulin resistance and diabetes.



## Physiological Function

- Iron is required for the production of red blood cells (a process known as hematopoiesis), but it's also part of hemoglobin (that is the pigment of the red blood cells) binding to the oxygen and thus facilitating its transport from the lungs via the arteries to all cells throughout the body. Once the oxygen is delivered, the iron (as part of hemoglobin) binds the carbon dioxide which is then transported back to the lung, from where it gets exhaled. Iron is also involved in the conversion of blood sugar to energy.
- The production of enzymes (which play a vital role in the production of new cells, amino acids, hormones and neurotransmitters) also depends on iron, this aspect becomes crucial during the recovery process from illnesses or following strenuous exercise.
- The immune system is dependent on iron for its efficient functioning. Physical and mental growth require sufficient iron levels, particularly important in childhood and pregnancy, where the developing baby solely depends on its mother's iron supplies.

## Clinical Manifestations of Excess/ Risk for Toxicity

Iron levels are typically evaluated in conjunction with other iron tests or a full anemia panel. High levels of serum iron can occur as the result of multiple blood transfusions, excessive iron supplementation or injections, lead poisoning, liver or kidney disease. Elevated iron levels can also be due to the genetic disease hemochromatosis-when too much iron accumulates in the body and can damage organs.

High iron levels from dietary or supplementation are more likely in men, and women after menopause because they do not lose iron in blood.

## How it gets depleted

Iron is lost by the body through a variety of ways including urination, defecation, sweating, and exfoliating of old skin cells. Bleeding contributes to further loss of iron which is why women have a higher demand for iron than men. If iron stores are low, normal hemoglobin production slows down, which means the transport of oxygen is diminished, resulting in symptoms such as fatigue, dizziness, lowered immunity or reduced ability for athletes to keep up with their training programs. Since our bodies can't produce iron itself, we need to make sure we consume sufficient amounts of iron as part of our daily diet.

## Clinical Manifestations of Depletion

Mild iron deficiency can be prevented or corrected by eating iron-rich foods and by cooking in an iron skillet. Because iron is a requirement for most plants and animals, a wide range of foods provide iron. Good sources of dietary iron have heme-iron as this is most easily absorbed and is not inhibited by medication or other dietary components. Two examples are red meat, and poultry.

Non-heme sources do contain iron, though it has reduced bioavailability. Examples are lentils, beans, leafy vegetables, pistachios, tofu, fortified bread, and fortified breakfast cereals. Iron from different foods is absorbed and processed differently by the body; for instance, iron in meat (heme iron source) is more easily absorbed than iron in grains and vegetables (non-heme iron source) but heme/hemoglobin from red meat has effects which may increase the likelihood of colorectal cancer. Minerals and chemicals in one type of food may also inhibit absorption of iron from another type of food eaten at the same time. For example, oxalates and phytic acid form insoluble complexes which bind iron in the gut before it can be absorbed.

Because iron from plant sources is less easily absorbed than the heme bound iron of animal sources, vegetarians and vegans should have a somewhat higher total daily iron intake than those who eat meat, fish or poultry. Legumes and dark-green leafy vegetables like broccoli, kale and oriental greens are especially good sources of iron for vegetarians and vegans. However, spinach and Swiss chard contain oxalates which bind iron making it almost entirely unavailable for absorption. Iron from nonheme sources is more readily absorbed if consumed with foods that contain either heme- bound iron or vitamin C.

## Food Sources

Symptoms of iron deficiency can occur even before the condition has progressed to iron deficiency anemia. Symptoms of iron deficiency are not unique to iron deficiency.

Iron is needed for many enzymes to function normally, so a wide range of symptoms may eventually emerge, either as the secondary result of the anemia, or as other primary results of iron deficiency. Symptoms of iron deficiency include: fatigue, dizziness, pallor, hair loss, twitches, irritability, weakness, pica, brittle or grooved nails.

## Supplement Options

Frequently used forms of iron in supplements include ferrous and ferric iron salts, such as ferrous sulfate, ferrous gluconate, ferric citrate, and ferric sulfate. Because of its higher solubility, ferrous iron in dietary supplements is more bioavailable than ferric iron. High doses of supplemental iron (45 mg/day or more) may cause gastrointestinal side effects, such as nausea and constipation. Other forms of supplemental iron, such as heme iron polypeptides, carbonyl iron, iron amino-acid chelates, and polysaccharide-iron complexes, might have fewer gastrointestinal side effects than ferrous or ferric salts. Many medicinal herbs can offer iron boosting properties to those who suffer from iron deficiency. These medicinal properties can easily be assimilated into the bloodstream as a hot water infusion (tea). Iron enhancing herbs include yellow dock, red raspberry leaf, gentian, yellow root, turmeric, mullein, nettle, parsley, ginseng, watercress, and dandelion.

# METABOLITES



### Physiological Function

Choline is metabolized within cellular mitochondria resulting in production of trimethylglycine; TMG plays a role in supporting methyl donation processes either directly (methylating homocysteine) or indirectly through supporting production of S-adenosyl methionine (SAMe). Choline is converted into acetylcholine (ACh).

### How it gets depleted

Depletion of choline is typically not a concern, and limited information exists on how depletion would happen primarily, however, lower intake of choline may lead to inefficient methylation.

### Clinical Manifestations of Depletion

- Deficiency in dietary choline is known to increase hepatic triglyceride accumulation. This results in lower blood triglycerides, but increased accumulation of triglycerides in the liver.
- Subjects with a mutation in the MTHFR enzyme seem to place more burden on choline in methylation cycles. Depletion of choline can also lead to muscle damage.

### Food Sources

Eggs, liver, and peanuts are the best sources of choline. Poultry, fish, and cruciferous veggies are good sources of choline.

\*Dietary choline sources, including lecithin (phosphatidylcholine), may increase serum TMAO in humans, although the evidence is mixed.

### Supplement Options

- The AI for choline is 425 mg/day for women and 550 mg/day for men.
- The UL is 3,500 mg/day.
- Choline bitartrate is the most common supplemental form of choline for most general purposes, such as liver health.
- CDP-Choline and Alpha-GPC are commonly used for nootropic purposes.
- Supplemental choline can enhance systemic methylation. Excessive consumption of choline  $\geq 7,500$  mg has been associated with low blood pressure, excessive sweating, fishy body odor, and gastrointestinal side effects.

## Physiological Function

Inositol derivatives are used in the cellular signaling process after the insulin receptor is activated; it is crucial for the development of peripheral nerves, helps move fats out of the liver, promotes the production of lecithin, and is anti-arteriosclerotic, and anti-atherogenic.

## How it gets depleted

Inositol can be released from phytate compounds via intestinal bacteria breaking phytate-degrading enzymes (*Lactobacillus plantarum*, *Lactobacillus brevis*, *Lactobacillus curvatus*, *L. gasseri*, *B. subtilis* and *Saccharomyces cerevisiae*).

If many courses of antibiotics are used, there may be some depletion of inositol from microbiome conversion.

Inositol is also stored in the liver, spinal cord nerves, and in the brain and cerebral spinal fluid.



## Clinical Manifestations of Depletion

- There do not appear to be any clinical manifestations of depletion of inositol. Inositol can be synthesized in the human body from glucose-6-phosphate, a derivative of glucose, therefore, deficiency would be rare.
- Urinary levels of inositol derivatives (D-chiro-inositols and myo-inositols) are seen as a biomarker for insulin resistance.
- Conditions associated with depletion of inositol, however, are depression, anxiety, PCOS, diabetes, CVD, and obesity.

## Food Sources

Good dietary sources of inositol include: oranges, cantaloupe, prunes, navy beans, grapefruit, limes, blackberries, kiwis, rutabagas, fresh green beans, unrefined molasses, stone ground wheat, bran flakes, and pumperknickel.

## Supplement Options

- There is currently no established RDA, AI, or UL for inositol. Myo-inositol is noted for its benefits to female fertility and insulin sensitivity, and is used often in treatment for PCOS in dosages of 2-4g/day.
- Higher doses of inositol are used to treat psychiatric conditions like depression and anxiety/OCD in much higher doses of 12-18 g/day; some mild gastrointestinal distress is noted with the higher doses and may need to be consumed in split doses.
- Lowering blood glucose can be seen with doses of inositol around 2-4 g/day.
- Currently supplementation of inositol has shown some promise in treating Alzheimer's to reduce progression of fibril formation.
- Inositol may decrease LDL-C and ApoB in persons with metabolic syndrome with doses of 5-10 g/day.
- Doses of inositol of 4 g/day have been associated with improvement of all markers of glycemic control and insulin resistance in gestational diabetes.

## Physiological Function

Carnitine is an essential co-factor in the metabolism of lipids and the production of cellular energy. It promotes neuroprotection through antioxidant properties and modulation and promotion of synaptic neurotransmission. Carnitine can be rate-limiting in ketone body uptake by brain astrocytes, and also reduces oxidative stress.

## How it gets depleted

Carnitine deficiency is rare in individuals who consume an omnivorous diet. Iron and Vitamin C are required for endogenous carnitine synthesis, and endogenous synthesis can also be impaired by severe liver disorders.

Deficiency may be found in vegetarians and vegans, and individuals with impaired absorption of nutrients, such as in inflammatory bowel disorders and celiac disease.

There may be increased demand for carnitine during ketosis.



## Clinical Manifestations of Depletion

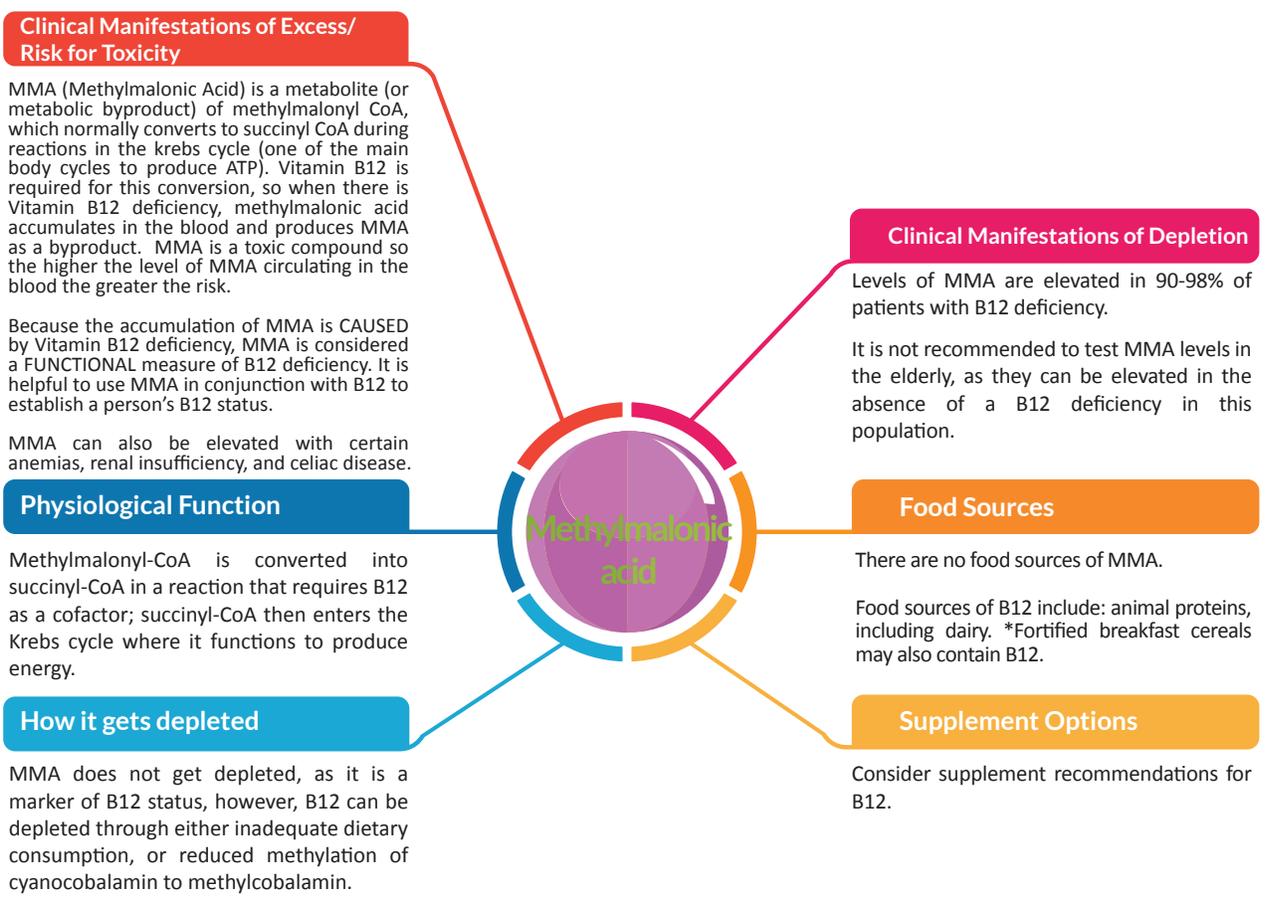
Symptoms of carnitine depletion or deficiency include: male infertility, impaired muscle metabolism of energy, which can cause myopathy, hypoglycemia, muscle necrosis, myoglobinuria, lipid-storage myopathy, hypoglycemia, fatty liver, and hyperammonemia with muscle aches, fatigue, confusion, and cardiomyopathy.

## Food Sources

Carnitine is found naturally occurring in high amounts in red meat, eggs, and dairy products.

## Supplement Options

- There is currently no established RDA, AI, or UL for carnitine intake.
- Supplementation of carnitine has been used in treatment of chronic degenerative diseases of the brain and for slowing down the progression of Alzheimer's disease.
- Carnitine supplementation in athletes has not been shown to consistently produce performance benefits.
- Carnitine comes in supplement form as L-carnitine.
- Some research suggests that diets high in carnitine may have associations with cardiovascular inflammation due to the over-abundance of opportunistic microbes that convert dietary carnitine to trimethylamine oxidase (TMAO). Consider testing levels of these bacteria to assess if TMAO levels are due to intestinal dysbiosis.



## AMINO ACIDS

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### Physiological Function

Asparagine is a non-essential amino acid required for development and function of the brain.

Asparagine can be synthesized from glutamine and aspartate. Asparagine is also required for DNA and RNA synthesis and removal of the cellular waste product ammonia.

### How it gets depleted

Asparagine deficiency is not likely due to its endogenous synthesis and ubiquitous presence in both plant and animal foods.



### Clinical Manifestations of Depletion

There are no known deficiency symptoms of asparagine that have been well reported or well studied, but possible symptoms of asparagine depletion could include fatigue or cognitive decline in adults.

### Food Sources

Dietary sources of asparagine include: dairy, whey, beef, poultry, eggs, fish, seafood, asparagus, licorice root, legumes, nuts, seeds, soy, and grains.

### Supplement Options

There is currently no established RDA, AI, or UL for asparagine.

Asparagine is rarely supplemented directly, due to its endogenous production in the body, but could be indirectly supplemented through glutamine.

## Physiological Function

- Glutamine is a conditionally essential amino acid (conditional mainly during times of disease or muscle wasting, such as HIV/AIDS, cancer, or severe infections).
- In the intestinal lining, glutamine is the preferred source of fuel for intestinal epithelial cells and the main energy source for leukocytes (immune cells).
- Other important functions of glutamine include: transporting nitrogen between cells, acting as a precursor to glutathione production, acting as a precursor to nucleotides (for DNA and RNA synthesis), participating in gluconeogenesis in the absence of adequate carbohydrate intake, blunting the rise of blood glucose after consuming carbohydrate-rich meals, and regulating intestinal tight junctions.

## How it gets depleted

Glutamine is known to be depleted in certain types of physiological stress such as burns, major trauma, and cancers that consume available intra-cellular glutamine stores more rapidly than skeletal muscle can generate it, leading to increased muscle wasting.

During physical activity, serum glutamine is consumed for longer endurance events (2+ hours); some evidence exists that chronic endurance exercise reduced glutamine levels to affect immune cell function and proliferation.



## Clinical Manifestations of Depletion

Glutamine depletion or deficiency is rare, as glutamine can be made endogenously and is ubiquitous in the food supply from both plant and animal sources.

Some studies suggest an increase in intestinal permeability when intestinal epithelial cells lack sufficient glutamine, as well as insufficient availability for leukocyte function.

## Food Sources

Very good sources of glutamine include: whey, casein, milk, white rice, corn, and tofu.

Good sources of glutamine include: meat and eggs.

## Supplement Options

- There is currently no established RDA, AI, or UL for glutamine.
- Glutamine is typically sold as L-glutamine and doses have been studied in humans ranging from 500 mg/day – 50g/day. Higher doses (>10 g/day) are commonly used in the treatment of intestinal barrier permeability.
- Supplementation of glutamine has not been shown to enhance muscle growth in healthy individuals.
- Typically an increase in serum insulin results after consumption of glutamine due to increased conversion to glucose. This may impact individuals with insulin resistance.
- Glutamine supplementation is also potentially beneficial to improve mental focus and concentration, as well as curbing cravings for sugar and alcohol.
- In some individuals, glutamine is converted more efficiently to glutamate, which can lead to a neuro-excitatory state, increased anxiety, tension headaches/migraines, and even tachycardia. If any of these symptoms occur after consuming glutamine, discontinue supplementation and discuss with your provider.

### Physiological Function

D-serine is a neuromodulator, produced in glial cells of the brain, and modulates the functions of neurons. Serine can be considered a nootropic nutrient.

Serine enhances binding of other compounds at NMDA (N-methyl-D-aspartate) receptors.

### How it gets depleted

Serine can be synthesized endogenously from dietary glycine, which is not considered an essential amino acid.

Serine deficiency would be rare, however, supra-physiological doses may be necessary to confer benefit over standard dietary intake.

### Clinical Manifestations of Depletion

It does not appear that depletion of serine is common, but side effects of low levels of serine in the brain appear to be correlated with a higher risk for addiction behaviors and some neurodegenerative conditions.

### Food Sources

Foods high in glycine include: fish, meat, dairy, sugar cane, soybeans, spinach, kale, cauliflower, cabbage, pumpkin, banana, kiwi, cucumber, and beans.

### Supplement Options

- There is currently no established RDA, AI, or UL for serine supplementation or intake.
- Serine can be supplemented to reduce symptoms of cognitive decline and reduce symptoms of cocaine dependence and schizophrenia.
- Phosphatidylserine is a common supplemental phospholipid that contains serine.
- Doses of 30mg/kg of bodyweight are commonly used in cognitive decline patients.

### Physiological Function

L-Arginine is a conditionally essential amino acid found in the diet. It is a dietary supplement used mostly by athletes because it is the amino acid that directly produces nitric oxide via the nitric oxide synthase enzymes.

Arginine helps heal injuries, aids kidneys in removing waste, and boosts immune system function.

### How it gets depleted

Arginine is important during periods of illness and chronic conditions like hypertension and type II diabetes, as these states tend to be characterized by an increase in the enzyme that degrades L-arginine (known as arginase) resulting in a transient deficiency; this precedes an increase in blood pressure in these states, and can be partially remedied by an increase in L-arginine intake or resolution of the illness/disease state.

### Clinical Manifestations of Depletion

Arginine is one of the three substrates to form creatine which is a vital nutrient (deficiency induces mental retardation) and is also used to form agmatine, a signalling molecule in the body. Arginine is an intermediate in both the urea cycle (with L-ornithine, L-citrulline, and arginosuccinate) and the nitric oxide cycle (with ornithine and arginosuccinate), and vicariously through ornithine it produces polyamine structures which can regulate cellular function. In some individuals with viral infections such as shingles, arginine supplementation may exacerbate symptoms and consultation with a healthcare provider is recommended.

### Food Sources

Dietary arginine accounts for 40-60% of serum arginine. Food sources include: turkey, pork, chicken, pumpkin seeds, soybeans, peanuts, spirulina, dairy, chickpeas, lentils.

### Supplement Options

- To maintain elevated arginine levels throughout the day, arginine can be taken up to three times a day, with a combined dose total of 15-18g. Note: L-citrulline supplementation is more effective at maintaining elevated arginine levels for long periods of time.
- Taking more than 10g of arginine at once can result in gastrointestinal distress and diarrhea.

### Physiological Function

Citrulline is an amino acid that is not one of the essential amino acids nor a common dietary amino acid (named after its only good natural source, watermelons), but is interconverted in the body and serves roles similar to L-arginine and L-ornithine.

### How it gets depleted

Citrulline can be produced by arginine by one of two mechanisms: either directly via arginine giving off a nitric oxide molecule (which is the path involved in the nitric oxide cycle), or indirectly via arginine's conversion into ornithine (which is involved in the urea cycle), sequestering ammonia.

### Clinical Manifestations of Depletion

The majority of L-citrulline either floats in the blood passively or gets transported to the kidneys for conversion into arginine.

### Food Sources

Food sources of L-citrulline include watermelon, muskmelons, bitter melons, squashes, gourds, cucumbers, and pumpkins.

### Supplement Options

There is mixed evidence as to whether citrulline supplementation can help with muscle protein synthesis.

### Physiological Function

Isoleucine is an essential branched-chain aliphatic amino acid found in many proteins. It is an isomer of leucine. It is important in hemoglobin synthesis and regulation of blood sugar and energy levels. Isoleucine is one of nine essential amino acids in humans (present in dietary proteins). It has diverse physiological functions, such as assisting wound healing, detoxification of nitrogenous wastes, stimulating immune function, and promoting secretion of several hormones.

### How it gets depleted

Isoleucine is necessary for hemoglobin formation and regulating blood sugar and energy levels. Isoleucine is concentrated in muscle tissues in humans. Deficiency is primarily due to low total protein intake, but may be found in individuals with prolonged or severe reduced digestive capacity, particularly those who have trouble digesting protein or with more severe hypochlorhydria.

### Clinical Manifestations of Depletion

Isoleucine deficiency is marked by muscle tremors. All 3 BCAAs are decreased in patients with liver disease, such as hepatitis, hepatic coma, cirrhosis, or extrahepatic biliary atresia. L-isoleucine is found to be associated with maple syrup urine disease, which is an inborn error of metabolism.

### Food Sources

Isoleucine is found especially in meats, fish, cheese, eggs, and most seeds and nuts.

### Supplement Options

### Physiological Function

Valine is a branched-chain essential amino acid that has stimulant activity. It promotes muscle growth and tissue repair. It is a precursor in the penicillin biosynthetic pathway. As a glycogenic amino acid, valine maintains mental vigor, muscle coordination, and emotional calm.

### How it gets depleted

Despite their structural similarities, the branched amino acids have different metabolic routes, with valine going solely to carbohydrates, leucine solely to fats, and isoleucine to both. The different metabolism accounts for different requirements for these essential amino acids in humans: 12 mg/kg, 14 mg/kg and 16 mg/kg of valine, leucine and isoleucine respectively.

### Clinical Manifestations of Depletion

Valine deficiency is marked by neurological defects in the brain.

### Food Sources

Valine is obtained from soy, cheese, fish, meats, and vegetables

### Supplement Options

Valine supplements are used for muscle growth, tissue repair, and energy. Because food sources are plentiful, supplementation is typically not necessary in the face of optimal total protein intake from a variety of sources.

### Physiological Function

Leucine is one of nine essential amino acids in humans (provided by food). Leucine is important for protein synthesis and many metabolic functions. Leucine contributes to regulation of blood-sugar levels, growth and repair of muscle and bone tissue, growth hormone production, and wound healing. Leucine also prevents breakdown of muscle proteins after trauma or severe stress and may be beneficial for individuals with phenylketonuria.

### How it gets depleted

Leucine is available in many foods and deficiency is rare.

### Clinical Manifestations of Depletion

Leucine supplementation alone exacerbates pellagra and can cause psychosis in pellagra patients by increasing excretion of niacin in the urine. Leucine may lower brain serotonin and dopamine.

### Food Sources

Leucine is more highly concentrated in foods than other amino acids. A cup of milk contains 800 mg of leucine and only 500 mg of isoleucine and valine. A cup of wheat germ has about 1.6 g of leucine and 1 g of isoleucine and valine. The ratio evens out in eggs and cheese. One egg and an ounce of most cheeses each contain about 400 mg of leucine and 400 mg of valine and isoleucine. The ratio of leucine to other BCAA is greatest in pork, where leucine is 7 to 8 g and the other BCAA together are only 3-4 grams.

### Supplement Options

BCAAs, and particularly leucine, are among the amino acids most essential for muscle health. Supplementation is typically not necessary if total protein intake from a variety of sources is optimal.

## ANTIOXIDANTS

### Physiological Function

CoQ10 is a fat-soluble compound primarily synthesized by the body and also consumed in the diet. It is found in virtually all cell membranes and participates in the mitochondria to convert carbohydrates and fatty acids into ATP. CoQ10 also supports cell signaling, gene expression, stimulation of cell growth, inhibition of apoptosis, control of thiol groups, formation of hydrogen peroxide, and control of membrane channels.

### How it gets depleted

CoQ10 is most commonly depleted through use of cholesterol-lowering medication, such as statins. Other causes of CoQ10 deficiency include genetic mutations that limit biosynthesis, unknown reasons in the aging process, cancer, and smoking.



### Clinical Manifestations of Depletion

Signs of CoQ10 deficiency include muscle weakness and fatigue, high blood pressure, and slowed thinking; more extreme symptoms of CoQ10 deficiency include chest pain, heart failure, and seizures.

### Food Sources

Food sources of CoQ10 are considered poor sources of the nutrient. Foods that contain more CoQ10 than others include organ meats from red meat sources. Nuts are considered a moderate source but would have to be eaten in extreme amounts to get the daily requirement.

### Supplement Options

- There is currently no established RDA, AI, or UL for CoQ10.
- CoQ10 comes in both ubiquinone and ubiquinol forms; ubiquinol is considered the active form, however, the body uses both forms as needed.
- Typical doses required to restore minimum CoQ10 levels while using statin drugs are 100-200 mg/day.
- Intestinal absorption of CoQ10 is limited, but optimized if consumed with a meal containing fat.
- There are really no adverse symptoms with high dose CoQ10 supplementation; however, supplementation is typically not recommended for pregnant or lactating women due to lack of controlled studies.

## Physiological Function

- Cysteine has antioxidant properties itself, but is also a precursor molecule to glutathione production, the master antioxidant.
- Cysteine is also an important source of sulfide for iron-sulfide metabolism.
- Cysteine will bind metals easily to its thiol group, such as iron, nickel, copper, zinc, and heavy metals such as mercury and lead, which may confer some chelation benefits.
- Cysteine counteracts acetaldehyde effects from consumption of alcohol and can reduce hangovers.

## How it gets depleted

Cysteine can be synthesized endogenously as long as sufficient methionine is available in the diet. Depletion is extremely rare.



## Clinical Manifestations of Depletion

Depletion or deficiency of cysteine is not common, as cysteine can be made endogenously, but can conditionally be required in greater amounts due to its strong antioxidant and detoxification properties.

## Food Sources

Dietary sources of cysteine include: meat, poultry, eggs, dairy, red peppers, garlic, onions, broccoli, Brussels sprouts, oats, granola, wheat germ, and lentils.

## Supplement Options

- There is currently no established RDA, AI, or UL for cysteine.
- Cysteine is typically purchased in supplement form as N-acetyl-cysteine (NAC).
- Cysteine can be purchased as L-cysteine in powder form.
- For general antioxidant support, doses start at 500mg/day and can increase depending upon direction from medical provider.

**AVOID: D-cysteine or D-cystine, which are toxic**

## Physiological Function

- Glutathione is the master intracellular antioxidant.
- Glutathione is the main non-enzymatic antioxidant in intestinal epithelium.  
The only cells in the body that have been found to be able to absorb intact GSH are hepatocytes, intestinal mucosal cells, and retinal cells.
- GSH can also conjugate target compounds for removal through hepatic/renal excretion or through removal into the intestinal lumen and through fecal elimination.
- Alpha-lipoic acid appears to support the transport of cystine (two bonded cysteine molecules) between cells for uptake to generate glutathione, and therefore, may increase glutathione synthesis provided that cysteine levels are adequate.

## How it gets depleted

- Glutathione levels deplete naturally during aging, however, this could be related to decreased protein intake in aging individuals.
- Pro-inflammatory states and elevated oxidative stress will drain GSH stores and require a conditionally greater intake of either high cysteine foods or NAC as a supplement to increase endogenous GSH production.
- Conversion of depleted glutathione back to its active state is achieved through an NADPH-dependent enzyme, so it stands to reason that low levels of NAD (or niacin, nicotinic acid) could further limit this conversion back to active GSH forms.
- Consider mutations in GSHPx gene to determine if deficiency or depletion is genetically influenced.



## Clinical Manifestations of Depletion

Symptoms of glutathione depletion or deficiency include: fatigue, increased oxidative stress, inflammation, cancer, and infections.

## Food Sources

Dietary glutathione consumption does not correlate with systemic levels of glutathione, but sources of glutathione are fruits and vegetables such as: asparagus, avocado, spinach, broccoli, cantaloupe, tomato, carrot, grapefruit, orange, zucchini, strawberry, watermelon, papaya, red bell pepper, peaches, lemons, mangoes, cauliflower, and cabbage.

## Supplement Options

- There currently is no RDA, AI, or UL established for glutathione intake.
- Glutathione cannot enter cells intact, and must be synthesized inside the cell in order to be effective, therefore, supplementation usually has negligible benefit.
- Supplementing the building blocks such as N-acetyl-cysteine, glutamic acid and glycine, of which NAC is the only one that may be necessary to supplement, may increase cellular production of glutathione.
- Direct glutathione supplementation has only been shown to benefit slowing the breakdown of nitric oxide in the bloodstream.



## WHOLE BLOOD OMEGA FATTY ACIDS

## Physiological Function

- Eicosapentaenoic acid (EPA) is an omega-3 fatty acid that participates in the health of cellular membranes, mediates lipid actions, and reduces inflammatory responses in the body.
- EPA and DHA influence the types of inflammatory response mediators made in favor of anti-inflammatory eicosanoids such as leukotrienes, prostaglandins, and thromboxanes. EPA and DHA are also noted for moderate to strong anti-depressant effects.
- Specific to EPA, it has been shown to suppress signaling of TNF- $\alpha$  in adipocytes.
- EPA also increases cerebral oxygenation.
- EPA appears to have some beneficial influence on regulating levels of leptin and increasing adiponectin.
- EPA may enhance adaptive immunity by stimulating B cell responsiveness.

## How it gets depleted

Lower dietary intake of omega-3 fatty acids is the primary reason for deficiency of EPA, or low levels of EPA.

Certain genetic polymorphisms such as reduced activity of the FADS1 and FADS2 genes may lead to reduced conversion of ALA into EPA and DHA.

## Clinical Manifestations of Depletion

EPA can be manufactured in the body from ALA, as well as retroconverted from DHA. However, relying solely on intake of ALA to provide adequate levels of EPA is not recommended due to poor or inefficient conversion from ALA to EPA.

Lower levels of EPA or deficient intake of EPA have been linked to increased risk for cardiovascular disease, arrhythmia, blood clots, heart attacks, stroke, elevated triglyceride levels, increased growth of atherosclerotic plaque, reduced vascular endothelial function, skin cancer, and increased inflammation.

Lower levels of EPA are also associated with lower brain mass in older adults.

## Food Sources

Good sources of EPA include: fatty fish such as Pacific herring, salmon, oysters, tuna, and omega-3 enriched eggs.

Food sources of ALA, the essential fatty acid EPA precursor include: flaxseeds and flaxseed oil, chia seeds, walnuts, and canola oil.

## Supplement Options

- Currently, no official dietary intake recommendations have been established.
- Several official health organizations have proposed a minimum dietary intake level of 500 mg/day of EPA+DHA.
- Because the efficiency of conversion of ALA to EPA is so low, supplementing EPA is generally recommended to meet therapeutic doses.
- High dose supplementation of omega-3 fatty acids (including EPA) has been shown to reduce the need for non-steroidal anti-inflammatory drugs (NSAIDS).
- Persons suffering from ulcerative colitis have been shown to need fewer corticosteroids when supplementing with high dose omega-3 fatty acids.
- Adverse side effects observed with high dose omega-3 fatty acids from supplement form include gastrointestinal upset and loose stools.
- Omega-3 supplements including EPA and DHA should be used with caution in persons with clotting disorders or on anti-clotting medication.



### Physiological Function

Docosapentanoic acid (DPA) is a structurally similar omega-3 fatty acid to EPA.

DPA is an intermediary omega-3 fatty acid between the conversion of EPA and DHA.

DPA supports the production of healthy blood vessels and reduces clotting.

### How it gets depleted

Deficiency of DHA is typically due to low dietary intake of high DPA foods.



### Clinical Manifestations of Depletion

Low levels of DPA are associated with increased risk of thrombosis and stroke death.

### Food Sources

Good sources of DPA include: fish oil, fatty fish such as salmon, and grass-fed beef.

### Supplement Options

Adverse side effects observed with high dose omega-3 fatty acids from supplement form include gastrointestinal upset and loose stools.

### Physiological Function

Arachidonic acid is considered a conditional essential fatty acid and is a structural component of cell membranes-particular cell membranes of the central nervous system (nerve and brain cells).

AA is also a metabolic precursor for proinflammatory signaling molecules (eicosanoid) synthesis.

### How it gets depleted

A low AA level with a high or normal LA level likely indicates a delta-6-desaturase deficiency. Activity of this enzyme can be impaired with increased age, alcohol use, certain genetic defects or nutrient deficiency or excess.



### Clinical Manifestations of Depletion

Low levels of AA are somewhat rare but can lead to an impairment to cell membrane functions of the central nervous system. Children with attention deficient or hyperactivity disorders have been shown to have low levels. Low levels could also lead to an inappropriate or insufficient immune response or delayed wound healing.

In western cultures, high levels of AA tend to be more problematic as they are associated with many proinflammatory conditions including heart disease, diabetes, arthritis and other autoimmune conditions. High levels of AA stimulate the production of proinflammatory cytokines.

### Food Sources

AA can be made endogenously inside the body from the parent compound Linolenic Acid. The rate of conversion is largely dependent on the activity of the delta-6-desaturase.

### Supplement Options

It is rarely necessary to supplement with arachidonic acid. If levels are deficient consider linolenic acid levels and factors that could influence delta-6-desaturase enzyme.

To reduce endogenous AA production, reduce dietary intake of vegetables oils high in LA (corn, soy, canola, safflower oil).

Fish oil supplementation or increased intake of EPA fatty acids in the diet can also lower AA.

## Physiological Function

Omega-3 Index is the sum of EPA % and DHA % as measured in whole blood, and derived by validated calculations to yield the equivalent sum of EPA % and DHA % in red blood cell membranes. Please note this value is a percentage, with the denominator being the sum of all Fatty Acids measured in the blood and thus the index can vary based on fatty acid composition of the diet.

The index can be used as an indicator of risk for sudden cardiac death and nonfatal cardiovascular events and as a therapeutic target. It can also be used to assess adherence to omega-3 therapy and/or success or failure of such therapy. Optimal omega-3 index positively impacts heart rate, blood pressure, triglyceride levels, myocardial efficiency, inflammatory responses, and endothelial function while also improving cognitive function.

## How it gets depleted

The Omega-3 Index is a validated biomarker of tissue membrane omega-3 (n-3) polyunsaturated fatty acid (PUFA) status. The ratio is expressed as a percentage where the denominator is the sum of all fatty acids measured in the blood. Thus, a decrease in the ratio can be caused by a low intake of omega-3 fatty acids and incorporation of those fatty acids into cell membranes; or due to a proportionally high intake of other dietary fatty acids (saturated fatty acids, mono-unsaturated fatty acids and omega-6's poly unsaturated fatty acids)



## Clinical Manifestations of Depletion

Low levels of omega-3 index are associated with increased risk for cardiac death.

## Food Sources

If omega-3 index is <8.0% it is advised to increase dietary sources of omega-3's (EPA and DHA) from both plant and animal sources. Because the omega-3 index is a relative ratio of omega-3 compared to all other fatty acids in the blood, it is also important to evaluate intake of all other dietary fatty acids (saturated fatty acids, mono-unsaturated fatty acids and omega-6's poly

## Supplement Options

- Currently, no official dietary intake recommendations have been established.
- Several official health organizations have proposed a minimum dietary intake level of 500 mg/day of EPA+DHA.
- Because the efficiency of conversion of ALA to DHA is so low, supplementing DHA is generally recommended to meet therapeutic doses.
- The recommended minimum level of DHA supplementation in adults is 250 mg per day.
- Pregnant and lactating women are recommended to consume at least 200 mg DHA per day.
- Diabetic individuals may benefit from supplementing DHA (along with EPA) due to its triglyceride-lowering effects.
- High dose supplementation of omega-3 fatty acids (including DHA) has been shown to reduce the need for non-steroidal anti-inflammatory drugs (NSAIDs).
- Persons suffering from ulcerative colitis have been shown to need fewer corticosteroids when supplementing with high dose omega-3 fatty acids.
- Adverse side effects observed with high dose omega-3 fatty acids from supplement form include gastrointestinal upset and loose stools.
- Omega-3 supplements including EPA and DHA should be used with caution in persons with clotting disorders or on anti-clotting medication.