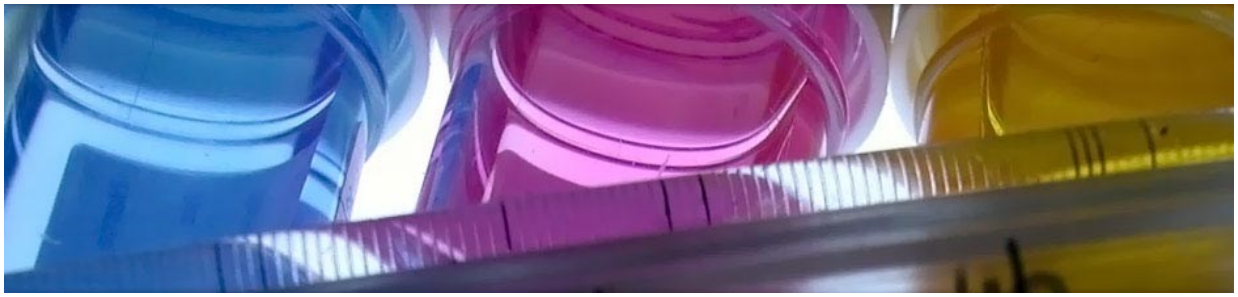
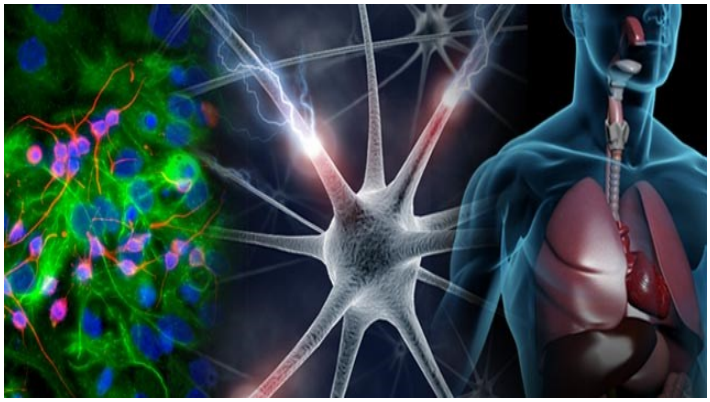
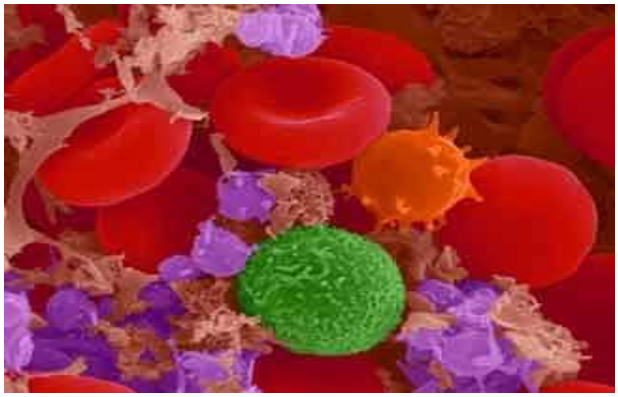


Holistic Blood Chemistry and Urinalysis Reference Manual





Dr. Brandon M. Lundell

DC, APC, DABCI, IFMCP, Dipl.Ac, N.E.

Fourth Edition

About the Author

Dr. Brandon M. Lundell DC, APC, DABCI, IFMCP, Dipl. Ac., NE, CAC
Doctor of Chiropractic
Advanced Practice Chiropractic Physician (New Mexico)
Board Certified in Diagnosis and Internal Disorders (ABCI)
Institute of Functional Medicine - Certified Functional Medicine Practitioner (IFMCP)
Diplomate in Acupuncture and Oriental Medicine (IACA)
Board Certified in Naturopathic Endocrinology (ANMA)
Certified Animal Chiropractor (AVCA)

Dr. Lundell graduated *cum laude* from Parker College of Chiropractic in 2004 with a Doctor of Chiropractic degree. (DC). He received his B.A. from the University of Colorado, Boulder in 1999 with a double major in Political Science and Classical Studies. While in school full-time obtaining his Doctor of Chiropractic degree, Dr. Lundell completed a three year diplomate in acupuncture and oriental medicine. He has also completed a Naturopathic Endocrinology (NE) certification from the National Institute of Endocrine Research in California. He has attained Advanced Practice (AP) certification which allows expanded scope of practice to include IV and injectable nutrients as well as pharmacological training. He is a board-certified Chiropractic Internist through the American Board of Chiropractic Internists (DABCI) which educates and certifies chiropractors in internal disorders, diagnostics, natural medicine and alternative therapies for conditions ranging from heart disease, autoimmune and neurology to pediatrics. He was also among the first practitioners in the country to complete the functional medicine certification program through the Institute of Functional Medicine (IFMCP). Dr. Lundell has developed and teaches several functional medicine courses at the university level and teaches these courses all over the country. Topics of his classes include blood chemistry/pathology, functional endocrinology, inflammatory basis of disease, detoxification, autoimmune, diet, lifestyle, nutrition, methylation, functional genetics and more.

In his 15 years of clinical experience, Dr. Lundell has built a waiting-list only practice. His focus is on integrative primary care, family practice and holistic functional medicine. He believes that functional medicine physicians can provide a much needed service in the current health care environment by filling both a primary care/general practice void as well as offering functional, holistic, science-based treatments which emphasize the correction of the ***Causes*** of illness, ***Prevention*** and ***Wellness*** throughout the lifespan.

His holistic practice includes chiropractic, clinical laboratory testing and analysis (including blood, urine and saliva), functional endocrinology emphasizing *restoration and balance* (rather than just hormone replacement), nutraceuticals, acupuncture, visceral manipulation, homeopathy, detoxification, pre-conception/prenatal planning, functional exercise training, dietary-nutritional education, and more. Dr. Lundell can be reached at his office in Longmont, Colorado: Harmony Healing Center, 303-651-1502, HarmonyHealingCenterPC@comcast.net. Or on the web: www.drbrandonlundell.com

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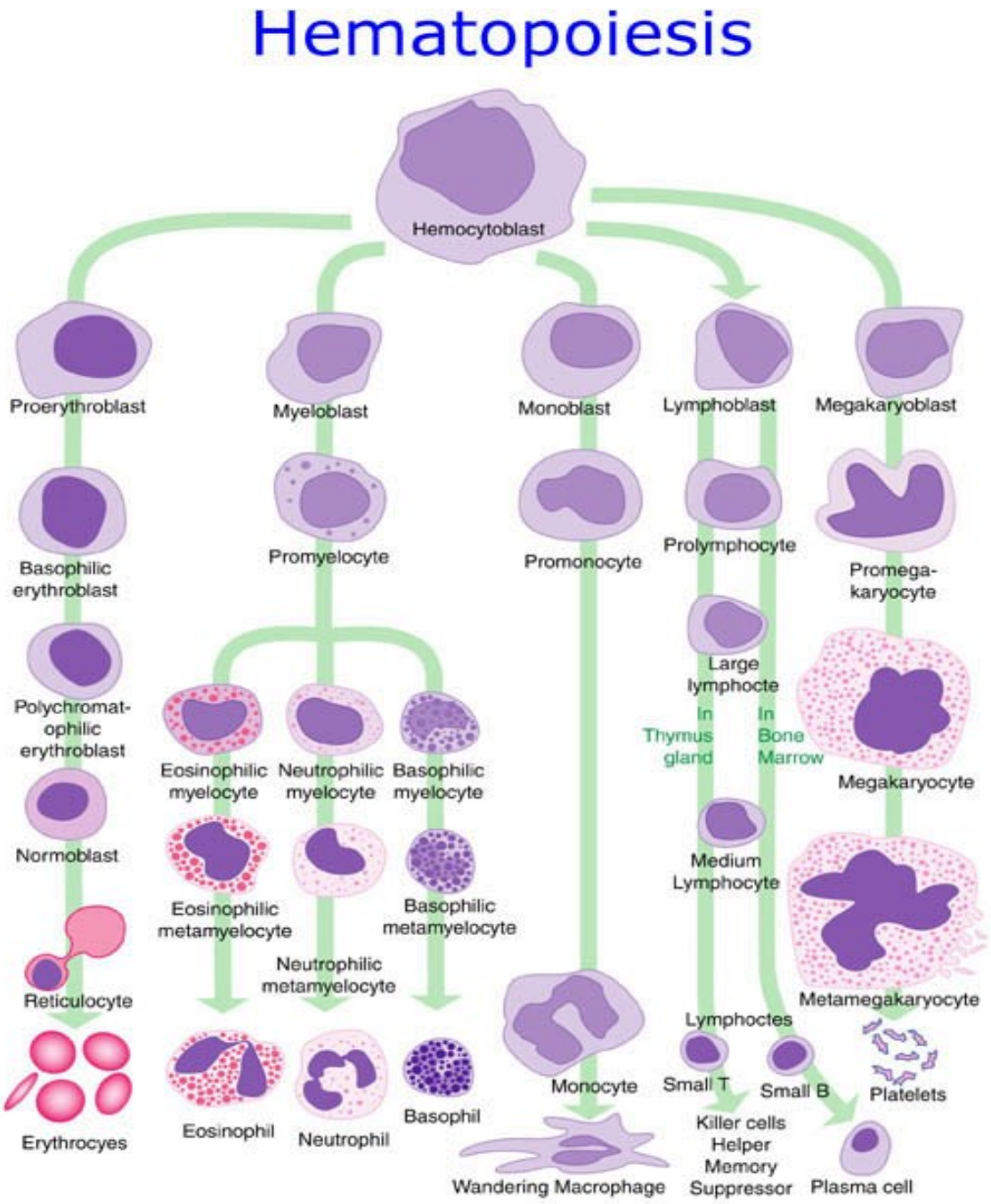
BLOOD CHEMISTRY

Complete Blood Count with Differential



White Blood Cell Count Optimal: 5.5 – 8.5 thous/ml

White blood cells are the first line of defense against microorganisms as well as the mediators of inflammation and tissue repair/destruction. They are grouped into two classes: Granulocytes (Basophils, Eosinophils, and Neutrophils); and Agranulocytes (Monocytes and Lymphocytes). This is both a morphologic as well as functional distinction. These two groups not only look different but have different roles within the complex immune system. The differential is often given in **absolute** numbers (actual count by a lab tech or done by automated cell counters) as well as a **percentage** of total WBC's. The former is usually more accurate and reliable because percentages may be influenced by each other without being necessarily abnormal. The exception to this is neutrophil percentage which is more sensitive to infection than total WBC count.

The role of each WBC will be discussed under their respective differential below. In general the granulocytes are non-specific macrophages which scavenge the body for non-self-organisms, defective cells, and debris. The agranulocytes are part of the humoral immune response and the cell-mediated immune response, which play important roles in cytokine regulation and production. Lymphocytes differentiate into T cells and B cells which produce antibodies.

Leukocytosis is an increase in any or all WBC's. Leukopenia is a decrease in WBC's. A "leukemoid" reaction is a temporary spike in WBC count associated with acute infection. Ranges are influenced by age, sex, ethnicity, environmental, dietary and lifestyle factors.

High (leukocytosis)

- Acute bacterial infection
- Acute viral infection
- Stress (acute)
- Hyperthyroidism
- Pregnancy (late)
- Childhood diseases (measles, mumps, rubella, chicken pox, etc.)
- Leukemia (>15,000/ml)
- Inflammation – leading to insulin resistance, diabetes, cancer and other diseases
- Dehydration
- Leaky gut (intestinal mucosal dysfunction can lead to multiple microorganisms as well as tissue degrading material into the general circulation)
- Malignancy
- Spleenectomy
- Neonates (the first few days of life demonstrate elevated WBC's)
- Steroids (short term)

Low (leukopenia)

- Chronic viral infections
- Chronic bacterial infections
- Immunosenescence (the age-related deterioration of the immune system which is advanced by environmental and lifestyle factors)
- Aplastic anemia (bone marrow failure often due to leukemia)
- Bone marrow suppression / failure / myelofibrosis (hormonal, chemical, autoimmune, congenital and chronic infectious influences)
- Hypothyroid
- Nutrient deficiency – Vit.C, zinc, iron, B12, B6 and folate deficiency affect WBC production.

- Autoimmune (SLE, RA etc.) - anti-neutrophil antibodies will often be present.
- Alcoholism (usually causes nutrient deficiency such as B12, folate etc.)
- Hypersplenism – spleen sequestration of WBC's and RBC's.
- Thymus involution / dysfunction
- Antibiotics – chronic use
- Leaky gut, chronic (over time, leaky gut will deplete the immune system due to inflammation and/or infection as well as cause nutrient malabsorption)
- Chronic illness
- Steroids (long term)
- Drug induced – chemotherapy, immunosuppressant etc.

Functional Considerations

There is a slight diurnal variation of all WBC's, especially the neutrophils, with the peak at 4pm and the nadir at 7am. This is important in interpreting borderline laboratory results. This also explains why symptoms for some immune challenges like the cold/flu may be worse in the evening as the WBC's increase their interleukin and cytokine production, which is actually what produces most of the symptomatology of illness.

Suboptimal WBC counts (high or low) can often be one of the only signs of chronic inflammation. Several studies link slightly elevated WBC counts with increased risk for diabetes, cancer and heart disease. Low WBC can also mean chronic inflammation and increased infections (EBV, CMV etc.).

The immune system is very complex and is influenced by many internal and external factors. It is clear that without supporting the immune system with diet, exercise, meditation (stress reduction), nutrient therapy and careful investigation and specific treatment of chronic microorganism burdens, then the body cannot long experience health and vitality.

Many tests are available to further assess immune function. **One must determine what the etiology behind the apparent abnormal laboratory findings are.** If a microorganism is suspected, then determine what the most likely may be. Treat the immune system as a whole first to see if covering the basics is enough to restore balance. If the patient is chronic or does not respond, then more intensive investigation is required to find underlying causes and how to best support the immune system. Careful not to overlook chronic dental infections such as old root canals that have become re-infected.

Related Tests

CBC w/Diff.: Allows for more complete marrow analysis as well as nutrient factor associated pathology.

Lymphocyte Subset Panel: Helps differentiate T and B cell dysfunction as well as general immune deficiency/dysfunction.

Cytokines: Assesses IL and TNF's associated with immune function. Can give a more in-depth assessment of immune challenges such as causative microorganisms, autoimmune and inflammatory disorders.

Lyme's: Western blot, PCR and antigen subset tests are available to identify past or present B. burgdorferi exposure. At best, these tests have only 70% sensitivity.

Viral Panel: Herpes varieties, EBV, cytomegalovirus, rubella etc.

West Nile: More common than is currently recognized, especially in rural areas.

Food Allergy: Food allergens and sensitivities will both stimulate and weaken the immune system over time.

G.I. Panel: In addition to parasites, functional GI panels will assess microbiota and digestive capabilities. ***Leaky gut is one of the most important factors to address in any immune challenge***.

Autoimmune Markers: ANA complete, RF, Citrillunated peptide, anti-mitochondrial antibodies etc.

Cancer Antigens

Thyroid Panel: Thyroid hormones greatly impact all phases of production, maturation and function of immune cells.
Adrenal Panel: Adrenal hormones, especially cortisol directly impact immune system function.
Spectracell™ Micronutrient Analysis: This test takes WBC's from serum and exposes them to different nutrient rich or nutrient deficient environments, and measures its functional response. Can give specific recommendations on nutrients that may support proper WBC function, as well as total body.
Bone marrow biopsy – most definitive test to determine cause of severe leukopenia

Neutrophils Optimal: 2000 – 6000 cells/mcl; 45 – 65%

Most frequently associated with inflammation as well as infection, neutrophils are sometimes referred to as polymorphonuclear segmented neutrophils (PMN's), or "polys". They are most often associated with bacterial infections whereas viral infections are associated with normal or even low counts of polys (especially percentage). However, about 20% of viral infections may contribute to PMN elevation. *Neutrophils have very short lives - only a few hours in circulation,* so relatively acute disturbances can cause dramatic shifts in PMN levels.

The term "shift to the left" is an older term used to describe an increase in immature PMN's due to rapid mobilization from infection, inflammation or cancer. It was originally used by lab techs who counted the number of immature cells by "stabbing" a punch card on the left side which was used to count the number of different cells in blood.

High

- Bacterial infection (acute)
- Viral (acute or severe)
- Inflammation- acute or chronic (one of the hallmarks of inflammation is recruitment and activation of leukocytes, especially neutrophils)
- Leukemia
- Acute stress (physical or emotional)
- Gout
- Thyroiditis
- Trauma
- Cigarette smoking
- Corticosteroids (can cause rapid elevations, often persisting for 2 – 3 weeks or more after resolution of stressor)

Low

- Blood diseases (aplastic anemia, pernicious anemia, etc.)
- Viral infection
- Chronic stress
- Immunosenescence (the age-related deterioration of the immune system which is advanced by environmental and lifestyle factors)
- Addison's disease
- Hypersplenism
- Vitamin D deficiency (Vit D regulates many aspect of immune cell production and function)
- Radiation
- Adrenal dysfunction (hypoadrenalism can cause neutropenia due to loss of corticosteroid stimulation)

- Overwhelming bacterial infection (poor prognostic indicator if levels drop dramatically)
- Idiopathic cyclic neutropenia (approximately 5 – 10% of population, not including the elderly)

Functional Considerations

Non-infectious rises in PMN's are common and associated with acidity (uremia, toxicity, gout, etc.) as well as chemicals and drugs. Rule these out before jumping to the conclusion the patient has infection. It is wise to run a UA since it is estimated that up to 20% of women and 10% of men currently have an undetected, asymptomatic urinary tract infection. PMN's will often be elevated at first, then severely decreased. Also look to lungs, heart and teeth for hidden sources of infections.

Since many factors increase PMN's temporarily, consider running another CBC w/diff 2-3 days after an initial abnormal finding. Considering a CBC is less than $10, this may save the physician and the patient much time and money in unnecessary treatments and procedures.

Related Tests

CBC w/Diff.: Allows for more complete marrow analysis as well as nutrient factor associated pathology.
Urinalysis: Many chronic infections are subacute urinary tract infections that may exist for months or even years before they are symptomatic.
Lymphocyte Subset Panel: Helps differentiate T and B cell dysfunction as well as general immune deficiency/dysfunction.
Cytokines: Assesses IL and TNF's associated with immune function. Can give a more in-depth assessment of immune challenges such as causative microorganisms, autoimmune and inflammatory disorders.
Lyme's: Western blot, PCR and antigen subset tests are available to identify past or present B. burgdorferi exposure. At best, these tests have only 70% sensitivity.
Viral Panel: Herpes varieties, EBV, cytomegalovirus, rubella etc.
West Nile: More common than is currently recognized, especially in rural areas.
Food Allergy: Food allergens and sensitivities will both stimulate and weaken the immune system over time.
G.I. Panel: In addition to parasites, functional GI panels will assess microbiota and digestive capabilities. ***Leaky gut is one of the most important factors to address in any immune challenge***.
Autoimmune Markers: ANA complete, RF, Citrillunated peptide, anti-mitochondrial antibodies etc.
Cancer Antigens
Thyroid Panel: Thyroid hormones greatly impact all phases of production, maturation and function of immune cells.
Adrenal Panel: Adrenal hormones, especially cortisol directly impact immune system function.
Spectracell™ Intracellular Analysis: This test takes WBC's from serum and exposes them to different nutrient rich or nutrient deficient environments, and measures its functional response. Can give specific recommendations on nutrients that may support proper WBC function, as well as total body.

Lymphocytes Optimal: 1500 – 3300 cells; 25 – 35%

Lymphocytes differentiate (mature) into T cells, B cells and NK cells. B cells are the source of humoral immunity (antibody-mediated) and are manufactured in the bone marrow. T cells are so called because they mature in the thymus, and they regulate the immune system through a balance of cytotoxic, regulatory and suppresser mechanisms.

Elevated lymphocytes (lymphocytosis) is associated with normal or low total WBC. The most common reason is viral infections. Often the *percentage* will increase, while the absolute count will remain the same due to a relative deficiency in other WBC's during viral infections. Some viruses will elevate WBC count as well as absolute lymphocytes such as pertussis, lymphocytosis, EBV, cytomegalovirus and viral hepatitis.

High

- Childhood infections (measles, mumps, rubella, chicken pox etc.)
- Acute and chronic viral infection
- Infectious mononucleosis
- Inflammation
- Systemic toxicity
- Chronic bacterial infection
- Multiple myeloma
- Toxoplasmosis
- Addison's (glucocorticoids have inhibitory effects on lymphocytes)
- Leukemia

Low

- Chronic viral or bacterial infections
- Free radical activity
- Recent influenza or common cold infection (unlike other viruses, these lower lymphocyte count)
- Immunosenescence (the age-related deterioration of the immune system which is advanced by environmental and lifestyle factors)
- Active bacterial infection
- Aplastic anemia
- Leukemia
- SLE
- Immunodeficiency
- Radiation
- Acute stress

Functional Considerations

If lymphocytes are elevated, it is most likely a viral source. Be aware that chronic bacterial infections will raise absolute lymphocytes as well as create a relative percentage increase due to low neutrophils.
Lymphocytes are often elevated if the patient is consuming inflammatory foods and food allergies.

Related Tests

CBC w/Diff.: Allows for more complete marrow analysis as well as nutrient factor associated pathology.
Urinalysis: Many chronic infections are subacute urinary tract infections that may exist for months or even years before they are symptomatic.
Lymphocyte Subset Panel: Helps differentiate T and B cell dysfunction as well as general immune deficiency/dysfunction.
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Monocytes Optimal: 250 – 750 cells/mcl; 3 – 7%

Monocytes are phagocytic cells which clean up inflammatory cellular damage as well as debris from destroyed microorganisms. They differentiate into macrophages. They play a major role in tissue repair. Without monocytes, muscles would not be able to heal after injury or exercise. This is why it is important to have **no caffeine** in the recovery phase of an injury or training regimen because cortisol and adrenaline will lower macrophage count and activity. They also secrete paracrine hormones and cytokines, making then essential to normal everyday function of the cells as well as mediators of inflammation. One of those cytokines is interferon, which is perhaps the body's most potent immune stimulant, and low amounts of this is associated with numerous pathologies including neoplasm.

High

- Recovery phase of infection
- Subacute bacterial endocarditis (the most common *pathologic* elevation)
- Parasites
- Chronic inflammation
- Benign prostatic hypertrophy (BPH)
- Viral infection
- Ulcerative colitis
- Autoimmune conditions (rheumatoid, MCT, SLE)
- Liver dysfunction (due to elevated tissue destruction)

Low

- Corticosteroids
- Adrenal dysfunction
- Immunosenescence (the age-related deterioration of the immune system which is advanced by environmental and lifestyle factors)
- Hypothyroid
- Stress
- Hairy cell leukemia

Functional Considerations

If monocytes are low, healing from injury will be delayed. Support for the immune system is important and often ignored after injuries. It is important that patients do not take anti-inflammatories for several weeks after an injury, especially if monocytes are low.

Monocytes are also elevated very commonly in autoimmune diseases and may be the only early indicator of oncoming autoimmune crises.

Related Tests

See lymphocytes

Eosinophils Optimal: 10 – 300 cells/mcl; 1 – 3 %

Eosinophils are granulocytes which react to antigen-antibody complexes and are mobilized to phagocytize foreign microbes. Often Eosinophils are erroneously mobilized in autoimmune conditions, especially psoriasis, which may actually have a viral etiology in many cases.

High

- Intestinal parasites (most often roundworms and various flukes. Look for Hx of international travel)
- Food and environmental allergies/sensitivities
- Asthma
- Eczema
- Methylation defects (need for methylation cofactors)
- Leukemia
- Autoimmune diseases
- Polyarteritis nodosa
- Hodgkin's
- Cancer (ovarian or other serous secreting tissue most common)

Low

- Increased adrenal steroid production
- Immunosenescence (the age-related deterioration of the immune system which is advanced by environmental and lifestyle factors)
- Leukemia
- Stress
- Hypersplenism

Functional Considerations

Most likely elevations are due to allergies and/or parasites. Patients often present with both as intestinal mucosal dysfunction is associated with increased allergen sensitivity and weakened defense systems allowing for parasitic infiltration.

Related Tests

See Neutrophils

Basophils Optimal: 10 – 100 cells/mcl; 0 – 1 %

Also called mast cells, these cells contain histamine, heparin and serotonin, and are involved in allergic reactions and inflammatory responses. Basophils can invade dermal tissue and create hives. Mast cells are very sensitive to inflammatory cytokines and are part of the inflammatory pathogenesis of many illnesses.

High

- Tissue inflammation
- Intestinal parasites
- Allergies (chronic)
- Myeloproliferative disease (most often chronic myelogenous leukemia)
- Hypothyroidism

Low

- Hyperthyroidism
- Acute allergy
- Stress
- Glucocorticoid therapy
- Hypersplenism

Functional Considerations

Consider food allergies as well as parasites if elevated. If low, consider chronic stress as main factor.

Related Tests

CBC w/Diff.: Allows for more complete marrow analysis as well as nutrient factor associated pathology.
Urinalysis: Many chronic infections are subacute urinary tract infections that may exist for months or even years before they are symptomatic.
Lymphocyte Subset Panel: Helps differentiate T and B cell dysfunction as well as general immune deficiency/dysfunction.
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Red Blood Cell Count

Optimal Female: 4.1 – 4.7 mill/mcl
Optimal Male: 4.4 – 5.2 mill/mcl

Red blood cells, or erythrocytes, are non-nucleated cells responsible for transporting oxygen, carbon dioxide, minerals, nutrients, hormones and other biochemical constituents in the blood. They have very pliable cell membranes which allow them to fold and squeeze through tiny microcapillaries. RBC's are produced in the marrow under stimulation by erythropoietin. The average lifespan of the RBC is about 120 days. The spleen removes aged and damaged RBC's where they are lysed and the heme component is recycled into bilirubin. When RBC's are low, the patient is anemic. Anemia's can be classified according to three criteria: 1. **Deficiency** of raw material (B12, iron etc.); 2. Altered **Production** (bone marrow depletion, hypothyroidism etc.), or; 3. **Loss** of RBC's (hemolysis, GI bleeding, hypersplenism). Anemia's can also be classified according to morphology, such as microcytic, macrocytic, hyperchromic, normochromic etc. The RBC indices (MCV, MCH etc.) are essential in determining etiology of abnormalities.

High

- Dehydration
- Respiratory distress: asthma or emphysema (low Po2 levels stimulate erythropoietin)
- High altitude
- Polycythemia (relative to other blood cells, or absolute elevation)
- COPD
- Hemochromatosis
- Hemoglobinopathies
- Congenital heart disease
- Intense exercise training

Low

- Anemia - iron, B6, B12 / folate deficiency
- Internal bleeding
- Digestive inflammation
- Vitamin C deficiency
- Splenomegaly / hypersplenism
- Hemoglobinopathies (sickle cell, hemoglobin C)
- Vitamin E deficiency
- EFA deficiency
- Glutathione deficiency
- Cirrhosis
- Chronic illness
- Pregnancy (normally on the low end of normal but needs to be monitored. Low iron during pregnancy is associated with birth defects and decreased I.Q. for the child)
- Renal disease
- Autoimmune (rheumatoid, collagen-vascular disease, lupus)
- Menses
- Bone marrow failure
- Antibiotics

Functional Considerations

RBC's are very susceptible to oxidative stress, since their job is to carry oxidative, free radical producing iron, oxygen, carbon dioxide and a host of other nutrients and biochemicals. Therefore, RBC's serve as sensitive total body anti-oxidant capacity measurements. If any sign of RBC hemolysis is present (low ferritin, low RBC, high RDW, high serum iron) suspect glutathione deficiency either primary (production deficit) or secondary (accelerated depletion). Replace with high amounts of antioxidants, NAC, glutathione as well as liver support formulas. Search for causative factors such as heavy metal, stress and inflammatory dietary habits.

Thyroid is often overlooked as a cause of low RBC's. Hypothyroidism is a major cause of subclinical anemia and may produce macrocytic, normo or hypochromic RBC's.
Because most labs run automated cell counters, they can miss a small percentage of RBC abnormalities. If the clinician has access to a microscope, there can be invaluable information obtained by adding a histological exam (with proper slide preparation technique) to basic hematological lab tests. One will often catch an abnormality that the other one misses. Doing a microscopic exam should not replace basic laboratory testing, but rather a compliment to it.

Related Tests

CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.
F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.
Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.

Hemoglobin

Optimal Female: 13 – 14.5 gm/dl
Optimal Male: 14.5 – 16 gm/dl

Hemoglobin (Hgb) is the oxygen carrying component of the RBC and is made up of heme (iron and protoporphyrin). It is also an important acid – base buffer in the blood. Hgb values are used as an indirect measurement of RBC count. Hgb and Hct are more sensitive to changes in plasma volume than total RBC counts are. Typically, what affects RBC's will also affect Hgb and Hct. There is a diurnal variation with the peak at 9am and nadir at 8pm with an average difference of up to **2 gm/dl**.

High

- Dehydration
- Respiratory distress: asthma or emphysema (low Po2 levels stimulate erythropoietin)
- Polycythemia (relative to other blood cells, or absolute elevation)
- COPD
- High altitude
- Increased risk for stroke and organ infarction
- Hemochromatosis
- Hemoglobinopathies
- Congenital heart disease
- Intense exercise training
- Hyperlipidemia

Low

- Anemia - iron, B6, B12 / folate deficiency
- Internal bleeding
- Digestive inflammation
- Increased risk for angina, heart attack and stroke (heart must work harder to maintain oxygen carrying capacity of blood)
- Vitamin C deficiency
- Splenomegaly / hypersplenism
- Hemoglobinopathies
- Vitamin E deficiency
- EFA deficiency
- Glutathione deficiency
- Cirrhosis
- Chronic illness
- Pregnancy (normally on the low end of normal but needs to be monitored. Low iron during pregnancy is associated with birth defects and decreased I.Q. for the child)
- Renal disease
- Autoimmune
- Menses
- Bone marrow failure
- Antibiotics

Functional Considerations

IDA and B2 (riboflavin) deficiency both can result in angular stomatitis. This brings up an important topic, namely the epidemic of *malabsorption*. This may be due in part to celiac disease (whether severe or subclinical) or it may be due to chronic inflammation of the intestines, stress, intestinal mucosal dysfunction, hypochlorhydria and leaky gut. In any case, ingesting micronutrients is very different from absorbing them, not to mention the proper utilization of these essential nutrients. It has far too long been assumed that just because some vitamins and nutrients are in the diet, or given in supplements that deficiencies are impossible or rare.

Related Tests

CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.
F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.

Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.

Hematocrit

Optimal Female: 37 – 45%
Optimal Male: 42 – 48%

Hematocrit is a measurement of the RBC volume in the serum after it has been centrifuged. The RBC's will fall to the bottom and the height of this will be compared to the height of the rest of the plasma and expressed as a percentage of the total volume of blood. It is generally similar to RBC and Hgb except when there is micro or macrocytosis (which will then affect total volume and not reflect the number of RBC as accurately). The plasma concentration also will greatly affect this test and can be used to

determine dehydration, as lower plasma will artificially raise RBC concentration. It is possible to have a macrocytic anemic patient who is also dehydrated come back with a normal or even slightly elevated Hct. This is why it is important to look at all RBC values and indices together.

High

- Dehydration
- Respiratory distress: asthma or emphysema (low Po2 levels stimulate erythropoietin)
- Polycythemia (relative to other blood cells, or absolute elevation)
- COPD
- High altitude
- Hemochromatosis
- Hemoglobinopathies
- Congenital heart disease
- Intense exercise training

Low

- Anemia - iron, B6, B12 / folate deficiency
- Internal bleeding
- Digestive inflammation
- Vitamin C deficiency
- Splenomegaly / hypersplenism
- Hemoglobinopathies
- Vitamin E deficiency
- EFA deficiency
- Glutathione deficiency
- Cirrhosis
- Chronic illness
- Pregnancy (normally on the low end of normal but needs to be monitored. Low iron during pregnancy is associated with birth defects and decreased I.Q. for the child)
- Renal disease
- Autoimmune
- Menses
- Bone marrow failure
- Antibiotics

Functional Considerations

RBC, Hct and Hgb are all affected by age, sex and overall health of the patient. An elevated WBC count may artificially lower Hct due to larger number of WBC's in plasma.

Related Tests

CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.
F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.
Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.

MCV Optimal: 83 – 92 femtoliters (fl)

Mean corpuscular volume is a measure of the diameter of RBC's. Knowing the morphology of RBC's allows for more accurate determination of anemia as well as nutritional and environmental factors affecting the health of the RBC. Collectively, MCV, MCH, MCHC and Reticulocytes (or RDW) are known as RBC indices, or "Wintrobe" indices. The MCV is calculated by dividing the Hct with the total number of RBC's. MCV should not be used as absolute evidence of macrocytosis. A significant number of patients with actual macrocytosis will not have an elevated MCV because of Hct variations.

High

- Megaloblastic anemia - B12 / folate deficiency (lack of these nutrients will cause impairment of DNA synthesis of healthy new RBC's. The most common cause of this condition is due to pernicious anemia which is an autoimmune destruction of parietal cells)
- Macrocytic non-megaloblastic anemia (hypothyroidism can cause macrocytic anemia with sufficient B12/folate levels)
- Macrocytosis – large RBC's often exist without anemia present (see functional cons. below)
- Intestinal dysbiosis / parasites (causes malabsorption of B12, folate and other nutrients)
- Vitamin C deficiency
- Alcoholism
- Chronic liver disease
- Smoking
- Acute blood loss (a rise in RDW will artificially raise MCV due to elevated Hct and low RBC)

Low

- Anemia - iron, B6 deficiency
- Chronic illness
- Internal bleeding (chronic loss of RBC causes loss of iron and microcytic cells)
- Thalassemia
- Glutathione deficiency

Functional Considerations

Supplementation of macrocytic anemia with B12 and folate does not always result in return to normoblastic erythrocytes. This is often due to hypothyroidism.

Check homocysteine as this will often be elevated if there is a functional B6, B12 and folate deficiency. It is commonly seen that as one ages, the ability to absorb these nutrients is greatly diminished, thereby explaining, at least in part, why MCV values increase with age.

MCV and RDW may be abnormal before actual anemia is present, and anemia can often take months or even years to develop even when MCV and RDW are abnormal.

Hypothyroidism is also another very common and overlooked cause of elevated MCV. This can occur with overt or subclinical hypothyroidism (also called thyroid insufficiency). The RBC's need sufficient thyroid hormones to mature and the absence of healthy levels will cause impaired RBC development and elevated MCV.

Related Tests

CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.

F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.
Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.

MCH Optimal: 28 – 31 pg

Mean corpuscular hemoglobin is a calculated value to estimate the amount of hemoglobin weight in each RBC. This is done by dividing the total hemoglobin by the number of RBC's. It provides a quick and fairly accurate way to assess the size of RBC's and the amount of hemoglobin each one carries.

High

- Anemia - B12 / folate deficiency
- Hypochlorhydria
- Intestinal dysbiosis / parasites (causes malabsorption of B12, folate and other nutrients)

Low

- Anemia-iron, B6 deficiency
- Internal bleeding
- Heavy metals
- Vitamin C deficiency

Functional Considerations

MCH values parallel MCV. See MCV.

Related Tests

CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.
F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.
Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.

MCHC Optimal: 32.5 – 35%

Mean corpuscular hemoglobin concentration is a calculated value to estimate how much Hg concentration is in each RBC. It is determined by dividing the total hemoglobin with the Hematocrit concentration.

A low MCH is considered hypochromic. An elevated MCH is hyperchromic. This is useful in the differentiating of certain anemias.

High

- Anemia - B12 / folate deficiency
- Hypochlorhydria
- Intestinal dysbiosis / parasites (causes malabsorption of B12, folate and other nutrients)

Low

- Anemia - iron, B6 deficiency

- Heavy metals
- Internal bleeding
- Vitamin C deficiency

Functional Considerations
MCHC closely parallels MCV.

Related Tests
CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.
F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.
Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.

RDW Optimal: 11 – 13 %
Red blood cell distribution width is an indication of the variation in RBC size. Normally RBC's are about the same size. If blood loss is occurring, or there is a production defect in RBC's, then there will be many abnormal sizes of erythrocytes. Newer, immature blood cells are larger, and in iron deficiency anemia (IDA), there will microcytosis. This test is useful in detecting *short term* changes in the morphology of RBC's. Even if there are abnormal sizes in RBC's, such as in pernicious anemia or IDA, the longer the condition persists the more all RBC's will reflect the abnormal size and the RDW will return to normal. This test gives the clinician somewhat of a timeline and body response marker. If the RDW is high, one is said to have anisocytosis (many different RBC sizes).

High (anisocytosis)
- Anemia - iron, B12 / folate (MCV and RDW may be abnormal before actual anemia is present, and anemia can often take months or even years to develop even if MCV and RDW are abnormal)
- Pernicious anemia
- Menses
- Internal bleeding recovery
- Hemolytic anemias
- Vitamin E deficiency (Vitamin E is the only lipid soluble antioxidant for RBC's)
- Decreased antioxidant status (glutathione is the main antioxidant for RBC's and one of the functional signs of depletion is elevated RDW due to accelerated RBC turnover)
- Recovery from acute/chronic illness
- Travel between different altitudes (moderate time in high altitudes may temporarily elevate RDW due to a short term increase in release of immature blood cells.)
- Inflammation - acute

Low or Normal (if anemia is present)
- Thalassemia
- Chronic disease
- Chronic anemia
- Inflammation - chronic

Functional Considerations

RDW is almost never low, even if severe anemia. It can however be normal in the case of severe anemia or chronic illness. RDW is sometimes the most sensitive indicator of abnormal RBC morphology. One can have abnormal RBC production due to several different reasons (B12, iron deficiency, hemolysis, cancer, internal bleeding etc.) for months and even years before actual anemia becomes apparent. RDW will sometimes be abnormal, even if MCV is normal. This makes RDW one of the most important markers of RBC production evaluation.

One of the first things to consider with elevated RDW is decreased glutathione and antioxidant status. This can be due to several reasons such as nutritional deficiencies of selenium, glutamine or sulfur containing amino acids such as cysteine. It can also be due to elevated free radical production such as acute inflammation, smoking, toxic exposure or stress. Keep in mind this can occur with or without other clinical reasons for elevated RDW such as internal bleeding and menses. Be careful not to assume that menstruation is the only cause of elevated RDW in a female patient. As always, clinical correlation is required to correctly interpret this finding. Often a trial of high doses of antioxidants, glutathione precursors and natural inflammation modulators will result in lowering of RDW confirming this condition.

Related Tests

CBC w/Diff: MCV, MCH, MCHC, Hgb, Hct. RBC and WBC with differential.
Iron Panel: Ferritin, iron, transferrin saturation, and binding capacity.
F.I.T.: Fecal immunochemical test. More sensitive measurement than occult blood.
Homocysteine: Helps assess functional B12, B6, and folate deficiency.
Thyroid Panel: Thyroid hormone is needed to stimulate healthy RBC and WBC production.
Glutathione, serum: Checking glutathione status may be helpful in differentiating cause of elevated RBC's.
Vitamin D: Often low in chronic inflammatory states and blood loss.

Platelet Count Optimal: 195 – 320 thousand/mcl

Platelets are also called thrombocytes as they play a major role in forming clots in order to maintain vascular integrity. They also play numerous other roles in cytokine formation, act as a back-up transport mechanism for hormones and nutrients, contain serotonin, and can regulate vasoconstriction. Platelets also act as a store for essential fatty acids and phospholipids. They are made in the bone marrow as megakaryocytes and mature as small, round, non-nucleated cells. The half-life of platelets is about 6 days.

High

- Dehydration
- Malignancy
- Rheumatoid arthritis (may be due to cytokine signaling and systemic inflammation, especially due to antibodies to vascular collagen)
- Anemia (IDA or hemorrhagic anemia which will stimulate pluripotent stem cells. Platelets do not need iron for production and maturation.)
- Polycythemia vera
- Atherosclerosis increased risk (look for elevated homocysteine, CRP, and fibrinogen)
- Inflammation and increased inflammatory potential (platelets initiate the arachidonic acid pathway of inflammation and contain many phospholipids that can be potentially oxidized, damaged and inflammatory.)

- Thrombocythemia (platelet counts above 1 million)
- Post-splenectomy or hypospleeninsm (low spleen function)

Low

- Idiopathic thrombocytopenia (acute is common in children and is usually self-limiting. The chronic form is found in adults and can be life threatening if not treated. Often this has a viral etiology and is found often coexisting with autoimmune conditions.)
- Pernicious anemia (platelets do need B12 and folate just like RBC's. If RBC and platelet is low, this can rule out IDA)
- Hemolytic anemia
- Kidney failure (uremic patients may have low platelets. Elevated BUN will be seen)
- Heavy metals
- Free radical increase
- Drug induced (some antibiotics, antimalarials, and blood pressure medications)
- Chronic infection (sepsis, viral, HIV, etc.)
- Hypersplenism – increased clearance of platelets and other blood cells due to liver dysfunction, cancer, irritation, infection or autoimmune
- Bone marrow dysfunction (cancer, myelofibrosis, old age)
- Autoimmune disease (antibodies to platelets are common in SLE, cold agglutinin disease and MCT disorders)
- Leukemia
- Increased risk for prolonged bleeding from injury, hemorrhage, petechiae and ecchymosis
- H.E.L.L.P. Syndrome (considered a form of pre-eclampsia, an acronym for **H**emolytic anemia, **E**levated **L**iver enzymes and **L**ow **P**latelets)

Functional Considerations

Laboratory error is considered to be about 10 -15% due to agglutination, so caution is advised when interpreting marginal values. Run repeat tests if any doubt exists as to whether the test value represents a pathology or dysfunction.

Platelets are designed to be very sensitive to chemicals of inflammation and oxidation, as this usually signals vascular wall damage and need for clotting. Therefore, if platelets are elevated, it is often a sign that the patient is undergoing oxidative stress due to toxicity, infection, stress etc. To prevent or mitigate atherosclerotic formation (a consequence of elevated platelets) in the short term while the underlying factors are addressed, give plenty of antioxidants and support liver detoxification with herbs such as silymarin, curcumin and SAM'e.

Low platelets are often a sign that shows up in several autoimmune diseases such as RA and Lupus. This can be explained by either cross reactivity of autoimmune antibodies and clearing of platelets, and/or autoimmune destruction of bone marrow.

Related Tests

MPV: Measures the size of platelets and can give information as to the cause of platelet abnormality.

PT/INR: Pro-time/International normalized ratio is used to further evaluate the hemostasis and coagulation system, including the extrinsic and common pathways. Not a sensitive test to determine hypercoagulability, but is used to monitor patients on blood thinning medication to avoid hypocoagulability and increased bleeding risk.

Fibrinogen: Used to assess increased risk for bleeding as well as heart attack/stroke risk.

Platelet Aggregation Function: Test used to determine where and if an abnormality exists in platelet action. Will uncover conditions such as von Willebrand's and other factor deficiencies.

Platelet Antibody: Tests for autoimmune antibody to platelets.
Bleeding Time: Performed by cutting the patient usually on the arm and recording the time it takes for the wound to stop bleeding.
CRP: Evidence of inflammation and in the case of cardio CRP, heart damage specifically.
Homocysteine: Elevated Hcys will cause increase vascular wall damage and increase platelet aggregation, even when platelet count is normal or even low normal.
Liver Enzymes: Many diseases which affect the liver can produce platelet abnormalities.
Nutrient and Toxic Element: Assesses for heavy metal burden and nutrient status.

Mean Platelet Volume Optimal: 8 – 10.5 fl

Mean platelet volume is the average size of each platelet. When compared to the size of RBC's (MCV) it is plainly evident that platelets are indeed very small. Immature, newly formed platelets are larger than normal platelets. Unlike RBC's, platelets do not need iron, but do need B12 and folate in the same way erythrocytes do. MPV is useful in determining cause of platelet count abnormality as well as differentiating causes of anemia.

High

- B12 / folate deficiency (platelets produced in pernicious anemia and/or B12 / folate deficiency are larger in size, just as RBC's are)
- Leukemia
- Hypersplenism (liver dysfunction and cirrhosis can cause portal hypertension – a major cause of splenomegaly)
- Intestinal dysbiosis / parasites (causes malabsorption of B12, folate and other nutrients)
- Internal bleeding

Low

- Aplastic anemia
- Chronic iron deficiency
- Heavy metals
- Wiskott-Aldrich syndrome (eczema, immune deficiency, and thrombocytopenia)
- Post splenectomy or hypospleenism

Functional Considerations

Elevated MPV can help confirm B12 deficient anemia if MCV is also elevated. If MCV is elevated and MPV is not, suspect hypothyroidism.

Related Tests

Platelets: MPV is always considered with total platelet count.
PT/INR: Pro-time/International normalized ratio is used to further evaluate the hemostasis and coagulation system, including the extrinsic and common pathways. Not a sensitive test to determine hypercoagulability, but is used to monitor patients on blood thinning medication to avoid hypocoagulability and increased bleeding risk.
Fibrinogen: Used to assess increased risk for bleeding as well as heart attack/stroke risk.
Platelet Aggregation Function: Test used to determine where and if an abnormality exists in platelet action. Will uncover conditions such as von Willebrand's and other factor deficiencies.
ESR: A non-specific test for increased inflammation and coagulation potential.

Platelet Antibody: Tests for autoimmune antibody to platelets.
Bleeding Time: Performed by cutting the patient usually on the arm and recording the time it takes for the wound to stop bleeding.
CRP: Provides evidence of general inflammation and in the case of *cardio*- specific CRP, heart damage specifically.
Homocysteine: Elevated Hcys will cause increase vascular wall damage and increase platelet aggregation, even when platelet count is normal or even low normal.
Liver Enzymes: Many diseases which affect the liver can produce platelet abnormalities.
Nutrient and Toxic Element: Assesses for heavy metal burden and nutrient status.

ESR Optimal: 4 – 10 mm/hr

Erythrocyte sedimentation rate is a useful, albeit non-specific, test for inflammation, infection, neoplasms, as well as a functional marker for blood viscosity and heart attack/stroke risk. It is not diagnostic for any specific disease. However, this test can uncover hidden etiologies and therefore provide the clinician with valuable information. For instance, if a patient has chest pain due to a heart attack, the ESR will be elevated due to tissue destruction. If the chest pain is due to angina, the ESR will be normal and a heart attack is unlikely. Given that it is an inexpensive test, it is often included in routine laboratory examinations.

The test is performed by collecting a venous sample of blood and letting it sit for 1 hour. At that time the remaining clear liquid (plasma) is measured. Therefore, a high rate means that the RBC's have agglutinated (stuck together) which has made them denser and have fallen faster.

High

- Non-specific tissue inflammation or destruction
- Renal disease (increased proteins and inflammation)
- Severe anemia
- Hyperproteinemia
- Infection
- Autoimmune (rheumatoid collagen disease, polyarteritis nodosa)

Low

- Blood hypercoagulation
- Dehydration
- Polycythemia
- Congestive heart failure
- Hypoproteinemia (see protein, serum. Less proteins means less aggregation on RBC's and slower sedimentation)
- Vitamin E deficiency
- Liver disease

Functional Considerations

It is estimated that 90% of all chronic degenerative diseases are inflammatory related. This test is helpful in determining persistent elevations of certain types of inflammation that effect globulins and proteins. Heart disease risk is elevated when ESR is elevated. ESR will often be elevated for months or possibly

years before there is any symptomatology for disease. An elevated ESR is a serious sign, especially if significantly elevated (>50). ESR levels often parallel fibrinogen and other acute phase reactant proteins. Keep in mind, low levels of ESR is associated with congestive heart failure and increased risk for heart attack for different reasons than elevated ESR. Therefore, both high and low levels are associated with increased risk for heart attack and stroke.

Because elevations of ESR are almost always associated with excess proteins in the blood, consider short term, high dose enzyme therapy. Caution should be used with enzymatic therapy, as this could irritate the enterocytes of unhealthy gut mucosal membranes. Enzyme therapy should not be done in high doses for long periods of time as this may lead to auto-digestion of the body's own cells and cell structures.

Related Tests

CRP: Provides evidence of general inflammation and in the case of *cardio*- specific CRP, heart damage specifically.
Homocysteine: Elevated Hcys will cause increase vascular wall damage and increase platelet aggregation, even when platelet count is normal or even low normal.
Liver Enzymes: Many diseases which affect the liver can produce platelet abnormalities.
Nutrient and Toxic Element: Assesses for heavy metal burden and nutrient status.
Cytokine Panel: Checking which cytokines may be elevated will help determine nature of inflammation.
Autoimmune Panel: Since many elevations in ESR are autoimmune related, checking for ANA, Thyroid, RA antibodies and more may elucidate reasons for elevations.

Comprehensive Metabolic Panel

Glucose, Fasting (10-12 hours) Optimal Range: 70 – 88 mg/dl

Glucose levels are tightly regulated in human blood. Because glucose is the main energy source for human cells through the citric acid cycle, it is necessary for the cells to have enough for metabolism, but not too much to overwhelm the capacity of cellular metabolism. Not enough glucose and cells will inefficiently look for other sources of energy such as fats and proteins, and readily available energy will diminish. Too much glucose will overwhelm metabolic cellular function, damage and congest tissues causing systemic inflammation. Therefore, the body uses many hormonal mechanisms to ensure just the right amount is available in the serum and tissues.

When fasting, the blood sugar drops and glucagon from the pancreas, cortisol and epinephrine from the adrenal gland, growth hormone from the hypothalamus and pituitary and thyroid hormone are excreted to stimulate gluconeogenesis (GNG) raising glucose levels. When blood sugar elevates, beta cells in the pancreas secrete insulin. Insulin binds to insulin receptors, activating glucose transport proteins on cell surfaces which escort glucose into the cell, thereby lowering blood glucose. Glucose cannot enter cells without insulin. When blood sugar imbalances occur, it is usually one or more of these hormonal mechanisms that is being affected.

Traditionally, blood sugars need to be extremely elevated to make a diagnosis of diabetes. However, dysglycemia is increasingly understood as a spectrum disorder. With more sensitive optimal ranges, early signs of blood sugar dysregulation can clearly be seen and reversed long before disease symptoms manifest.

High >88

- Insulin resistance (IR) - see functional considerations below.
- Diabetes (>126) - see functional considerations.
- Gestational diabetes - predisposes mother to diabetes later in life. Usually insulin resistance is part of the physiology.
- Metabolic syndrome - a constellation of symptoms of which elevated glucose is one. Essentially the same as IR but with other advanced signs of dysglycemia such as elevated blood pressure, triglycerides, and cholesterol.
- Thiamine deficiency - thiamine is needed for conversion of glucose to energy in the electron transport chain.
- Cortisol resistance - elevated secretions of ACTH and hypercortisolism lead to stimulation of gluconeogenesis.
- Fatty liver - consequence of elevated glucose, cholesterol, triglycerides, etc.
- Liver congestion - consequence of elevated glucose, cholesterol, triglycerides, etc.
- Severe stress during blood draw - epinephrine and cortisol are released causing hyperglycemia.
- Cushing's syndrome - can be either exogenous glucose administration or endogenous adrenal dysfunction.
- Corticosteroid therapy - cortisol stimulates gluconeogenesis (GNG).
- Certain diuretics - stimulates adrenal cortisol secretion.
- Antidepressants - pathophysiology is multifactorial, essentially due to effects on pituitary.
- Beta blockers - beta blockers cause lower metabolism and promote IR.

Low <70

- Reactive hypoglycemia - see functional considerations.
- Hypoglycemia secondary to low glycogen levels in liver or impaired GNG.
- Cancer – certain cancers will cause hypoglycemia such as testicular, liver, pancreatic.
- Over medication with diabetic drugs - insulin overdose is the most common cause of severe hypoglycemia.
- Hyperinsulinism - endogenous production of insulin is increased in insulin secreting tumors, acute infections, impaired liver detoxification, autoimmune against pancreas and some rare genetic defects.
- Adrenal hypofunction - low production of cortisol lowers glucose during fasting.
- Hypothyroid - liver cells involved in gluconeogenesis need thyroid hormone to function properly.
- Hypopituitarism- growth hormone and ACTH are major anti-insulin hormones that stimulate GNG.
- Addison's disease - low production of cortisol lowers glucose during fasting.
- Prolonged fasting (>12 hrs.)
- Acetaminophen - this drug impairs liver function affecting glucose metabolism.
- Alcohol - about 3-4 hours post ingestion there is an observed hypoglycemia.

Functional considerations

Glucose will rarely be elevated out of normal levels *by itself*. Most often elevated blood glucose will have to be correlated with other laboratory sub-optimal findings in order to get an accurate picture of the causes of elevated glucose as well as the extent of systemic involvement. If glucose is elevated by itself, it may represent either a non-fasting state, ingestion of caffeine or someone who was exceptionally anxious about the blood draw.

The most common reason for blood sugar outside the **optimal** range is insulin resistance. This may be the most common condition seen in a primary care practice when running labs. It is a "silent" disease in that most of the signs and symptoms do not occur until much later in the disease process. Therefore, most people with insulin resistance are unaware that they have this condition. This makes it especially important for integrative health practitioners to become familiar with its causes, effects and treatments.

The difference between diabetes and insulin resistance, physiologically speaking, is pancreatic insufficiency. After years of elevated blood sugar and insulin release, the beta cells in the pancreas eventually wear down. When this happens, insulin levels drop, blood sugar levels rise rapidly and stay elevated. The progression from IR diabetes often is very fast once this occurs. Since diabetics already are insulin resistant, the elevating levels of blood sugar continue to stimulate insulin release from the pancreas, wearing it down very fast. This is why it is imperative to treat dysglycemia while the pancreas is still intact and capable of healing. This is true whether Type I or Type II.

There is emerging evidence that waiting to put a Type I diabetic on insulin, and working with dietary and immunologic factors, may actually give the young patients' pancreas a chance to rebuild and become functional again. This should be done with a knowledgeable functional endocrinologist. It may be necessary to put the Type I patient on metformin or some other type of blood sugar lowering medication while the pancreas heals.

Often the earliest sign of insulin resistance is actually a **low** fasting blood sugar. This signals that the patient is dysglycemic and may eventually progress to elevated blood sugar and/or diabetes. This is termed reactive hypoglycemia (see conditions below). Essentially this happens because the patient has early insulin resistance which at times causes an elevation of blood sugar. The pancreas is still functional, so it will over-secrete insulin thereby causing a rapid decline in blood sugar. Other physiological mechanisms are at play, which include adrenal fatigue and hypocortisolism. All of which result in the patient not being able to manage serum glucose levels. Furthermore, reactive hypoglycemic patients often feel the hypoglycemic (shaky, tired, nervousness) and will crave sweets and simple carbs, which only advance the pathophysiology.

Related Tests

Hemoglobin A1C: Test used for determining average levels of blood glucose over the last 3 months. Used to determine level of progression of insulin resistance, diabetes and diabetic risk. Also useful as a marker of treatment effectiveness.
Oral Glucose Tolerance Test(OGTT): Often used to determine response to glucose load. Not as useful clinically as HA1C. It may be easier on the patient to administer a post-prandial glucose test, rather than subjecting the patient to a harsh glycemic load. This test is most often used to detect gestational diabetes.
Diabetes Mellitus Autoantibody Panel: Type I diabetes (insulin dependent diabetes mellitus) can be autoimmune related. Tests for antibodies against beta cells are found in nearly 90% of IDDM patients. Do not use this test if patient is already on exogenous glucose.
Insulin: Measurement of insulin levels fasting and PP are useful in determining etiology of IR or DM.

Hemoglobin A1c Optimal Range: 4.7 - 5.4 %

Also known as Glycosylated Hemoglobin. There are several subtypes of hemoglobin. HbA_{1c} is a type that binds strongly and fairly predictable to glucose. The more glucose exists in the blood, the more it binds to hemoglobin. Once glycosylation occurs, it is irreversible. Therefore, it is an accurate measurement of average blood glucose levels over the course of the RBC lifespan (approx. 120 days). This test is not affected by short term variations such as eating, exercise, stress etc.

High 5.5 or greater

- Diabetes mellitus
- Insulin resistance
- Reactive hypoglycemia (if fasting glucose is low)
- Spleen dysfunction - the spleen is responsible for RBC destruction. If spleen is removed or dysfunctional, the RBC lifespan is increased, giving more time for glycosylation.

Low <4.7

- Hypoglycemia (see low glucose for associated conditions)
- Adrenal insufficiency - cortisol's main action is to maintain healthy blood sugar levels.
- Infection / chronic illness - many chronic illnesses can affect RBC production and lifespan as well as glucose production. Furthermore, chronically ill patients are often malnourished causing low blood glucose.
- Anemia - if the patient is anemic this test can be falsely lowered. Hemoglobin A levels can be relatively low in relation to other Hg. Also, the RBC lifespan is shortened, giving less opportunity for glycosylation.
- Antioxidant insufficiency – if glutathione is deficient, RBC life span is shortened, creating less A1c to be glycosylated, giving a falsely low value.

Functional considerations

Traditionally this test is only used once a diagnosis of IR or diabetes has been established using fasting blood glucose (FBG). While HA1c should not be used to diagnose diabetes, it is an extremely useful functional test for blood sugar metabolism. It is often quite possible for a borderline diabetic or IR patient to fast for 12 hours and produce a normal fasting glucose. HA1c however cannot be manipulated so easily. Therefore it is useful as a screening test for detecting dysglycemia long before a fasting blood sugar is abnormal. This makes it one of the most useful functional tests in laboratory evaluations. Many cases of IR present with normal FBG but abnormal HA1c. This is due to the fact that diabetes is defined as a relative or absolute deficiency in insulin. In the case of "pre-diabetes" or insulin resistance, the pancreas is still functioning and able to secrete enough insulin to eventually normalize glucose. Not using HA1c as a more sensitive marker of dysglycemia in the traditional medical community represents an inability to value **prevention,** instead opting to wait until the pancreas has become insufficient and the disease has progressed. Oral glucose tolerance tests are sometimes used to detect dysglycemia and diabetes. However, this test is time consuming and somewhat expensive so that it is not an ideal screening test.

Because glycosylation happens predictably, mathematical equations are used to determine average blood glucose levels in mg/dl. This is represented as Mean Plasma Glucose, and is usually included in a HA1c.

Related tests

See Fasting Glucose above as all tests apply here.

Glycosylated Fructosamine: A 15-20 day measurement of average blood glucose. Glucose will bind to fructosamine in the same way it will bind to Hg. However, the lifespan of fructosamine (a carrier protein) is about 3 weeks. If one requires a more immediate indication of treatment effectiveness, this is a useful test.
Alpha Hydroxy Butyrate: In large studies, this organic acid was the most sensitive predictor of insulin resistance and subsequent diabetes.
Triglycerides: Elevated triglycerides is a very sensitive marker for insulin resistance as one of the actions of insulin is stimulation of hepatocytes to form TG's from glucose in the blood. Elevated cholesterol and other lipids will also follow.
Uric Acid: Will often be elevated in IR due to increased formation and decreased clearance due to kidney damage.

BUN Optimal: 12-19 mg/dl

Blood Urea Nitrogen is the measurement of urea in the blood which is formed primarily in the liver as an end product of protein metabolism. Amino acids undergo deamination and ammonia is formed. Most of this process occurs by bacteria in the gut. BUN is both a liver and kidney function test, though predominately considered a part of the renal function study. Once produced by the intestines and liver, it must be excreted by the kidney. Most kidney diseases result in impaired filtration and subsequent elevation of urea and creatinine. Elevated BUN is referred to as azotemia or uremia. There are pre-renal, renal and post renal causes of azotemia.

Pre-renal: The excessive production of urea due to increased protein intake, tissue destruction, or decreased renal blood flow from various etiologies such as CHF, nutritional deficiency, inflammation etc.
Renal: Accumulation of urea due to direct renal structural deterioration due to autoimmune destruction, acute toxicity or idiopathic causes
Post-renal: Most often due to urinary obstruction. Oliguria is the result. Diagnosis is often made by a urinalysis showing infection or kidney stones (crystals).

High

- Renal disease
- Renal insufficiency
- Dehydration
- Hypochlorhydria
- Diet - excessive protein intake
- Adrenal hyperfunction
- Dysbiosis / bacterial and microbial overgrowth
- Anterior pituitary dysfunction
- Congestive heart failure
- Myocardial infarction
- Sepsis
- Excessive fasting
- Eating disorders
- Urinary tract infection
- U.T. obstruction

Low

- Diet - low protein

- Malabsorption / celiac disease
- Antibiotic use / dysbiosis (intestinal flora is the largest producer of ammonia in the body)
- Pancreatic insufficiency
- Liver dysfunction
- Over hydration
- Pregnancy
- Low muscle mass
- Anabolic steroids

Functional Considerations

BUN levels are very sensitive to hydration levels. Not only will dehydration artificially elevate BUN levels because the serum is more concentrated, it also limits the glomerular filtration rate and ability of the kidney to excrete urea as well as all other toxic substances and metabolites. Also, BUN levels tend to be lower in the morning and peak in the evening.

When creatinine levels are normal, BUN is more of a liver function test as urea is made in the liver. Usually a lower urea level signals a loss of liver function. It may also signify a need for dietary protein. If dietary intake is within acceptable limits, digestion and absorption dysfunction (such as low HCL or pancreatic function) is a consideration.

In males with elevated BUN by itself, it may signal prostate obstruction due to prostate disease. It is common to see elevated uric acid along with BUN because both are by-products of protein metabolism. Often gout can be seen in these patients. If gouty crystals have not had time to form, patients may still complain of diffuse, often systemic joint pain. This is often exacerbated by the fact that most people will then take a NSAID or other pain killer which will further damage kidneys and progress the dysfunction.

It is often reported that in kidney dysfunction, it is BUN that will rise before creatinine. Chronic use of NSAID's is the most common cause of kidney damage. Since the kidneys are one of the main detoxifiers in the body, an elevated BUN could represent impaired detoxification and should be addressed with kidney support formulas (astragalus, corn silk etc.), far-infrared, acupuncture, ginger or castor oil packs. Check urine for proteinuria signifying serious kidney damage. Do not put the patient on a Detox protocol until kidney issues have been resolved. Loosing stored toxins and increasing toxic burden without proper liver and kidney function will only serve to make the patient sicker.

Related Tests

Creatinine: A more pure kidney function test as creatinine is not as subject to extra-renal influences. It is influenced however, by muscle mass and metabolism.
Cystatin C: Unlike creatinine, Cystatin C is produced at a more constant rate than creatinine regardless of metabolic state. This is an even more accurate and sensitive marker for renal dysfunction and patient mortality. If kidney disease is suspected or part of a patient's history, this test is very useful.
Urinalysis: UA will show proteinuria if renal destruction is cause of elevated BUN.
Creatine Clearance: A 24 collection of urine to more accurately measure kidney function. This test is most often run in a hospital or in-patient setting. It is a direct measure of glomerular filtration rate.
eGFR: Estimated Glomerular Filtration Rate is a mathematical equation based on creatinine, age, sex, ethnicity etc. It is reported to be fairly accurate if a renal disease is present. It is subject to the same limitations of creatinine. It is usually automatically reported by most labs and can be useful in tracking kidney function over time, and response to treatment.

Creatinine Optimal: .6 - .9 mg/dl

Creatinine (Cr) is a byproduct of muscle contraction and is released in varying amounts according to muscle mass, activity level and time of day. It is used as a marker of kidney clearance as creatinine should be excreted at a steady and sufficient rate. When Cr levels rise, kidney dysfunction is suspected. However, an elevated creatinine must be correlated with other lab and clinical findings. If Cr is elevated by itself, it most likely represents recent exercise or muscle trauma. Inquire the patient about such possibilities. This is why pt.'s must be instructed to avoid exercise for at least 36 hours before the blood draw. Also, body types with large muscle mass releases more Cr naturally and is not considered pathological. One abnormal value is also of limited value and follow tests several days apart should be repeated.

If BUN is elevated along with Cr, then the likelihood of a kidney disease is significant and the etiology of the dysfunction needs to be investigated with related lab tests and/or diagnostic imaging studies and perhaps renal biopsy if indicated. Cr, like BUN has a nadir in the morning and a peak in the evening.

High

- Prostate enlargement
- UT obstruction (renal calculi, chronic infection, tumor)
- Renal disease
- Renal insufficiency
- Congestive heart failure
- Uterine disorders
- Rhabdomyolysis (tissue destruction causes myoglobin release which is toxic to kidneys)
- Large muscle mass
- High protein diet
- Exercise <36 hrs. before test or on athlete who exercises vigorously
- Creatine supplementation
- Acromegaly (increase in GH will cause larger muscle mass)
- Medications

Low

- Muscle atrophy
- Protein insufficiency or impaired digestion
- Risk for osteoporosis
- Low muscle mass
- Sedentary lifestyle

Functional Considerations

In a healthy person Cr levels will remain constant and within tight parameters. Therefore, this test is useful as a *long-term marker* to trace any developing changes in kidney function before overt disease is apparent. Common non-renal causes of elevated Cr in a primary care setting are exercise induced elevations, dehydration, prostate hypertrophy in males, and uterine disorders in females. Only if BUN and Cr are elevated is a renal cause likely. However, creatinine is a more sensitive and specific marker for kidney disease so if it is elevated chronically, early kidney insufficiency may be likely. Find cause for kidney damage (such as insulin resistance, toxic exposure, drugs etc.) and also support kidney function with curcumin (turmeric), green tea and astragalus.

High Vit. C together with dehydration or diuretics can potentially cause oxalate stones to form, damaging kidney function thus raising Cr levels. However, if the patient is properly hydrated and not on BP lowering medications such as diuretics, then high dose Vit. C, even IV doses up to 50g, has been reported to repair kidney damage and lower creatinine and BUN levels. If calcium oxalate stones are forming (urinalysis), then the patient may need more magnesium and remove high oxalate foods (spinach, rhubarb, chard).

Related Tests

BUN: This test is another measurement of kidney clearance ability and function.
Cystatin C: Unlike creatinine, Cystatin C is produced at a more constant rate than creatinine regardless of metabolic state. This is an even more accurate and sensitive marker for renal dysfunction and patient mortality. If kidney disease is suspected with a patient's history, this test can be very useful.
Urinalysis: UA will show proteinuria if renal destruction is cause of elevated BUN or Cr.
Creatine Clearance: A 24 collection of urine to more accurately measure kidney function. This test is most often run in a hospital or in-patient setting.
Electrolyte Excretion: Excretion of sodium is usually very constant. Measuring the amount of sodium intake and excretion over a given time period. It is useful in differentiating prerenal azotemia and renal failure.
eGFR: Estimated Glomerular Filtration Rate is a mathematical equation based on creatinine, age, sex, ethnicity etc. It is reported to be fairly accurate if a renal disease is present. It is subject to the same limitations of creatinine. It is usually automatically reported by most labs and can be useful in tracking kidney function over time, and response to treatment.

BUN/CREATININE RATIO Optimal: 12 - 18

This is a calculated ratio which assesses overall kidney and liver function. It is limited in usefulness due to the high variability of BUN and Cr formation and excretion. It can aid however, in differentiating renal vs. hepatic dysfunction.

High

- Renal dysfunction
- Liver dysfunction
- Dysbiosis/ intestinal mucosal dysfunction (often correlated with brain degeneration, an increase in inflammatory cytokines is associated with breakdown of endogenous proteins leading to elevated BUN. In addition, intestinal hyperpermeability allows more undigested proteins and ammonia compounds into the blood where the liver converts them to urea)
- High protein diet
- See elevated BUN or low Cr

Low

- Low protein
- See elevated Cr or low BUN
- Liver disease

Functional Considerations

Optimal kidney and liver function should produce a fairly even and constant BUN/Cr ration of around 15. Track changes over time to detect early organ dysfunction.

Related Tests

See BUN and Creatinine.

Uric Acid

Optimal Female: 3.5 - 6 mg/dl
Optimal Male: 4 - 6.5 mg/dl

Uric acid (UA) is a nitrogenous end product of purine (nucleotide) metabolism. Two factors affect UA levels in the blood: 1. Production of UA; 2. Excretion of UA by the kidney and intestine. Synthesis of UA depends on the amount animal protein available for catabolism. Two sources are available – dietary intake and endogenous tissue breakdown. Many diseases can cause tissue breakdown and careful correlation with other laboratory and clinical findings are warranted. Decreased excretion is also multifactorial. UA normally is excreted at a constant rate by the kidney, therefore is a useful kidney function test. Hypothyroidism can also cause decreased clearance as well as affect purine formation. The kidney can only excrete so much UA, and many substances compete for tubular binding excretion sites such as ketones and organic acids. Elevated levels are called hyperuricemia.

UA is a potentially inflammatory molecule. As it builds up in the blood it can cause endothelial damage leading to an increased risk for atherosclerosis, which may be why most people with CHD have elevated UA levels in their blood. It also can precipitate out into all fluid in the body, not just joint tissue. Patients may complain of generalized muscle and joint pain and stiffness. Because of its inflammatory nature, it is no wonder why it is considered and independent risk factor for heart disease.

High

- Gout
- Atherosclerosis
- Arthralgias
- Dehydration
- Rheumatoid arthritis (due to autoimmune destruction of kidney as well as joint inflammation)
- Genetic disorder in purine metabolism – either a decreased utilization or increased production defect.
- Methylation deficit – MTHFR SNP's and methylfolate deficiencies
- Renal insufficiency / renal disease
- Circulatory disorders (hypoxia will trigger xanthine oxidase enzyme responsible for UA formation)
- UT obstruction
- Insulin Resistance/ Diabetes
- Leaky gut syndrome
- Dysbiosis (may cause increase in organic acids which compete for renal excretion)
- Low dose aspirin (<100 mg/day)
- Metastatic cancer
- Chemotherapy
- Rhabdomyolysis
- Stress (catecholamines will cause increased catabolism and UA formation as well as affect kidney tubule reabsorption)

Low

- Molybdenum deficiency
- Anemia - B12 / folate deficiency
- Copper deficiency

- High dose aspirin (>300 mg Daily)
- Heavy metal toxicity
- Impaired detoxification
- Severe liver disease
- Multiple Myeloma
- Autoimmune – Sjogrens, Hashimoto's
- Increased risk for **Multiple Sclerosis** (could be due to metabolic dysfunction, increased oxidant formation and low inosine leading to increased oxidation of neuro-phospholipids)
- Increased Risk for Parkinson's, Alzheimer's and other dementia's.

Functional Considerations

UA is affected by many medications. Of note is aspirin. As more doctors are prescribing low dose aspirin as a supposed heart disease risk reducer, they are unaware this may chronically elevate UA causing many other untoward effects. It is not a coincidence that there has been a steady rise in gouty arthritis and those who take aspirin daily are at increased risk. Aspirin is an example of a biphasic substance in which it will cause a UA raising effect at low dose and a UA lowering effect at high dose. The heart and kidneys are in turn affected by hyperuricemia.

Reducing protein in the diet, no matter the initiating factor of hyperuricemia is always a prudent treatment. Focus on plenty of vegetables to alkalize the system which will allow increased UA excretion. Kidney support formulas as well as magnesium, N-acetyl-cysteine, folic acid and B complex will lower UA while the true etiology is repaired. Infections can be a common hidden source of inflammation and tissue destruction.

Low Uric Acid can also present problems. UA is considered a moderate antioxidant and several studies have shown low levels to be present in many diseases. Careful that patient was not overhydrated for sample collection which could artificially decrease UA (and other analytes).

Related Tests

Nutrient and Toxic Element: Nutrient status and toxic burden both affect UA formation and excretion.

Uric Acid, Urine: Uric acid in the urine is called uricosuria. If UA is present in the urine it suggests an overproduction etiology. If hyperuricemia is present with hypouricosuria, then a renal disease etiology is implicated.

Comprehensive Metabolic Panel: Looking at other liver and renal function tests will help elucidate a correct etiology.

Inflammatory Markers: Tests such as ESR, CRP, Ferritin and Homocysteine can give a picture of overall inflammatory state associated with hyperuricemia.

Urinalysis: Can also give clues as to the functioning of the kidney. If proteinuria is present for example, this leads one to suspect a renal cause of hyperuricemia. Bacterial infections and kidney stones also can directly contribute to UA levels.

Potassium Optimal: 4 - 4.6 mmol/l

Potassium (K) is a cation which exists 90% intracellularly. The role of potassium is both a buffer of acid-base within the cell and outside on extracellular fluid as well. It further acts as an electrolyte within the cell responsible for electrical potential and function. It also serves as an important osmotic pressure stabilizer. K levels are tightly controlled in the blood and minor changes can significantly alter cellular function. The kidneys and adrenals are the organs responsible for potassium balance and use sodium as the major counterbalance. As sodium (Na) is reabsorbed, potassium excretion is hastened. Since the kidney cannot reabsorb potassium and cannot limit excretion, dietary replenishment is crucial to avoid hypokalemia.

Potassium levels have profound effects on heart and neurological tissue. Hypokalemia is associated with cardiac arrhythmias. Hyperkalemia causes irritability, cramping, spasms, diarrhea and heart abnormalities. Many drugs including diuretics affect the levels of potassium. Potassium sparing diuretics such as spironolactone will increase K levels, while other diuretics (furosemide) cause increase excretion.

High

- Adrenal dysfunction
- Dehydration
- Tissue destruction
- Hemolysis due to improper handling of specimen. If no other clinical indications explain hyperkalemia, run an additional CMP to rule out lab error.
- Metabolic acidosis (potassium bicarbonate is major buffer and will be increased in acidosis)
- Excessive dietary intake
- Renal failure
- Addison's disease
- Glutathione deficiency (RBC destruction if severe enough will elevate potassium)
- Infection
- Diabetes/Insulin Resistance (potassium follows glucose into cells and if glucose transport is impaired then potassium builds up in extracellular spaces and serum)
- Chronic stress (will deplete mineralocorticoids leading to excess loss of Na thereby sparring K)

Low

- Adrenal dysfunction
- Drugs: diuretics, antibiotics, insulin (antibiotics damage kidney function while insulin administration causes sudden drop of K due to rapid glucose uptake by cells.)
- Essential hypertension
- Burns
- Dietary insufficiency (a common yet mostly unsuspected phenomenon in the western diet)
- Malabsorption (leaky gut, inflammation, Crohn's etc.)
- Increased refined sodium intake (as sodium levels rise, potassium levels tend to fall)
- Cushing's disease (glucocorticoids have weak aldosterone-like effects)
- Hyperaldosteronism (aldosterone and other mineralocorticoids increases absorption of Na and hastens loss of K. This can be caused by stress and hyper adrenal function)
- Estrogen therapy (K levels have been shown to drop by both renal and extrarenal mechanisms)
- Licorice ingestion (amplifies mineralocorticoids receptor activity by inhibiting 11-B-hydroxysteroid dehydrogenase which will increase excretion of K while retaining Na)

Functional Considerations

Supplementation with potassium in hypokalemic states, while important and necessary, does not address the underlying causative factors as simple dietary insufficiency of K is relatively rare in the United States. Adrenal dysfunction is of primary concern in relation to K and electrolytes. Electrolyte balance cannot be achieved without proper adrenal function, and proper adrenal function cannot happen without electrolyte balance. This is a crucial concept to understand.

Since K is involved in all nerve cell activity, the neuro-endocrine implications of hypokalemia are infinite. Muscles, nerves, hormonal secretion all depends on adequate K levels. GERD, stroke, insulin

resistance, neuro-degenerative disorders, kidney stone formation all are related to K deficiency. When supplementing with K, Mg is usually concomitant and will aid in absorption and utilization.

Related Tests

Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.
Adrenal Function Assay: Adrenal secretion of cortisol, aldosterone and DHEA directly affect electrolyte levels. Adrenal dysfunction, whether in hyper or hypo or dysrhythmic states will alter electrolytes.
Gastrointestinal Panel: GI function is critical for both absorption of K as well as the prevention of loss of K due to dysbiosis, parasites and fluid loss.

Sodium Optimal: 138 - 142 mmol/l

Sodium (Na) along with Chloride (Cl) is the most abundant extracellular cation. Na helps to maintain the osmotic gradient so that serum and extracellular fluid volume is maintained. Na also is major cation for nerve conduction, as well as many ligand based receptors on cell surface membranes and acid–base buffering. The major regulators of Na are the mineralocorticoids, Renin, glomerular filtration rate, dietary intake (to a lesser degree because the body has many homeostatic controls of Na so that excretion usually equals intake over a wide range of salt intake), Anti-diuretic hormone, Natriuretic hormone, as well as direct sympathetic innervation to the kidney tubule and glomerulus.

Hyponatremia is often caused by excessive water intake coupled with electrolyte loss in the sweat and urine. All nerve conduction slows and the patient becomes lethargic and even delirious. Hypernatremia results in dry mouth, thirst, restlessness and irritability.

High

- Adrenal dysfunction
- Cushing's disease
- Dehydration
- Diabetes insipidus
- Hyperaldosteronism
- Severe burns
- Corticosteroid administration

Low

- Adrenal dysfunction
- Addison's disease
- Edema
- Drug diuretics
- Hyperglycemia (glucose will attract water therefore diluting relative salt concentration)
- Congestive heart failure
- Hypothyroid
- SIADH (syndrome of inappropriate secretion of ADH)
- Severe burns

Functional Considerations

It is interesting to note that the salt and other mineral ratios in salt water are roughly equal to human blood. Salt is more concentrated in salt water but it demonstrates how nature uses all minerals to achieve pH balance and electrical neutrality. It has even been shown that animals and humans can survive if blood is replaced by salt water (Quinton), and diluted, sterilized sea water has been used in emergency transfusions in both World Wars.

Since sodium is inter-dependent with all other electrolytes and trace minerals, it has been observed that replacing refined sodium with unrefined sea salt which contains other electrolytes and minerals in natural ratios, can regulate fluid volume and actually lower blood pressure, even if the amount of sodium intake increases. **Serum Na is also one of the most sensitive functional tests of adrenal function**. When adrenals are acutely stressed, more mineralocorticoids will be secreted, raising Na levels. Chronic stress and adrenal depletion will result in less mineralocorticoid production and patients will often complain of excess urination ("water is going right through me"). This can change dramatically throughout the day. If low sodium is seen on a morning fasting blood draw, this very likely indicates Hypoadrenal function.

Careful to consider hydration status at the time of blood draw as being dehydrated will slightly raise Na levels. If patients are properly hydrated (1/2-2/3 oz. per lb. of body weight) it is advised that the water have added electrolytes and minerals, especially if drinking reverse osmosis or distilled water. In any case it is wise to supplement the water directly with minerals and electrolytes.

Related Tests

Urine Sodium: Measures sodium in urine to determine rate of excretion in the kidney.
Aldosterone: The major hormone in Na homeostasis. Run if hypothalamic-pituitary-adrenal pathology is suspected.
BNP (Brain Natriuretic Peptide): This test is used as a marker of and risk factor for congestive heart failure. Run if sodium is low and patient is complaining of shortness of breath.
Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.
Adrenal Function Assay: Adrenal secretion of cortisol, aldosterone and DHEA directly affect electrolyte levels. Adrenal dysfunction, whether in hyper or hypo or dys-rhythmic states will alter electrolytes.
Gastrointestinal Panel: GI function is critical for both absorption of Na as well as the prevention of loss of Na due to dysbiosis, parasites and fluid loss.

Chloride

Optimal: 100-107 mmol/l

Chloride is an anion and is coupled with sodium to maintain electrical neutrality. Cl is under the same control mechanisms that Na is subject to. It has an important role in acid/base balance as it is closely related to the other major anion bicarbonate (HCO_3^-) in an inverse pattern. If the body is experiencing metabolic acidosis, HCO_3^- will be moved into the cell and Cl will be pushed out, raising Cl levels in the serum. Cl urinary excretion is also decreased in this situation. In general, if Cl levels are abnormal, then acid/base balance is dysfunctional.

High

- Metabolic acidosis
- Adrenal dysfunction
- Dehydration
- Renal tubular acidosis
- Eclampsia

- Cushing's disease

Low

- Hypochlorhydria
- Metabolic alkalosis
- Adrenal dysfunction
- Overhydration
- SIADH
- Addison's disease
- Edema
- Drug diuretics
- Hyperglycemia
- Congestive heart failure (diluted electrolytes due to water retention)
- Hypothyroid
- Severe burns

Functional Considerations

Cl, like Na is mainly influenced by adrenal function. Mineralocorticoids exert the same effect on Cl as Na due to the fact that Cl will follow sodium.

Related Tests

See Sodium

CO2 Optimal: 22 – 28 mmol/l

CO2 levels are actually a measurement of the bicarbonate anion, HCO_3^- , in the blood. CO2 in the blood dissolves into HCO_3^- and is the major acid-base buffer in the body. This test is not a highly accurate measurement of either CO2 or pH but it can serve as a rough guide to acid-base abnormalities. pH is maintained very tightly in the blood between 7.35 and 7.45. Any diversion from this will cause enzymes in the body to stop functioning, or function less efficiently. This is what makes pH of intra and extracellular fluids so important. Kidneys produce most of the body's bicarbonate. It is important to remember that HCO_3^- levels do directly determine pH, but rather is a response to the actual pH.

Metabolic acidosis (MA) is when there is an excess of acids (H+) in the ECF. It occurs when the kidney either produces less HCO_3^- than is needed or the body is producing more acid. This can occur with hypoxia or diabetic ketoacidosis. Lactic acid is another major acid that can cause MA and can occur in anaerobic conditions. Renal disease and renal failure can cause diminished excretion of HCO_3^-.

Respiratory acidosis is high CO2 in the blood due to hypoventilation. It is an acidic state, as in MA, with a respiratory cause and not a metabolic one.

Metabolic alkalosis is when the body is producing too much HCO_3^-, increased intake or retention. Vomiting can cause a sudden decrease in chloride and the body will try to compensate by raising HCO_3^- levels.

Respiratory alkalosis is a decrease in CO2 due to hyperventilation and thus less carbonic acid is produced and relatively more HCO_3^- exists in the blood. Treatment is breathing into a paper bag to increase CO2 levels.

High
- Metabolic alkalosis
- Adrenal dysfunction / hyperaldosteronism
- Hypochlorhydria (the kidney will respond to low Cl by retaining bicarbonate)
- Hypoproteinemia (protein is the major buffer in the blood and if low bicarbonate will try to counterbalance)
- Respiratory acidosis (asthma or other obstructive airway disease, not allowing sufficient CO2 exchange)
- COPD
- Vomiting

Low
- Metabolic acidosis
- Citric acid cycle dysfunction (CAC produces CO2 as a by-product)
- Respiratory alkalosis
- Diarrhea
- Ketoacidosis
- Excessive exercise
- Renal failure

Functional Considerations
Rarely will a primary care setting see grossly abnormal values of CO2 (HCO_3^-). However, this test can give a basic guideline as to the acid-base buffering of the patient. When a high CO2 is observed, it is often due to decreased respiration. Breathing techniques are important and can dramatically improve acid-base balance immediately. It is a good idea to have a pulse oximeter in the office to demonstrate to patients that they may have suboptimal PO2% (optimal: >98%). Have the patient breathe deeply for 1 minute, retest and see the dramatic difference that rhythmic, deep breathing has on oxygen, and at the same time, CO2 levels. Another important fact is that when PO2% is below 95% and CO2 levels rise, the autonomic (sympathetic) nervous system is activated. This is why most stress reducing techniques incorporate some type of breathing exercise. Activation of the diaphragm is also largely a parasympathetic activity, while heavy, labored breathing using the ancillary upper thoracic respiratory muscles activate the sympathetic.

A good technique for isolating a cause of low CO2 is called the paper bag technique. Find a weak muscle and have the patient breathe into a paper bag 5-7 times. If this strengthens the muscle, or the patient reports feeling better, then this is a good indicator that the patient may have impaired CAC function. A CAC test may be ordered, or nutrients to support CAC (B-vitamins, biotin, CoQ10, succinic, malic acid, fumaric acid, magnesium etc.) may be given on a trial basis, or individual nutrients may be tested in a biofeedback way (i.e. muscle, pulse testing, Vega machine etc.).

Many factors influence CO2 levels in the blood so take care in correlating abnormal findings with other clinical and laboratory clues.

Related Tests
Anion Gap: Rough measurement of acid/base cations and anions. Helps determine cause of MA.
Aldosterone: The major hormone in Na homeostasis. Run if hypothalamic-pituitary-adrenal pathology is suspected.

Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.
Adrenal Function Assay: Adrenal secretion of cortisol, aldosterone and DHEA directly affect electrolyte levels. Adrenal dysfunction, whether in hyper or hypo or dys-rhythmic states will alter electrolytes.

Anion Gap Optimal: 8-12

A mathematical equation to determine the difference between the major anions and cations in the extracellular fluid. AG = (sodium and potassium) – (Chloride and CO2). This does not take into account other major anions in the blood and ECF such as lactate, phosphate, sulfates and proteins. However, as these anion levels rise, bicarbonate levels decrease and the anion gap will increase.

High (Low CO2 or high sodium)

- Thiamine need / citric acid cycle dysfunction
- Metabolic acidosis
- Respiratory alkalosis
- Diarrhea
- Ketoacidosis
- Excessive exercise
- Toxicity / heavy metal exposure
- Renal failure
- Hyperaldosteronism (aldosterone stimulates Na retention and acid excretion. Acid levels will rise in absence of aldosterone and bicarbonate will combine with the acids and levels fall)

Low (Low sodium or high CO2)

- Antacid ingestion
- Hypoproteinemia (proteins are major anions. If decreased due to diet or nephritis syndrome, kidney will secreted more CO2)
- Multiple myeloma (globulins are cationic proteins and they will be increased in MM)
- Neoplasia (increase in calcium will cause anion gap to decrease)
- Lithium toxicity (lithium is a cation and will decrease other measured cations)

Functional Considerations

Useful but somewhat limited test for acid/base measurements. It is influenced by many factors so care is exercised when interpreting results. Often a high anion gap is caused by recent exposure to organopesticides or heavy metal, or during a Detox. If this is suspected, run a toxic element of hepatic profile to determine cause.

Related Tests

Anion Gap: Rough measurement of acid/base cations and anions. Helps determine cause of MA.
Aldosterone: The major hormone in Na homeostasis. Run if hypothalamic-pituitary-adrenal pathology is suspected.
Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.
Adrenal Function Assay: Adrenal secretion of cortisol, aldosterone and DHEA directly affect electrolyte levels. Adrenal dysfunction, whether in hyper or hypo or dys-rhythmic states will alter electrolytes.

Total Protein Optimal: 6.9 – 7.5 g/dl

Total proteins (TP) in the blood are a measurement of albumin, prealbumin, and globulins. Albumin comprises 60% of TP and its major role is a carrier molecule for hormones, enzymes and nutrients, as well as a buffering agent and osmotic regulator. Globulins are the other major constituent, and their role is largely immunologic. However, globulins also play a small role in osmotic regulation, and transportation molecules (hormone binding globulins). A smaller percentage of TP is made up of other proteins such as ferritin, lipoproteins, enzymes, plasmins and haptoglobins.

Since the liver is the major producer of albumin, this is an indirect measurement of liver function. However, in chronic liver disease, albumin is lowered and globulins remain normal so TP is often normal. In immunodeficiency states, globulins are low but albumin may be normal or elevated (especially in dehydration) so again TP is normal.

Nutrition affects TP levels. Low amount of dietary protein can lower TP. Many dysfunctional states also lead to impaired absorption of proteins and G.I. function may be investigated.

TP is affected by the kidneys. In nephrotic syndromes and autoimmune conditions, proteins will be lost in the kidney, even though globulins may be normal or elevated.

High

- Dehydration
- Inflammation
- Acute infection
- Iron deficient anemia
- Anabolic steroids
- Progesterone
- Multiple myeloma
- Food / environmental allergies

Low

- Hypochlorhydria
- Starvation / malnutrition
- Digestive dysfunction and/or inflammation
- Liver dysfunction
- Pregnancy (third trimester)
- Over-hydration
- Autoimmune disorder (RA, SLE etc.). Secondary to KI damage
- Kidney nephropathy
- Chronic infection
- Oral contraceptives / excess estrogen

Functional Considerations

TP must be correlated with albumin and globulin levels as these are the major components of TP. However, when TP is elevated and the albumin and globulin are normal, consider inflammation. Most acute phase reactants are proteins that are made in the liver in response to inflammation or even infection. These include CRP, alpha1-antitrypsin, ferritin and homocysteine. If the body is in an acute or even chronic state of inflammation, TP will be slightly elevated independent of albumin or globulin.

If TP is low, consider the patient to be malnourished, not simply because they may have low intake of protein, but proteins such as albumin and prealbumin are carriers for vitamins, minerals and other nutrients. Regardless of why they have low protein, pt.'s with low protein need extra nutrients so that tissue levels can be restored, as well as supporting liver and kidney function, which may be the cause of low TP in the first place.

If TP is high consider running a protein electrophoresis to determine exactly which protein(s) is/are elevated. This will help determine the etiology of the disease/dysfunction.

Related Tests

Protein Electrophoresis: Shows levels of Alpha, Beta and Gamma globulins to better differentiate causes of TP elevations.
Immunoglobulin Electrophoresis: Will provide a breakdown of specific gammaglobulins (IgG, IgA, IgM, IgE) and differentiate different types of gammaglobinopathies.
Prealbumin: A more sensitive marker of liver function and synthesis of proteins. It is a valuable nutrient status marker and therapeutic response element. Prealbumin levels are low in zinc deficiency, inflammation and malignancy.
Bence Jones Protein, Urine: BJP is ordered if TP and/or IgM globulins are elevated on Ig electrophoresis. BJP is pathognomonic for multiple myeloma.
Urine Protein Electrophoresis: Similar to serum protein electrophoresis. Order if serum tests are inconclusive, inconsistent or unavailable.
Food Allergy Panel: Increase in exposure to food allergies upregulate Ig production.
Inflammatory Markers: CRP, Hcys, Ferritin, etc. to determine inflammatory causes of elevated TP.
G.I. Panel: Assesses malnutrition and leaky gut as possible etiologies for abnormal TP.

Albumin Optimal: 4 – 4.7 g/dl

Albumin is the main constituent protein in the serum and extracellular fluid (ECF). It is produced in the liver and its main role is maintaining oncotic pressure between ECF and plasma as well as being responsible for about 15% of the total buffering capacity of the blood. It also serves as an important transport carrier protein for hormones, vitamins, minerals, fatty acids, enzymes, amino acids and drugs. It has a half-life of about 4-5 days. It is excreted by the kidneys and synthesis in the liver is triggered by low levels, under a positive feedback system.

High

- Dehydration
- Kidney nephrosis (Excessive albumin is lost due to kidney damage. Synthesis is upregulated in the liver. Albumin levels may be elevated or normal in the beginning stages. As more protein is lost, the liver may not be able to keep up demand and albumin levels will drop as disease progresses.)

Low

- Hypochlorhydria
- Liver dysfunction
- Inflammation – negative acute phase reactant (lowers in response to acute infection/illness
- Oxidative stress

- Vitamin C need
- Congenital hypoproteinemia
- Pregnancy
- Cancer / metastasis
- Kidney nephropathy – consider running a microalbumin urine test- very sensitive for Kidney disease often associated with diabetes. This test can predict kidney disease by up to 10 years.

Functional Considerations

The main reason for albumin to be elevated is dehydration. This is very commonly seen in clinical practice and is an excellent opportunity to discuss proper hydration with the patient. For proper hydration and body function, about 1/2 - 2/3 oz. per pound of body weight is recommended. The reasons for this are too numerous to discuss here. Many practitioners will not work with a patient until they agree to do this because healing is so limited in times of chronic dehydration. If the patient is resistant or non-compliant, try lancing a finger, as if doing a blood stick, and if they are dehydrated the blood will not flow more than a drop or two on its own. If properly hydrated, and not in a state of inflammation / hypercoagulation, the blood will flow easily for about a minute with light pressure above the prick site. For more information on the importance of proper hydration, see "Your Body's Many Cries for Water" by F. Batmanghelidj, M.D.

Functionally low albumin is most often associated with liver dysfunction and chronic inflammation. As inflammatory proteins are made in the liver, albumin levels will decrease. Livers are over-burdened in modern society and need extra support with antioxidants, hepatic protection and bile clearance. Many formulas exist that contain milk thistle, phosphatidyl choline, glutathione (GSH) or GSH precursors such as NAC. Hypochlorhydria and digestive malabsorption is also a major contributor to low albumin. However, this is not specific or sensitive for digestive disorders as the body will break down endogenous proteins in order to synthesize adequate levels of albumin and other proteins. If albumin is low it needs to be correlated with other clinical and laboratory findings to illuminate true causation.

Very low albumin is a very serious disorder as it is related to liver and kidney function. Low albumin is a sign that severe liver damage, body stress, and/or kidney disease has progressed. It is an **ominous sign** often indicating advanced neoplasms and/or metastasis.

Related Tests

Protein Electrophoresis: Shows levels of Alpha, Beta and Gamma globulins to better differentiate causes of TP elevations.
Prealbumin: A more sensitive marker of liver function and synthesis of proteins. It is a valuable nutrient status marker and therapeutic response element. Prealbumin levels are low in zinc deficiency, inflammation and malignancy.
Urine Protein Electrophoresis: Similar to serum protein electrophoresis. Order if serum tests are inconclusive, inconsistent or unavailable.
Food Allergy Panel: Increase in exposure to food allergies upregulate Ig production.
Inflammatory Markers: CRP, Hcys, Ferritin, etc. to determine inflammatory causes of elevated TP.
G.I. Panel: Assesses malnutrition and leaky gut as possible etiologies for abnormal TP.
Urinary Vitamin C: An excellent test for oxidative stress and Vit. C levels in the body.

Globulin Optimal: 2.5 – 3.2 g/dl

Total Globulins (tG) are a group of proteins mainly used as building blocks for antibodies (immunoglobulins). There are subclasses of globulins; alpha, beta and gamma. Gamma globulins are the largest component of tG and are the immunoglobulins. Therefore, the tG is really a measure of

immunoglobulins. However, the other subunits do contribute to the tG and a protein electrophoresis as well as immunoglobulin electrophoresis is run when levels are elevated.

Alphaglobulins consist of alpha1 and alpha2 subunits. Alpha1globulin is mostly Alpha1-antitrypsin which is an acute phase reactant and protects cells from damage due to oxidative, enzymatic destruction. A1 also includes the hormone binding globulins. Alpha2 globulins include haptoglobin which binds hemoglobin in the blood as it is released from the RBC during hemolysis. Ceruloplasmin is another A2 globulin which is responsible for carrying copper and other metals in the blood. Prothrombin, clotting factor enzymes, cholinesterase are also A2 globulins. Beta globulins include other complement proteins, fibrinogen, transferring and lipoproteins which make up HDL and LDL.

High

- Acute infection
- Hypochlorhydria (proteins are digested insufficiently, causing increased dysbiosis, urea formation and immunoglobulin production due to food allergies/leaky gut)
- Liver inflammation (some liver diseases affect albumin production but not globulins)
- Oxidative stress
- Heavy metal toxicity
- Inflammation
- Multiple myeloma
- Leaky gut

Low

- Digestive dysfunction (if pancreatic dysfunction, HCL deficiency and leaky gut are chronic, total protein levels go down and the body cannot produce globulins)
- Immune deficiency (chronic infections, steroid use, immunosenescence)
- Weight loss

Functional Considerations

In a PC setting, very often one will encounter low globulin due to immune deficiency. Careful investigation is required to find causative organisms or underlying disorder contributing to immune deficiency. In women, look for chronic bladder infections. Another common area of hidden infection is in the teeth. Sometimes a Thermogram can detect these or other areas of hidden infections. Parasites are common as well, as are chronic food allergies. Globulins are also a good general overview of nutriture and health. Very often in chronic illness or fatigue you will see patients who just are not healthy. They don't exercise, eat right or take supplements. Often times covering the basics is enough to restore proper immune function. For example, Vit A deficiency will lead to immune compromise. Supplementing with a good multi and added Vit A can stimulate immune function. Furthermore, it is becoming evident that many toxic chemicals and heavy metal create immunodeficiency through many mechanisms. One mechanism is that many of these xenobiotics are stored in bone and marrow and overtime cause a fibrosis to infiltrate and replace vital marrow tissue. As one gets older, this is often described as Immunosenescence. This is a difficult situation to deal with once it develops and why it is so important to emphasize PREVENTION and wellness to patients. What we are doing now will affect us many years down the road. And what we don't know, CAN kill us.

If acute infection or elevated cholesterol, tG will be elevated. Also many active autoimmune diseases will produce elevated tG.

See WBC and differential for more info. on immune function.

Related Tests

Albumin/Globulin Ratio: Can help differentiate causes of abnormal globulin and albumin levels. Many diseases will have normal TP levels but slightly abnormal A or G levels.
WBC w/Differential: Can give additional information on immune function and potential causes for acute/chronic immune issues.
Protein Electrophoresis: Shows levels of Alpha, Beta and Gamma globulins to better differentiate causes of TP elevations.
Prealbumin: A more sensitive marker of liver function and synthesis of proteins. It is a valuable nutrient status marker and therapeutic response element. Prealbumin levels are low in zinc deficiency, inflammation and malignancy.
Urine Protein Electrophoresis: Similar to serum protein electrophoresis. Order if serum tests are inconclusive, inconsistent or unavailable.
Food Allergy Panel: Increase in exposure to food allergies upregulate Ig production.
Inflammatory Markers: CRP, Hcys, Ferritin, etc. to determine inflammatory causes of elevated TP.
G.I. Panel: Assesses malnutrition and leaky gut as possible etiologies for abnormal TP.
Urinary Vitamin C: An excellent test for oxidative stress and Vit C levels in the body.

A/G Ratio Optimal: 1.4 – 1.8

A mathematical ratio to compare levels of albumin and globulin. This is helpful to catch subtle abnormalities when albumin and globulin levels may be slightly abnormal but when viewed together can elucidate a functional disorder.

High (High albumin and/or low globulin)

- Chronic infection
- Dehydration

Low (High globulin and/or low albumin)

- Liver dysfunction (liver disease will cause hepatocyte damage and will the liver will lose the ability to make albumin while retaining the ability to make globulins).
- Immune activation (acute infections will raise globulin levels)
- Inflammation (globulins are acute phase reactants and will rise during times of inflammatory stress and decrease albumin levels at the same time)
- Cancer
- Autoimmune (collagen vascular disorders such as lupus can create nephropathy, increased capillary permeability – loss of albumin into ECF – as well as increased globulins)
- < 1 is considered an ominous sign of severe pathology, no matter the etiology.

Functional Considerations

Elevated A/G ratio almost always is a sign of dehydration. Often is can be elevated in immunocompromised patients if albumin is normal and globulin is low.

Low A/G ratio is multifactorial and must be correlated with other clinical and laboratory findings. A person is not optimally healthy if the A/G ration is abnormal

Related Tests

See albumin and globulin.

Calcium Optimal: 9.2 – 9.8 mg/dl

Calcium (Ca) is the most abundant mineral in humans. 99% of calcium is stored in bones and teeth. The remaining is dissolved in blood, half of which is ionized (free) and the other half is bound to albumin. Calcium is important in several physiological processes and cell functioning, including nerve transmission, muscle contraction, intracellular signaling, cell receptor activity, and wound healing (complement factor activation).

Parathyroid hormone stimulates osteoclasts and mobilizes calcium form bone when levels drop. When elevated, calcitonin will stimulate Ca reabsorption in bones and other connective tissues. Vit. D levels are also critical for proper calcium levels as Vit. D stimulates calbindin production in enterocytes which helps absorption of calcium. Vit. D also limits excretion of Ca by the kidney. Several kidney disorders can also alter Ca status.

Hypocalcemia will often be asymptomatic, or present with tetany, muscle spasms, paresthesias, cardiac arrhythmias, bronchospasms, seizures and if sub-clinical for extended periods, will contribute to osteoporosis and osteopenia.

Hypercalcemia may often present with nausea, vomiting, loss of appetite, constipation, cramping, polyuria, mood swings, confusion and in severe cases coma or death.

An elevation of calcium above 10.5 is considered an ominous sign.

High (Hypercalcemia)

- Hyperparathyroidism
- Hyperthyroid - thyrotoxicosis
- Dehydration
- Diuretics
- Carcinoma (produce PTH, thereby raising calcium)
- Hypervitaminosis D (Vit. D excess stimulates PTH and upregulates calcium absorption)
- Milk-Alkali syndrome
- Sarcoidosis, tuberculosis (inflamed and infected lung tissue can stimulate PTH activity and enhance Vi.t D production)
- Addison's disease (glucocorticoids inhibit Vit. D activity and synthesis. If glucocorticoids are absent, Vit. D is largely unopposed and will raise calcium levels)
- Adrenal hypofunction
- Bone disease (destruction of bone releases calcium into serum)
- FBHH – familial benign hypocalciuric hypercalcemia
- Lithium therapy
- Hypervitaminosis A
- Renal Failure

Low (Hypocalcemia)

- Parathyroid hypofunction
- Dietary deficiency
- Hypochlorhydria
- Vitamin D deficiency
- Ulcerative colitis (intestinal inflammation is associated with mineral **malabsorption**)
- Pancreatitis (an increase in fatty acids can bind to calcium)
- Renal failure
- Diarrhea
- Magnesium deficiency (as magnesium is depleted intracellularly, Ca is driven into the cell in order to maintain electrical neutrality. Blood levels therefore drop).
- Antacid ingestion
- Hyperphosphatemia (laxatives and enemas can cause reactive hyperphosphatemia and low Ca)

Functional Considerations

Although usually tightly controlled, calcium levels can fluctuate for many different reasons. Always run another calcium test several days after the first abnormal reading to confirm any pathology. One will often see elevated calcium on one reading, and a few days later will be back into normal levels. If any calcium abnormality is suspected, take serial calcium readings (at least three or four) to accurately assess calcium status.

Hyperparathyroidism is predominantly found in females and should be suspected in younger women who present with hypercalcemia. As a generalization, if hypercalcemia is present in older patients, this most often represents a cancer. However, many younger women are developing breast and lung cancer, and hypercalcemia should be aggressively pursued. Also, with the popularity of Vit. D supplementation, it is more and more common to see Hypervitaminosis D and elevated calcium levels.

Elevated calcium and low phosphorous is seen in women who are sedentary and at an increased risk for osteoporosis. Chronically elevated calcium will contribute to cataracts. If a patient has cataracts, consider risk/benefit of Vit. D supplementation and caution is always advisable. Osteoporosis is not simply a calcium deficiency. It is, in my opinion, the result of lifestyle – sedentary and being indoors causing a lack of Vit. D. We do not see osteoporosis in third world countries to the extent we see it in industrialized nations. Women in third world countries are not taking calcium supplements, in fact many are considered to be malnourished. However, they are working all day, often out in the sun where they can synthesize enough Vit. D. Therefore, it is wise to counsel patients on lifestyle factors and get them out in the sun, increasing their exercise, especially weight-bearing to stimulate Wolf's law.

Always look at albumin in relation to calcium since 50% in the blood is carried by albumin. If albumin is low and calcium is normal, this patient might actually be hypercalcemic, a state that often exists with cancer.

Calcium and magnesium are regulated together. Often supplementation in one will cause a decrease in the other. High Ca supplementation (>500mg) may inhibit other mineral absorption. Therefore, consider supplementing calcium with a well-rounded complex of minerals including magnesium, iron, zinc iodine, manganese and phosphorous. Additionally, there is evidence that supplementing Ca with magnesium aids in Ca absorption. Furthermore, Ca needs HCL to be absorbed, so in patients with suspected hypochlorhydria, supplementation may be needed. As to the form of calcium, there is considerable variability in the research. One thing is certain, calcium carbonate is the least absorbed of all forms.

Calcium citrate, Ca hydroxyapatite, and calcium orotate have been proven to be better absorbed in some individuals.

Related Tests

PTH: Can detect hyperparathyroidism as cause for elevated Ca. Primary hyperparathyroidism is a major cause of elevated calcium, usually due to adenoma or carcinoma of PTH. There are numerous secondary causes of elevated PTH.
Ionized Calcium: If albumin levels are abnormal, ionized calcium will be more accurate.
Magnesium: Often deficient with Ca deficiency.
Albumin: Since albumin carries 50% of calcium in blood, it is a major factor in Ca levels.
Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.

Phosphorous Optimal: 3.2 – 4 mg/dl

Phosphorous (P) is the sixth most abundant mineral in the body and is the most abundant anion inside the cell. It is crucial to all forms of life as it supplies the energy-rich bonds of ATP. It is required for metabolism of carbohydrates, fats and proteins, is an integral part of cell structures and membranes, is crucial for B-vitamin utilization and is part of the acid-base buffering system. Phosphate is ubiquitous in the body, and is concentrated in the bones and teeth (85%). The rest is distributed throughout all tissues in the body, mostly intracellularly. Phosphorous exists in the body as inorganic and organic phosphates. This test measures inorganic phosphate and is a good representation of total body P.

The largest influence on P is PTH, which increases absorption of P form the intestine and increases its excretion in the kidney. The net effect of PTH is to lower the amount of P in the body. This is an inverse relationship to calcium, so that as Ca levels rise, P levels decrease and vice versa. Even though blood controls are in an inverse relationship, it is important to know that intestinal absorption of Ca and P usually happen together, largely through the action of Vit. D. Phosphorous deficiency in the diet is rare as most foods are abundant in P and the GI is efficient at absorbing P. However, there are malabsorption states that exist with chronic GI inflammation (Crohn's etc.), anorexia, bulimia, antacid ingestion and Vit D deficiency.

Low levels of phosphorous mirrors high levels of Ca in terms of clinical signs and symptoms. However low levels of P are most likely "asymptomatic" clinically. Because P is crucial for cellular energy, any sign of chronic fatigue may be a functional inability to utilize P. Shallow and rapid breathing may also be a sign of P deficiency.

Hyperphosphatemia is characterized by numbness, tingling, muscle spasms and seizures if severe. Chronically elevated P leads to excess Ca deposition and arteriosclerosis and a widening pulse pressure. DJD and arthritis can also be exacerbated by high P levels.

High

- Hypoparathyroidism
- Bone growth and/or repair
- Osteoporosis
- Hypervitaminosis D
- Excess phosphorous consumption
- Renal insufficiency

- Acromegaly
- Bone disease (neoplasm, infection etc.)
- Hypocalcemia (calcium and phos normally oppose each other)

Low

- Hyperparathyroidism
- Hypochlorhydria
- Hyperinsulinism (insulin drives glucose into cells. P is transported by glucose into cells)
- Hypercalcemia
- Chronic fatigue
- Antacid and/or laxative ingestion
- Malabsorption / G.I. inflammation (Crohn's)
- Vitamin D deficiency
- Diet - high in refined carbohydrates
- Alkalosis
- Kidney disease
- Stomach bypass surgery
- Alcoholism

Functional Considerations

If P is outside of the functional range on the low side, it often reflects a lack of bone activity due to a sedentary lifestyle. The prescription is more exercise along with mineral supplementation and Vit. D. GI malabsorption (and gallbladder dysfunction) are also important and should be addressed with a complete GI assessment, especially if other clinical and laboratory findings are consistent with a GI dysfunction. If P is low and calcium is high, check parathyroid hormone (PTH) for possible tumor.
One of the most common reasons for P to be abnormal (high or low but especially low) is hypochlorhydria. This is a common epidemic and other signs such as B12/Folate deficiency, low WBC's, low calcium and low globulins will also be seen.

High P and high Ca often signals bone disease. Consider hemolytic anemia if iron is elevated and RBC, Hgb is on the low side. Take a thorough history to rule out past parathyroid disease. Children will have elevated P due to increased bone activity. Also, excess Vit. D consumption is more common than many practitioners think. Many patients put themselves on high doses of Vit. D for long periods of time, which may in fact be detrimental to health and should be watched for carefully.

Related Tests

PTH: Can detect hyperparathyroidism as cause for lowered P. Primary hyperparathyroidism is a major cause of lowered P, usually due to adenoma or carcinoma of PTH. There are numerous secondary causes of elevated PTH.
Calcium: Ca and P exist in inverse relationship with each other and under many of the same mechanisms of influence.
Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.

Magnesium

Optimal: 2 – 2.5 mg/dl (Serum Mg)
5 – 7 mg/dl (RBC Mg)

Mg is the fourth most abundant mineral in the human body and is the second most abundant cation intracellularly. 50% is incorporated into bones, and the other half exists within the cell. Only about 1% of total body Mg exists in the serum. Mg acts as a cofactor in over 300 biochemical reactions in the body including nerve function, protein and nucleic acid synthesis, blood coagulation, and antioxidant production. It is responsible for recycling ADP to ATP and is an essential element in structural tissues such as bones, nerves and muscles.

Levels of magnesium are affected by nutrition status, kidney function, aldosterone and PTH. Clinical hypomagnesaemia presents as excitability, nervousness, spasms, muscle twitches, headaches, cardiac arrhythmia, hypertension and muscle pain to name a few. Hypermagnesemia is relatively rare except in severe renal dysfunction, or excessive intake of Mg containing antacids. Pts. with elevated Mg may experience slurred speech, blunted reflexes, sleepiness and bradycardia.

In a healthy gut, only about 40% of ingested magnesium is absorbed. This decreases significantly if there is a GI absorption issue, hypochlorhydria or inflammatory bowel. Vegetarians are often deficient in Mg in part because protein aids in Mg absorption.

High

- Renal dysfunction
- Hypothyroid
- Magnesium containing antacids
- Mg containing Laxatives
- Hemolysis of blood sample
- Adrenal dysfunction – low (Aldosterone deficiency will cause excessive sodium loss in urine. In this case, other minerals such as Mg will not be excreted.)

Low

- Malabsorption
- Dietary deficiency
- Dehydration
- Diuretics
- Antibiotics
- Hypercalcemia (excess calcium will cause accelerated excretion of Mg)
- Alcoholism
- Fatigue
- Hypoparathyroidism
- Epilepsy
- Tissue Injury

Functional Considerations

Because Mg is an intracellular cation, and levels of Mg are under strict control with other electrolytes, serum Mg levels are rarely abnormal. However, **when ordering RBC magnesium**, which measures the amount of Mg *within* the RBC (the largest store of Mg in the blood), a more accurate level of functional Mg levels can be seen. It is reported by some that over 80% of adults are RBC magnesium deficient. If

RBC's are deficient, this most likely is a reflection on all other tissues as well. Serum Mg levels are also useful but may not be as sensitive a marker of Mg levels in cells and tissues.

When supplementing with Mg, consider transdermal or Mg salt baths in those with GI imbalances. Mg is poorly absorbed in the GI tract in inflamed, which is why it is often used as a cathartic (laxative). It is often difficult to get enough absorbed without some parenteral route. A combination of different forms of Mg seem to work best for most people (glycinate, malate, citrate etc.)

Related Tests

RBC Mg: A measure of intracellular Mg which is the most accurate functional level of body Mg.
Electrolytes: All major electrolytes are included in a CMP and are routinely run at the same time because of their interrelationship.
GI Panel: Malabsorption is very common and associated with hypomagnesemia.
Adrenal Function: Adrenal function is critical in the homeostasis of all electrolytes and minerals.
Vit. D: In malabsorption and/or Vit. D deficiency, Ca will be low, causing Mg to be low as well.

Alkaline Phosphatase

Optimal Adult: 60–90 U/L
Optimal Child: 80–120 U/L

Alkaline phosphatase (ALP) is a cellular enzyme found in many tissues including hepatic, biliary, bone, intestines, epithelium and placenta. The highest concentrations are found in bone and liver. It is usually elevated due to disorders affecting either bone or liver but can be elevated for many other reasons as well. A full laboratory and clinical workup is necessary to discover the source of ALP elevation. When clinical and or other laboratory findings do not give a clear indication as to the source of ALP elevation, an isoenzyme test may be ordered.

It is often elevated due biliary tract obstruction for two main reasons. First is direct damage to the biliary tract epithelial tissue which will release ALP into the bloodstream. Second, ALP is a byproduct of normal cell turnover and is naturally excreted in the bile. Any obstruction or limitation in bile release will subsequently cause reabsorption of ALP. Often these two situations exist together because most disorders that cause biliary tissue damage will most likely cause obstruction.

Bone disease is the second most common source of elevated ALP and is seen in any situation, pathogenic or not, where skeletal tissue is highly metabolically active, or is being destroyed.

High

- Biliary tract obstruction (either intra or extrahepatic - especially if bilirubin is also elevated)
  Intrahepatic: liver cell acute injury; liver congestion; drug toxicity
  Extrahepatic: gallstones biliary stasis; pancreatic tumor or other space occupying lesion.
- Liver damage (most commonly seen with elevated liver enzymes AST/ALT)
- Bone metabolism (fracture, repair or rapid growth)
- Intestinal inflammation / infection (disorders affecting epithelial cells release intestinal ALP)
- Infection – herpes zoster, hepatitis, Lyme's disease, sepsis
- Bone disease (neoplasia of skeletal origin or metastasis to bone, Paget's, etc.)
- Hyperparathyroidism (PTH stimulates osteocyte activity and bone turnover)
- Pregnancy (ALP is made in placental tissue and will return to normal with a few weeks post-partum)

- Rheumatoid arthritis
- Myocardial infarction
- Thyrotoxicosis (severely elevated thyroid levels cause increased tissue turnover and ALP release)
- Liver metastasis (ALP is considered the most sensitive to liver metastasis)
- Children/adolescents during growth spurts (common for ALP to be about 3-5x's normal)
- Breast cancer

Low

- Zinc deficiency
- Oral contraceptives
- Hypophosphatemia
- Chologogue / choloretic use (herbs or drugs that cause increase contraction of gallbladder or increase secretion of ALP containing bile – these include taurine, dandelion, burdock and more)
- Hypothyroidism (slow metabolism causes decreased normal turnover of ALP containing tissue)
- Milk-Alkali syndrome
- Vitamin C deficiency
- Pernicious anemia
- Magnesium deficiency

Functional Considerations

ALP is a zinc dependent, cell membrane bound enzyme. It requires zinc, magnesium and other minerals to function properly. Therefore, zinc and mg deficiency is associated with low levels of ALP. Ultimately, ALP is most often used as a marker for tissue damage. If ALP is elevated, all enzymes as well as the clinical presentation of the patient must be considered in order to accurately identify where the tissue damage, inflammation is. Moreover, ALP does not give a diagnosis or cause of dysfunction, only an idea of location.

It is also important to note that a large meal the night before a fasting blood test (especially if it is high in fat) can elevate ALP, even many hours after ingestion of the meal.

Related Tests

AST: Liver enzyme test which can help differentiate source of ALP elevation.
ALT: Liver enzyme test which can help differentiate source of ALP elevation. ALT is slightly more liver specific than AST.
GGT: Hepatobiliary enzyme that when elevated along with ALP is suggestive of biliary disease.
5'-Nucleotidase: Hepatobiliary enzyme that when elevated along with ALP is suggestive of biliary disease.
Acid Phosphatase: Bone enzyme marker that is suggestive of bone disease. In males, this enzyme is also used to detect prostate cancer. Therefore, if this and ALP is elevated in a male, suspect prostate cancer that has metastasized to bone.
Bilirubin: Elevated bilirubin suggests obstructive biliary disease.
Creatine Kinase: A cellular enzyme which exists mainly in heart and skeletal muscle.
LDH: Nonspecific enzyme for tissue damage involving the heart, RBC's, muscle, brain, liver and lungs. Available in an isoenzyme fraction which can further differentiate source of elevation.
Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.

Zinc Taste Test: A low titer zinc solution (0.1%) that when held in a patients mouth and the patient cannot detect any taste whatsoever, can be indicative of low zinc levels. A low ALP can corroborate this.
ALP Isoenzymes: If clinical and other laboratory tests are inconclusive, this subfraction of ALP will further delineate source of ALP (liver, bone, intestines, etc.)

Lactate Dehydrogenase (LD or LDH) Optimal: 125 – 175 U/L

LDH is an intracellular enzyme that exists in virtually every cell. It is responsible for converting pyruvate, which is a by-product of the citric acid cycle, into lactate. Therefore, anytime glycolysis is increased, such as during exercise, LDH activity is increased. All cells produce lactate through LDH, which is then spilled into the blood stream and converted back to glucose primarily in the liver (aka: the Cori cycle). If there is severe liver dysfunction, lactate (and LDH) will accumulate in the blood. When tissues are hypoxic, they will produce more lactate and therefore more LDH is released from the cell. It takes only a relatively small amount of tissue damage to raise LDH levels which makes it a very **sensitive** marker. However, since virtually all tissues have some level of LDH (some higher than others) it is not a very **specific** marker at all. Further investigation is needed to isolate source.

LDH is highly concentrated in the heart, liver, skeletal muscles, RBC's, kidney, lung and lymphocytes, as well as cancer cells (which make it a good marker for cancer treatment effectiveness). Total LDH is non-specific for any disease. However, it can be subfractionated into its isoenzymes which can give a better indication of which tissues are being affected. It is also compared to other laboratory and clinical findings to be a useful marker for the extent and location of tissue damage.

Isoenzymes will be discussed here. LDH1 (if greater than LDH2) is indicative of acute MI, hemolysis or renal damage. LDH2 elevation is usually nonspecific as LDH2 is naturally the highest relative sub-fraction. LDH3 is indicative of lung pathology. LDH5 indicates liver and/or skeletal muscle damage. (see p 333, Clinical Laboratory Medicine by Ravel, for excellent graph).

High

(If LDH is high, run an isoenzyme test)

- Heart disease (CHF and severe atherosclerosis will cause chronic mild elevations)
- Myocardial infarction (will be elevated starting 24 -36 hours after MI and peaks at 2-3 days)
- Liver / biliary dysfunction
- Hemolysis (due to improper handling of specimen, glutathione deficiency, oxidative stress, hemolytic anemia)
- Pernicious anemia (may contribute to hemolysis. LDH fraction 1 will be elevated. MCV, MCHC, RBC and Hg are more specific for megaloblastic anemia)
- Systemic inflammation (often seen in SLE or RA)
- Strenuous exercise
- Viral infection
- Testicular cancer (tumor cells produce much lactate due to their high metabolism)
- Pulmonary disease (emboli, infection, COPD. Systemic hypoxia will cause increased cell death, increased glycolysis, as well as liver stagnation and decreased action of the Cori cycle)
- Intestinal disease (epithelial cells contain large amounts of LDH)
- Lymphoproliferative disorder (lymphocytes contain large amounts of LDH)

Low

- Reactive hypoglycemia (lowered cellular metabolism results is less LDH being released)
- Sedentary lifestyle
- Excessive fasting or ketogenic diet (ATP will be produced by fatty acid oxidation, not glycolysis, and LDH will decrease due to less lactate production)
- Heavy metal toxicity (HM's can cause reactive hypoglycemia through multiple mechanisms)
- High doses of Vit. C (presumably by hastening more oxidative glycolysis and less anaerobic glycolysis. Also, with higher Vit. C, cell membranes are better protected against oxidative damage and less cell death occurs which means less LDH spilling into blood)
- Genetic influences
- Zinc deficiency (zinc is required to form LDH and is also needed for insulin receptor function)

Functional Considerations

The most common reason for elevated LDH on routine laboratory evaluations is strenuous exercise. However, the second most common cause is sub-acute MI. Check cardio CRP to see extent of inflammation. This is often the case when patients are experiencing micro- capillary emboli in heart tissue. This is not immediately life threatening but nonetheless warrants immediate attention.

Be aware that many diseases exist as co-morbidities (acting at the same time). Therefore, many isoenzymes could be elevated making diagnosis complicated. Use all available clinical and laboratory findings to uncover true underlying cause of LDH elevation and not simply focus on the effects. For example, COPD can cause elevations in total LDH with or without affecting the heart. Isoenzymes may show heart fraction elevated but it is the lung congestion that is the cause, and the patient is not experiencing a heart attack. A thorough history and physical is always paramount to correctly interpreting laboratory results.

Viral pneumonia will elevate LDH whereas bacterial will not unless it is an overwhelming infection. *Pnemocytis carinii* will elevate LDH, which is often seen in AIDS patients.

Low LDH is often a sign of lowered cellular metabolism since this is an intracellular enzyme. I have seen this in many patients with CFS or Fibromyalgia. Always suspect reactive hypoglycemia or high protein, ketogenic diet in low LDH as well. Look at adrenal function as anyone with reactive hypoglycemia will have some level adrenal dysfunction.

Related Tests

Troponins: Cardiac Troponins are very specific and sensitive markers for myocardial injury. Can differentiate easily between skeletal injury and heart disease.
LDH Isoenzymes: LDH has five sub-fractions or isoenzymes which can help differentiate where the dysfunction leading to elevated LDH is coming from.
AST: Liver enzyme test which can help differentiate source of LDH elevation.
ALT: Liver enzyme test which can help differentiate source of LDH elevation. ALT is slightly more liver specific than AST.
ALP: Alk. Phos. may be elevated in liver disease or bone disease. May be low with low LDH if zinc deficiency.
GGT: Hepatobiliary enzyme that when elevated along with LDH is suggestive of biliary disease.
5'-Nucleotidase: Hepatobiliary enzyme that when elevated along With LDH is suggestive of biliary disease.

Acid Phosphatase: Bone enzyme marker that is suggestive of bone disease. In males, this enzyme is also used to detect prostate cancer. Therefore, if this and ALP is elevated in a male, suspect prostate cancer that has metastasized to bone.
Bilirubin: Elevated bilirubin suggests obstructive biliary disease.
Creatine Kinase: A cellular enzyme which exists mainly in heart and skeletal muscle. The CK-MB fraction is more sensitive to MI than LDH as it will rise immediately after an MI.
Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.
CBC with differential: Can demonstrate anemia, hemolysis, or infectious source of LDH elevation.
Saliva Hormone: Adrenal dysfunction is associated with reactive hypoglycemia and low LDH

LDH Isoenzymes

LDH isoenzymes can be useful when total LDH is elevated. Many tissues have different concentrations of the isoenzymes so seeing elevations in one or more can help isolate LDH source. Isoenzymes can also be useful if total LDH is normal, but a clinical dysfunction is suspected. For example, a person with reactive hypoglycemia may have normally low LDH, then experience a mild heart attack, but total LDH is still within population normal. Running an isoenzyme will uncover that the fractions are abnormal and do show a typical M.I. pattern.

In another example of the usefulness of LDH isoenzymes, many diseases can coexist. A person may have long-standing liver disease with elevated LDH. A M.I. may be missed unless an isoenzyme test reveals a change in isoenzyme pattern.

LDH1: RBC's, heart and kidney
LDH2: Pulmonary, heart, RBC's, lymph
LDH3: Pulmonary, to a lesser degree: kidney, spleen, and pancreas
LDH4: Kidney, pancreas, placenta
LDH5: Liver, to a lesser degree: skeletal muscle

Common Abnormal Patterns

A. Normally LDH2 is greater than LDH1. In acute MI, the ratio is flipped and LDH1 is elevated and becomes greater than LDH2. Other fractions are normal. CK isoenzymes are more helpful in the first 24 hours after acute M.I.
B. LDH 5 is elevated in liver disease (hepatitis, cirrhosis, hepatocellular carcinoma, etc.). Also elevated in intense exercise or muscle injury.
C. LDH2 and 3 are elevated in pulmonary disease (emboli, CHF, COPD, pneumonia, viral infection). This pattern can also be seen in lymphoproliferative disorders, myeloma, pancreatic cancer.
D. LDH2-5 elevated seen in pulmonary congestion with liver involvement (often seen in advanced CHF). Also seen in Epstein-Barr (mono) and cytomegalovirus infection.
E. All LDH enzymes can be elevated with multi-system disorders such as systemic hypoxia, malignancy, trauma, infection, active cirrhosis and others.
F. Many illnesses listed above do not have typical isoenzyme pattern for various reasons, including the fact that many disorders exist to varying degrees at the same time in the same individual.

SGOT/AST Optimal: 12 – 27 U/L

Serum glutamic oxaloacetic transaminase (SGOT) is now referred to as Aspartate aminotransferase (AST). A non-specific enzyme found in metabolically active tissues such as heart, liver, skeletal muscle and RBC's. It is predominately referred to and used as a liver biomarker since large quantities of AST are

found in the liver. Since AST in an intracellular enzyme, levels rise in cell death associated with acute injury to the tissue. Once levels rise outside of healthy ranges, the degree of elevation corresponds to the degree of injury. However, AST is cleared fairly rapidly from the serum (within a few days), so elevations associated with chronic disease are often transitory unless a very large portion of the organ is affected, or multiple organs are affected at the same time, such as COPD affecting heart, lung and congested liver.
AST is responsible for transferring an amino group of aspartate to make glutamate. Therefore, it is an essential enzyme in liver detox pathways.
AST is normally slightly higher than ALT because it is found in greater concentrations in other tissues than the liver. If AST is elevated over ALT greater than 1.5, the tissue damage may be coming from extrahepatic sources (heart, kidney, gallbladder, pancreas etc.).

High

- Liver dysfunction
- Extrahepatic liver / biliary obstruction
- CHF (congestive heart failure - associated with hypoxia and cell death to heart, liver and other tissues)
- Acute MI
- CAD (coronary artery disease)
- Skeletal muscle injury or disease
- Infectious mononucleosis, viral hepatitis, CMV (AST/ALT is often <1)
- Thyroid dysfunction (hypothyroidism can cause elevations of AST due to hypo-function and increased cell death of hepatocytes)
- Non-viral hepatitis (the AST/ALT ratio > 1)
- Liver cancer (metastatic tumor to the liver shows an AST/ALT ratio >1)
- Alcoholic cirrhosis (the AST/ALT ratio >1)
- Drug-induced liver toxicity

Low

- B6 deficiency (AST is a B-vitamin dependent enzyme.)
- Severe alcoholism (because of severe nutrient deficiency, the liver cannot function and enzyme production falls)
- Thyroid dysfunction
- Thiamine deficiency (Beriberi and subclinical B1 deficiency can affect AST levels.)
- Pregnancy
- Renal disease (elevated BUN and creatinine are often seen with kidney disease)
- Diabetes

Functional Considerations

It is often observed that AST will rise and quickly fall within a matter of days or weeks upon retesting. This is most likely associated with acute infection, skeletal muscle injury, acute renal or pancreatic dysfunction, or alcohol ingestion within 24-36 hours before the test. Always re-run abnormal tests to

confirm it is not a transitory elevation. Confirm patient did not ingest alcohol or engage in intense exercise for at least 48 hours, especially for retesting.
If AST is low due to a B-6 deficiency, it can be assumed that some level of detoxification and/or methylation is impaired. It would be wise to not only supplement with B-6 and other B vitamins but with liver detox supporting herbs and supplements as well. If patient is suffering from chronic health issues, checking for heavy metals and toxic compounds in the blood may be more accurate than urine. This is also true of AST if it is elevated beyond optimal limits but not elevated more than 2x the laboratory limit. Overwhelmed hepatocytes due to toxicity will undergo accelerated cell death and release AST into the blood.

Related Tests

ALT: Liver enzyme test which can help differentiate source of AST elevation. ALT is slightly more liver specific than AST. If both are elevated, this tends to suggest liver disease.
ALP: Alk. Phos. may be elevated in liver disease or bone disease. May be low with low LDH if zinc deficiency.
Bilirubin: Elevated bilirubin suggests obstructive biliary disease.
Thyroid Panel: Liver enzymes are often elevated in hypothyroidism.
Troponins: Cardiac Troponins are very specific and sensitive markers for myocardial injury. Can differentiate easily between skeletal injury and heart disease.
Homocysteine: This can check for altered methylation by assessing B12, B6 and mineral deficiency.
LDH: Nonspecific enzyme for tissue damage involving the heart, RBC's, muscle, brain, liver and lungs. Available in an isoenzyme fraction which can further differentiate source of elevation.
LDH Isoenzymes: LDH has five sub-fractions or isoenzymes which can help differentiate where the dysfunction leading to elevated LDH is coming from.
GGT: Hepatobiliary enzyme that when elevated along with AST is suggestive of obstructive hepatobiliary disease.
Serum Toxic Elements: If liver enzymes are abnormal (high or low) it may be assumed that the patient has some level of detoxification impairment.
5'-Nucleotidase: Hepatobiliary enzyme that when elevated along with AST and ALT is suggestive of biliary disease.
Creatine Kinase: A cellular enzyme which exists mainly in heart and skeletal muscle.
Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.
CBC with differential: Can demonstrate anemia, hemolysis, or infectious source of AST elevation.
Viral Panel: If infection is suspected, check for EBV, CMV, hepatitis panel and Lyme's.

SGPT/ALT Optimal: 12 – 27 U/L

Serum glutamic-pyruvic transaminase (SGPT) is now referred to as alanine aminotransferase (ALT). ALT is much more of an isolated liver enzyme than AST. It exists predominantly in the liver and to a lesser degree other tissues such as heart, skeletal muscle and kidney. When ALT rises along with other liver signs and symptoms such as jaundice, it can be concluded that the source of jaundice is indeed the liver and not hemolysis from RBC's. There does seem to be some genetic/racial variation such that African-American and Hispanic males often have 50% higher or more levels than Caucasians.

High

- Liver disease / dysfunction
- NAFLD (non-alcoholic fatty liver disease associated with metabolic syndrome)
- Extrahepatic biliary obstruction

- Rhabdomyolysis
- Cirrhosis
- Mononucleosis
- MI (if severe damage has occurred)
- Pancreatitis
- Thyroid dysfunction (hypothyroid or acute hyperthyroid storm may cause elevated ALT)
- Viral hepatitis (ALT > AST)

Low

- B6 deficiency
- NAFLD (non-alcoholic fatty liver disease associated with metabolic syndrome)
- Liver congestion
- Autoimmune (SLE, RA and others have been associated with this finding)
- Chronic hyperthyroidism
- Alcoholism
- Pregnancy

Functional Considerations

Patients taking statins, or other drugs (a very long list including antibiotics) affecting the liver will often have marked elevations of ALT and possibly AST. As in AST, if ALT is abnormally high or low assume impaired liver detoxification ability and altered methylation.

Related Tests

AST: Liver enzyme test which can help differentiate source of ALT elevation.
ALP: Alk. Phos. may be elevated in liver disease or bone disease. May be low with low LDH if zinc deficiency.
Bilirubin: Elevated bilirubin suggests obstructive biliary disease.
Homocysteine: This can check for altered methylation by assessing B12, B6 and mineral deficiency.
Troponins: Cardiac Troponins are very specific and sensitive markers for myocardial injury. Can differentiate easily between skeletal injury and heart disease. Occasionally severe heart damage will elevate ALT, even though ALT is predominantly a liver enzyme.
Thyroid Panel: Liver enzymes are often elevated in hypothyroidism.
LDH: Nonspecific enzyme for tissue damage involving the heart, RBC's, muscle, brain, liver and lungs. Available in an isoenzyme fraction which can further differentiate source of elevation.
LDH Isoenzymes: LDH has five sub-fractions or isoenzymes which can help differentiate where the dysfunction leading to elevated LDH is coming from.
GGT: Hepatobiliary enzyme that when elevated along with AST is suggestive of obstructive hepatobiliary disease.
Serum Toxic Elements: If liver enzymes are abnormal (high or low) it may be assumed that the patient has some level of detoxification impairment.
5'-Nucleotidase: Hepatobiliary enzyme that when elevated along with AST and ALT is suggestive of biliary disease.
Creatine Kinase: A cellular enzyme which exists mainly in heart and skeletal muscle.
Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.
CBC with Differential: Can demonstrate anemia, hemolysis, or infectious source of AST elevation.
Viral Panel: If infection is suspected, check for EBV, CMV, hepatitis panel and Lyme's.

GGT/GGTP

Optimal Female: 10-30 U/L
Optimal Male: 10-40 U/L

Gamma glutamyl transferase (GGT) is a sensitive marker for hepatic and biliary injury. It has a long half-life (up to 28 days) so it can be useful in determining acute or chronic progression of illness. GGT exists mainly in liver cells and the canalicular cells lining the epithelium of the biliary tract. It is often elevated with chronic alcohol intake and levels of GGT roughly correlate with amount of ethanol ingestion. It also exists in other tissues in smaller amounts such as intestines, heart, brain, pancreas and spleen. Its function is to transport amino acids across cell membranes, regulating the structural integrity of cell membranes and the metabolism of glutathione.

High

- Biliary canalicular injury (if ALP is elevated along with GGT, then biliary tree injury is likely)
- Biliary obstruction / stagnation
- Primary biliary cirrhosis (see antimitochondrial antibodies under related tests)
- Liver disease (cirrhosis, hepatitis, other infections – see below)
- Metastatic liver tumor (GGT is about 90% sensitive to liver cancer. Run an Alphafeto-protein test if liver cancer is suspected.)
- Alcoholism
- Liver infections (GGT is elevated in 90% of patients with acute EBV infection)
- Acute / chronic pancreatitis
- Pancreatic insufficiency
- Impaired or overburdened toxicity (heavy metals, free radicals, ionizing radiation, chemicals, pesticides, etc.)
- Prostate irritation (GGT exists in fair quantities in prostate)
- MI (will be elevated if liver is affected or severe heart damage. May be elevated for weeks post MI)

Low

- B6 deficiency
- Magnesium deficiency
- Hypothyroidism
- Increased risk for kidney damage (renal epithelial cells require GGT more than other tissues)
- Glutathione deficiency
- Impaired or overburdened toxicity (heavy metals, free radicals, ionizing radiation, chemicals, pesticides, etc.)
- Pregnancy

Functional Considerations

A common cause of elevated liver enzymes (AST and ALT) especially in women, is hypothyroidism. For various reasons, GGTP is actually low in hypothyroidism and this pattern can be used to support hypothyroidism even if thyroid hormone tests are fairly normal. Of course, other labs for hypothyroidism may be abnormal as well such as elevated triglycerides, cholesterol and inflammatory markers.

GGT is also sensitive for oxidation potential. If GGT is high, the patient may be experiencing an acute free radical pathology. Use high amounts of antioxidants and pro-glutathione nutrients to protect liver cells while the source of toxicity is being investigated. If GGT is low, the patient may have impaired

detoxification/glutathione metabolism. This may be due to altered methylation (check homocysteine) or mineral deficiency (check RBC magnesium).

Dietary consideration: people with chronically or congenitally low GGT may not be able to process proteins as efficiently and cannot transport amino acids into cells.

Related Tests

ALT: Liver enzyme test which can help differentiate source of GGT elevation.
AST: Liver enzyme test which can help differentiate source of GGT elevation.
ALP: Alk. Phos. may be elevated in liver disease or bone disease. May be low with low LDH if zinc deficiency. GGT is not elevated in bone disease so if ALP is solely elevated, liver disease may be ruled out.
Bilirubin: Elevated bilirubin suggests obstructive biliary disease.
Homocysteine: This can check for altered methylation by assessing B12, B6 and mineral deficiency.
Antimitochondrial Antibodies: Seen more commonly in women, primary biliary cirrhosis is often part of an emerging understanding of multi-organ autoimmune. This is often seen in SLE and MS patients.
Troponins: Cardiac troponins are very specific and sensitive markers for myocardial injury. Can differentiate easily between skeletal injury and heart disease. Occasionally severe heart damage will elevate GGT, even though GGT is predominantly a liver enzyme.
Thyroid Panel: GGT is often elevated in hyperthyroidism, and decreased in hypothyroidism.
LDH: Nonspecific enzyme for tissue damage involving the heart, RBC's, muscle, brain, liver and lungs. Available in an isoenzyme fraction which can further differentiate source of elevation.
LDH Isoenzymes: LDH has five sub-fractions or isoenzymes which can help differentiate where the dysfunction leading to elevated LDH is coming from.
Serum Toxic Elements: If liver enzymes are abnormal (high or low) it may be assumed that the patient has some level of detoxification impairment.
5'-Nucleotidase: Hepatobiliary enzyme that when elevated along with ALP and GGT is suggestive of biliary disease.
Creatine Kinase: A cellular enzyme which exists mainly in heart and skeletal muscle.
Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.
CBC with Differential: Can demonstrate anemia, hemolysis, or infectious source of GGT elevation.
Viral Panel: If infection is suspected, check for EBV, CMV, hepatitis panel and Lyme's.

Total Bilirubin Optimal: .2 – .8 mg/dl

Total bilirubin is a measure of conjugated and unconjugated bilirubin. Bilirubin is made from heme mostly from the breakdown of red blood cells as well as heme containing proteins such as the cytochrome enzymes. Bilirubin is produced by cells of the reticulo-endothelial (RE) system which includes the Kuppfer cells of the liver, phagocytes, spleen and bone marrow.

Abnormalities in bilirubin can be thought of as a result of either acquired or inherited disorders. The acquired disorders that result in elevated bilirubin can be thought of as either an over production of bilirubin or undersecretion. If undersecretion is the culprit, it is the result of either intrahepatic or extrahepatic biliary tract obstruction. Looking at whether conjugated or unconjugated bilirubin is elevated gives clues as to where the obstruction is coming from.

The RE cells breakdown the heme proteins into an unconjugated, hydrophobic bilirubin. This is transported by albumin to the liver where the hepatocytes conjugate the bilirubin to make it more

hydrophilic. It is then secreted into the bile ducts and excreted through the bile. Therefore, if unconjugated is elevated, it is most likely either an overproduction (as in hemolysis) or intrahepatic blockage such as cirrhosis, which is not allowing the liver cells to conjugate it. If the conjugated bilirubin is elevated, then it may be assumed that an extrahepatic blockage is occurring, such as gallstones or pancreatic cancer blocking the bile duct. Most of the congenital defects result in a rise in unconjugated bilirubin due to some form of enzyme deficiency which does not allow formation of conjugates.

Total High >.8

- Biliary stasis or obstruction
- Oxidative stress
- Thymus dysfunction
- Liver dysfunction (liver cell damage due to cirrhosis, infections and metastases from pancreatic, breast, lung and GI cancer)
- Hypersplenism
- RBC hemolysis
- Hypothyroidism (can cause decreased bile excretion with increased serum bilirubin. Often the unconjugated /indirect bilirubin will be slightly higher in proportion to conjugated/direct bilirubin)
- Gilbert's syndrome
- Severe hematoma or tissue injury
- Crigler-Najjar (congenital deficiency of conjugating enzymes)
- Fasting, prolonged (>12 hours)
- Many drugs

Indirect / Unconjugated Bilirubin High .2 - .8 mg/dl

- RBC hemolysis
- Gilbert's syndrome
- Crigler-Najjar (congenital deficiency of conjugating enzymes)
- Sepsis
- Hepatitis
- Liver disease
- Pernicious anemia
- Glutathione deficiency (increased RBC destruction)

Direct / Conjugated Bilirubin High 0 - .2 mg/dl

- Biliary tract obstruction
- Biliary calculi / obstruction (usually extra hepatic)
- Pancreatic tumor
- Sympatheticotonia

Total Low < .2

- Spleen insufficiency
- High dose aspirin (>300mg)
- Possible risk factor for CAD in males
- Oral contraception/ estrogen replacement (estrogen increases bile clearance)

Functional Considerations

The most common cause for elevated bilirubin is biliary obstruction (gallstone) or insufficiency often seen in hypothyroidism. In fact, hypothyroidism may be one of the main etiological factors in the formation of gallstones. It has been shown that biliary cells need thyroid stimulation to work properly due to the high metabolic nature of the biliary system. If total cholesterol, liver enzymes and total bilirubin are elevated, suspect a thyroid issue. Of course, deal with the obstruction first and rule out more serious hepatic pathology, especially if unconjugated is highly elevated.

Also of note is the fact that in males, low bilirubin has been associated with increased risk for heart disease. This may be due to the fact that bilirubin is thought to act as an antioxidant as well and anti-inflammatory, thereby protecting the endothelial lining from atherosclerosis and clot formation. Low bilirubin may be due to chronic anemia, liver dysfunction and/or altered metabolism. Increase antioxidants, liver support and check homocysteine metabolism for low bilirubin.

Related Tests

Urine Bilirubin and Urobilinogen: If there is elevated serum bilirubin and no urobilinogen in urine, it may be deduced that the patient has a complete biliary obstruction since urobilinogen is made in the intestines from excreted bilirubin in the bile. If no bilirubin is excreted, then urobilinogen will not be formed, reabsorbed and excreted by the kidney.
ALT: Liver enzyme test which can help differentiate source of GGT elevation.
AST: Liver enzyme test which can help differentiate source of GGT elevation.
ALP: Alk. Phos. may be elevated in liver disease or bone disease. May be low with low LDH if zinc deficiency. GGT is not elevated in bone disease so if ALP is solely elevated, liver disease may be ruled out.
Homocysteine: This can check for altered methylation by assessing B12, B6 and mineral deficiency.
Antimitochondrial Antibodies: Seen more commonly in women, primary biliary cirrhosis is often part of an emerging understanding of multi-organ autoimmune. This is often seen in SLE and MS patients.
Thyroid Panel: GGT is often elevated in hyperthyroidism, and decreased in hypothyroidism.
LDH: Nonspecific enzyme for tissue damage involving the heart, RBC's, muscle, brain, liver and lungs. Available in an isoenzyme fraction which can further differentiate source of elevation.
LDH Isoenzymes: LDH has five sub-fractions or isoenzymes which can help differentiate where the dysfunction leading to elevated LDH is coming from.
Serum Toxic Elements: If liver enzymes are abnormal (high or low) it may be assumed that the patient has some level of detoxification impairment.
5'-Nucleotidase: Hepatobiliary enzyme that when elevated along with ALP and GGT is suggestive of biliary disease.
Creatine Kinase: A cellular enzyme which exists mainly in heart and skeletal muscle.
Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.
CBC with Differential: Can demonstrate anemia, hemolysis, or infectious source of GGT elevation.
Viral Panel: If infection is suspected, check for EBV, CMV, hepatitis panel and Lyme's.

Creatine Kinase (CK, CPK)

Optimal Adult Female: 40 – 90 U/L
Optimal Adult Male: 60 – 135
Optimal Infant to Toddler: 65 – 350

Creatine Kinase is an intracellular enzyme found predominantly in skeletal muscle, heart and in nervous tissue in the brain. This test is used to detect injury to these tissues because cells must be lysed in order to release intracellular components. There is always a small amount of tissue turnover constantly happening so levels will never be close to zero. However, they will rise in times of injury, autoimmune destruction, heart attack, stroke etc. When used as an indicator of heart disease, CK has a peak value approximately 2 hrs. after an MI event and returns to normal 2-4 days post MI.

Be sure to have the patient abstain from exercise/strenuous physical activity for at least 36-48 hrs. before blood draw as this will naturally increase CK levels since most of the circulating CK found in the blood is form skeletal muscle and is not an abnormal finding. When seeing an elevated reading, rule this out first. Also, keep in mind that the normal amount of CK is very unique for each individual and is dependent on the muscle mass of the individual. As such, a very large man will naturally have CK levels in the upper limits of normal, whereas a petite female may have levels in the lower limits. This is why it is important to track this value over time and if an unexplained rise occurs outside of that individual's "normal", then it warrants investigation.

When CK is chronically elevated or is slowly rising over time, this may indicate a chronic degenerative disorder such as cardiovascular disease of autoimmune process.

This test is traditionally used to detect damage after a heart attack or stroke. If elevated outside of laboratory or critical ranges, then an "isoenzyme" may be performed to further elucidate which tissue has been affected. Isoenzymes are as follows

CK-BB (CK1): more specific for brain and lung (should not be detected in non-disease states)

CK-MB (CK2): heart specific – some may exist due to natural cell turnover (< 5% total CK). Isoenzymes of CKMM are MM1 and MM3. If MM3 is greater than MM1 it is indicative of acute myocardial injury.

CK-MM (CK3): skeletal muscle - major circulating isoenzyme in normal person (95-100% total CK). There are further isoenzymes under CKMB called MB1 and MB2. When MB2 is greater than MB1, this may indicate acute heart disease.

High

- Muscle injury (exercise, trauma etc.)
- Myocardial infarctions or cardiac ischemia
- Ventricular arrhythmias
- Brain injury (stoke, hemorrhage, seizure, Reye syndrome)
- Pulmonary embolism
- Rhabdomyolysis (may be seen with statin drug use)
- Drugs/alcohol (antibiotics, anticoagulants, dexamethasone, furosemide, lithium, propranolol, morphine, aspirin, succinylchloride)
- Autoimmune disease (SLE, Rheumatoid initial stages, and neuro-autoimmunity may elevate CK if active tissue damage)
- Muscular dystrophy
- Hypothyroidism (metabolic rate of cells too low to sustain optimal activity, therefore cells die more rapidly than normal, spilling the intracellular components)
- Cancer (especially of breast, brain, prostate and lung)
- Liver disease
- Infection

Low

- Muscle atrophy
- Small stature
- Chronic fatigue syndrome (may be either elevated or decreased depending on stage of illness)
- Chronic subclinical hypothyroidism

Functional Considerations

Obviously if CK is elevated and you suspect MI, refer to hospital immediately. Quiz the patient first to rule out natural causes such as exercise or bodily injury. You may want to run a troponin and isoenzyme if you do not suspect MI or stroke. Anyone with an elevated CPK outside of critical lab ranges should have an isoenzyme test.

From a functional perspective, CK may actually be useful for detecting chronic inflammation in an otherwise non-diseased individual. If CK is chronically elevated outside of *optimal* values but within lab ranges, look for where the injury is coming from. Often this may be due to medications such as statin drugs and/or alcohol. It may also be due to total body hypoperfusion where the individual is systemically inflamed. If this is the case, then increasing antioxidants, CoQ10 and EFA's may be helpful. Other anti-inflammatories and nutrients for slightly elevated CK that may be useful include bromelain, phosphatidyl choline, curcumin, boswellia, green tea extract, glutamine, quercetin, SAMe and EFA's, n-acetyl cysteine, glutathione and antioxidants Vit. A,D,C,E. These are also good nutrients to stabilize cell membranes reducing unnecessary cell turnover.

If CK is very low and the patient is complaining of fatigue, this may signal a loss intracellular energy production. Consider methylation support (B12, Methylfolate, B6, B1, B3, B2) as well as mitochondria support (all the methylation support plus CoQ10, carnitine, glutathione and EFA's).

Related Tests

CK isoenzymes: See above for description of CK isoenzymes.

Troponins: Cardiac Troponins are very specific and sensitive markers for myocardial injury. Can differentiate easily between skeletal injury and heart disease.

LDH: Another intracellular enzyme showing tissue damage.

LDH Isoenzymes: LDH has five sub-fractions or isoenzymes which can help differentiate where the dysfunction leading to elevated LDH is coming from.

AST: Liver enzyme test which can help differentiate source of CK elevation. If elevated it may be heart disease or liver damage. May also be elevated with brain injury.

ALT: Liver enzyme test which can help differentiate source of CK elevation. ALT is slightly more liver specific than AST.

GGT: Hepatobiliary enzyme that when elevated along with LDH is suggestive of biliary disease.

5'-Nucleotidase: Hepatobiliary enzyme that when elevated along With LDH is suggestive of biliary disease.

CRP: Elevated in times of heart damage and inflammation.

ALP: Alk. Phos. may be elevated in liver disease or bone disease. May be low with low LDH if zinc deficiency.

Leucine Aminopeptidase: Hepatobiliary enzyme that can be elevated in liver or gallbladder dysfunction.

CBC with differential: Can demonstrate anemia, hemolysis, or infectious source of CK elevation.

Thyroid panel: Hypothyroid may cause CK elevation if severe enough. Chronic hypothyroid may cause low CK.

Basic Lipid Panel

Triglycerides

Optimal: 30 – 85 mg/dl

Triglyceride (TG) is a fatty acid transport molecule. It consists of a glycerol molecule (derived from glucose) and three fatty acids. TG's are abundant in the diet and are broken down and repackaged as chylomicrons in the intestinal enterocytes. From there they are absorbed into the lymphatic vessels and deposited in the blood stream. TG's from the diet are further broken down by cellular lipase enzymes into glycerol (which can then be reconverted into glucose) and free fatty acids to be used for energy. Endogenous sources of TG's are produced in the liver in response to many factors. Insulin will trigger hepatocyte production of TG's as well as high glucose. Liver production of TG's is accompanied by VLDL production which acts as a carrier protein for TG's.

High >85

- Metabolic syndrome/Insulin Resistance – TG's are made directly from sugar
- Early stage hyperglycemia / diabetes
- Fatty liver (NAFLD)
- Non-fasting test (must fast for minimum of 8 hours)
- Hypothyroidism
- Liver congestion
- Cardiovascular disease
- Atherosclerosis
- Poor metabolism and utilization of fats
- Hyperlipidemia / hyperlipoproteinemia (familial)
- Adrenal cortical dysfunction
- Alcoholism

Low <30

- Liver / gallbladder dysfunction
- Excessive fasting
- Thyroid hyperfunction
- Autoimmune processes
- Adrenal hyperfunction
- Malabsorption / enterocyte dysfunction
- Malnutrition

Functional Considerations

It is extremely important to obtain a fasting measurement of TG's in order to accurately assess the metabolic features associated with TG's. Because dietary TG's give us limited information (how much the patient ate recently), instruct the patient to fast at least 12 hours. Elevated TG's are the main component in advancing IR. Insulin will stimulate lipogenesis and the production of TG's. Therefore, elevated glucose and a high glycemic diet must be eliminated or reduced. It is not fat that elevated TG's necessarily. Rather, it is sugar and carbohydrates which contribute to elevated fasting levels of TG's.

TG's are important in cardiovascular disease because it will elevate VLDL and contribute to atherosclerosis. This can lead to kidney microvascular damage and elevate blood pressure as well. Many patients with elevated TG's also present with low HDL. Elevated TG's will also contribute to fat cell proliferation in all tissues, especially liver and adipose tissue, leading to fatty liver and/or obesity.

Another important functional correlation with TG's is thyroid function. In a hypothyroid state, the metabolism of most cells declines, leaving a surplus of glucose, fatty acids and glycerol. The liver will then be forced to produce a higher number of TG's, making this an excellent marker of thyroid *function*, regardless of whether the thyroid analyte numbers (TSH, T4 etc.) are abnormal or not. In contrast, if the thyroid is hyper-functioning, cells will be metabolizing glucose and fats at an accelerated rate, which will outpace the body's ability to form TG's, thereby lowering TG levels.

Adrenal hormones also influence TG production and warrants consideration in any abnormal TG level. In hypercortisolism, TG's are produced in response to gluconeogenesis and metabolism up-regulation. Catecholamines will also stimulate TG production and mobilization. In chronic stress however, TG's may decline due to the malabsorption and continued increase in metabolism. These patients are the high-strung patients of excess catecholamine production and possibly impaired clearance caused by a genetic polymorphism.

A further functional consideration for abnormal TG's is liver toxicity. Look at other related tests to show signs of liver toxicity such as Hcys, uric acid, cholesterol etc. In acute toxicity the liver will try to transform the pollutant using phase I and phase II detoxification. Most people however have impaired phase II and will therefore produce a lipophilic compound. This may damage hepatocytes and trigger cholesterol and TG production. In chronic liver damage, hepatocytes can no longer function and its capacity to produce TG's decrease. In either case, an abnormal TG is cause to investigate detoxification function.

Related Tests

Lipoprotein Fractionation (Cardio IQ, Spectracell™ etc.): This test measures the subclasses of lipoproteins and their sizes, including Lp(a). It is a good test for estimating atherogenic tendencies of cholesterol, as well as familial lipid abnormalities. Often patients will present with normal lipid values but elevated Lp(a), thereby increasing their risk of clot formation and atherosclerosis.
Lipid Panel: Cholesterol, LDL, HDL and HDL/Cholesterol ratio.
Homocysteine: An important cardiovascular health marker. If CVD is suspected, this test is highly useful.
Cardio CRP: An important inflammatory marker indicative of coronary tissue damage if elevated.
Apolipoproteins: Test measuring the protein components of lipoproteins. Since it is these proteins which are highly atherogenic, and not just the cholesterol or lipid itself, this test can help further define a person's heart disease risk factor.
Insulin: Because elevated TG's are closely associated with IR, a post prandial and fasting insulin can be performed to demonstrate hyperinsulinemia and IR.

Cholesterol

Optimal Female: 140-195mg/dl
Optimal Male: 145-185mg/dl

This test is usually run as part of a lipid panel which includes total cholesterol, HDL, TG's and calculated LDL. Cholesterol is both a lipid and a hormone. Its role as a lipid includes cell membrane structure, myelin sheath integrity, a source of energy, transport and storage of toxins, and a major component of bile. Its role as a hormone includes being the precursor for all steroid hormones as well as Vit. D. Cholesterol is a fatty substance and as such cannot be dissolved in water-based blood plasma. Therefore, it requires a hydrophilic carrier called lipoproteins (LP). These lipoproteins largely determine the pathogenic/physiologic activity of cholesterol. That is, it is the LP which determines if the cholesterol has good (HDL) or bad (LDL) activity in the body. LDL is largely responsible for delivering cholesterol and TG's from the liver to the tissues, while HDL is associated with delivering cholesterol back to the liver

for metabolic processing and excretion. Too much LDL is a sign that the liver is not able to handle the excess cholesterol or TG's due to many influences, such as hormonal regulation and diet. Other important factors determine whether cholesterol or lipoprotein is pathogenic. It is not just total amount of these substances but also how they act and are influenced by peripheral tissues. For instance, if the tissues are free-radical dense, then the LP's become oxidized and are less likely to be metabolized and more likely to be atherosclerotic. A host of other nutritional and genetic variances are involved, such as peripheral lipase enzyme concentration in tissues and endothelium, which is why simply lowering cholesterol has not proven to effectively lower risk of death from a cardio-vascular event.

Many factors influence total cholesterol. Diet accounts for only 10-25% of total cholesterol, another reason why low fat/cholesterol diets have failed. Endogenous production is largely under hormonal regulation. An elevated insulin level in response to elevated glucose is the major stimulator of cholesterol production. Other hormones such as thyroid, catecholamines and cortisol play key roles in the formation and function of cholesterol.

High >185(M);195(F)

- Primary hypothyroidism
- Adrenal cortical dysfunction
- Cardiovascular disease
- Atherosclerosis
- Biliary stasis
- **Insulin resistance**
- Poor metabolism and utilization of fats
- Fatty liver (NAFLD)
- Early stage hyperglycemia / diabetes
- Metabolic syndrome
- Multiple sclerosis
- Pregnancy
- High carbohydrate diet
- Andropause (decreased testosterone)
- Beta blockers
- Alcoholism
- Cushing's disease
- Leaky gut
- Hyperlipoproteinemia (familial)

Low <145(M);140(F)

- Oxidative stress
- Heavy metal body burden
- Liver / biliary dysfunction
- Advanced liver disease (cirrhosis, hepatitis etc.)
- Diet - malnutrition
- Thyroid hyperfunction
- Autoimmune processes
- Adrenal hyperfunction
- Menopause
- Advanced cancer (cholesterol below 140 is considered an "ominous" sign. Look for low albumin as another ominous sign of severe disease or cancer)

- Pernicious anemia
- Statin drugs
- Vegan diet (strict vegans or raw food diets may not include sufficient cholesterol for optimum health)

Functional Considerations

If cholesterol is elevated the first concern is reduce lipid peroxidation (the transformation of cholesterol into a free radical and atherosclerotic molecule). Increase antioxidants immediately while taking steps to lower cholesterol. Always find the underlying mechanism of elevated cholesterol rather than just trying to "artificially" lower cholesterol. Using red yeast rice to lower cholesterol is not addressing the underlying pathological conditions which have contributed to the elevated cholesterol. Only in cases where cholesterol is elevated to dangerous levels (>300) would one consider nutraceutical or pharmaceutical cholesterol lowering agents. Instead, focus on the underlying issues such as **inflammation**, toxicity, insulin resistance, nutritional deficiencies, and hormonal dysregulation. Use an anti-inflammatory diet and vigorous exercise as first line treatments. If other cardiovascular markers are elevated, such as ESR, Hcys, CRP, Fibrinogen, TG's etc., then use heart support formulas including but not limited to: garlic, Hawthorne, acetyl-l-carnitine, ribose, CoQ10, EFA's, Vit E and Proteolytic enzymes (on empty stomach) to break down potential clots. Address other lifestyle factors immediately such as smoking, drinking and stress reduction and lowering blood pressure if elevated.

One of the earliest signs of hypothyroidism is high cholesterol. Because metabolism decreases with low thyroid, cholesterol will elevate often much earlier than abnormalities in TSH or total thyroid. A complete thyroid panel is warranted in any case of elevated cholesterol. It is not uncommon to see cholesterol levels drop 100 points once thyroid hormones are balanced.

Reiterate to the patient that elevated cholesterol and other cardiovascular markers need to be taken seriously. According to the American Heart Association, about 1/3 of people who experience their **first** heart attack do not have any warning signs and do not get a second chance as it results in death. Patients must be educated not to go by how they "feel". They must take preventive and proactive steps to avoid costly and potentially fatal consequences. Reassure the patient that natural therapies are quite effective and pharmaceutical medication is a last resort.

Patients who choose to take statins must be supported with CoQ10 as all who take statins are deficient, whether or not they have side-effect symptoms.

If heart damage is apparent, such as elevated CK, LDH, and Troponins, medical management may be necessary to stabilize the patient until the functional consideration can be addressed.

Related Tests

Lipoprotein Fractionation (Cardio IQ, Spectracell™ etc.): This test measures the subclasses of lipoproteins and their sizes, including Lp(a). It is a good test for estimating atherogenic tendencies of cholesterol, as well as familial lipid abnormalities. Often patients will present with normal lipid values but elevated Lp(a), thereby increasing their risk of clot formation and atherosclerosis.

Lipid Panel: Cholesterol, LDL, HDL and HDL/Cholesterol ratio.

Homocysteine: An important cardiovascular health marker. If CVD is suspected, this test is highly useful. An elevated Hcys can double or quadruple risk for coronary artery disease.

Cardio CRP: An important inflammatory marker indicative of coronary tissue damage.

Creatine Kinase: If elevated run an isoenzyme test to isolate if it is heart tissue that has been damaged and released CK.

Troponins: The most accurate marker of acute MI. Run this test if you suspect the patient has had a recent MI.

LDH: If elevated, run an isoenzyme test to isolate if it is the heart muscle that has been damaged or other tissue in the body.
Fibrinogen: Fibrinogen is a blood clotting biomarker. High levels are associated with increased risk for CHD, stroke, MI and elevated blood pressure.
Hepatic Detox Panel: Liver detoxification is essential in lowering elevated cholesterol. Many people with elevated cholesterol also show impaired detoxification ability in either Phase I or Phase II or both.
Nutrient and Toxic Element: Elevated cholesterol is associated with nutrient deficiency and/or increased heavy metal burden. It is theorized that heavy metal damage to endothelium is the trigger for plaque formation, and not elevated cholesterol by itself.
Apolipoproteins: Test measuring the protein components of lipoproteins. Since it is these proteins which are highly atherogenic, and not just the cholesterol or lipid itself, this test can help further define a person's heart disease risk factor. *The apo A1/ apo B ratio is considered to be the best single indicator of CVD.*
Insulin: Because elevated TG's and cholesterol are closely associated with IR, a post prandial and fasting insulin can be performed to demonstrate hyperinsulinemia and IR as contributing factors to dyslipidemia.

LDL Optimal: < 100 mg/dl

Low density lipoproteins are the major carrier of cholesterol and TG's in the blood. Low density refers to the non-cholesterol components of LDL, making LDL actually higher in cholesterol density. LDL is sometimes referred to the "lousy" cholesterol due to its propensity for plaque formation. LDL is formed in the liver predominantly from VLDL. LDL's physiological role is to carry cholesterol to peripheral tissues where it is metabolized by lipoprotein lipase and used for structural maintenance of cells and energy. It is when this mechanism is overwhelmed that a buildup of LDL occurs and can form plaque and block micro-capillaries first, then larger arteries. Levels of LDL are genetically influenced.
However, it has been shown that environmental factors (diet, lifestyle etc.) are far more important in the etiology of elevated lipoproteins and increased risk for CVD. Most labs still estimated the LDL based on the Friedwald formula which is: LDL= Total Cholesterol – ([TG's/5]-HDL). To get an actual number, a specialty lab must be used, or check with your local lab to see if they use an actual or estimated LDL. This formula however has been shown to be fairly accurate in terms of total LDL number, unless total TG's are over 400mg/dl. LDL subclasses are more useful in determining risk for cardio-vascular events. LDL subclasses are also useful in determining congenital/familial patterns.

High >100

- Diet - high in refined carbohydrates
- Metabolic syndrome
- Increased risk for atherosclerosis
- Liver / gallbladder dysfunction
- Hypothyroid
- Fatty liver / hyperlipidemia
- Oxidative stress
- Increased toxic burden
- Multiple myeloma (high levels of globulins prevent metabolism)
- Kidney disease
- Glycogen storage disease
- Leaky gut

Very Low <40

- Oxidative stress
- Heavy metal body burden
- Liver / biliary dysfunction
- Diet - malnutrition
- Thyroid hyperfunction
- Autoimmune processes
- Adrenal hyperfunction
- Menopause
- Advanced cancer
- Pernicious anemia
- Statin drug use
- Vegan diet

Functional Considerations

Since LDL represents most of the cholesterol and fatty acids in the blood, this test is useful as risk factor for CVD, hypothyroidism and liver toxicity. An important consideration is to educate the patient that familial hyperlipidemia is still mostly influenced by choices yesterday, today and tomorrow. Reducing oxidation, refined carbohydrates/sugar, inflammation, stress and liver toxicity while increasing metabolism through exercise is almost always enough to lower LDL and CVD risk if the patient is willing to do what is necessary. An important test to run is the lipoprotein fractionation subclasses to determine CVD risk more accurately. The larger the LDL size, the lower the risk of CVD.

Related Tests

Lipoprotein Fractionation (VAP™, Spectracell™ etc.): This test measures the subclasses of lipoproteins and their sizes, including Lp(a). It is a good test for estimating atherogenic tendencies of cholesterol, as well as familial lipid abnormalities. Often patients will present with normal lipid values but elevated Lp(a), thereby increasing their risk of clot formation and atherosclerosis.
Lipid Panel: Cholesterol, LDL, HDL and HDL/Cholesterol ratio.
Homocysteine: An important cardiovascular health marker. If CVD is suspected, this test is highly useful. An elevated Hcys can double or quadruple risk for coronary artery disease.
Cardio CRP: An important inflammatory marker indicative of coronary tissue damage.
Creatine Kinase: If elevated run an isoenzyme test to isolate if it is heart tissue that has been damaged and released CK.
Troponins: The most accurate marker of acute MI. Run this test if you suspect the patient has had a recent MI.
LDH: If elevated, run an isoenzyme test to isolate if it is the heart muscle that has been damaged or other tissue in the body.
Fibrinogen: Fibrinogen is a blood clotting biomarker. High levels are associated with increased risk for CHD, stroke, MI and elevated blood pressure.
Hepatic Detox Panel: Liver detoxification is essential in lowering elevated cholesterol. Many people with elevated cholesterol also show impaired detoxification ability in either Phase I or Phase II or both.
Nutrient and Toxic Element: Elevated cholesterol is associated with nutrient deficiency and/or increased heavy metal burden. It is theorized that heavy metal damage to endothelium is the trigger for plaque formation, and not elevated cholesterol by itself.
Apolipoproteins: Test measuring the protein components of lipoproteins. Since it is these proteins which are highly atherogenic, and not just the cholesterol or lipid itself, this test can help further define a

person's heart disease risk factor. *The apo A1/ apo B ratio is considered to be the best single indicator of CVD.*
Insulin: Because elevated TG's and cholesterol are closely associated with IR, a post prandial and fasting insulin can be performed to demonstrate hyperinsulinemia and IR as contributing factors to dyslipidemia.

HDL Optimal: 60-90 mg/dl

High Density Lipoprotein is considered the "good" cholesterol because of its role in being able to take cholesterol from peripheral tissues back to the liver to be metabolized to form hormones, bile and structural fatty acids (phospholipids), thereby reducing TC in the periphery. There is a strong inverse relationship between HDL and atherosclerosis. It is also a sign of proper hepatocyte function and low HDL is a marker of liver dysfunction, stagnation and toxicity. Always consider all CVD risk factors and not just one marker by itself. Elevated HDL can down regulate the apoB-100 receptor in liver and peripheral tissue cells thus lowering the detrimental effects of LDL.

High > 90

- Excessive exercise
- Genetic predisposition
- Autoimmune processes
- Liver Inflammation

Low < 60

- Hyperlipidemia / fatty liver
- Atherosclerosis
- Metabolic syndrome
- Oxidative stress
- Heavy metals
- Hyperthyroidism
- Lack of exercise / sedentary lifestyle
- Genetic hypoalpha-lipoproteinemia

Functional Considerations

Hypothyroidism may be elevated HDL along with total cholesterol and LDL so that while elevated HDL may be desirable, the increase in other risk factors far outweigh the benefits of elevated HDL. Often you will see elevated HDL first in hypothyroid disorders before TC and LDL increase, so it is wise to consider a complete thyroid function panel.

Exercise is the most reliable way to increase HDL. It is also the most beneficial lifestyle modification that a person can make because it will address many other issues of ill health and while lowering CVD risk. Also, eliminating alcohol, smoking and some medications where appropriate can also increase HDL. Also, HDL must be considered along with the other lipids. A low HDL is not necessarily a risk factor if total cholesterol and TG's are also low. However no matter the TC or TG levels, HDL above 45 is desirable.

Related Tests

For low HDL see related tests for elevated LDL.

Cholesterol/HDL Ratio Optimal: < 3.0

This is a ratio of TC to HDL and is considered a better indicator of heart disease risk than either TC or HDL by itself. It is simply a mathematical equation which has been shown in large scale models to more accurately predict a cardio-vascular event.

Iron Studies

Serum Iron Optimal: 60 – 135 ug/dl

Serum iron measures the amount of iron in the blood that is bound to transferrin which represents only a small fraction of total body iron. 70% of body iron is in the form of hemoglobin. Most of the rest is stored as ferritin or hemosiderin (used by bone marrow to make RBC's). Serum iron levels should be carefully related to other iron indices such as TIBC, ferritin, transferrin saturation and the RBC indices. Serum iron levels alone do not give a clear picture of iron metabolism if interpreted by itself.

As iron is absorbed in the small intestine, it is bound to transferrin and transported to the liver, bone marrow and any excess is stored as ferritin in peripheral tissues. Iron is required for oxygen transport, energy metabolism (cytochromes is the mitochondria), detoxification/biotransformation (CyP450), and immune defenses. Total body iron is about 3-4 grams.

High

- Liver dysfunction (liver inflammation causes increase in iron uptake as well as cytochrome release)
- Hemochromatosis / hemosiderosis
- Factor deficiency anemia (with pernicious anemia and B-6 deficiency, RBC's are not being made and iron therefore will be stored and elevate in serum)
- Viral infection (acute hepatitis, EBV, CMV, chronic infection)
- Excess iron consumption
- Hypersplenism
- Estrogen therapy (increases transferrin)
- Hemolysis
- Lead toxicity

Low

- Chronic blood loss (GI cancer is the most common cause, Coumadin therapy, cerebral infarction ulcerative colitis, Crohn's)
- Malabsorption (low HCL or Vit. C. Intake of dairy, coffee, sugar inhibits Fe absorption. Pt. with ulcers and/or gastritis may have both decreased absorption as well as increased blood loss)
- Antacids decrease absorption of iron
- Pregnancy (usually last trimester - the baby will most likely be iron deficient as well)
- Cancer
- Copper deficiency (mucosal enzymes needed to absorb iron are copper-containing)
- Dietary insufficiency (vegetarians)
- Excessive menstrual bleeding

Functional Considerations

Mild hiatal hernias are associated with decreased absorption of iron as well as other nutrients. If you have the training, assess for HH and use manual/visceral manipulation techniques to resolve. This is often associated with women who have frequent iron-deficiency headaches, with or without anemia.

When treating someone for pernicious anemia, iron levels initially fall due to rapid utilization in RBC production and maturation. It is recommended to wait 30-60 days after starting B12/folate to recheck for possible iron deficiency. If iron levels are dropping, then supplementation may be necessary for a few months.

Iron is needed for macrophages and neutrophils to make myeloperoxidase which is responsible for killing microorganisms. If a patient is iron deficient, they may be immunocompromised as well. Immune support is appropriate especially if chronic infection is present or suspected. It may even be possible that a chronic infection may be the source of iron depletion, setting up a downward cycle in health often seen with iron deficiency.

Excess iron is extremely toxic and if persistent, a chelator such dexosferamine may be used to lower iron levels. Whenever iron is high regardless of the reason, copious antioxidants (i.e. glutathione, Vit. E) should be administered to protect cells from oxidative, free radical damage that free iron can produce. Be careful to find the cause of excess iron and avoid Vit. C as this may increase iron absorption. Also, avoid all refined or enriched foods as they most likely contain added iron.

Keep in mind that someone with iron deficiency may be borderline anemic even when Hg, RBC, and are normal. This is often seen when a patient has iron deficiency and at the same time is dehydration, which is often the case. If ferritin is low, TIBC is high and serum iron is low, suspect sub-clinical IDA, especially if RDW is high normal or elevated, or MCV is low normal or low.

Related Tests

RBC indices: These are useful in determining type and extent of iron deficiency.
Ferritin: A measure of iron stores. Will often show abnormality before serum iron.
Transferrin: A liver function marker as transferrin is made in the liver.
Transferrin Saturation: Can help determine cause of abnormal iron and TIBC levels. It will be decreased in iron deficient anemia but elevated hemolytic or pernicious anemia)
TIBC: An indirect but accurate measurement of transferrin.
Fecal Occult Blood: Use of fecal immunochemical test (FIT) plus transferrin can be up to 85% sensitive for GI cancer.
GI Panel: To check for absorption issues, parasites, inflammation etc.
CA Tests: To check for possible cancer, especially if administration of iron works initially then drops again.

Ferritin

Optimal Male: 25 - 125 ng/ml
Optimal Female: 20 - 90
Optimal Female (menopause): 25 - 115

Ferritin is a protein that exists in virtually all tissues. Its main activity is to bind to iron when iron is in the extracellular spaces and acts as a storage source. When it is not bound to iron it is referred to as apoferritin. Serum ferritin closely reflects tissue ferritin. Ferritin levels will rise in response to persistently elevated serum iron levels. Serum iron and ferritin will both be elevated. However, as iron levels become depleted, ferritin will give up its iron to maintain normal serum iron levels. Running just a serum iron therefore can miss a developing iron deficiency. Ferritin levels will decrease even before RBC indices show signs of microcytic, hypochromic anemia. This is why it is imperative to look at all iron indices to determine if and why iron levels are abnormal. Ferritin is also considered an acute phase reactant and liver production of Ferritin will increase as inflammatory cytokines are released due to infection, tissue damage, stress and toxicity. High levels of ferritin are associated with increased hydroxyl ions in the body, which is the body's most potent free radical. Elevated ferritin is associated with increased risk of multiple cancers, and especially coronary vascular disease. According to the American Heart Journal (2011) those with ferritin levels around 75 had the lowest risk of CVD.

High

- Hemochromatosis / hemosiderosis (increased available iron raises ferritin. Often ferritin will be elevated above 500 or more)
- Excess iron consumption
- Inflammation / inflammatory disease (cardio-vascular disease, collagen-vascular disease, Autoimmune, etc.)
- Liver dysfunction (hepatitis, cancer, other infection)
- Pernicious anemia
- Hemolytic anemia (iron may be elevated or normal. Serum LDH may be elevated)
- Non-hepatic cancer
- Chronic illness – anemia of chronic disease is marked by low iron but elevated ferritin)
- Pregnancy (early only. Late pregnancy is associated with low ferritin)
- Copper deficiency (check serum Ceruloplasmin)

Low

- Anemia (due to iron deficiency - chronic)
- Pregnancy (late)
- Severe protein deficiency
- See low iron for other causes

Functional Considerations

Ferritin is an acute phase reactant protein, quite possibly because neutrophils and other WBC's need iron to form cytochrome enzymes which help regulate inflammation. Levels will rise 24-48 hrs, peak in 3-5 days and can stay elevated for up to five weeks after resolution of the inflammation. Therefore, when there is an acute or persistent chronic inflammation, ferritin levels may rise without iron levels being affected. In fact, in most cases transferrin levels will decrease since transferrin is a negative acute phase reactant and will be down-regulated. Therefore, iron levels may actually be low and the person with chronic inflammation may present with elevated ferritin but still be anemic.

Be aware that acute inflammation can hide an iron deficiency. Ferritin will be up-regulated during, say, a trauma. However, the patient may be experiencing iron deficiency due to blood loss. If the patient is suspected of having a true iron deficiency (RBC's show anemia), if ferritin levels are normal, suspect a coexisting inflammatory condition.

When ferritin levels rise and iron levels are normal or near normal, suspect acute infection or inflammation. Look at RBC indices to check for possible hemolysis. In this case, LDH may also be elevated. If elevated ferritin levels are due to hemochromatosis, then iron levels will most likely be elevated, as well as transferrin and transferrin saturation.

Related Tests

RBC Indices: These are useful in determining type and extent of iron.
Iron: Serum iron can give a more present-moment iron picture.
Transferrin: A liver function marker as transferrin is made in the liver. Negative phase reactant.
Transferrin Saturation: Can help determine cause of abnormal iron and TIBC levels. It will be decreased in iron deficient anemia but elevated hemolytic or pernicious anemia)
TIBC: An indirect but accurate measurement of transferrin.
Fecal Occult Blood: Use of fecal immunochemical test (FIT) plus transferrin can be up to 85% sensitive for GI cancer.
GI Panel: To check for absorption issues, parasites, inflammation, etc.
CA Tests: To check for possible cancer, especially if administration of iron works initially then drops again.

TIBC Optimal: 275 – 375 mcg/dl

Total iron binding capacity is a measurement of all proteins available for iron binding. Since the majority of those proteins are transferrin (a small portion is also albumin), this is really an indirect measurement of transferrin in the serum. It must be correlated however, with iron and ferritin levels as well as transferrin saturation in order to correctly interpret the results.

Typically as TIBC levels rise, it is due to an iron deficiency anemia. TIBC is the amount of transferrin that is *available* to bind to iron. Therefore it is often in an inverse relationship to iron. One can think of TIBC as the number of cars on a train. Each car represents a transferrin. If the car is full of iron, it will not be counted because its capacity is full. So the TIBC is the number of available cars that have no iron. Since iron does not stay on the train long, it is an accurate measurement of how many cars are on the train. If iron is absent, as in iron deficiency, more cars will be available and TIBC will elevate. Since transferrin is made in the liver, if the liver is dysfunctional there will not be very many cars produced and the TIBC will go down.

High

- Anemia - iron deficiency
- Pregnancy
- Estrogen therapy (promotes binding protein production in the liver)
- Chronic blood loss (if not hemolytic or internal. Blood loss must be such that iron is not reabsorbed)
- Hypochlorhydria
- Cancer (some cancers deplete iron without affecting transferrin levels, so TIBC will elevate)
- Vegan / vegetarian diet

- Excessive menstrual bleeding
- Pregnancy

Low

- Hemochromatosis / hemosiderosis / iron overload
- Microscopic bleeding
- Chronic infection
- Diet - protein malnutrition
- Liver disease
- Pernicious anemia
- Hemolysis

Functional Considerations

TIBC can be thought of as a measurement of liver function, as transferrin is produced by the liver. Transferrin is also a negative acute phase reactant which means in time of stress and/or inflammation, transferrin levels will go down. This can be misleading as often an iron deficiency is seen at the same time as an inflammatory disease or cirrhosis. This will lower TIBC even though the patient may be iron deficient.

Up to half of patients with iron deficiency have normal or even low TIBC so this is not the most sensitive test for ID. However, it can be used to see the larger picture of iron metabolism and liver function. Laboratory as well as clinical findings must be integrated so that the clinician can fully appreciate the underlying mechanisms.

In hemochromatosis, TIBC is often unchanged as this is an iron storage overload and the amount of transferrin does not always change. The % saturation however is elevated in hemochromatosis.

Related Tests

RBC Indices: These are useful in determining type and extent of iron.
Iron: Serum iron can give a more present-moment iron picture.
Transferrin: A liver function marker as transferrin is made in the liver.
Transferrin Saturation: Can help determine cause of abnormal iron and TIBC levels. It will be decreased in iron deficient anemia but elevated hemolytic or pernicious anemia)
Ferritin: Measurement of stored iron.
Fecal Occult Blood: Use of fecal immunochemical test (FIT) plus transferrin can be up to 85% sensitive for GI cancer.
GI Panel: To check for absorption issues, parasites, inflammation etc.
CA Tests: To check for possible cancer, especially if administration of iron works initially then drops again.

% Transferrin Saturation Optimal: 21 – 35%

Transferrin saturation is a calculated measurement of the amount of iron that is bound to all available iron binding proteins (most of which is transferrin). It is based on serum iron and TIBC using the equation: serum iron X 100/ TIBC. It is a more sensitive measurement of iron status as saturation of iron binding sites will take place before TIBC changes. Low saturation is diagnostic of iron deficiency. Chronic illness

affecting the liver or depleting iron will result in low serum iron and low TIBC, therefore the % saturation will be normal.

High

- Hemochromatosis / hemosiderosis
- Hemolytic anemia
- Excess iron intake
- See increased iron levels

Low

- Iron deficiency
- Chronic illness (iron levels are low and the TIBC levels increase)
- See decreased iron levels

Related Tests

RBC Indices: These are useful in determining type and extent of iron.
Iron: Serum iron can give a more present-moment iron picture.
Transferrin: A liver function marker as transferrin is made in the liver.
TIBC: Total iron binding capacity measures the amount of available transferrin
Ferritin: Measurement of stored iron.
Fecal Occult Blood: Use of fecal immunochemical test (FIT) plus transferrin can be up to 85% sensitive for GI cancer.
GI Panel: To check for absorption issues, parasites, inflammation, etc.
CA Tests: To check for possible cancer, especially if administration of iron works initially then drops again.

Thyroid Section

"The classic picture of hyperthyroidism or hypothyroidism is frequently not complete and may be totally absent [on laboratory results]… the multiplicity of tests implies that none is infallible or invariably helpful."
- Ravel, Clinical Laboratory Medicine

TSH (Thyrotropin) Optimal: 1.0 – 2.5 mU/L

Thyroid stimulating hormone is now referred to as thyrotropin, although TSH is still commonly used. Thyrotropin is a hormone released by the pituitary in response to thyrotropin releasing hormone (TRH) from the hypothalamus, which monitors levels of T4 in the blood. When blood levels of T4 and T3 go down, TRH and subsequently TSH is then secreted if the hypothalamic sensitivity is functioning properly. TSH then acts upon TSH receptors on the thyroid epithelial cells and stimulates all aspects of T3 and T4 production, and blood levels of thyroid hormone are elevated. TSH is diurnal, with peak levels at about 10pm and lowest levels at 10 am. The difference between the peaks and valleys can sometimes be 2-3 times baseline levels.

Primary hypothyroidism refers to a dysfunctional thyroid gland and TSH levels are usually elevated as the hypothalamus and pituitary continue to secrete TRH and TSH respectively, in response to low hormone levels. In secondary hypothyroidism, TSH levels are low because the pituitary is not functioning properly. It tertiary hypothyroidism, the hypothalamus is faulty and TRH and subsequently TSH are both decreased.

TSH has long been thought to accurately reflect thyroid function. However, it is only useful if used as part of a complete thyroid survey utilizing actual T3 and T4 hormone levels as well as other thyroid function tests (see related tests).TSH does not always accurately reflect the functional end-tissue utilization of thyroid hormone and consequently, some individuals may be considered "euthyroid sick" (normal TSH but clinical manifestations of hypothyroidism). Because abnormal TSH cannot be considered absolute evidence of thyroid disease, nor can normal TSH be considered absolute evidence of a fully functional thyroid, TSH can be best utilized as a rough guide to thyroid gland function. TSH can also be used to monitor thyroid treatment effectiveness as well. TSH can also serve to differentiate primary, secondary and tertiary thyroid dysfunction.

TSH "ultrasensitive" or "third generation" refers to the sensitivity TSH has in the low range, and therefore its sensitivity to differentiate hyperthyroidism (no TSH present) and non-thyroid illness (low but not zero).

High

- Primary hypothyroidism
- Thyroid resistance (with elevated T3 and/or T4. This is due to peripheral tissue resistance and/or Pituitary dysfunction from chronically elevated ACTH or other neurotransmitter imbalance)
- Pituitary tumor
- Iodine supplementation
- Autoimmune thyroiditis
- Lithium intake
- Chronic illness
- Myxedema

- Cretinism (infant hypothyroidism)
- Medications (such as amiodarone and many others)
- Addison's disease (CRH / ACTH secretion may stimulate TRH / TSH as well)

Low

- Hyperthyroidism
- Secondary hypothyroidism (pituitary dysfunction causing low TSH output)
- Tertiary hypothyroidism (hypothalamic dysfunction)
- Heavy metals (heavy metals cross the BBB and can affect pituitary and hypothalamic dysfunction, causing multiple endocrine disorders. Consider heavy metal assays on patients with any suspected or diagnosed neuro-endocrine disorder)
- Dopamine (increased dopamine levels can suppress TSH through hypothalamic and pituitary inhibition)
- Cortisol (chronic stress or exogenous administration causes hypothalamic and/or pituitary insensitivity to normal stimuli, therefore lowering TRH, TSH release, respectively)
- Chronic illness
- Thyroid medications
- Antidepressants
- Elderly

Functional Considerations

Proper thyroid assessment is both crucial to a primary care practice and complicated at the same time. The thyroid gland is proving to be an "indicator" organ (much like indicator species) that is very sensitive to environmental and physiological stressors including emotional stress, chemicals, pollutants, heavy metals, diet and nutritional deficiencies. Diagnosis of hyperthyroid states using laboratory evaluations is fairly straightforward. However, with hypothyroidism, the clinician must use more extensive laboratory evaluations together with clinical findings to develop an accurate picture of the thyroid's impact on an individual's health. Thyroid function is also affected by many disease states and is often dysfunctional in any chronic illness. Therefore, no matter what the patient complains of, if it is a chronic condition, then thyroid support may be crucial for proper healing and recovery. Because all cells in the body require thyroid hormone, it affects the health and function of every tissue in the body.

It is imperative that the clinician be well acquainted with natural treatment recommendations for thyroid support which include diet (gluten and dairy free), lifestyle (exercise and meditation) and nutraceutical (of which there are many). Please refer to the thyroid section for more info.

Related Tests

TSH Stimulation Test: Administration of TSH can help differentiate primary hypothyroidism vs. secondary or tertiary. Because bovine TSH is used, some develop antibodies to TSH following this test.
TRH Stimulation: Administration of TRH allows for assessment of primary, secondary and tertiary hypothyroidism. TRH is given to a patient and TSH is then measured. In primary hypothyroidism, there is an exaggerated TSH elevation. In secondary hypothyroidism, TSH is not significantly elevated. In tertiary hypothyroidism, TSH is slightly elevated into normal levels but the release is delayed about 30 minutes. If the patient is hyperthyroid, the TSH will not elevate after TRH is given. This test has been used to differentiate bipolar (normal TSH response) vs. clinical depression (blunted response) indicating pituitary dysfunction.

T4: Thyroxin is the major thyroid hormone produced by the thyroid (97%). Free T4 gives a better picture of thyroid output as well as tissue exposure. Total T4 is essentially bound T4 and is affected by TBG values.
T3: Triiodothyronine is the active thyroid hormone and requires peripheral conversion from the liver and other tissues. About 3% of total thyroid hormone secreted by the thyroid is T3. It has a very short half-life (2-4 hours), therefore serum T3 not only measures thyroid output, but the ability of peripheral conversion through the selenium-dependent deiodinase enzymes.
rT3: Reverse T3 is produced in peripheral tissues such as liver and intestinal epithelial cells from T4 which has been converted by deiodinase enzymes. rT3 elevates due to many illnesses and conversion problems.
Thyroid Antibodies (Anti-TPO, Anti-thyroglobulin, TSI): These tests are useful for the diagnosis of autoimmune thyroid disorders (i.e. Grave's and Hashimoto's).
FTI: Free thyroxine index (now called free T4 index, but previously referred to as T7) and is a mathematical calculation of free T4 by trying to compensate for TBG levels. This test gives an estimate of free T4. It is only useful when compared to the total T4 and T3 uptake, as well as T3 and TBG.
T3 Uptake: This test measures the amount of thyroid hormone and the amount of TBG.
TRH: Thyrotropin releasing hormone is secreted by the hypothalamus and can be useful in differentiating between primary, secondary and tertiary hypothyroidism.
TBG: Thyroid binding globulin affects the bioavailability and transport of thyroid hormones and is itself affected by many medications and illnesses.
Cholesterol: Will often be elevated in hypothyroid states even if thyroid panels are normal. Cholesterol is often decreased in hyperthyroidism and thyrotoxicosis as well.
RBC Indices: Hypothyroid states can cause elevated MCV and MCH.
Liver Enzymes: AST and ALT may be elevated is early or severe hypothyroidism.
Food Allergy Testing: Detecting and eliminating potential food allergens and immune dysregulators is imperative in treating and supporting thyroid function. The most common foods that aggravate the thyroid are gluten, dairy and soy).
Iodine Clearance Test: If the patient is suspected of having a frank or functional iodine deficiency, this test will help determine need.

Free Thyroxin (FT4) Optimal: 1.0 – 1.5 ng/dl

Approximately 95-97% of thyroid hormone output is T4. Up to 99% of T4 is bound to protein and less metabolically active. T4 is unbound and available for conversion to T3 in peripheral tissues. Since protein levels can impact total T4 levels, the free fraction is a more accurate of thyroid function as well as a functional indicator of tissue exposure to active thyroid hormone as it is mostly unaffected by fluctuating TBG and albumin, prealbumin and other proteins. Many conditions and factors affect binding protein levels which make free T4 essential in assessing whether the thyroid is functioning properly.
T4 is considered the storage and transport form of thyroid hormone and itself has only weak biological activity within the cell. It must be converted to T3 in the peripheral tissues.

High

- Primary hyperthyroidism
- Thyroid medication
- Acute illness
- Autoimmune thyroiditis
- Struma ovarii (ectopic thyroid tissue commonly seen in the ovarian teratogenic tumors)
- Pregnancy

Low

- Primary hypothyroidism
- Secondary hypothyroidism
- Iodine deficiency
- Pregnancy (late)
- Chronic, non-thyroid illness
- Anti-thyroid medications (i.e. propylthiouracil)
- Administration of iodine contrast media for radiology (I-131)

Functional Considerations

Many laboratory reference ranges are influenced by a relatively large percentage of persons on synthroid (synthetic T4). Therefore it is often seen that T4 levels appear low in patients who have normal T4 production. A similar predicament exists with T3. Many people have conversion problems and the population reference range can be low. As a result, the T3 levels on a patient who is hypothyroid may actually appear normal. Using the optimal ranges gives a clearer picture of thyroid health than the laboratory ranges.

Free T4 outperforms FTI in separating euthyroid patients from hypo or hyper thyroid ones.

Please read entire section on Thyroid (and Dr. Lundell's educational recordings). Having a mastery of thyroid conditions is encouraged to effectively treat thyroid imbalances as well as prevent thyroid problems for euthyroid patients. Of special note is the research linking drinking water, organophosphates (pesticides) and other pollutants to thyroid damage.

Related Tests

TSH: Secreted by the pituitary, thyrotropin can give information as to causes of thyroid dysfunction.

T3: Triiodothyronine is the active thyroid hormone and requires peripheral conversion from the liver and other tissues. About 3% of total thyroid hormone secreted by the thyroid is T3. It has a very short half-life (2-4 hours), therefore serum T3 not only measures thyroid output, but the ability of peripheral conversion through the selenium-dependent deiodinase enzymes.

rT3: Reverse T3 is produced in peripheral tissues such as liver and intestinal epithelial cells from T4 which has been converted by deiodinase enzymes. RT3 elevates due to many illnesses and conversion problems.

Thyroid Antibodies (Anti-TPO, Anti-thyroglobulin, TSI): These tests are useful for the diagnosis of autoimmune thyroid disorders (i.e. Grave's and Hashimoto's).

FTI: Free thyroxine index (now called free T4 index, but previously referred to as T7) and is a mathematical calculation of free T4 by trying to compensate for TBG levels. This test gives an estimate of free T4. It is only useful when compared to the total T4 and T3 uptake, as well as T3 and TBG.

T3 Uptake: This test measures the amount of thyroid hormone and the amount of TBG.

TRH: Thyrotropin releasing hormone is secreted by the hypothalamus and can be useful in differentiating between primary, secondary and tertiary hypothyroidism.

TBG: Thyroid binding globulin affects the bioavailability and transport of thyroid hormones and is itself affected by many medications and illnesses.

TSH Stimulation Test: Administration of TSH can help differentiate primary hypothyroidism vs. secondary or tertiary. Because bovine TSH is used, some develop antibodies to TSH following this test.

TRH Stimulation: Administration of TRH allows for assessment of primary, secondary and tertiary hypothyroidism. TRH is given to a patient and TSH is then measured. In primary hypothyroidism, there is an exaggerated TSH elevation. In secondary hypothyroidism, TSH is not significantly elevated. In tertiary hypothyroidism, TSH is slightly elevated into normal levels but the release is delayed about 30 minutes. If the patient is hyperthyroid, the TSH will not elevate after TRH is given. This test has been used to

differentiate bipolar (normal TSH response) vs. clinical depression (blunted response) indicating pituitary dysfunction.
Cholesterol: Will often be elevated in hypothyroid states even if thyroid panels are normal. Cholesterol is often decreased in hyperthyroidism and thyrotoxicosis as well.
RBC Indices: Hypothyroid states can cause elevated MCV and MCH.
Liver Enzymes: AST and ALT may be elevated is early or severe hypothyroidism.
Food Allergy Testing: Detecting and eliminating potential food allergens and immune dysregulators is imperative in treating and supporting thyroid function. The most common foods that aggravate the thyroid are gluten, dairy and soy).
Iodine Clearance Test: If the patient is suspected of having a frank or functional iodine deficiency, this test will help determine need.

Total T4 (TT4) Optimal: 7.5 – 11 mcg/dl

Total T4 is a measure of bound (97%) and unbound (3%) thyroxine. This test is specific for hypothyroid and hyperthyroid states, although not as sensitive as free T4. This test is influenced by TBG levels since a rise or absence of TBG will affect circulating T4 levels. The more TBG is present, the longer T4 will stay in circulation, giving a false impression of hyperthyroidism. Conversely, if TBG is depressed, or clearance is elevated through the liver and kidney for various non-thyroid reasons, then the test will yield a false reading of hypothyroidism.

High

- Hyperthyroidism
- Thyroid medication
- TBG elevation (hepatitis, heavy metal exposure, estrogen, tamoxifen, genetic TBG elevation)
- Struma ovarii
- Acute illness
- Autoimmune thyroiditis
- Pregnancy

Low

- Primary hypothyroidism
- TBG depression (severe liver disease, kidney disease, androgens, steroids, Cushing's, beta blockers, Dilantin etc. These medications actually interfere with the binding ability of TBG by preferentially binding to TBG in greater affinity than thyroid hormone itself)
- Protein deficiency (malabsorption, malnutrition, nephropathy, severe burns)
- Excess iodine administration (There is an initial decrease in T3 and T4 release by the thyroid. This will return to normal if iodine administration is reduced or discontinued. Doses are typically 150-300mg.)
- Iodine deficiency (long-term iodine deficiency and/or exposure to perchlorates, chlorine, bromine and fluoride will create a "functional" deficiency of iodine)
- PCOS (loss of estrogen causes androgen dominance and low TBG. See T3 uptake)
- Pregnancy (late)
- Chronic illness
- Administration of iodine contrast media for radiology (I-131)

Functional Considerations

Total T4 is affected by TBG and other proteins in non-thyroid conditions. Look at free T4 as well as FTI and all other thyroid markers. This test is still useful for detecting advanced cases of hypo or hyper thyroid states.

If the free T4 value is elevated, and the T3 uptake is decreased, suspect TBG elevation due to a non-thyroidal issue, along with a hyperthyroid state. If free T4 value is low and the T3 uptake is high, suspect TBG decrease due to non-thyroidal illness such as liver or kidney disease.

Related Tests

See free T4

Total T3 Optimal: 115 – 185 ng/dl

Total serum triiodothyronine is assayed by the same technique as TT4. It is a measurement of the bound (99%) and free (1%) of T3. Total T3 represents about 3% of total thyroid hormone circulating in the blood. It is affected by TBG and protein alterations the same as T4 (see T4 section). T3 is the bioavailable thyroid hormone. It is produced from T4 by deiodinase enzymes in the hepatocytes, epithelial cells and in almost every tissue in the body. One iodine molecule is cleaved from T4. Depending on which iodine is removed, T3 or rT3 is produced. Deiodinase enzymes are selenium dependent and selenium deficiencies will cause lowered T3 levels when T4 is normal.

T3 has a very short half-life (2-4 hrs.) therefore it serves as the most bioavailable thyroid hormone. T4 has a very long half-life and is considered the storage and transport form of thyroid hormone. T4 does have some bioactivity within the cell, but it is T3 that has the greatest affinity for nuclear receptors and therefore is the major hormone responsible for thyroid action within the cell.

Many factors affect both production of T3 by the thyroid as well as peripheral conversion. It has hereto for been a poorly understood mechanism and more understanding on the many factors affecting T3 is still being discovered.

High

- Hyperthyroidism
- Iodine deficiency (thyroid production of T3 is elevated when iodine is deficient)
- TBG elevation (hepatitis, heavy metal exposure, estrogen, tamoxifen, genetic TBG elevation)
- Pregnancy
- Struma ovarii
- Thyroid medication (desiccated or synthetic T3)
- Acute illness
- Autoimmune thyroiditis

Low

- Primary hypothyroidism
- TBG depression (severe liver disease, kidney disease, androgens, steroids, Cushing's, beta blockers, Dilantin etc. These medications actually interfere with the binding ability of TBG by preferentially binding to TBG in greater affinity than thyroid hormone itself.)
- Protein deficiency (malabsorption, malnutrition, nephropathy, severe burns)
- Iodine deficiency (non compensated)
- PCOS (loss of estrogen causes androgen dominance and low TBG. See T3 uptake)

- Pregnancy (late)
- Chronic illness
- Selenium deficiency
- Hepatic disease (affects conversion of T4 to T3)
- Administration of iodine contrast media for radiology (I-131)

Functional Considerations

Probably the most common thyroid dysfunction found in clinical practice is thyroid underconversion. Laboratory evaluations can help elucidate this dysfunction. However, it is still possible for T3 to be normal and the quality of T3 is impaired such that patients are considered "euthyroid" sick, or "subclinical" hypothyroid.

Keep in mind as well, that conversion problems are often present at the same time as other thyroid disorder. It is quite common for someone to be clinically hypothyroid *and* have a conversion issue at the same time. These patients are often more sick than there labs may indicate. Always correlate laboratory findings with clinical indications and patient history. Clinical experience shows that supporting this conversion pathway helps thyroid patients immensely.

Many people have been placed on synthroid therapy for many years. This can deplete selenium over time as more deiodinase enzymes are needed to convert the synthetic T4 into T3, leaving them with less T3.

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Iodine Clearance Test: If the patient is suspected of having a frank or functional iodine deficiency, this test will help determine need.

Free T-3 Optimal: 2.7 – 3.7 pg/ml

Like free T4, free T3 is unaffected by protein levels on non-thyroidal illnesses. It is therefore a more accurate picture of thyroid function and conversion than total T3. See total T3 for discussion on T3 activity.

High

- Hyperthyroidism
- Iodine deficiency (compensated: in times of iodine deficiency the thyroid will make more T3)
- Pregnancy
- Thyroid medication [desiccated (Armour) or synthetic (liothyronine)]
- Acute illness
- Autoimmune thyroiditis
- Struma ovarii (ectopic thyroid tissue commonly seen in the ovarian teratogenic tumors)

Low

- Primary hypothyroidism
- Selenium deficiency
- Pregnancy (late)
- Iodine deficiency (non-compensated)
- Hepatic disease (much of the conversion of T4 to T3 takes place in the liver)
- Secondary hypothyroidism (pituitary insufficiency)
- Chronic, non-thyroid illness (cancer, Cushing's, renal failure)
- Antithyroid medications (i.e. propylthiouracil)
- Administration of iodine contrast media for radiology (I-131)

Functional Considerations

See total T3 for discussion. In addition, see free T4 as TBG variations will affect T3 similarly to T4. It is also often seen that patients who are put on desiccated thyroid glandulars (Armour) will show normal T4 levels with elevated T3 levels on subsequent laboratory evaluations. This does not necessarily mean the patient in on too much thyroid. It is usually an issue of laboratory reference ranges being skewed due to a population that is taking T4 (synthroid), which is void of T3, and also has thyroid conversion issues, thereby artificially lowering the reference range of T3.

Related Tests

See Total T3.

T-3 Uptake/THBR Optimal: 27 – 33 %

T3 uptake actually has little to do with T3 levels which is why it is often referred to as thyroid hormone binding ratio (THBR). It is an indirect measurement of T4 levels as well as thyroid binding globulin (TBG). The test is performed by putting radioactive T3 (RT3, not to be confused with reverse T3= rT3) along with a binding resin into the sample of blood. The T3 that is not able to bind to the non-occupied binding sites on TBG is forced to bind to the resin which is then re-"uptaken" and measured as percentage of that which was added to the serum initially. If there are not a lot of binding sites available, either due to low production of TBG or high amounts of T4, then a high number of RT3 is produced. If there are plenty of binding sites available, either due to accelerated production of TBG or low amounts of T4, then the RT3 uptake will be low as all the RT3 will bind to the available sites and not to the resin.

When T3 uptake is interpreted along with T4 it can serve as a useful confirmatory test for T4 levels as well as give an idea of TBG production and how it is affecting the functional capacity of cells to receive thyroid hormone. If T4 is high, and T3 uptake is also high, then hyperthyroidism is confirmed. If T4 levels are normal and T3 uptake is abnormal, it is most likely a non-thyroid issue, which can still affect the ability of cells to receive thyroid hormone. For example, if T3 uptake is low in the presence of normal T4 levels, then the patient may have a functional hypothyroid due to the fact that there could be less free, bioavailable hormone available is there is an abundance of TBG.

High

- Hyperthyroidism
- Thyroid hormone replacement (especially synthroid which will elevate T4 levels)
- Medications [some medications decrease TBG or production or occupy TBG binding sites such as Dilantin, valproic acid (Depakote), dicumerol, heparin and high dose aspirin]
- Insulin resistance (IR is associated with elevated testosterone also PCOS)
- Elevated testosterone
- Liver disease (chronic liver disease is marked by hypoproteinemia)
- Nephrotic syndrome (severe loss of albumin leaving less binding sites available for RT3)

Low

- Primary hypothyroidism
- Secondary hypothyroidism - anterior pituitary dysfunction
- Selenium deficiency
- Iodine deficiency
- Increased TBG production (in addition to those listed here, other diseases and factors may cause elevated production of TBG such as congenital variances, HIV and some medications)
- Pregnancy
- Liver disease (cirrhosis and acute hepatitis)
- Oral contraception / estrogen therapy

Functional Considerations

T3 uptake is elevated in many females with PCOS because elevated levels of testosterone, Luteinizing Hormone and DHEA associated with IR and PCOS may decrease TBG production. Elevated T3 uptake can serve as a confirmatory test for insulin resistance. When people have IR the body has many compensating mechanism to try to maintain energy production. One of these is to increase insulin like growth factor (IGFBP-1) which down regulates hormone binding quantity and quality in an attempt to make more anabolic hormones available, thereby raising metabolic activity. Without hormone binding proteins, there are more "free" hormones available to attach to receptors.

Related Tests

TSH: Used to evaluate thyroid function and help differentiate primary, secondary or tertiary hypothyroidism. It is part of the evaluation of the hypothalamic-pituitary-thyroid (HPT) axis.
T4 Total and Free: Measuring the actual thyroxine level is helpful in evaluating thyroid function.
T3 Total and Free: Measuring the actual triiodothyronine level is helpful in evaluating thyroid function.
Thyroglobulin Antibodies: This may be seen in autoimmune conditions affecting the thyroid such as Hashimoto's or Graves' disease.
Thyroid peroxidase Antibodies: Often seen in autoimmune thyroiditis and Hashimoto's.
TBG: Measures the actual level of TBG output by the liver and can help in the full evaluation of thyroid function.
Thyrotropin - Releasing Hormone: Evaluates the HPT axis. TRH can help differentiate the causes of thyroid dysfunction by evaluating the release of and response to the TRH from the hypothalamus.
TSH Stimulation: Evaluates the HPT axis. A useful test in evaluating the cause of hypothyroidism by stimulating the thyroid with exogenous TSH.

Reverse T3 (rT3) Optimal: 12-20ng/dl

About 95% of all thyroid hormones produced by the thyroid is T4. T4 must be converted in the Liver, GI and peripheral tissues into T3. There are two main forms of T3: "regular" T3 and "reverse" T3. They are made in approximately equal amounts in the body as part of a buffer system. T3 is very biologically active, while rT3 is biologically "inactive" and is therefore considered an antagonist to thyroid function. It may occupy a thyroid receptor without eliciting a response while keeping regular T3 from binding to the receptor. This is done in order to keep the amount of T3 from overwhelming thyroid receptors.

There are many reasons why the body may decide to make more rT3 rather than regular T3. The deiodinase enzymes responsible for cleaving iodine from T4 making T3 are influenced by many factors. A specific deiodinase enzyme which makes rT3 is activated by inflammatory cytokines in the body. Therefore, if the body is under a great deal of inflammatory stress due to infection, illness, injury or severe nutrient depletion, these cytokines will activate the rT3 deiodinase enzyme in order to conserve energy. It is often seen in terminally ill patients that rT3 will spike late in the illness.

Looking at rT3 by itself is of limited value. It must be part of a complete thyroid laboratory and clinical analysis. Often the most useful part of rT3 is the FreeT3/ReverseT3 ratio. This will give a better picture of peripheral conversion.

High >20

- Hyperthyroidism (all thyroid hormones and metabolites will be elevated)
- Functional Hypothyroidism (see FT3/rT3 ratio below)
- Inflammation
- Tissue Injury
- Infection
- Selenium deficiency
- Iodine deficiency
- Vitamin D deficiency
- Oral contraception / estrogen therapy

Low < 12

- Primary hypothyroidism
- Secondary hypothyroidism - anterior pituitary dysfunction
- Selenium deficiency
- Iodine deficiency
- Increased TBG production (in addition to those listed here, other diseases and factors may cause elevated production of TBG such as congenital variances, HIV and some medications)
- Pregnancy
- Liver disease (cirrhosis and acute hepatitis)
- Oral contraception / estrogen therapy

Free T3 / Reverse T3 ratio (FT3/rT3) Optimal: > .2

Be careful with conversion of measurements. This optimal ratio is using pg/ml for free T3 and ng/dl for reverse T3. Look at your labs to see what your units are and if they are different there are many websites you can visit to do the conversion for you so you get to these units here.

The idea here is that you want to check not just levels of hormone but how your body is converting T4. Remember T4 can be converted and biotransformed into T3, reverse T3 but also T2 and T1. This is why looking at ratios can give a more accurate picture of what the body is doing with thyroid hormone at the cellular level. This ratio has been called the single greatest marker of actual tissue thyroid levels.

A low conversion ratio means the tissues are preferentially making reverse T3 over free T3.

Low < .2

- Functional hypothyroidism (this ratio cannot in itself be a diagnosis of hypothyroidism. However, it can illuminate the fact that many "normal" thyroid patients have an elevated reverse T3 conversion essentially creating a situation where the cells themselves are not supplied with adequate normal T3)
- Inflammation
- Tissue Injury
- Illness
- Selenium deficiency
- Vitamin D deficiency
- Iodine deficiency
- Increased TBG production (in addition to those listed here, other diseases and factors may cause elevated production of TBG such as congenital variances, HIV and some medications)
- Pregnancy
- Liver disease (cirrhosis and acute hepatitis)
- Oral contraception / estrogen therapy

Additional Tests

C-Reactive Protein

Optimal: < .5 mg/L
Persistent levels of .5 – 5 = chronic inflammation
>5 = suspect bacterial infection or MI

C- reactive protein is a protein produced in the liver in response to inflammatory cytokine production in the body. It is a non-specific marker for inflammation that is more sensitive and rapidly elevated than ESR, ferritin or fibrinogen (other acute phase reactants) when inflammation is present. This is why it is called 'highly sensitive" CRP or hsCRP by some labs. Like all non-specific markers of inflammation, it will not indicate the cause of inflammation exactly. However, it is not elevated in all cases of inflammation making it more specific than other acute phase reactants. Its synthesis is stimulated in the presence of antigen-immune complexes (such as in autoimmune), bacteria, fungi, trauma and tissue damage such as heart attacks, strokes or injury. The main trigger for CRP production in the liver is inflammatory cytokines such as IL-6.

It has been observed that CRP tends to be elevated in bacterial infections and not for viral infections. This makes acute elevations of CRP a sensitive and somewhat specific marker for bacterial infections when an illness is suspected, such as upper respiratory illness or meningitis. CRP therefore has been proposed as an excellent biomarker to indicate when to use or not use antibiotic therapy for many infections.

Persistent, mild elevations of CRP have been clearly linked to cardio vascular disease risk. Since vascular compromise to tissues in the heart and brain (and all other tissues as well) lead to chronic low levels of inflammation, CRP can be used to detect and monitor treatment efficacy for heart disease. This is why it is now called "cardio CRP" in most labs.

Short term inflammation in response to injury or illness is appropriate and healthy. However, **there is no optimal safe level of chronic inflammation in the body**. Therefore, it has been proposed that *any* elevation of CRP is abnormal and should be addressed. Healthy individuals have no elevation in CRP and any rise in CRP, no matter the amount, should be investigated, tracked over time and preventive strategies such as diet, exercise and supplementation should be considered.

In general, the higher the CRP the more acute the inflammation and/or trauma is. Elevations above 7mg/L are most likely acute infections and trauma. Mild elevations of .5 – 7 is more than likely chronic, systemic inflammation such as in atherosclerosis and heart disease.

High > .5

- Bacterial infections (respiratory, urinary, meningeal, etc.)
- Autoimmune conditions (RA, SLE, collagen vascular disease, etc.)
- Injury or trauma (severe tissue injury, surgery, soft tissue trauma)
- Cardio-vascular disease
- Myocardial infarction
- Increased risk for stroke
- Neurological disorders (Parkinson's, Alzheimer's, cognitive decline)
- Arthritis
- MTHFR gene polymorphism (will need methylation factors to reduce inflammation)

- Cancer / malignancy
- Systemic inflammation (stress, nutrient deficiency etc.)
- G.I. inflammation (Crohn's, UC, IBS, infection)
- IUD (intra-uterine devices work by causing inflammation in the uterus and may elevate CRP levels)

Functional Considerations

In general, the more elevated the CRP the more acute and severe the trauma. If CRP is mildly elevated and persists for weeks, months or years, then the likelihood of heart disease is greatly enhanced. **Keep in mind that someone taking NSAID's or steroids may have falsely low levels of CRP, but may actually be experiencing one of the above conditions.**

The suggested way to interpret elevated CRP is to order the test twice, about 1-2 weeks apart and observe the trend. If it is initially elevated and subsequent test is going down without therapeutic intervention, then it is likely a self-limiting infection (still may require immune support and natural anti-inflammatories such as curcumin, boswellia etc. for a protective effect). If CRP stays elevated, then it is likely a long-term inflammatory state and should be investigated and treated (the most common – heart disease, autoimmune, nutrient deficiency, stress). Most likely the source of inflammation will be found on physical examination, history and/or other laboratory biomarkers.

There is no safe long-term elevation in CRP. This should be monitored in all individuals as it is a relatively inexpensive test that yields valuable information about that person's inflammatory state. Since inflammation is linked to most chronic degenerative diseases such as arthritis, heart disease, neurological disorders, autoimmune etc., elevated CRP should be aggressively investigated and the source of inflammation found. Natural interventions are the most effective at dealing with inflammation. This test exemplifies PREVENTIVE medicine at its best since early detection and treatment of inflammation could save countless lives and unnecessary illness.

Of course, the underlying source of inflammation needs to be found and resolved. However, the inflammation itself can be immediately addressed using several natural nutrients. Curcumin, boswellia, fish oils, pancreatic enzymes, green tea, grape seed extract, resveratrol, quercetin, N-acetyl cysteine, bromelain and high dose Vit. C have all been found effective at reducing inflammation and CRP levels.

Related Tests

ESR: A non-specific marker of inflammation that will aid in evaluation if systemic inflammation.

Ferritin: Acute phase reactant that will be elevated in acute and chronic inflammation, especially heart disease.

Fibrinogen: Acute phase reactant that when elevated signals increase risk for clotting, heart attack, stroke, emboli, etc.

Creatine Kinase: CRP levels correlate very well with CK in cases of myocardial infarction. If CK levels are high, suspect acute MI.

Alkaline Phosphatase: Enzyme found in bone, liver, soft tissue and will be elevated when those tissues are damaged due to injury, cancer, osteoporosis, etc.

Lactate Dehydrogenase: A marker of tissue damage in heart and muscle.

AST/ALT: Liver enzymes that may be elevated in liver inflammation such as cirrhosis and hepatitis.

Homocysteine: When elevated can contribute to cardio-vascular inflammation.

WBC w/Diff: Helpful in discerning acute from chronic, and bacterial from viral infections.

Autoimmune Panel: Anti-nuclear antibody, rheumatoid factor, uric acid, anti- CCP and anti-streptolysin O may be used to evaluate autoimmune causes of inflammation.

Homocysteine

Optimal Male: 5 – 8umol/L
Optimal Female: 4 – 7umol/L

Homocysteine (Hcys) has been called the best single indicator of whether you are likely to live long or die young. It is both an indicator of many diseases as well as a contributor to other diseases. This means that it will be elevated as a **result of** some diseases and illnesses such as hypothyroidism, autoimmune, and genetic polymorphisms, as well as **contributing to** the risk of heart attacks and strokes by damaging the endothelial lining of the arterial system. It is linked to over 100 diseases in the scientific literature such as heart disease, cancer, stroke, advanced aging, genetic defects, autoimmune, metabolic syndrome, diabetes and inflammation etc. Elevated Hcys (hyperhomocysteinemia) has been investigated for decades and has been the strongest and most consistent predictor of cardio-vascular disease currently known. Familial homocystinuria was investigated in the 1960's by Dr. Kilmer McCully and the children he observed with this condition due to genetic abnormalities suffered from accelerated atherosclerosis and premature aging, often dying of heart disease before the age of 10.

Hcys is an amino acid intermediate formed in the liver as part of the methylation pathway. Methylation is the second largest biochemical action in the body and elevated Hcys is often elevated when a disorder of methylation exists. If methylation is impaired, it may have global body significance due to its role in regulating and protecting gene translation, hormonal control and neurotransmitter regulation.

Most laboratory reference ranges for Hcys are set by looking at populations with the highest risk for cardio vascular disease and setting an upper limit which reflects twice the risk for heart disease. What this means is that, according to most labs with upper limits around 11 mmol/L, by the time you reach this limit, you are now at a significant higher risk for cardio-vascular disease than the general population which dies of cardio-vascular disease. Optimal reference ranges are set by looking at population ranges and mean distributions. This is more of a traditional and accepted way of developing reference ranges. When this method is employed, the numbers are closer to 4-8 mmol/L.

High

- Cardio-vascular disease
- Methylation defect (genetic SNP's such as MTHFR and CBS gene)
- B12 deficiency
- Folate deficiency
- Alzheimer's
- High protein diet
- Hypothyroidism
- Cerebro-vascular disease
- Parkinson's
- Metabolic syndrome
- Autoimmune (SLE, RA, etc.)
- Diabetes (Type I and II)
- Pernicious anemia
- Megaloblastic anemia
- Osteoporosis
- Liver disease
- Systemic inflammation
- High stress (regular meditation has been shown to lower Hcys)

Low

- Malnutrition / malabsorption (protein deficiency, especially sulfur containing amino acids such as methionine, taurine and cysteine)
- Glutathione deficiency
- Hyperthyroidism
- Medications (antibiotics, birth control, tamoxifen, to name a few)
- Liver disease
- Kidney disease (greater mortality in those with CKD and low Hcys)

Functional Considerations

Elevation of Hcys is not always as simple as a B12, B6, folate, magnesium or other nutrient deficiency. Many other factors such as inflammation, liver damage, diet, sedentary lifestyle and prescription drugs may contribute to elevated Hcys. If Hcys is elevated, the cause must be investigated rather than simply giving B vitamins mentioned above. Studies have shown that simply lowering Hcys with large doses of B12, B6 and folate, while effective at lowering Hcys, did not provide the desired cardio-protective or overall mortality protection. This is due to the fact that the underlying cause is not always nutrient deficiencies.

With Hcys, the lower is not always the better. Because Hcys is involved in glutathione production, if Hcys is too low, then there may be impairment in GSH production. Hyperthyroidism may cause low Hcys as well as other disease states.

When Hcys is elevated above 15, it is imperative that it be reduced immediately due to the vascular damage it is causing. This is most significant in the aging brain. Probably the strongest correlation with high Hcys is cognitive and neurological impairment. When the blood supply is compromised due to the obliteration of the micro-vascularization, then that tissue undergoes cell death more rapidly. This is especially true in highly metabolically active tissue, such as in brain and heart. And when this happens in the brain, the effects can be devastating and permanent. This is why it is imperative to be checking these levels in all age groups of the population, so the detrimental effects of hyperhomocysteinemia may be PREVENTED.

Many studies and empirical evidence has shown that vigorous exercise can lower Hcys significantly. Also, removing sugar from the diet and other free radical producing substances such as cigarette smoke, coffee, fried foods and alcohol can also significantly lower Hcys. Interestingly, regular meditation has also been shown in research to lower Hcys. Be careful not to practice bad medicine by simply throwing nutrients or drugs at a problem. Investigate and treat the underlying cause with lifestyle medicine first, and the nutrient supplements will work even better.

Related Tests

See CRP above as all inflammatory markers for cardiovascular disease should be evaluated.

Serum B12: One of the most often overlooked causes of elevated Hcys in elderly and pernicious anemia.

MMA: Urinary MMA is a good indicator of functional B12 status.

MTHFR Gene: Genetic polymorphisms may explain elevated Hcys in which case methyl donors such as SAM'e and Betaine and methylated folate may be necessary to lower levels.

Lipid Panel: Looking at lipids and fractionated lipid profiles can further elucidate true cardiovascular risk. Also, consider apolipoproteins as they are more atherosclerotic and with elevated Hcys greatly increase CVD risk.

Thyroid Function Studies: Thyroid has a significant impact on Hcys production. **Hypothyroidism will elevate CRP and Hcys.**

Vitamin D, 25-OH

Optimal: 40 – 65 ng/ml
Pregnancy: 50 – 75 ng/ml
Short Term Increased Need (athlete, disease states): 75 – 120 ng/ml

Vitamin D3, or cholecalciferol, is a fat-soluble vitamin that acts both as a cofactor in many enzymes, and also a pro-hormone with independent actions on gene and cellular function similar to steroid hormones. The main action of the ***activated*** Vitamin D [1,25 (OH)2 D3] is binding the vitamin D receptor (VDR) found in nearly all tissues. The VDR is involved in regulating (activating or suppressing) nearly a thousand genes in the human genome. Once activated the VDR gene regulates proteins involved in calcium absorption in the gut, cellular apoptosis, osteoblastic activity, calcium/phosphorous balance within the cell as well as plasma, and regulates anion/cation exchange at the cellular membrane level – which is important in cellular respiration and exocytosis. In essence, most cells cannot function properly without Vitamin D.

Food sources are relatively non-existent with only small amounts occurring in fish and cod liver oil, egg yolk, cheese and bovine liver. The body uses sunlight (UVB) to synthesize D3 from cholesterol metabolites made in the liver and skin. D3 must be converted to 1,25 OH Vitamin D in the kidney for the vitamin to be activated. **It is interesting to note that as 25-OH levels rise, 1,25 OH levels may actually decrease.** This paradoxical reaction is why extremely high levels of D3 intake may not be optimal long term. It is estimated by Dr. Holick, one of the foremost researchers of Vitamin D, that in order to make sufficient levels of Vitamin D, it takes a *minimum* of 15 minutes of 80% skin exposure, 3 x week, during the months of April to September (when the sun is not at as much of an oblique angle to the earth) during the daytime hours of 11 am to 4 pm. A minimal erythemal dose is required, which can be seen as the skin getting warm and flushed, but before burning. This is not part of our culture and therefore it is observed that most people who do not take Vitamin D as a supplement are likely to be deficient, especially given the concerns over sunlight exposure and skin cancer.

Vitamin D is one of the most important nutrients for optimal health and the further one lives from the equator, the greater the incidence of Vitamin D deficiency. It is beyond the scope of this lab manual to list the myriad of diseases and ailments associated with low vitamin D. They can be readily found in a multitude of sources. A short list of Vitamin D deficiency and insufficiency - associated illnesses include rickets (<15 ng/ml), depression, anxiety, schizophrenia, bone loss, joint/ muscle pain, increased risk of infection, autoimmune disease progression, cancers such as bone, colon, ovarian, prostate and breast, migraines/other headaches, diabetes, obesity, heart disease, high blood pressure, cardiovascular disease and much more.

THE VITAMIN D CONTROVERSY:

There is a healthy debate among scientists about optimal levels. It has become quite popular in nutritional circles to recommend high doses of Vitamin D for all patients, regardless of blood levels or absence of validated clinical rational. There is a surprising shortage of long term (>2 or even 5 years) studies showing the efficacy of high dose (> 2,000 iu/day) supplementation of Vit D. It is this author's recommendation, after much research and clinical experience, that caution should be used in using high dose Vitamin D for long term. It is abundantly clear the RDA of 400-800 iu/day is grossly insufficient. But recommending levels above 2000 iu should be done with caution and appropriate clinical rationale.

Each person's needs of vitamin D will vary quite a bit based on many factors. Stress, pregnancy, obesity, age, sex, diseases such as infection, autoimmune, multiple sclerosis and cancer, all influence the need and

therapeutic value for Vitamin D supplementation. It is impossible to give a recommendation such as "everyone should be 5,000 or 10,000 iu/day." This is both irresponsible and dangerous.
Over reliance on blood levels. Blood levels of vitamin D do not always reflect true Vitamin D status. There are many metabolites, such as 1,25 OH D3 that are more bioactive but have relatively short half lives and therefore cannot be tested accurately. Furthermore, not everyone needs to be at the same level for optimal function.

A popular method of determining individual Vit. D need is to test for VDR SNP's. This is a genetic test that tests for *possible* decreases in VDR function and number. This should be looked at very cautiously. SNP testing is often overemphasized by practitioners. One should not look at a SNP test and say "you have a VDR SNP therefore you should take more Vit. D." Again, this is both irresponsible and potentially dangerous and reflects a misunderstanding of how genetics work. A SNP is a tendency but not an actual reflection of gene function. Genes are more under the control of EPIGENETIC influences than genetic code. Meaning, genes respond to environmental, lifestyle and dietary cues first and foremost and do not operate solely based on its coded instruction. An example of this for Vit D is that elevated levels of Vitamin D beyond normal physiological amounts, has been shown to downregulate the receptor. Therefore, giving someone high doses of Vit D just because they have a SNP could cause a paradoxical effect of suppression of Vitamin D function. Also, elevated Vitamin D can cause Vitamin D toxicosis, sarcoidosis or worsening of illness.

This author believes that most people will benefit from at least some amount of Vitamin D supplementation. However, the main message here is that high doses of Vitamin D administration long term has not been scientifically validated and moreover, may cause more harm. For example, several studies have shown long term optimal health outcomes improve and all-cause mortality decreases when levels are naturally maintained between 36-40 ng/ml (Am J Clin Nutr 2006). The first recommendation of intake should be based on an initial blood test to determine deficiency. If less than 20 nmol/L and no major illnesses are apparent, start with 2500 – 5000 iu/day and retest in 6-8 weeks. Adjust dosage appropriately to achieve and maintain optimal levels. If a disease such as Crohn's/UC, other malabsorption states or history of cholecystectomy, the required amount of supplementation to achieve higher serum levels may need to be increased to 10,000iu/day.

A person that is relatively healthy, or achieves relative health after treatment, this author recommends that optimal levels be maintained through sunlight exposure as much as possible without burning, and Vitamin D supplementation of 800 – 2,000 iu/day. At these dosages, repeat Vitamin D testing should not have to be done very often once baseline levels are stable and no major changes in a person's health status. If elevated doses of 5,000 iu or greater are given, then testing of Vitamin D, serum and ionic calcium and parathyroid levels should be done at least twice a year.

For further information on Vitamin D, an excellent and well researched article can be found in Dr. Alan Gaby's book Nutritional Medicine (see bibliography).

BASIC (ROUTINE) URINALYSIS

Urinalysis is one of the oldest forms of physical examination and should always be considered a part of a complete examination of a patient. For centuries, physicians have observed the appearance, odor, characteristics and even taste (not recommended this day and age!) of urine to determine the health or illness of the patient. Urine is not only a direct assessment of kidney function, but also blood health and environmental influences on the patient's metabolism. Today, it is still one of the most useful physical examination techniques available, especially with advancing microscopic and exam technology together with a more complete understanding of the complex physiology required for urine formation.
In healthy individuals, urine reflects blood levels for most analytes. Therefore, comparing blood and urine levels of the same analyte can provide insight as to the function of the kidneys. There are also some products that should never be in the urine in any appreciable amounts such as glucose and albumin or proteins. Their presence always signals kidney damage and/or extremely high amount in the blood.
It is very important to note that if one is to do a complete workup of the bodily fluid, it is recommended to do a urinalysis test ***with microscopic*** as opposed to just using a dipstick. The dipstick test, while convenient (can be done in any office or home and results are immediate), is of more limited value compared to a microscopic examination of urine. The dipstick test will show gross abnormalities and acute conditions. However, it will not detect minute changes in urine balance and its preventive value is limited. Much can be hidden in urine that will not show up on dipstick tests. An acute eye can see, under the microscope, urine that has bacteria, small amounts of casts, microalbuminuria, or even crystals signaling a chronic, low-level often asymptomatic condition. This is why it is imperative to order a urinalysis with microscopic from your lab, or perform it yourself if you have a microscope and are trained to do so. This is different from dark-field microscopy, which is useful in its own right.

There are several reasons to run a urinalysis on patients regularly. These include diagnosing and or monitoring renal or urinary tract disease such as glomerulonephritis, to detect metabolic illness such as diabetes or multiple myeloma (Bence-Jones protein), identification of urinary tract infections, kidney stones and even more advanced analyte testing such as hormones and heavy metals.
In general, it is a good idea for a basic urinalysis to be done on the first morning void. This will ensure that the urine is not too diluted and the chance for detecting abnormalities is greater because of the longer period of urine collection in the bladder.

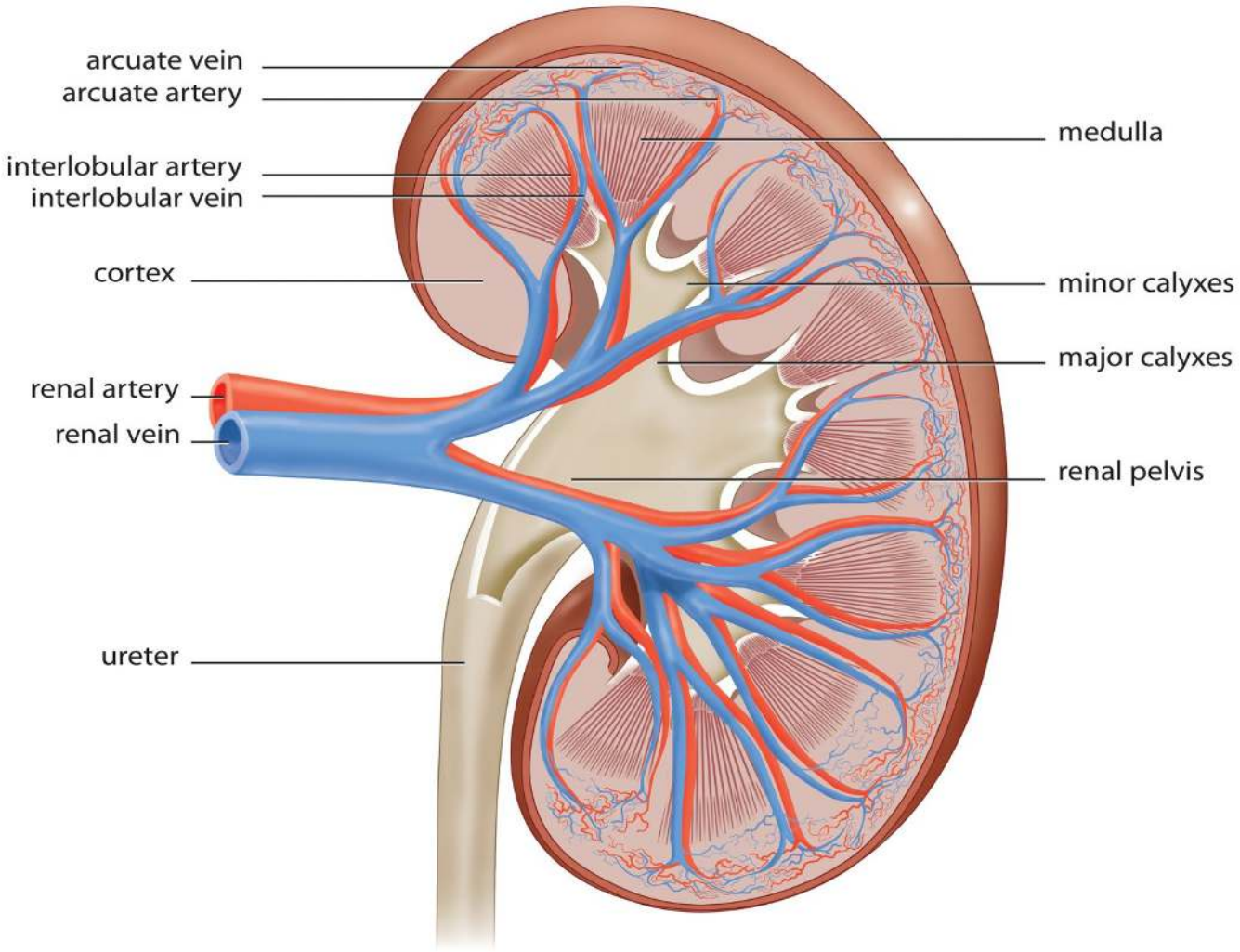
The kidneys are rather affected by internal and external influences. Once damaged, it may be very difficult to repair. Toxins, drugs, pollutants, elevated blood sugar, acids, free radicals, etc. all wear on the kidneys overtime. This modern polluted world and current lifestyle habits are no doubt to blame for the exponential rise of kidney disease. The kidneys main job is to filter out exogenous and endogenous pollutants. If this be impaired in any way, then the entire person and every organ system is affected by increased toxic burden.

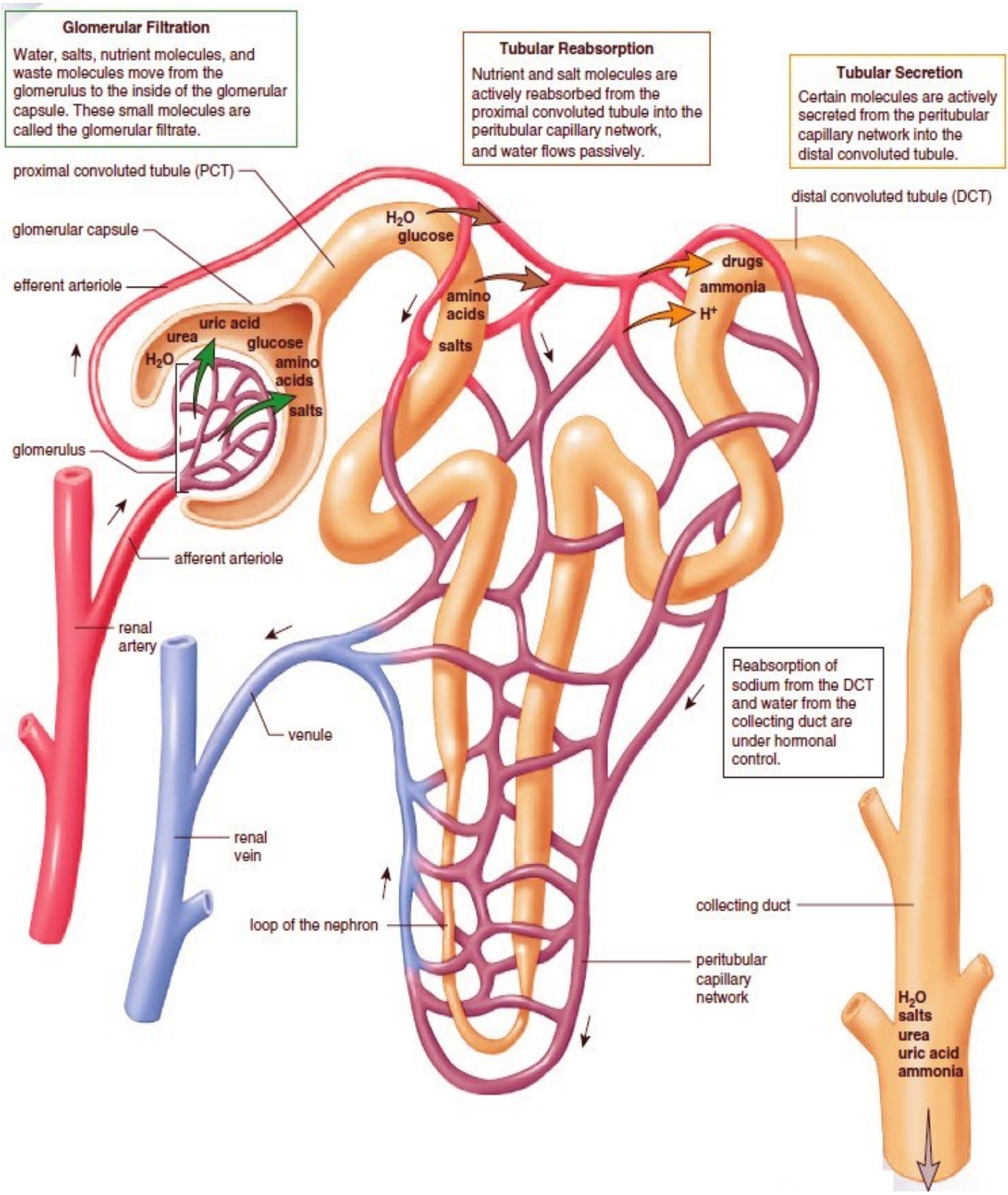
The kidneys require first and foremost blood perfusion. Approximately 1200ml of blood is filtered through the adult kidney **every minute**. Kidneys receive 25% of cardiac output. The glomerular filtration rate produces 180L of urine output per day! Most of this is reabsorbed so that the final urine volume in an adult is about 1-2L per day.

Impairment in kidney perfusion is perhaps the first insult to kidneys as atherosclerosis runs rampant and filtration is therefore limited. This is the main reason why there is so much hypertension, as the kidneys

are responding the decreased blood flow by activating the Renin-Angiotensin System (RAS). If one tries to lower the blood pressure artificially (pharmaceutically), then more toxins and inflammation build up. The kidneys are especially susceptible to free radical damage which is why it is imperative to provide ample amounts of antioxidants and precursors for our own free radical quenchers such as glutathione, cysteine and B-vitamins.

A routine analysis may not detect early kidney damage, which is why it is imperative to assess kidney function using blood and physical examination together with a urinalysis.
The following will provide a functional and traditional perspective on abnormalities in urinary tract system.





Appearance and Characteristics

Optimal: pale to straw yellow and clear of visible solutes, with typical aromatic smell

The yellow color of normal urine is mostly due to the pigment urochrome, which is a bile pigment that is a byproduct of heme metabolism. Bile is converted to urobilinogen by intestinal bacteria and then to urobile or urochrome in the kidneys. The most common influence on color and appearance of urine is hydration level. Hyperhydration will cause pale to clear urine, while dehydration will cause a darker, browner color.

It is important to note that many drugs, metabolites, foods and even urine specimen handling will affect color and appearance of urine. For a list of drugs that effect urine color –see Mosby's Manual of Laboratory and Diagnostic Tests, 4th ed., pp. 1002; or visit http://www.globalrph.com/urine.htm.

Odor:

- Normal urine has an aromatic odor due to volatile acids
- Ammonia/foul – infection
- Sweet – diabetic ketoacidosis or Maple Syrup Urine Disease
- Fecal odor – enterovesical fistula
- Asparagus – consumption of asparagus
- Musty - phenylketonuria

Clear:

- Normal urine should appear clear, with no visible signs of mucous, crystals or cloudy appearance
- Other disorders may produce clear urine such as diabetes mellitus and insipidus so clear urine does not rule out renal or urinary tract disorders.

Cloudy:

- Urinary Tract Infection – due to presence of bacteria, WBC's, pus, necrotic tissue
- Kidney stones and/or crystals – oxalates, phosphates and others
- Mucous due to kidney/bladder disease and or infection
- Phosphaturia – due to renal abnormality in reabsorption of phosphate. If phosphaturia is suspected, put a few drops of vinegar in the urine and it should turn clear.
- Prostatitis
- Sperm in urine
- Vaginal creams
- Lipiduria – triglycerides and cholesterol appear in the urine with nephrotic syndrome
- Chyluria – could be due to filariasis (parasite) infection or lymphatic blockage due to infection or tumors in the UTI causing lymphatic vessel rupture and spillage of lymph fluid into urine.

Red Color:

- Most often due to blood in the urine (hematuria)
- Menstruating female
- Rhabdomyolysis (Myoglobinuria)
- Hemoglobinopathy (hemolytic anemia, sickle cell, RBC destruction due to drugs etc.)
- Tissue injury/trauma
- Hemochromatosis

- Kidney disease – glomerulonephritis, interstitial nephritis, acute necrosis and pyelonephritis
- Severe urinary tract infection
- Kidney or bladder cancer
- Prostatitis
- Porphyria
- Beet consumption
- IV or IM B12 nutrient
- Rifampin and other drugs

Yellow-brown or green-brown color

- Bilirubinemia due to biliary obstruction – shaking specimen will produce a yellow foam

Dark brown or black

- Hemoglobin or myoglobin in more acidic urine will be dark brown. These are present in urine from tissue breakdown, rhabdomyolysis, cancer, hemolytic anemia, hemoglobinopathies etc.
- Bilirubinemia – bile obstruction
- Malignant melanoma
- L-dopa
- Herbs cascara and senna (will also cause colon staining seen on colonoscopy)

Green

- Pseudomonas infection
- Bilirubinemia

Blue – green

- Indican - small intestine bacterial overgrowth / infection
- Certain medications

Orange

- Urobilinogen
- Drugs – phenothiazine, ethoxazene, phenindione, rifampin

Intense Yellow

- B-vitamin intake, especially B1 (thiamine), B2 (riboflavin) and B6 (pyridoxine)
- Dehydration

Urine Specific Gravity Optimal: 1.010 – 1.023

Specific gravity (SG) is measurement of concentration of total solutes in the urine. Since kidney function keeps reabsorption rates tightly controlled, SG may reflect the health of the kidneys. Urea and sodium chloride make up half of total dissolved solutes and total specific gravity.

High

- Dehydration – low H20 intake, diarrhea, vomiting, sweating
- Syndrome of inappropriate antidiuretic hormone – due to pituitary dysfunction
- Reduced renal blood flow – heart failure, renal artery stenosis, hypotension, overmedication of blood pressure drugs.
- Glycosuria (diabetes)
- Proteinuria (kidney disease) – will see other evidence of kidney failure on serum blood tests

Low

- Overhydration
- Diuretics
- Diabetes insipidus
- Renal failure
- Adrenal dysfunction (hypoadrenia)

Urine pH Optimal: 5.5 – 7.5

Urinary pH is both a measure of serum acid-base balance as well as kidney function. Urinary pH reflects dietary habits. An alkaline urine is common after meals. Metabolic acids must be secreted by the kidney so a low pH could reflect system acidosis. An alkaline urine could reflect the kidneys inability to excrete acids (hydrogen, ammonium) and therefore still reflect systemic acidosis. This is why urine pH should always be evaluated with a salivary pH if abnormalities are suspected. Salivary pH will more closely reflect systemic pH than urine in many cases. In most cases, acidic urine reflects an acidic body, while a more basic urine reflects a healthier system.

Foods that increase pH are alkaline foods. These include most vegetables, berries, fish and organic poultry. Acidic foods include sugar, grains, beef, coffee, cheese, cranberries and processed foods.

High (Alkaline)

- Alkalemia – secretion of excess base from blood due to metabolic or respiratory imbalance
- UTI
- Vomiting
- Renal tubular dysfunction – inability of renal tubules to secrete acids
- Kidney stone formation – calcium carbonate, calcium phosphate and magnesium phosphate. The urine should be kept more acidic to prevent formation of these stones.
- HCL deficiency in stomach

Support: If the urine is too basic, it may signal a problem with renal clearance of acids. See general kidney support below. Look at both serum and urine markers for evidence of kidney problems, such as carbon dioxide/anion gap, BUN, Creatinine and crystal formation. Always make sure kidneys are hydrated – drink ½ oz. per pound of body weight minimum.

Low (Acidic)

- Acidemia – excess acids in urine such as sulfuric, phosphoric, hydrochloric, lactic and uric acids
- Ketoacidosis – diabetes, starvation, ketogenic diet (high protein and fat)
- Pancreatic insufficiency – insufficient bicarbonate production
- Acidic diet

Support: Acidic urine is often a sign of dietary habits. Ingestion of sugars, carbohydrates and refined foods lead to acid formation, kidney stones and kidney disease. Remove the acid foods and add plenty of organic vegetables and filtered water. Exercise also facilitates the removal of acids and supports kidney function. Putting four ounces of lemon juice in 2 liters of water will increase pH and decrease calcium oxalates. Stress will also increase acid formation so stress reduction is imperative.

Supplemental Support:

- B-6 (50-100mg)
- Sodium Bicarbonate
- Citrate forms of all minerals, especially magnesium and potassium
- Calcium (yes, calcium supplementation will bind to oxalates in blood and prevent urine formation)
- Trace minerals

Urine Protein

Optimal: 4 – 15mg/DL of urine, usually reported as "Negative."

Protein is a sensitive indicator of kidney function. Normally there should be a very small amount of protein in urine. This is because the glomerular basement membrane is tightly packed and does not allow large molecules such as proteins to pass. Most of the protein in urine is actually from globulins lining the UTI and are post-renal in nature.

If there is a large amount of protein in urine, reported usually as +1, +2 or simply "positive" is usually a sign of glomerular dysfunction and therefore kidney disease. Most of the protein found abnormally is albumin. This can be detected very early in kidney dysfunction and therefore can provide justification for preventive strategies. One must first determine the source of kidney destruction such as oxidative stress, homocysteinemia, drug intake, elevated blood glucose, heavy metals, infection, autoimmune and cardiovascular disease to name a few.

High

- Kidney disease – glomerulonephritis, polycystic kidney disease, nephrotic syndrome etc.
- Malignant hypertension
- Heavy metal poisoning
- Pyelonephritis (infection)
- Autoimmune kidney disease – SLE, Goodpasture
- Congestive heart failure
- Trauma
- Postural proteinuria – as many as 25% of adults may have standing proteinuria but not while lying down. This could be due to kidney ischemia from hyperlordosis or congenital kidney abnormalities. The finding is usually incidental and no other kidney problems seem to manifest.
- Preeclampsia
- Rhabdomyolysis
- Prostatitis

- Bladder cancer
- Amyloidosis

Support: See Kidney support below.

Urine Glucose Optimal: Negative

Normally there should be no glucose in urine. If the concentration of glucose in the blood exceeds 180mg/dL, then glucose is forced through the glomerular apparatus. This can also occur in severe kidney disease.

High

- Elevated blood glucose - Diabetes mellitus, Cushing's, liver disease etc.
- Kidney disease

Support: See Kidney support below.

Urine Ketones

High

- Diabetes mellitus
- Alcoholism
- Starvation, severely restricted diet, anorexia
- Ketogenic diet – no carbohydrates
- Hyperthyroidism
- Severe illness
- Excessive aspirin intake

Support: See Kidney support below.

Urine Blood Optimal: Negative

High

- Kidney stones
- Kidney disease
- Urinary tract infection
- Trauma
- Excessive exercise
- Cancer of urinary tract
- Bladder atrophy (as in the case of menopause or hormone depletion)
- Prostatitis
- Hemolytic uremic syndrome
- Autoimmune hemolysis

Support: See Kidney support below.

Urine Bilirubin Optimal: Negative

There is only a very small amount of bilirubin in normal urine. Bilirubin must be conjugated in the liver in order to be water soluble and therefore pass through the glomerular membrane into urine. If bilirubin is in the urine, it means there is excess bilirubin in the blood, usually due to Hepatobiliary obstruction.

High

- Gallstones
- Extrahepatic duct obstruction – pancreatic tumor, fibrosis, inflammation etc.
- Intrahepatic obstruction – liver metastasis, tumor, hepatocellular disease
- Dubin-Johnson syndrome
- Rotor syndrome

Support: See Kidney support below.

Urine Urobilinogen Optimal: Negative

Urobilinogen is an end product of conjugated bilirubin that has been excreted in the bile and converted by intestinal bacteria into urobilinogen. It is then reabsorbed and re-excreted. Elevations in urobilinogen are therefore a sign of increased load of bilirubin and or decreased excretion by the liver. It accumulates in the blood and enters the urine at when concentrations are high. If urobilinogen is elevated and there is no bilirubin, this is due to hemolysis, and probably not a liver problem.

High

- Elevated RBC destruction - hemolytic anemia, pernicious anemia, hemolysis due to drugs, hematoma, ecchymosis etc.
- Hepatitis
- Liver poisoning

Support: See Kidney support below.

Urine Nitrites Optimal: Negative

Nitrites in the urine are most often due to the presence of bacteria in the urinary tract. Bacteria convert dietary nitrates into nitrites. Keep in mind that not all microorganisms do this and it is possible to have a UTI and this test is negative. It is a rule-in test, not a rule out test. Consider a urine culture if this is positive.

High

- UTI

Support: See Kidney support below.

Leukocyte Esterase Optimal: Negative

Leukocyte esterase is produced by neutrophils. The presence of LE in the urine signals excess WBC's in the urinary tract. This is most often due to infection, but inflammation from other sources is also possible. Consider a urine culture if this is positive.

High

- Possible UTI
- Urethritis
- Cystitis
- UT tumors
- Kidney stones

Support: See Kidney support below.

Urine WBC Optimal: 0-5 cells/ high power field (HPF)

Same as LE but is a direct measurement of WBC and therefore more sensitive and specific. This is only done using a microscopic and not a dipstick.

High

- Possible UTI
- Urethritis
- Cystitis
- UT tumors
- Kidney stones
- Lupus nephritis

Support: See Kidney support below.

Epithelial cells and casts Optimal: 0-5 cells/HPF

Epithelial cells and casts (degenerated cells) are cells that line the urinary tract. Epithelial cells can slough off during injury or inflammation. There are several different types of epithelial cells tested for and can point to source of tissue damage.

Squamous cells usually come from the bladder or urethra and can signal infection, inflammation and/or injury. Normally a small amount of epithelial cells slough off during void. Anything above five cells/hpf signals an abnormal process. Squamous cells are also skin cells and can signify improper collection or handling of specimen. **Transitional** cells are usually in the bladder or urethra. **Renal** tubular cells and casts are highly suggestive of kidney infection or injury. There should be very little to no renal cells present in urine (0-3 cells/hpf)

High

- Infection
- Glomerulonephritis
- Tumor
- Polyps
- Urinary tract injury or trauma
- Inflammation

- Eclampsia
- Heavy metal poisoning

Support: See Kidney support below.

Urine RBCs

Optimal: 0-3 RBC's/HPF

Red blood cells can enter the urine at any point from kidney glomerulus to ureters to bladder to urethra. RBC's can be gross or microscopic (occult). RBC casts suggest kidney glomerulonephritis and kidney origin of disease.

High

- Kidney disease
- Urinary tract infection
- Kidney stones
- Subacute bacterial endocarditis
- Renal infarct
- Trauma to UT
- Excessive exercise
- Cancer of urinary tract
- Prostatitis
- Bladder atrophy (as in the case of menopause or hormone depletion)
- Lupus nephritis
- Goodpasture syndrome
- Malignant hypertension

Support: See Kidney support below.

Urine Casts

Optimal: None Seen

Casts are clumps of dead or degenerated cells and/or cell fragments. They form in renal distal and collecting tubules. For casts to form the urine must be fairly concentrated and acidic. Therefore, they are usually associated with high concentrations of protein, fat or cells and cell fragments. There is usually some degree of renal stasis as well. Casts should not be seen upon routine urine examination.

Hyaline Casts

- Hyaline casts are protein fragments and indicate proteinuria
- Strenuous exercise
- Fever
- Orthostatic proteinuria
- Congestive heart failure
- Chronic renal disease

Granular Casts

- Granular casts can be WBC's or epithelial cells
- UTI
- Renal disease – glomerulonephritis, acute tubular necrosis, nephrosclerosis
- Lead poisoning
- Stress
- Renal transplant rejection

Waxy Casts

- Waxy cast can be cellular fragments or hyaline fragments
- Chronic renal disease
- End stage renal disease – renal failure, nephropathy
- Malignant hypertension
- Glomerulonephritis

Fatty Casts

- Fatty material from degenerated cells coalesce and form fatty droplets with protein
- Nephrotic syndrome
- Diabetic nephropathy
- Glomerulonephritis
- Mercury poisoning
- Fat embolism

Support: See Kidney support below.

Urine Crystals Optimal: None Seen

Normally there should be no visible crystals in the urine. If there are some present, the next step is determining the type of crystal formed. There are many reasons crystals may form in the urine. The most common is kidney stone formation. If crystals are seen in fresh specimens, the person may be forming or have already formed significant stones (nephrolithiasis). In the absence of stones, crystals may form if the urine is too concentrated due to dehydration, or the kidneys are not functioning well (kidney stasis).
pH is one of the most important factors in crystal formation, as different types of crystals only appear in certain pH ranges. A small number of crystals are often non pathologic, but may signal an abnormal process which may eventually lead to pathology. Large amounts of crystals are almost always pathologic.

Calcium Oxalate

- Most commonly formed crystal
- Kidney stone formation
- Formed in normal acid urine < 7
- Increased consumption of oxalate rich foods – spinach, rhubarb, chard, almonds, sesame seeds, soy milk, chocolate, peanuts and others.
- UTI
- Hyperparathyroidism – increase in calcium levels in blood and urine
- Chronic renal disease – if high amount of crystals
- **Large doses of ascorbic acid intake in some individuals will produce oxalates.** If a person develops oxalates while on high doses of vitamin C, reduce to 500mg/day

Support: Acidic urine is often a sign of dietary habits. Ingestion of sugars, carbohydrates and refined foods lead to acid formation, kidney stones and kidney disease. Remove the acid foods and add plenty of organic vegetables and filtered water. Exercise also facilitates the removal of acids and supports kidney function. Putting four ounces of lemon juice in 2 liters of water will increase pH and decrease calcium oxalates. Stress will also increase acid formation so stress reduction is imperative. REMOVE oxalate foods. Remove coffee and caffeine.

Nutrients:

- B-6: pyridoxyl-5-phosphate (50-100mg)
- Sodium bicarbonate salts (500-2000mg bid)
- Calcium (yes, calcium supplementation will bind to oxalates in blood and prevent urine formation)
- Citrate forms of all minerals, especially magnesium and potassium
- Magnesium (200 – 1200 mg)
- Potassium (500mg-1500mg)
- Trace minerals
- Vitamin D (2,000-10,000 iu)

Calcium Carbonate

- Forms in alkaline urine
- Rare

Uric Acid

- Gout
- High protein diet
- Kidney disease
- Forms in acidic urine < 5.5
- Kidney stones
- Lesch-Nyhan syndrome

Support: Gout is multifactorial. The body is usually very acidic, therefore an alkaline diet is recommended (see pH). Although removal of proteins in the diet is important for short–term relief, in most cases it is not just an overconsumption of meats that is the problem. Methylation is also necessary for the proper utilization and elimination of purines, and many gout sufferers have methylation problems. Exercise is also of primary importance to support kidney function.

Nutrients:

- Methylation cofactors (L-5MTHFR, B12, B6, SAMe)
- Devil's claw
- Cherry
- Quercetin
- HCL
- L-Arginine
- Ginger
- Turmeric
- Green tea extract
- Magnesium

Phosphates (calcium, magnesium)

- Usually formed on alkaline urine > 7
- Increased phosphate consumption
- Kidney disease
- UTI
- Vinegar test will confirm phosphate content (see pH discussion)

Support: To acidify the urine, some supplements may be needed. Follow general kidney support suggestions.

Nutrients:

- Cranberry Extract
- Aloe
- UTI support supplements
- Kidney support supplements

Struvite

- UTI
- Forms in alkaline urine so treatment should be to acidify urine

Microorganisms Optimal: None Seen

Properly collected urine from a healthy individual is sterile. Microscopic examination will identify general type of organism (bacteria or yeast). **If positive, order a culture and sensitivity**. If positive, approx. 80% is from E. coli bacteria and a C&S does not have to be performed if you initiate a trial treatment and it is successful. There is some controversy as to whether treatment should be initiated if asymptomatic. Form a functional medicine pro-active perspective, it is not a normal finding and is therefore best treated prophylactically to prevent complications.

Microalbumin Optimal: < 2mg/L

Albumin is the main protein in both blood and urine, making up nearly 60% in both. Therefore, it is easily detected and serves as an early indicator of kidney damage. Albumin is a large protein and is therefore not normally allowed into the urine through the glomerular membrane. A small amount of albumin does get through but is actively reabsorbed. Any disturbance in the glomeruli will allow more albumin through than can be reabsorbed.

Microalbumin (MA) is the term for a small but significant rise in the amount of albumin in the urine. The most common rise in MA is diabetic nephropathy due to increased oxidative stress and glucose damage to the glomeruli. MA can identify kidney disease 5 years before blood tests show abnormalities. If diabetics have positive MA, it is associated with a 5-10 fold increase in CVD mortality.

If a single MA is positive, it is recommended to do a 24 hour collection to better assess extent of kidney damage. It is also evaluated in the context of creatinine since hydration levels can affect MA. **The MA/Creatinine ratio should be 0-25 mg/g.**

High

- Kidney damage, inflammation
- Insulin resistance
- Nephropathy
- Diabetes
- Tissue injury causing elevation of proteins in urine
- Autoimmune kidney disease
- Atherosclerosis
- Cardiovascular disease
- Multiple Myeloma (Bence-Jones proteinuria)

Support: See Kidney support below.

Kidney Support

What makes kidney disease so insidious and so widespread lies in the fact that it is a SILENT KILLER with little to no symptoms until late stage disease is apparent. There is no doubt the kidneys are one of the most crucial organs for health. And there is little doubt that they are one of the organs most affected by our modern lifestyle. Therefore, it is important to remember that in most cases, except rare congenital defects, ***kidney disease is a lifestyle disease.***

The kidneys provide multiple crucial functions. The first is to maintain electrolyte balance and this is directly affected by adrenal input. Therefore, looking at renal health requires addressing adrenal problems immediately. Another function of kidneys is to remove toxic compound from the blood and excrete them from the body. Any impairment in the kidney's ability to do so will have systemic-wide consequences such as heart disease, brain degeneration and cancer.

Therefore it is important to test for kidney function routinely and pay attention to the fine details and signs of kidney problems. Renal health is also one of the top priorities in PREVENTIVE medicine and steps should be taken daily to ensure kidney health. These include:

1. **Exercise everyday**
2. **Drink plenty of clean purified water**
3. **Get regular body work such as chiropractic and massage**
4. **Avoid toxins, plastics and non-organic foods**
5. **Keep blood sugars as low as possible**
6. **Eat an anti-inflammatory diet**
7. **Infrared Sauna (30-60min/day) make sure to shower after and drink plenty of water**
8. **Take supplements which support kidney health daily (see below)**

The first and foremost requirement for kidneys is *adequate blood flow*. The two main reasons for decreased blood flow to the kidneys are

1. **Sedentary Lifestyle**
2. **Atherosclerosis**

The first is a byproduct of our modern world and lack of exercise. The most studied and scientifically accepted way to repair and prevent kidney damage is through moderate, consistent exercise. This is more than just walking through the park once or twice a week. This means doing some high intensity training. Please see Dr. Lundell's 5-element exercise plan for more detail on how to implement a balanced and healthful exercise routine. This is PARAMOUNT for the kidneys!

Atherosclerosis is buildup of fats and scar tissue in the arteries and causes hardening, stiffening and compromised blood flow to the end organ, in this case we are talking about the kidneys. The two main reasons for this are diet and pollutants. Please see Dr. Lundell's anti-inflammatory diet for details on which foods support health and life and prevent atherosclerosis. Pollution is also a major cause of arterial damage and causes inflammation and subsequent depletion of nitric oxide in vessels, causing further damage and narrowing. The best way to avoid toxins is eating organically, removing chemicals from the home, using a water purifier and air purifier.

Note about Proteins and Kidneys: There is some evidence to suggest that protein may contribute to kidney damage. This is only partially true in some end-stage renal disease (ESRD). Many studies have shown

that adverse effects from a protein deficiency outweigh any benefit of protein restriction. High amounts of protein only damage the kidney if it is immuno-stimulatory and from undigested proteins which leak into the blood stream and cause immune reactions and elevated cytokines. Furthermore, the quality of protein is of important consideration. It has been noted in the veterinary community for some time that predatory animals that eat wild game live longer without kidney problems than do animals that are fed domesticated, toxic, obese meat. Human epidemiological studies have confirmed this as well. Therefore, consumption of wild, grass fed, non-domesticated proteins is actually nephron-protective, and will eliminate the iron deficiency of ESRD.

In ESRD, sodium and potassium should be avoided as the filtering mechanisms do not work properly and they may build up in the blood.

And probably the most common source of nephrotoxic compounds is pharmaceutical drugs, especially NSAID's and other over-the-counter medications such as proton pump inhibitors, allergy medication and topical anti-fungals. Antibiotics can also cause kidney damage. Addressing the underlying condition causing the need for such medications is important and is the functional medicine approach.

Another important cause for kidney damage is toxicity, or nephrotoxic compounds. The most common nephrotoxic compounds are glucose and glucose by-products (AGE's) which accumulate with insulin resistance and diabetes. This is related to atherosclerosis because these same compounds also cause atherosclerosis and damage the micro-capillaries to the kidneys. And the AGE's also do direct damage to the basement membrane of the glomerulus. In addition, the more than 100,000 chemicals and drugs which are ingested and/or absorbed on a daily basis, known or unknown, do damage to the delicate filtration mechanisms 24-seven.

Methylation is important for kidney health and a build-up of homocysteine is an important sign of methylation defects and B-vitamin need. See Methylation defect section in blood chemistry pattern section for recommendations on methylation support.

There is scientific evidence now that blunted kidney development and lifelong kidney impairment begins in the womb especially in mothers who are insulin resistant, have compromised blood flow and/or elevated levels inflammatory cytokines during gestation. This damages kidney development and the child is more likely to develop kidney problems in the future. This makes reducing IR and inflammation in our mothers-to-be extremely important for the future of our children.

Hypertension (HTN) is both caused by kidney damage and in turn causes kidney damage. Therefore, if one has HTN, all of the kidney recommendations apply. In order to reduce the damage to the kidneys, it is important to lower the BP to at least 130/90. Remember, BP below 100/70 in an adult over 40 is associated with depression, Parkinson's, Alzheimer's and fatigue. If the kidneys are healthy, the BP will be tightly controlled around 110-120/75-85. Keep in mind, when it comes to **BP – EVERYONE IS UNIQUE.** The most important thing is to track it overtime and only when there is a noticeable and or sharp trend up or down that something needs to be addressed.

Heavy metals are another source of kidney damage. It is recommended that if you find a kidney problem in lab work or the person is diagnosed with renal diseases, run a urinary HM test. Be careful to support kidneys with nutrient supplementation if doing a provocative test which uses chelators to pull HM's from body tissues. This places an increased burden on kidneys and therefore they should be protected. ESRD is not necessarily a contraindication for provocative urinary or blood HM testing. However, if concern is great, you may want to use hair analysis.

Finally, an often overlooked source of kidney damage is chronic UTI's. It is standard practice in medicine to not even look for infection until symptoms appear. It is also standard practice that if bacteria are found on routine UA, it should be left untreated. This is an example of passive medicine and a more proactive approach should be taken to avoid damage due to long-term mild UTI's. See UTI section and run microscopic examinations of urine at least once/year.

Please see below for Autoimmune kidney disorders, as there are a few more considerations in addition to the general kidney health recommendations.

NUTRIENT RECOMMENDATIONS FOR KIDNEY HEALTH:

All of the following have been extensively researched for kidney health. You may not need all of these nutrients, and each person is individual in their specific needs. However, the main point is to ensure plenty of vitamins, antioxidants, free radical quenchers and anti-inflammatories. Many of these compounds have been shown to reverse, yes reverse, kidney damage, especially curcumin, cordyceps, resveratrol, and lipoic acid. These nutrients have multiple effects such as lowering blood pressure, decreasing inflammation and stimulating repair of membrane damage.

- Resveratrol (100-300 mg)
- Quercetin (150-500 mg)
- Curcumin/turmeric
- Lipoic acid (300-1,200 mg)
- Cordyceps (200-500 mg)
- Vitamin D (2,000-10,000 IU)
- Vitamin E (400 mg full spectrum tocopherols and tocotrienols)
- EFA's – broad spectrum containing EPA, DHA, GLA, ALA (2-6 gr)
- L-carnitine (500 – 100 mg)
- Arginine (1,000 - 4,000 mg)
- Multivitamin with plenty of B's (support cellular health and prevention of AGE's)
- Glutathione (GSH is the most potent protector of cells against free radicals)
- NAC (500-2000 mg)
- Olive leaf extract (oleuropein) (100-200 mg)
- Methylation co-factors (homocysteine is extremely nephrotoxic)
- CoQ10 (100-600 mg)
- Adrenal support (see adrenal section in blood chemistry patterns)
- Electrolytes, especially magnesium (200-1000 mg) and calcium (400-1200 mg)
- Iron (if low in blood and on meat restricted diet in ESRD)
- Ginkgo (120-250 mg)
- Green tea extract (500-1000 mg)

UTI

As stated before, approximately 25% or more of women and slightly less in men, have an asymptomatic UTI. The best way to catch this is a microscopic UA as dipsticks will miss most low-level UTI's. The first thing to do for UTI's is to eliminate all sugar. This is the food source for bacteria and while there normally is no glucose in urine, blood and tissue concentrations will go up enough to support bacterial/microbial growth and survival. All carbohydrates and sugars should be eliminated for at least 6 weeks. It may take up to 3 months to completely eradicate a chronic, stubborn UTI.

The next approach should be to increase water consumption in order to increase urine volume and excretion of bacterial colonies in the UT. One of the main causes of UTI in the first place is dehydration,

in many cases due to excess consumption of coffee (which is most often consumed with large amounts of sugar and dairy). Dairy is another food that should be avoided due to its mucogenicity. This will create more mucous for the bacteria to form biofilms and colonies. The AI diet is essential for UTI resolution.
Another important but often overlooked aspect of silent UTI (asymptomatic bacteriuria) is its contribution to immune dysregulation and autoimmune disease. Chronic stimulation of cytokines due to UTI is akin to chronic yeast or bacterial infection in the gut. This leads to abnormal signaling in cytokine production and can lead to TH1/TH2/TH17 and T regulatory cell imbalance. In genetically susceptible persons, this can lead to autoimmune diseases ranging from lupus, to RA to autism in children, even brain degeneration and Alzheimer's in adults. Chronic immune activation can also lead to early immune deficiency and even UTI cancers. Chronic infection has long been associated with development of certain types of cancers. Chronic UTI can also lead to incontinence.
Since most (>90%) of UTI is due to E. coli from the GI tract and over 95% of all UTI is due to some other microbe from the GI system, proper GI health is imperative. If a person has UTI, especially if chronic, a leaky gut and dysbiosis is almost assured to be comorbidity. The AI diet and leaky gut protocol is also imperative (see Leaky Gut rec. under Blood Chemistry Pattern section). SIBO is also likely and should be checked. This means that digestive enzymes and HCL would need to be looked at as well.
Lastly, sexually transmitted diseases can also mask, mimic or contribute to UTI's so take care to test for common STD's if suspected through history or physical exam. Ask patient about sexual intercourse habits and proper hygiene.
Acute and chronic UTI's should follow all the lifestyle recommendations for kidney health. This is the only way to prevent and treat effectively. Of course, if it is a serious UTI, then appropriate antibiotic therapy should be administered. It is my experience however, that most UTI's can be treated naturally, if the person is willing to follow the following recommendations:

1. **Exercise every day, especially high-intensity intervals 3-4x/wk.**
2. **Drink plenty of clean purified water (at least 2/3oz/lb. of body weight for UTI's)**
3. **No carbohydrates or sugars**
4. **Eat an anti-inflammatory diet**
5. **Practice good genito-urinary hygiene**
6. **Treat leaky gut/dysbiosis if present**
7. **Get regular body work such as chiropractic and massage**
8. **WBV can be helpful for pain and for increased urine elimination**
9. **IR sauna is also very helpful (30-45min/day)**
10. **Take supplements which support kidney health daily and antimicrobial (see below)**

<u>Nutrient Recommendations for UTI</u>

- D-Mannose - inhibits adhesion of e. coli to mucous membrane and increase sIgA: 2-4 gr/day
- Aloe extract (200:1): 1,000-4,000 mg
- Berberine (Goldenseal extract): 250-500 mg/day
- Cranberry extract – contains d-mannose and other antimicrobials: 1000-3000 mg. May also do unsweetened cranberry-only juice 4 – 12 oz. day in divided doses.
- Cat's claw: 200-400 mg
- Uva Ursi: 200-400 mg
- Garlic extract (allicin): 500-1000mg
- Probiotics, both oral and vaginal – lactobacillus rhamnosus and reuteri, bifidobacterium, saccharomyces boullardii (5-50 billion cfu, more if on pharmaceutical antibiotics)
- Vitamin C: 2-4gr in divided doses
- Vitamin D: 5,000-10,000 iu
- Zinc: 15-75 mg

- Douche with Yin Care and or 1:1 solution of white vinegar (4 oz. per wash, let sit in vaginal canal for at least 20 min while lying in empty bathtub)
- Hormones – run an adrenal and sex steroid panel as evidence shows that hormonal depletion can be a contributing factor to chronic UTI

Autoimmune Kidney Disease

The first thing to understand in any autoimmune disease (AD) is that while many of them have different signs and symptoms, current scientific understanding reveals that the underlying mechanisms are the same across most autoimmune disorders. The immune system is under constant strain from pollution, stress, nutritional deficiency, increased free radicals and so on. This eventually leads to immune dysregulation where the immune activation by cytokines becomes unable to return to baseline or normal. Immune cells are stimulated and the regulatory mechanisms are overwhelmed. Once a person's immune system learns to make antibodies to (and fails to stop the subsequent immune cascade resulting in cell damage or destruction) then this mechanism can be repeated for many different tissues within the body. Therefore, AD should be looked at as more an underlying immune dysregulation that affects the whole system regardless of whether or not symptoms appear. The classical medical approach is to wait until symptoms are present to treat. This has proven too passive and with nutritional medicine research advancing, the prevention and elimination of autoimmune disease is the preferred method.

It is imperative to protect and monitor the kidneys in any AD. The kidneys are often damaged in many AD such as lupus, RA, Sjogren's and others. The common denominator is INFLAMMATION, INFLAMMATION, INFLAMMATION. It is then the task of the healthcare provider and patient to detect sources for this inflammatory immune dysregulation. Since the kidneys filter out so much of the blood components, the inflammatory cytokines and immune complexes tend to conglomerate, adhere and linger in the kidneys more than anywhere else in the body.

Prevention and eliminating AD is possible. AD can be seen DECADES before symptoms appear. Early detection is key as the longer the immune system is imbalanced, the more difficult it is to reverse. Furthermore, the advancing understanding of what triggers autoimmune diseases in the first reveals common mechanisms that should be addressed in anyone diagnosed with AD. A brief checklist for the provider to refer to is as follows. The proper way to use this checklist is to address all of them systematically and treat what you find, whether the precise mechanism of how this relates to the specific AD disease symptom is understood or not.

1. **Leaky gut (LG) and dysbiosis** – probably the single greatest source of SYSTEMIC immune dysfunction. Repairing the gut is an absolute must. Functional stool tests are invaluable at evaluating pathologic and commensal microbial environments and can be of great aid in directing individual therapy. See LG section for more detailed treatment recommendations.
2. **Hormones** – quite possibly the second most important factor behind LG. Several AD display higher female preferences. This is most likely explained, at least in part, by the influence of hormones on the immune system. Imbalances in steroid hormones may negatively affect immune balance and should therefore be addressed as part of a functional AD workup.
3. **Food allergies** – eating certain foods, especially in the presence of LG, may create immune complexes and activate inflammatory mechanisms. Certain food can also cross react with self-proteins, thereby mimicking an antigen and triggering an immune response.
4. **Detoxification** – many AD persons have impairment in biotransformation and elimination. A thorough look at Phase I and Phase II capabilities is imperative. This is often done with genetic testing to look at SNP's and genetic susceptibility, all of which can be modified using diet, lifestyle and targeted nutritional therapy

5. **Heavy metals and other pollutants** – some people have immune reactions to heavy metals and pollutants. In addition to being potentially inflammatory at any level regardless of sensitivity or not, there are certain individuals that either make antibodies to or cross react (or both) to pollutants and xenobiotics. Studies have confirmed that in some individuals who develop glomerulonephritis, a recent exposure in inhaled chemicals (paint, fuel etc.) was more frequently found than in controls.
6. **Stress** – almost anyone with Crohn's disease will tell you that stress is one of the biggest triggers.
7. **Diet** – sugars impair WBC function. Dysglycemia seems to be correlated with many AD's as well as consumptions of pollutants, GMO's and inflammatory, processed foods.
8. **Infection** – infection with certain viruses or bacteria, even parasites, have been shown to trigger autoimmune attacks in some. Look to common sources or chronic fulminant infection such as gut, lungs, teeth, urinary tract as well as systemic infections such as Lyme's or CMV.
9. **Cytokine assay** – checking cytokine and CD4/CD8 ratios can help determine how the immune system is behaving and how best to modulate it as there are certain nutritionals that can help dampen specific cytokines, or stimulate others in order to bring more balance and harmony to the immune.
10. **Elimination** – eliminate caffeine, alcohol and OTC medications.

Nutritional support for AD and Kidney AD

- In addition to the above mentioned kidney supported nutrients (see kidney support section), the following are studied immune modulators that can help support immune balance:
- DHEA has been shown to be very helpful in many AD: 25-100 mg
- Melatonin: 500 mcg-10 mg; has potent immunomodulatory effects
- Boswellia: 100 mg
- Grape seed: 100-400 mg
- Plant sterols: 20-50 mg
- Probiotics: run stool analysis to determine which ones
- Ginger: 2-4 gr/day as either capsule or tea
- Glutamine: 2-5 gr bid; may help repair basement membrane
- Chlorella: 500-2,000 mg
- Selenium: 400 – 1,200 mcg
- Zinc: 25-150 mg; make sure to add small amount of copper if on zinc for more than 6 weeks
- See NFkB modulators in functional medicine notes – NFkB has been shown to be upregulated in most AD.

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Lab Evaluation Form – Traditional Groupings

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
CBC (INCL. DIFF/PLT):						
White Blood Cell Count	5.5 - 8.5 thous/uL					
Red Blood Cell Count	Fem 4.1-4.7 mill/uL Male 4.4-5.2 mill/uL					
Hemoglobin	Fem 13 - 14.5 g/dL Male 14.5 - 16 g/dL					
Hematocrit	Fem 37 - 45% Male 42 - 48%					
MCV	83-92 femtoliters (fL)					
MCH	28 - 31 pg					
MCHC	32.5 – 35 g/dL					
RDW	11 - 13%					
Platelet Count	195 - 320 thousand/uL					
Mean Platelet Volume	8 - 10.5 fl					
Neutrophils	45 - 65%					
Lymphocytes	25 - 35%					
Monocytes	3-7%					
Eosinophils	1 - 3%					
Basophils	0 - 1%					
Neutrophils (Absolute)	2000 - 6000 cells/uL					
Lymphocytes (Absolute)	1500 - 3300 cells/uL					
Monocytes (Absolute)	250 - 750 cells/uL					
Eosinophils (Absolute)	10 - 300 cells/uL					

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Basophils (Absolute)	10 - 100 cells/uL					
ESR	4 - 10 mm/hr					
**********						
CMP:						
Glucose, Fasting	70 - 88 mg/dL					
Hemoglobin A1c	4.7 - 5.4%					
BUN (Urea Nitrogen)	12 - 19 mg/dL					
Creatinine	.6 - .9 mg/dL					
BUN/Creatinine Ratio	12 - 18					
eGFR	> 59					
Sodium	138 – 142 mmol/L					
Potassium	4 - 4.6 mmol/L					
Anion Gap	8 - 12					
Chloride	100 - 107 mmol/L					
CO2	22 - 28 mmol/L					
Phosphorus	3.2 - 4 mg/dL					
Calcium	9.2 - 9.8 mg/Ll					
Magnesium, serum	2 - 2.5 mg/dL					
Magnesium, RBC	5-7 mg/dL					
Uric Acid	Fem 3.5 - 6 mg/dL Male 4 - 6.5 mg/dL					
Protein, Total	6.9 - 7.5 g/dL					

Lab Evaluation Form – Traditional Groupings

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Albumin	4 - 4.7 g/dL					
Globulin	2.5 - 3.2 g/dL					
A/G Ratio	1.4 - 1.8					
Bilirubin, Total	.2 - .8 mg/dL					
Bilirubin, Indirect	.2 - .8 mg/dL					
Bilirubin, Direct	0 - .2 mg/dL					
Alkaline Phosphatase	Adult 60 - 90 U/L Child 80 - 120 U/L					
GGT	Fem 10 - 30 U/L Male 10 - 40 U/L					
Creatine Kinase (CK,CPK)	Fem 40 - 90 U/L Male 60 - 135U/L Infant to Toddler 65 - 350 U/L					
LDH (Lactate Dehydrogenase)	125 - 175 U/L (LD or LDH)					
AST (SGOT)	12 - 27 U/L					
ALT (SGPT)	12 - 27 U/L					
**********						
LIPID PANEL:						
Cholesterol	Fem 140 - 195 mg/dL Male 145 - 185 mg/dL					
Triglycerides	30 - 85 mg/dL					
LDL	< 100 mg/dL					
HDL	> 60 mg/dL					
LDL/HDL Ratio	1 - 2					
VLDL	10 - 30 mg/dL					

Lab Evaluation Form – Traditional Groupings

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
CRP, Cardiac	< .5 mg/L					
Homocysteine	Fem 4 - 7 umol/L Male 5 - 8 umol/L					
Fibrinogen Activity	250 - 350 mg/dL					
**********						
IRON STUDIES:						
Iron, Serum	60 - 135 ug/dL					
Ferritin	Fem 20 - 90 ng/mL Fem (meno.) 25 - 115 Male 25 - 125 ng/mL					
TIBC	275 - 375 mcg/dL					
UIBC	190 - 375 ug/dL					
Iron Saturation	21 - 35%					
**********						
THYROID:						
T-3 Uptake /THBR	27 - 33%					
T4 (Thyroxine) Total	7.5 - 11 mcg/dL					
T4 (Thyroxine), Free	1.0 - 1.5 ng/dL					
TSH (Thyrotropin)	1.0 - 2.5 mIU/L					
T-3, Total	115 - 185 ng/dL					
T-3, Free	2.7 - 3.7 pg/mL					
Reverse T-3 (rT3)	12 - 20 ng/dL					
Free T-3/ Reverse T-3 Ratio (FT3/rT3)	> .2					

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Thyroid Peroxidase	0-20 IU/mL					
Thyroglobulin Antibody	0-0.5 IU/mL					
Free T4 (Thyroxine) Index	2 - 3.5					
**********						
OTHER:						
Sex Hormone Binding Globulin	Fem 35 - 100 nmol/L Fem (Postmenopausal) 25 - 100 nmol/L Male 20 - 50 nmol/L					
Vitamin D (25-Hydroxy)	40 - 65 ng/mL					
Antinuclear Antibodies, IFA	Negative					
RA Latex	0-9 IU/mL					
**********						
URINALYSIS, COMPLETE:						
URINALYSIS GROSS EXAM						
Color	Yellow					
Appearance	Clear					
Specific Gravity	1.005 - 1.030					
pH	6 - 7					
Glucose	Negative					
Bilirubin	Negative					
Ketones	Negative					
Occult Blood	Negative					
Protein	Negative/trace					

Lab Evaluation Form – Traditional Groupings

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Nitrite, Urine	Negative					
WBC Esterase	Negative					
Urobilinogen, Semi-Qn	0.2 - 1.0 EU/dL					
MICROSCOPIC EXAMINATION						
WBC	0 - 5/HPF					
RBC	0 - 0.2/HPF					
Epithelial Cells (non-renal)	0 - 10/HPF					
Bacteria	Not seen/Few					
Casts	None seen					
Cast Type	N/A					
Mucus Threads	Not established					

Lab Evaluation Form – Traditional Groupings

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE

Lab Evaluation Form – LabCorp Spreadsheet

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
CMP:						
Glucose, Serum (Fasting)	70 - 88 mg/dL					
Hemoglobin A1c	4.7 - 5.4%					
Uric Acid, Serum	Fem: 3.5 - 6 mg/dL Male: 4 - 6.5 mg/dL					
BUN	12 - 19 mg/dL					
Creatinine, Serum	.6 - .9 mg/dL					
eGFR	>59					
BUN/Creatinine Ratio	12 - 18					
Sodium, Serum	138 - 142 mmol/L					
Potassium, Serum	4 - 4.6 mmol/L					
Anion Gap	8 - 12					
Chloride, Serum	100 - 107 mmol/L					
Carbon Dioxide, Total	22 - 28 mmol/L					
Calcium, Serum	9.2 - 9.8 mg/dL					
Phosphorus, Serum	3.2 - 4 mg/dL					
Magnesium, RBC	5-7 mg/dL					
Protein, Total, Serum	6.9 - 7.5 g/dL					
Albumin, Serum	4 - 4.7 g/dL					
Globulin, Total	2.5 - 3.2 g/dL					
A/G Ratio	1.4 - 1.8					

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Bilirubin, Total	.2 - .8 mg/dL					
Bilirubin, Direct	0 - .2 mg/dL					
Alkaline Phosphatase	Adult: 60 - 90 IU/L Child: 80 - 120 IU/L					
Creatine Kinase, Total, Serum	Fem 40 - 90 U/L Male 60 - 135 U/L Infant to Toddler 65 - 350 U/L					
LDH	125 - 175 IU/L (LD or LDH)					
AST (SGOT)	12 - 27 IU/L					
ALT (SGPT)	12 - 27 IU/L					
GGT	Fem 10 - 30 IU/L Male 10 - 40 IU/L					
Iron Bind. Cap. (TIBC)	275 - 375 ug/dL					
UIBC	190 - 375 ug/dL					
Iron, Serum	60 - 135 ug/dL					
Iron Saturation	21 - 35%					
Ferritin, Serum	Fem 20 – 90 ng/mL Fem (meno) 25 - 115 Male 25 - 125 ng/ml					
Vitamin D, 25-Hydroxy	40 - 65 ng/mL					
**********						
LIPIDS:						
Cholesterol, Total	Fem 140 - 195mg/dl Male 145 – 185 mg/dL					
Triglycerides	30 - 85 mg/dL					
HDL Cholesterol	> 60 mg/dL					

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
VLDL Cholesterol Cal	10-30 mg/dL					
LDL Cholesterol	< 100 mg/dL					
LDL/HDL Ratio	1 - 2					
C-Reactive Protein, Cardiac	< .5 mg/L					
**********						
THYROID:						
Homocysteine, Plasma	Female: 4 - 7 umol/L Male: 5 - 8 umol/L					
TSH	1.0 - 2.5 uIU/mL					
Thyroxine (T4)	7.5 - 11 ug/dL					
T3 Uptake	27 - 33%					
Free Thyroxine Index	2 - 3.5					
Triiodothyronine (T3)	115 - 185 ng/dL					
Triiodothyronine (T3) Free, Serum	2.7 - 3.7 pg/mL					
Reverse T3, Serum	12 - 20 ng/dL					
T4, Free (Direct)	1.0 - 1.5 ng/dL					
Thyroid Peroxidase (TPO) Ab	0 - 20 IU/mL					
Thyroglobulin Antibody	0 - 0.5 IU/mL					
**********						
IMMUNOASSAY:						
Sex Horm Binding Glob, Serum	Fem 35 - 100nmol/L Fem (postmeno) 25 - 100 nmol/L Male 20 - 50 nmol/L					

Lab Evaluation Form – LabCorp Spreadsheet

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
SEROLOGY/ IMMUNOLOGY:						
Antinuclear Antibodies, IFA	Negative					
RA Latex	0 - 9 IU/L					
Fibrinogen Activity	250 - 350 mg/dL					
**********						
CBC, PLATELET CL, AND DIFF:						
WBC	5.5 - 8.5 x10E3/uL					
RBC	Fem 4.1 - 4.7 Male 4.4 - 5.2 x10E6/uL					
Hemoglobin	Fem 13 - 14.5 g/dL Male 14.5 - 16 g/dL					
Hematocrit	Fem 37 - 45% Male 42 - 48%					
MCV	83-92 femtoliters (fl)					
MCH	28 - 31 pg					
MCHC	32.5 – 35 g/dL					
RDW	11 - 13%					
Platelets	195 - 320 x10E3/uL					
Neutrophils	45 - 65%					
Lymphs	25 - 35%					
Monocytes	3 - 7%					
Eos	1 - 3%					
Basos	0 - 1%					
Neutrophils (Absolute)	2.0 - 6.0 x10E3/uL					

Lab Evaluation Form – LabCorp Spreadsheet

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Lymphs (Absolute)	1.5 – 3.3 x10E3/uL					
Monocytes (Absolute)	0.25 - 0.75 x10E3/uL					
Eos (Absolute)	0.01 – 0.3 x10E3/uL					
Baso (Absolute)	0.01 – 0.1 x10E3/uL					
Immature Granulocytes	%					
Immature Grans (Abs)	0 - 0.1 x10E3/uL					
Sedimentation Rate-Westergren (ESR)	4 - 10 mm/hr					
**********						
URINALYSIS, COMPLETE:						
URINALYSIS GROSS EXAM						
Specific Gravity	1.005 - 1.030					
pH	6 - 7					
Urine-Color	Yellow					
Appearance	Clear					
WBC Esterase	Negative					
Protein	Negative/trace					
Glucose	Negative					
Ketones	Negative					
Occult Blood	Negative					
Bilirubin	Negative					

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE
Urobilinogen, Semi-Qn	0.2 - 1.0 EU/dL					
Nitrite, Urine	Negative					
MICROSCOPIC EXAMINATION:						
WBC	0 - 5/hpf					
RBC	0 - 0.2/hpf					
Epithelial Cells (non-renal)	0 - 10/hpf					
Casts	None seen					
Cast Type						
Mucus Threads	Not established					
Bacteria	Not seen/Few					

Lab Evaluation Form – LabCorp Spreadsheet

Patient Name _____ Age _____ Sex_____

ANALYTE	FUNCTIONAL RANGE	DATE	DATE	DATE	DATE	DATE