Blood Disorders
Anemia, Leukopenia, and Thrombocytopenia
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Like any part of the body, the blood can also be afflicted with diseases and disorders that can compromise your health. Disorders of the blood range from mild, with no symptoms, to life-threatening medical emergencies.

The majority of the blood is plasma, which accounts for about half of the blood volume. Plasma is mostly water and contains dissolved salts and proteins, as well as hormones, electrolytes, fats, sugars, minerals, and vitamins. The other components of blood include:

- **Red blood cells**—Red blood cells are responsible for carrying oxygen from the lungs to all other cells in the body, and for transporting carbon dioxide back to the lungs. Red blood cells are produced in the bone marrow. Each red blood cell has a life cycle of about 120 days, at which point they wear out and are destroyed in the spleen. Red blood cells are able to transport oxygen because of hemoglobin, an iron-containing molecule that binds to oxygen. About 90 percent of each red blood cell is hemoglobin, and each molecule of hemoglobin can carry four molecules of oxygen (Eastern Kentucky University 2005).
- **White blood cells**—White blood cells are the backbone of the immune system. They fight infection by engulfing invading organisms or abnormal cells. There are five basic kinds of white blood cells: neutrophils, monocytes, lymphocytes, eosinophils, and basophils. Neutrophils are the most common form of white blood cell and are responsible for fighting infection.
- **Platelets**—Platelets are responsible for blood clotting. They circulate constantly in the bloodstream. In the event of an injury, platelets gather (aggregate) at the injured site and touch off a chemical reaction that results in a blood clot. Abnormal platelet function may result in increased bleeding or the formation of dangerous blood clots where they don't belong, which can cause a heart attack or stroke.

In this chapter, we will review three blood disorders—anemia (low red blood cells), leukopenia (low white blood cells), and thrombocytopenia (low platelets). We will address how these disorders are diagnosed and conventionally treated and how to support the health of your red blood cells, white blood cells, and platelets with nutrition.

WHAT IS ANEMIA?

Anemia is a common blood disorder characterized by a decrease in the amount of red blood cells, or a decrease in the capacity of red blood cells to transport oxygen. This results in a lack of oxygen reaching the body's cells and tissues. Referred to as the "hidden hunger" by the World Health Organization, anemia poses significant health risks worldwide. It affects between 2 percent and 15 percent of people in the United States (Abrahamian FM et al 2005). Women are about twice as likely to be anemic as men. This is especially true of premenopausal women; between 4 percent and 8 percent of premenopausal women have iron deficiency anemia (Abrahamian FM et al 2005; Conrad ME 2005).

Anemia is associated with poor health outcomes. In patients who have had a heart attack, anemia sharply increases mortality (Wu RC et al 2001), and it is a strong predictor of overall mortality in the elderly. Over a 5-year period, anemic people aged 70 to 79, 80 to 89, and 90 to 99 were 28 percent, 34 percent, and 48 percent, respectively, more likely to die than people of the same ages who were not anemic. Stroke is commonly associated with anemia (Kikuchi M et al 2001).

Anemia is associated with the following symptoms (Abrahamian FM et al 2005):

- Weakness and fatigue
- Irritability
- Shortness of breath
- Headaches
- Sore tongue and bleeding gums
- Pallor
- Nausea and loss of appetite
- Faintness and dizziness
- Confusion and dementia

- Increased heart rate
- Heart failure (in severe cases)

Depending on its cause, anemia is generally classified in three ways: excessive bleeding, decreased red blood cell production, or increased red blood cell destruction.

Excessive bleeding

This form of anemia occurs when someone loses too much blood, either because of an injury (acute anemia) or a chronic disease. When the body loses a large amount of blood, the body reacts by pulling water from surrounding tissues into blood vessels to maintain a healthy blood pressure. This dilutes the blood, lowering the proportion of red blood cells.

Excessive bleeding can result in very serious anemia, depending on the nature of the injury. Acute anemia that involves the rapid loss of great volumes of blood can result in heart attack or stroke (Beers MH 2003). However, anemia related to chronic conditions, such as recurrent nosebleeds or ulcers in the stomach, develops more slowly and may not be as obvious. This type of anemia sometimes occurs as a result of cancer, especially colon cancer.

Chronic blood loss can cause a deficiency in iron. Iron deficiency anemia is the most common form of anemia (Leung AK et al 2001; Rasul I et al 2001), affecting about 2 billion people worldwide (Lynch SR 2005). It results in decreased red blood cell production.

Because it can take several months to deplete the body's supply of iron, it might take a long time for symptoms to develop. Iron deficiency anemia caused by blood loss is one of the most common forms of anemia in the United States (Beers MH 2003). In women, this condition is frequently related to excessively heavy menstrual bleeding; in men, it is often related to gastrointestinal bleeding.

Decreased red blood cell production

Red blood cells are manufactured in the bone marrow. This process relies on various nutrients, including iron, vitamin B12, and folic acid, as well as smaller amounts of vitamin C, riboflavin, and copper. Also, the production of red blood cells is stimulated by a hormone called erythropoietin. Deficiencies in any of these nutrients or in erythropoietin can result in anemia. Besides iron deficiency anemia caused by bleeding, other forms of anemia include:

- **Pernicious anemia (vitamin B12 deficiency)**—It is estimated that 300,000 to 3 million people in the United States have a vitamin B12 (cobalamin) deficiency (Diamond AL et al 2004). Vitamin B12 deficiency is rarely related to a dietary deficiency. Rather, vitamin B12 relies on intrinsic factor, a protein generated by cells in the stomach, to be bound to vitamin B12 and then absorbed in the ileum, the last segment of the small intestine. People who lack intrinsic factor cannot use the available vitamin B12, meaning that anemia can develop even if large amounts of vitamin B12 are consumed. Besides a lack of intrinsic factor, pernicious anemia can be caused by Crohn's disease, stomach surgery, or a strict vegetarian diet. Breast-fed infants of vegan mothers are particularly at risk of vitamin B12 deficiency.
- **Folic acid deficiency anemia**—Folic acid is abundant in green leafy vegetables. Because many people in industrialized countries don't eat enough vegetables, folic acid deficiency is more common than pernicious anemia. Folate deficiency is found in malnourished individuals (especially alcoholics), infants who are fed only cows' milk, pregnant women, and adults over age 60. It can also be caused by diseases that affect absorption in the small intestine, including Crohn's disease.
- **Anemia of chronic disease**—Anemia is associated with various chronic diseases and conditions, including infections, inflammatory diseases, and cancers that affect the ability of the body to produce red blood cells (Brill JR et al 2000; Bron D et al 2001). Diseases or conditions that are associated with anemia include cancer (Gillespie TW 2003; Knight K et al 2004), HIV/AIDS (Sullivan PS et al 1998), and testosterone deficiency (Bain J 2001; Zitzmann M et al 2000). In patients with cancer or HIV/AIDS, anemia is associated with increased mortality (Buskin SE et al 2004; Caro JJ et al 2001). Testosterone deficiency can cause anemia because the hormone helps stimulate kidneys and bone marrow to produce erythropoietin and stem cells. Symptoms of testosterone deficiency include decreased libido, impotence, infertility, fatigue, and decreased muscle mass and strength (Baker HWG 1995).

Additionally, aplastic anemia is a rare form of anemia that occurs when bone marrow fails to produce all three types of blood cells: red blood cells, white blood cells, and platelets. Causes of aplastic anemia include autoimmune diseases, viruses, or chemicals (e.g., benzene or pesticides). Symptoms include frequent infections (white blood cells are reduced), fatigue (red blood cells are reduced), and bleeding (platelets are reduced).

Increased red blood cell destruction

If the rate of red blood destruction is more rapid than the creation of new red blood cells, hemolytic anemia occurs. This form of anemia is less common than the other two. Hemolytic anemia can result from infection, certain drugs, autoimmune disorders in

which the body attacks and destroys its own red blood cells, and inherited disorders such as sickle cell anemia or thalassemia.

Additionally, an enlarged spleen can result in anemia. The spleen is responsible for destroying old red blood cells; an enlarged spleen can increase the rate of red blood cell destruction beyond the body's ability to manufacture new red blood cells.

Sickle cell anemia is the most common inherited blood disorder in the United States, affecting 1 in 500 African Americans and 1 in 2000 Hispanics of Caribbean or South or Central American descent (Pegelow C et al 2004). In this disease, the red blood cells are abnormally shaped (they resemble boomerangs), and their blood carrying capacity is reduced. These cells are fragile and break up as they travel through blood vessels, resulting in a reduced red blood cell count.

Thalassemia occurs when there is an imbalance in the production of one of the amino acid chains that makes up hemoglobin. Many people who have thalassemia also have mild anemia.

Autoimmune disorders can cause anemia if the body identifies red blood cells as invader pathogens and attacks them. In most people, the cause of autoimmune anemia is unknown (Beers MH 2003).

Diagnosing Anemia

Anemia is typically diagnosed with a complete blood count (CBC) test. Anemia is defined as a decreased number of red blood cells, a decrease in the quantity of hemoglobin, or a lowered hematocrit (the ratio of red blood cells to whole blood). The following Table shows the reference ranges for these measurements.

Reference Ranges for Blood Indicators*

Indicator	Men	Women
Red blood cell count	4.10-5.60 (×106/µL)	3.80-5.10 (×106/µL)
Hemoglobin	12.5-17.0 (g/dL)	11.5-15.0 (g/dL)
Hematocrit	36%-50%	34%-44%

*µL=microliter; g/dL=grams per deciliter.

If initial blood tests analyzing hemoglobin, red blood cell count, or hematocrit indicate anemia, additional testing should be done to determine the cause of anemia (Brill JR et al 2000). Additional tests may include:

- **Stool tests**—If a person has symptoms of anemia and has noticed bleeding, a physician may test for the presence of blood in the stool, which can indicate chronic bleeding that would cause anemia.
- **Iron deficiency tests**—Iron deficiency is best diagnosed by blood testing (Uthman E 2005). Additionally, physicians may test for levels of transferrin (a protein that carries iron) or for ferritin (a protein that stores iron).
- **Other tests**—Laboratory tests for vitamin B12 anemia are usually based on low serum vitamin B12 levels or elevated serum methylmalonic acid and homocysteine levels (Baik HW et al 1999). Similarly, folic acid levels can be measured to detect a deficiency in folic acid.

Managing Anemia

Management of anemia depends on the cause. If anemia is caused by chronic bleeding, for example, the goal is to stop the bleeding; the anemia may then resolve on its own. For instance, in patients with HIV/AIDS, anemia can be treated by temporarily suspending treatment with the antiretroviral drugs used to attack the virus. In extreme cases of acute blood loss, a transfusion may be necessary to raise the red blood cell count.

In some cases, anemia is treated by prescribing erythropoietin, a hormone that stimulates red blood cell production. Erythropoietin is a very expensive drug that is sometimes used to treat severe anemia caused by chemotherapy, certain anti-HIV drugs, testosterone deficiency, or chronic kidney failure. Erythropoietin, taken along with iron, may help reduce the need for a red blood cell transfusion. It is particularly important to supplement erythropoietin with iron because erythropoietin causes the iron to be utilized to form new red blood cells. A poor result may occur if an iron supplement is not prescribed concurrently with erythropoietin.

If the anemia is caused by a genetic disorder (such as sickle cell anemia), blood transfusions may be used to raise the red blood cell count while other drugs are prescribed to treat the genetic disorder itself.

Nutritional Support

Some forms of anemia respond well to nutritional therapy, including anemia caused by iron deficiency or folic acid deficiency.

Iron

In the United States, dietary iron deficiency is rare because of a diet high in iron-rich foods such as red meat, beans, egg yolks, whole-grain products, nuts, seafood, iron-fortified cereals, dark green leafy vegetables, and dried fruit. However, some people in the United States have a higher need for iron, including children, pregnant or menstruating women, strict vegetarians, and long-distance runners.

Oral iron supplements are available to treat iron deficiency anemia. However, gastrointestinal malabsorption syndromes may require the intramuscular or intravenous injection of iron dextran (Imferon) by a physician. Iron protein succinate (sold as a drug in Germany) may be the most effective oral treatment of iron deficiency anemia. This form of iron has been evaluated in multicenter clinical trials to determine efficacy and tolerability (Kopcke W et al 1995). The following effects were seen in anemic adults after only 60 days:

- 23 percent increase in percentage of red blood cells (hematocrit)
- 30 percent increase in blood oxygen-carrying capacity (hemoglobin)
- 6 percent increase in total number of red blood cells

One new and novel approach to iron supplementation is the use of ferritin, a protein that is involved in the storage of iron and can be found naturally in foods like beans. Newer studies have shown that ferritin supplementation may be able to boost iron levels without the side effects associated with iron supplementation (Theil EC 2004). In one study, a ferritin complex was shown to be effective in children who had anemia that was caused by hemodialysis (Warady BA 2005).

Folic acid
The recommended daily requirement of folate is difficult to obtain from food sources alone. Symptoms of folic acid deficiency may include diarrhea and other gastrointestinal problems. Because supplementation with folic acid can mask a vitamin B12 deficiency, folic acid and vitamin B12 should be taken together.

Anemia caused by folic acid deficiency normally responds quickly to oral folic acid and vitamin B12 supplementation. Anticonvulsants, antituberculosis drugs, alcohol, and oral contraceptives have been associated with low serum levels of folate (Lambie DG et al 1985).

Vitamin B12
In pernicious anemia, the body lacks intrinsic factor, which is needed to carry vitamin B12 from the digestive tract into the bloodstream. This condition often affects the gastrointestinal tract and the nervous system, with symptoms that range from weakness to vertigo to angina. Vitamin B12 is available as a supplement in multiple forms, including cyanocobalamin and methylcobalamin. The conventional treatment for pernicious anemia is an intramuscular injection of cyanocobalamin, often followed by lifelong supplementation with vitamin B12.

One study, however, showed that subjects given 1500 micrograms (mcg) of methylcobalamin orally daily for 1 to 3 months experienced prompt correction of their anemia, with recovery of neurological disturbances observed after 1 month and recovery of hemoglobin and serum concentrations within 2 months. These results imply that orally administered methylcobalamin may be as effective as traditional vitamin B12 injections for treatment of pernicious anemia (Takasaki Y et al 2002). If, however, red blood cell levels fail to respond to treatment with methylcobalamin, conventional treatment should be sought.

Copper, zinc, and selenium
Trace minerals can be an adjunctive nutritional therapy to reduce the effect of anemia on normal red blood cell function. Copper, zinc, and selenium are used in biochemical processes such as cellular utilization of oxygen, DNA and RNA reproduction, maintenance of cell membrane integrity, and sequestration of free radicals (Chan S et al 1998).

L-carnitine
Patients with anemia caused by end-stage renal disease respond to therapy with L-carnitine. In one study, L-carnitine therapy increased hematocrit and decreased resistance to erythropoietin (Horl WH 2002).

Testosterone therapy
Anemia associated with testosterone deficiency can be addressed with testosterone replacement therapy, which can stimulate erythropoietin production and increase hematocrit. Potential candidates for testosterone replacement therapy should undergo a complete physical examination including a complete medical history and a hormone profile (Morales A et al 2000).

WHAT IS LEUKOPENIA?

Leukopenia is a diminished white blood cell count. When white blood cells are depleted, the immune system is weakened and people are at increased risk of infection. Leukopenia is associated with diseases, medications, and genetic deficiencies.

The most common form of leukopenia is neutropenia, or a reduced number of neutrophils. Neutrophils comprise about 45 percent to 75 percent of the total white blood cell count. They are responsible for fighting bacterial, fungal, viral, and parasitic infections. Neutropenia is associated with increased risk of bacterial infections. If not treated during the early infectious phase, and if the level of neutrophils falls too low, septic shock and death often occur (Corapcioglu F et al 2004; Ochs HD et al 1996).

Diagnosis is dependent on a CBC test. Neutropenia in adults is defined as an absolute neutrophil count of less than 500 cells per microliter (µL). However, even a neutrophil count of less than 1000 cells/µL of blood can raise the risk of infection (Beers MH 2003).

Treatment of neutropenia depends on the cause and any associated conditions. Neutropenia can occur when the neutrophils are destroyed faster than they are created (by an autoimmune response, for instance), or when the production of neutrophils in the bone marrow is reduced (as with cancer, diseases such as influenza, or vitamin B12 or folic acid deficiencies). Neutropenia is also associated with radiation treatment that has affected the bone marrow. In fact, the most common cause of neutropenia is drugs or therapies that are used to fight cancer or autoimmune disorders. Other drugs that have been associated with neutropenia are antibiotics (including penicillin) and antiretroviral drugs used in the treatment of HIV/AIDS. Drug-induced neutropenia can often be reversed by discontinuing use of the drug.

It is possible to resolve neutropenia associated with other conditions by addressing the underlying health concern. For instance, bacterial neutropenia may be treated with broad-spectrum antibiotics, while a fungal infection caused by neutropenia may be treated with antifungals. For viral infections such as herpes, the use of acyclovir is common (Steiner I et al 2005).

If the neutropenia is caused by a genetic disease or chemotherapy, it will typically be treated with granulocyte colony-stimulating factor and other bone marrow–derived growth factors (Bradstock KF 2002; Cario G et al 2005). These drugs, approved by the US Food and Drug Administration (FDA), stimulate the production of neutrophils by increasing the number of bone marrow–neutrophil precursors (Cario G et al 2005). Additionally, melatonin has been shown to reduce neutropenia in patients who have undergone chemotherapy to treat cancer (Viviani S et al 1990).

If the neutropenia is caused by an autoimmune disorder, it may be treated with glucocorticoids, cyclosporine, or (Kasper DL et al 2004).

Additionally, vitamin E may be recommended for patients who have chemotherapy-induced neutropenia. In a study of 49 women undergoing chemotherapy for breast cancer, neutropenia was common. Ingestion of vitamin E or multivitamins resolved the condition (Branda RF et al 2004).

WHAT IS THROMBOCYTOPENIA?

Under normal circumstances, the blood contains about 150,000 to 350,000 platelets/µL. These platelets are involved in blood clotting. They circulate constantly in the bloodstream, looking for damaged areas. In response to an injury in a blood vessel, the platelets respond by sticking to the site and clumping together (platelet aggregation). This aggregation begins the clotting that prevents further bleeding (Troy GC 1988).

Thrombocytopenia occurs when the platelet count falls too low. At levels of 20,000 to 30,000 platelets/µL, bleeding can occur in response to relatively minor trauma. At platelet counts less than 20,000 cells/µL, spontaneous bleeding can occur, which increases the risk of bleeding that can result in shock and death (Rosthoj S et al 2003).

Like other blood disorders, thrombocytopenia can occur when the body either doesn't produce enough platelets, or if too many platelets are destroyed. Thrombocytopenia is associated with leukemia or lymphoma, aplastic anemia, vitamin B12 or folic acid deficiency anemias, an enlarged spleen, infectious diseases such as HIV/AIDS, and massive blood transfusions.

Two diseases that occur because of increased destruction of platelets are:

- **Idiopathic thrombocytopenic purpura (ITP)**—This disease occurs when antibodies attack and destroy the body's platelets for unknown reasons. In children, ITP can be an acute condition that occurs after infection. Acute ITP is rare in adults. More common is chronic ITP, a condition that may persist for years and most frequently affects women ages 20 to 40 years. If symptoms (such as bleeding or easy bruising) are present, a physician may prescribe prednisone to be taken for 4 to 6

weeks.

- **Thrombotic thrombocytopenic purpura (TTP)**—TTP is a life-threatening disease that occurs when small blood clots form suddenly throughout the body. It can result in cardiac hemorrhage and death (Burke AP et al 2005). It occurs more often in women and is associated with pregnancy, metastatic cancer, chemotherapy, HIV/AIDS, and some prescription drugs (such as ticlopidine). Patients with TTP experience kidney failure or decreased kidney function, fever, and neurological problems. The most common treatment is fresh-frozen plasma exchange, which is associated with a 90 percent survival for this once-fatal disease. Other therapies include vitamin E and kidney dialysis and transplant (Ruggenenti P 1990).

Supporting Healthy Blood Cells Through Nutrition

A number of nutrients have been studied for their ability to promote healthy blood and fight diseases of the blood cells, including thrombocytopenia and leukopenia. These include:

Antioxidant vitamins

In a series of animal studies, supplementation with vitamins C, E, and A was investigated to find out the effects of these vitamins on thrombocytopenia. Nutritional supplementation with vitamins C, E, and A diminished coagulation activation induced by surgery. In this series of studies, the use of vitamins C, E, and A diminished thrombocytopenia (Byshevskii AS et al 1994). Fewer deaths occurred after surgery in study animals pretreated with these vitamins (Byshevskii AS et al 1992a). The antioxidant effect of these vitamins is believed to diminish development of free radicals and thereby diminish platelet cell destruction (Byshevskii AS et al 1992b).

Omega-3 fatty acids

Dietary supplementation with omega-3 is associated with prolonged platelet viability, decreased platelet activation (and aggregation), and diminished production of free radicals. In a study comparing fish oil consumption to placebo, platelet survivability was shown to be significantly longer and platelet activation was diminished (Pirich C et al 1999). The results of this clinical study suggest that fish oil supplementation rich in omega-3 polyunsaturated fatty acids increases platelet survivability by decreasing cell loss due to platelet activation.

The extended platelet life span induced by omega-3 fatty acids may also be due to reduced generation of free radicals. In a study examining the effects of omega-3 on free radical production in neutrophils, the amount of free radical production was significantly lower in the group supplemented with omega-3 (Schneider SM et al 2001). Lipid peroxidation, a process that results in death of white blood cells and platelets, is promoted by free radical formation. Omega-3 diminishes free radical formation (Schneider SM et al 2001) and therefore diminishes destruction of platelets and white blood cells.

Shark liver oil

Shark liver oil is rich in a class of compounds known as alkylglycerols, which occur naturally in various mammalian tissues, including most organs responsible for producing blood cells. While most studies have focused on the ability of shark liver oil to fight cancer, it has also been shown to boost immunity by stimulating production of neutrophils and activating macrophages (another type of white blood cell) (Krotkiewski M et al 2003).

Copper and zinc

Leukopenia and thrombocytopenia can be caused by copper deficiency, which reduces production of red blood cells, white blood cells, and platelets. Effective copper replacement reverses leukopenia within 2 months (Takeuchi M et al 1993).

Zinc deficiency can result in leukopenia (Fraker PJ et al 2000). These findings are supported by murine studies in which a limited zinc diet was provided. Moderate zinc deficiency occurs in disorders such as sickle cell anemia, renal disease, and gastrointestinal disorders. The short-term use of zinc supplementation boosts the immune system and appears to protect against opportunistic infections (Fraker PJ et al 2000).

Melatonin

A number of studies have shown that melatonin can enhance blood health by supporting production of blood platelets and neutrophils.

In a pilot study, three patients with ITP were given melatonin for up to 46 months. All patients had an initial response after 1 month of treatment, and disease progression subsequently diminished. There were no manifestations of toxicity in any of the study subjects (Todisco M et al 2002). A follow-up case study of a patient with refractory ITP, which typically has a poor prognosis, showed that melatonin was able to successfully manage the symptoms of severe bleeding (Todisco M et al 2003). Melatonin has also been shown to enhance the production of platelets and resolve thrombocytopenia in a variety of patients (Lissoni P et al 1999).

In the newest melatonin research, scientists have delved into its ability to protect patients with cancer by boosting the health of bone marrow, among other benefits. Studies have reported that melatonin may decrease thrombocytopenia and neutropenia in patients with cancer (Abrial C et al 2005).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Scientific studies have shown that nutrients may be able to help manage some forms of blood disorders. For clarity, Life Extension Foundation recommendations have been organized according to various diseases of the blood. The Life Extension Foundation suggests:

For pernicious anemia (Note: If blood tests do not show rapid improvement, vitamin B12 injections must be administered. See your physician for more details.):

- **Vitamin B12**—2000 to 4000 mcg daily, orally or sublingually, in the form of methylcobalamin
- **Zinc**—30 milligrams (mg) daily
- **Copper**—2 to 3 mg daily
- **Selenium**—200 micrograms (mcg) daily

For folic acid deficiency anemia:

- **Folic acid**—1600 mcg daily
- **Vitamin B12**—2000 to 4000 mcg daily, sublingually
- **Zinc**—30 mg daily
- **Copper**—2 to 3 mg daily
- **Selenium**—200 mcg daily

For iron deficiency anemia:

- **Iron Protein Plus**—300 mg of iron protein succinate, equivalent to 15 mg of elemental iron per capsule daily
- **Zinc**—30 mg daily
- **Copper**—2 to 3 mg daily
- **Selenium**—200 mcg daily

To help maintain healthy blood (including healthy platelets and white blood cells):

- **Shark liver oil**—500-1000mg [containing 20% alkylgycerols (100-200mg)] a day.
- **Vitamin C**—2000 mg daily
- **Vitamin E**—400 international units (IU) daily
- **Vitamin A**—3000 IU daily
- **Zinc**—30 to 60 mg daily
- **Copper**—2 to 3 mg daily
- **Selenium**—200 mcg daily
- **Folate and vitamin B12**—800 mcg of folate and 300 mcg of vitamin B12 daily
- **Fish oil**—Two 600-mg soft-gel capsules of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) twice daily (for a total of 2400 mg daily)
- **Melatonin**—20 mg daily

BLOOD DISORDERS SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Copper

- Do not take copper supplements if you have Wilson's disease.
- Consult your doctor if you take copper supplements and have chronic liver failure and/or chronic kidney failure.
- Do not take high doses of copper. High doses of copper are extremely toxic.
- Copper can cause gastrointestinal symptoms such as nausea and diarrhea.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Folic acid

- Consult your doctor before taking folic acid if you have a vitamin B12 deficiency.
- Daily doses of more than 1 milligram of folic acid can precipitate or exacerbate the neurological damage caused by a vitamin B12 deficiency.

Iron

- Do not take iron if you have hemochromatosis or hemosiderosis.
- Consult your doctor before taking iron supplements if you have an elevated serum ferritin level, alcoholic cirrhosis, a pancreatic insufficiency, or a history of chronic liver failure, chronic alcoholism, gastritis, peptic ulcer disease, or gastrointestinal bleeding.

Melatonin

- Do not take melatonin if you are depressed.
- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a “heavy head,” or gastrointestinal symptoms such as nausea and diarrhea

Selenium

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

Shark Liver Oil

- Do not exceed the maximum recommended dose.
- Prolonged use (more than 30 days in a row) causes a rare side effect known as thrombocythemia (excess platelets), which can cause the blood to clot.
- Shark liver oil can cause rash, breath that smells like garlic, fatigue, irritability, and gastrointestinal symptoms such as nausea and diarrhea.

Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

Vitamin C

- Individuals with kidney stone disease or a history of renal insufficiency (defined as serum creatine greater than 2 and/or creatinine clearance less than 30) should avoid vitamin c supplementation.
- Individuals with hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia and erythrocyte G6PD deficiency might experience iron overload if they use large amounts of vitamin C.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.

- Discontinue using vitamin E 1 month before any surgical procedure.

Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix