STAY OPTIMAL

An Insider's Guide to Your Patients' Blood Biomarkers

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Introduction

As medical practitioners, how can we best provide our patients with insight into their health? If we're to do this in a truly valuable way, then our focus can't merely lie on our patients' illnesses and conditions — patients want more than just a diagnosis.

We need to offer guidance on the overall state of our patients' health, what conditions they are at risk for, and what actionable steps they can take to assist them in their journey toward optimal health.

This principle lies at the core of Functional Medicine. One of the most effective ways that practitioners can exercise this idea is through testing for their patients' blood biomarkers.

Blood biomarkers offer a window into the body's complex functions, and when examined via functional analysis, these same biomarkers provide a comprehensive and contextual roadmap of your patient's health.

Tracking biomarker changes over time will help you **provide answers and insights into your patients' health** — enabling them to live a more optimal life.

Learn more about OptimalDX >

How to use this guide

Blood testing can present an overwhelming array of biomarkers that may serve as direct indicators of your patient's health, as indirect clues toward the root of the problem, or even as red herrings.

This guide offers an overview of the most significant biomarkers associated with major systems in the body to help clarify the results of blood testing. You can skip ahead to the sections that seem most relevant to you, bookmark it to return to key sections later, or read through the guide in its entirety to gain a broad understanding of what the different biomarkers in a blood test may signify.

Each section discusses significant biomarkers in depth and what their increased or decreased levels may signify. These sections also include a list of additional, but less-significant biomarkers that may prove useful when assessing your patient's health.

Finally, we've included a section at the end of this guide labeled "Additional support for practitioners" that discusses useful tools and training to assist in measuring and tracking these biomarkers and supporting your efforts toward maintaining your patients' optimal health.

Limits of Liability & Disclaimer of Warranty

We have designed this book to provide information regarding the subject matter covered. It is made available with the understanding that the authors/publishers are not liable for the misconception or misuse of information provided.

The purpose of this book is to educate. It is not meant to be a comprehensive source for the topic covered and is not intended as a substitute for medical diagnosis or treatment or intended as a substitute for medical counseling. Information contained in this book should not be construed as a claim or representation that any treatment, process or interpretation mentioned constitutes a cure, palliative, or ameliorative. The information covered is intended to supplement the practitioner's knowledge of their patient. It should be considered as adjunctive support to other diagnostic medical procedures.

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Blood Sugar Regulation & Energy

These biomarkers can keep you informed of the functional health of your patient's blood sugar regulation. By measuring these biomarkers, you can see whether there is a growing trend towards hypoglycemia, metabolic syndrome, or insulin resistance. If left unassessed and untreated, long-standing blood sugar dysregulation may lead to hyperinsulinemia or type 2 diabetes.

GLUCOSE

Blood glucose levels are regulated by several important hormones, including insulin and glucagon. Glucose is directly formed in the body from carbohydrate digestion and by the conversion of other sugars, such as fructose, and fats in the liver.

- **Increased** blood glucose levels are associated with types 1 and 2 diabetes, metabolic syndrome, and insulin resistance.
- **Decreased** blood glucose levels are associated with hypoglycemia.

HEMOGLOBIN A1C

Hemoglobin A1C, also known as glycohemoglobin, is formed when glucose and hemoglobin combine over the course of a red blood cell's lifespan, which lasts about 120 days. The amount of glycohemoglobin formed is in direct proportion to the amount of glucose present in the bloodstream during this 120-day lifespan.

In the presence of high blood glucose levels (hyperglycemia), the amount of hemoglobin that is converted into glycohemoglobin increases, and a patient's **hemoglobin A1C levels will be high.**

Hemoglobin A1C is used primarily to monitor long-term blood glucose control and to help determine therapeutic options for treatment and management. The closer hemoglobin A1C levels are kept to normal, the less likely those patients are to develop the long-term complications of diabetes.

INSULIN: FASTING

Insulin is the hormone released in response to rising blood glucose levels and decreases blood glucose by transporting glucose into the cells. Often, people lose their ability to use insulin to effectively drive blood glucose into energy-producing cells. This is commonly known as insulin resistance and is associated with **increased levels of insulin** in the blood. Excess insulin is associated with greater risks of:

Heart attack | Stroke | Metabolic syndrome | Diabetes

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ADDITIONAL BIOMARKERS

In addition to the above, the following biomarkers and biomarker ratios can provide insight into your patient's blood sugar and energy regulation:

- Estimated average glucose (eAG)
- C-Peptide
- Fructosamine
- GlycoMark, or 1,5-anhydroglucitol
- Adiponectin
- ALT:AST ratio

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Electrolytes & Acid-Base Balance

An electrolyte imbalance can affect the body's acid-base system, hydration, and even the movement of ions across the cell membrane. Symptomatically, an electrolyte balance can show up as:

- Low blood pressure
- Cold hands or feet
- Poor circulation
- Swelling in the ankles
- Immune insufficiency

CHLORIDE

Chloride plays an important role in human physiology by regulating the acid-base balance in the body. The amount of serum chloride is carefully regulated by the kidneys.

- **Increased** chloride levels are associated with metabolic acidosis.
- **Decreased** chloride levels are associated with metabolic alkalosis.

Chloride is an important molecule in the production of hydrochloric acid in the stomach — as a result, decreased levels of serum chloride are associated with hypochlorhydria, or low stomach acid levels.

CARBON DIOXIDE (CO_2 OR BICARBONATE)

The CO_2 component of bicarbonate (HCO_3, a byproduct of the body's metabolism) is available for acid-base balancing. Bicarbonate neutralizes metabolic acids in the body.

- **Increased** CO_2 levels are associated with metabolic alkalosis and hypochlorhydria.
- **Decreased** CO_2 levels are associated with metabolic acidosis.

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POTASSIUM

Potassium is one of the main electrolytes in the body. It plays an essential role in:

- Nerve conduction
- The maintenance of osmotic pressure
- Muscle function
- Cellular transport via the sodium-potassium pump
- Acid-base balance

The majority of potassium in the body is intracellular. However, because of potassium's critical functions in human metabolism and physiology, it is essential for the body to maintain optimal serum levels even though only a small concentration is found outside of the cell. Additionally, potassium concentration is greatly influenced by adrenal hormones. As such, potassium levels can be a marker for adrenal dysfunction in addition to acid-base balance and general electrolyte status.

SODIUM

Sodium plays an important role as a blood electrolyte. It constitutes 90% of electrolytes in the extracellular fluid, where it is the most prevalent cation. Sodium functions to maintain osmotic pressure and acid-base balance and aids in nerve impulse transmission and renal, cardiac, and adrenal functions. Sodium serves as a general marker for acid-base balance and electrolyte status.

- **Increased** sodium levels are most often due to dehydration (sweating, diarrhea, vomiting, polyuria, etc.) or adrenal stress.

- **Decreased** sodium levels are associated with adrenal insufficiency and edema.

ANION GAP

The anion gap is the measurement of the difference between the sum of the serum cations (sodium and potassium) and the sum of the serum anions (CO2/bicarbonate and chloride). The difference between these two reflects the concentrations of other, unmeasured extracellular anions, such as phosphates, sulfates, ketones, proteins, and lactic acid. An increase in these unmeasured anions is associated with acidosis and thiamine deficiency.

ADDITIONAL BIOMARKERS

In addition to the above, the sodium:potassium ratio can assist you in assessing your patients' functional health.

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Enzymes

These enzyme biomarkers have traditionally been the go-to biomarkers for assessing and diagnosing acute pancreatitis and/or damage to the pancreas itself. From a more functional perspective, we can look at these enzyme biomarkers to aid in the detection of pancreatic inflammation, pancreatic insufficiency, and hepatobiliary dysfunction.

AMYLASE

Amylase converts starch into sugar and is produced primarily in the salivary glands and pancreas.

- **Increased** amylase levels are seen with inflammation of the pancreas (pancreatitis) or salivary glands.
- **Decreased** amylase levels are seen with pancreatic insufficiency, a dysfunction of the pancreas leading to a decreased output of pancreatic enzymes.

LIPASE

Lipase is produced primarily in the pancreas and supports the body in fat digestion.

- **Increased** lipase levels are seen with inflammation of the pancreas (pancreatitis) and gallbladder dysfunction.
- **Decreased** lipase levels may be seen with pancreatic insufficiency.

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Red Blood Cell Health & Oxygenation

The following biomarkers are primarily helpful for assessing the degree of anemia in your patient, a condition in which there are not enough healthy red blood cells to carry oxygen around to the tissues of the body. Knowing that your patient is anemic is not enough; you need to know the cause of the anemia.

Commonly, nutritional deficiencies are the culprit behind anemia, especially iron and vitamin B12, but you must also rule out other causes that are not nutrition-related. The biomarkers listed below can help you in this task, as well as the nutrient biomarkers covered elsewhere in this guide.

RED BLOOD CELL COUNT

A red blood cell count determines the total number of red blood cells, or erythrocytes, found in a cubic millimeter of blood. The red blood cell carries oxygen from the lungs to the body tissues and transfers carbon dioxide from the tissues to the lungs, where it is expelled.

- **Increased** red blood cell levels are associated with dehydration, stress, a need for vitamin C, and respiratory distress such as asthma.
- **Decreased** red blood cell levels are primarily associated with anemia.

HEMATOCRIT

The hematocrit represents the percentage of a known volume of centrifuged blood that consists of red blood cells.

- **Increased** hematocrit levels are associated with dehydration. This is also associated with, but by no means diagnostic of, asthma or emphysema. Because the blood is insufficiently oxygenated under these conditions, the body will increase the red blood cell count to increase the number of cells that can be oxygenated. The hematocrit will go up accordingly.
- **Decreased** hematocrit levels are associated with anemia, though observing decreased levels of hematocrit alone can't tell you much about the cause and type of anemia. The hematocrit should be evaluated with the other biomarkers on a complete blood count/hematology panel to learn more.

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HEMOGLOBIN

Hemoglobin carries oxygen in red blood cells. The oxygen-combining capacity of the blood is directly proportional to the hemoglobin concentration.

- **Increased** hemoglobin levels are associated with dehydration.
- **Decreased** hemoglobin levels are associated with anemia. Measuring hemoglobin is useful to determine the cause and type of anemia and for evaluating the efficacy of anemia treatment.

ADDITIONAL BIOMARKERS

These additional biomarkers can provide you insight into your patient's functional health as well:

- Mean corpuscular volume (MCV)
- Mean corpuscular hemoglobin (MCH)
- Mean corpuscular hemoglobin concentration (MCHC)
- Red cell distribution width (RDW)
- Platelets
- Mean platelet volume (MPV)

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Metabolic Health

The metabolic health biomarkers are helpful for assessing systems in the body associated with energy, strength, endurance, and overall performance.

CREATININE KINASE (CPK)

Creatine kinase (CPK) is a group of enzymes found in skeletal muscle, the brain, and the heart muscle. Damage to one or more of these tissues will liberate CPK into the serum, thus raising serum levels. CPK catalyzes the breakdown of adenosine triphosphate (ATP) into adenosine diphosphate (ADP), a process that liberates high-energy phosphate for metabolic processes such as muscle contraction.

- **Increased** CPK levels are associated with muscle damage or breakdown, damage to the heart muscle as in an acute heart attack, heavy exercise, and brain damage or inflammation. As levels of CPK increase, your patients may notice a negative shift in recovery time as well as impairment in endurance and overall performance indicators.

- **Decreased** CPK levels may be seen in chronic muscle atrophy.

URIC ACID

Uric acid is produced as an end-product of purine, nucleic acid, and nucleoprotein metabolism. Levels can increase due to overproduction by the body or decreased excretion by the kidneys.

- **Increased** uric acid levels are associated with gout, atherosclerosis, oxidative stress, arthritis, kidney dysfunction, circulatory disorders, and intestinal permeability.

- **Decreased** uric acid levels are associated with detoxification issues, molybdenum deficiency, B12/folate anemia, and copper deficiency.
  The typical focus of uric acid measurement is to assess the risk for gout, renal failure, and leukemia. However, this marker is also a strong indicator of potential inflammation and metabolic disturbance in the body.

ADDITIONAL BIOMARKERS

These additional biomarkers can be helpful in assessing your patients' metabolic health as well: Parathyroid hormone (PTH); Leptin

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Adrenal Health

The following biomarkers are helpful for assessing the functional health of your patient's adrenal glands.

The adrenal glands produce the glucocorticoid and mineralcorticoid hormones in response to stress, resulting in "the fight or flight" response.

Unfortunately, when the body is under constant stress — which is quite common — the adrenal glands become less functional. Adrenal dysfunction can be caused by an increased output of stress hormones (adrenal hyperfunction) or, more commonly, a decreased output of adrenal hormones (adrenal hypofunction).

DEHYDROEPIANDROSTERONE SULFATE (DHEA-S)

DHEA is produced primarily from the adrenal glands.

As the most abundant circulating steroid in the human body, DHEA influences more than 150 known anabolic repair functions throughout the body and brain.

Additionally, DHEA is the precursor for the sex hormones: testosterone, progesterone, and estrogen. DHEA-sulfate (DHEA-s) is the form of DHEA that we measure in the blood to give us a sense of DHEA levels in the body.

- **Increased** DHEA-S levels may be associated with adrenal hyperplasia, a condition that impairs the ability of the adrenal glands to produce cortisol and other glucocorticoids.

- **Decreased** DHEA-S levels are associated with adrenal insufficiency and many common age-related conditions, including diseases of the nervous, cardiovascular, and immune systems. These include metabolic syndrome, coronary artery disease, osteoporosis, mood disorders, and sexual dysfunction.

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CORTISOL

Cortisol is the most prominent glucocorticosteroid in the body and is essential for the maintenance of several body functions, including:

- Controlling blood sugar balance
- Regulating metabolism
- Reducing inflammation
- Controlling blood pressure

Like other glucocorticosteroids, cortisol is synthesized from the common precursor cholesterol in the adrenal glands. A serum cortisol test is used to identify dysfunction in the adrenal gland, such as adrenal hyperfunction or hypofunction.

Additionally, it can be used to monitor Cushing's Syndrome, a condition marked by an overproduction of cortisol, and Addison's Disease, a disease in which the adrenal glands do not produce enough cortisol.

ADDITIONAL BIOMARKERS

The following biomarkers and biomarker ratios also play a role in assessing your patient's functional health:

- Potassium
- Sodium
- Sodium:potassium ratio

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Sex Hormone Health – Male & Female

The blood levels of these crucial hormones diminish with age, contributing to age-related dysfunctions, such as low libido, blood sugar problems, excess weight, heart disease, and more.

ESTRADIOL

Estradiol (E2) is one of the most frequently measured estrogens, the others being estrone (E1) and estriol (E3).

- **In women,** low levels of estradiol can be a risk factor for osteoporosis and bone fracture. Estrogen hormone therapy may improve menopausal women's quality of life. Increased levels of estradiol in women suggest an increased risk of breast or endometrial cancer.

- **In men,** estradiol is a minor hormone that plays a role in male sex hormone physiology and is synthesized from testosterone and androstenedione. Low levels of estradiol in men affect bone density, raising men's risk for fractures as their estradiol level decreases.

  High levels of estradiol in men are associated with abdominal obesity, an increased risk of cardiovascular disease, insulin sensitivity, and blood sugar dysregulation.

TESTOSTERONE — TOTAL

Total testosterone levels encompass both the testosterone that is bound to serum proteins and the unbound form (or free testosterone). Testosterone is the primary sex hormone for men, but it also plays an important role in females as well.

- **In men,** total testosterone levels are useful for assessing gonadal, adrenal, and pituitary function.

- **In women,** total testosterone levels can help in the evaluation of polycystic ovarian syndrome, testosterone-producing tumors of the ovary, tumors of the adrenal cortices, and congenital adrenal hyperplasia.

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TESTOSTERONE — FREE

Free testosterone is unbound to serum proteins such as sex hormone–binding globulin (SHBG) or albumin.

- **In men**, elevated free testosterone levels may be seen in patients that are overusing supplemental testosterone, or it can be a sign of testosterone overproduction in the body.

  Decreased free testosterone levels in men are associated with several dysfunctions, including metabolic syndrome, an increased risk of cardiovascular disease, an increase in abdominal obesity, decreased libido, and erectile dysfunction.

- **In women,** elevated free testosterone levels are associated with excessive growth of hair on the face and chest (hirsutism), polycystic ovary syndrome, and an increased risk for insulin resistance. In women, low free testosterone levels have been linked to an increased risk for osteoporosis, decreased lean body mass, and decreased libido.

ADDITIONAL BIOMARKERS

These additional biomarkers allow you to do a more detailed analysis of your patient's sex hormone regulation:

- SHBG
- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Pregnenolone
- Progesterone
- Testosterone — bioavailable
- Testosterone — % free
- Testosterone — % bioavailable
- Prolactin
- Insulin growth factor-1 (IGF-1)

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Inflammation & Oxidation

These biomarkers are helpful for assessing the degree of oxidative stress and inflammation that your patient may be dealing with. Several biomarkers in the blood increase in the presence of dysfunctions and diseases associated with inflammation — cardiovascular disease, diabetes, hypertension, autoimmune diseases, and fibromyalgia, to name a few.

Oxidative stress arises when the levels of free radicals in the body are high and/or the levels of antioxidants in the body are low. The primary contribution to increased free radicals is the exposure to toxins from our environment. When this occurs, you may see shifts in the following biomarkers.

C-REACTIVE PROTEIN (CRP) & HIGH-SENSITIVITY (HS) CRP

C-reactive protein (CRP) is produced in the liver, primarily in response to increased levels of a pro-inflammatory molecule, interleukin 6. CRP levels can increase with:

- Infections
- Abdominal obesity
- Periodontal disease
- Smoking
- High blood pressure

High-sensitivity C-reactive protein (Hs-CRP) is a more sensitive CRP biomarker that can help indicate the level of chronic inflammation in the body. Increased Hs-CRP levels are associated with an increased risk of generalized inflammation, cardiovascular disease, stroke, and diabetes.

FIBRINOGEN

Fibrinogen is one of the principal blood clotting proteins. It is produced in the liver, and liver disease and dysfunction can cause a decrease in the level of circulating fibrinogen. Levels increase with tissue inflammation or tissue destruction.

Increased fibrinogen levels are associated with an increased risk of cardiovascular disease, heart attack, and stroke. Fibrinogen levels are often elevated in patients suffering from cancer, especially colon cancer.

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HOMOCYSTEINE

Homocysteine is a molecule formed from the incomplete metabolism of the amino acid methionine. Deficiencies in vitamins B6, B12, and folate cause methionine to be converted into homocysteine.

Homocysteine increases the risk of cardiovascular disease by causing damage to the endothelial lining of the arteries, especially in the heart.

- **Increased** homocysteine levels are associated with an increased risk of cardiovascular disease and stroke, as well as cancer, depression, and inflammatory bowel disease.

- **Decreased** homocysteine levels are associated with a decrease in the body's detoxification capacity and an increased risk of oxidative stress.

ADDITIONAL BIOMARKERS

These additional biomarkers may be useful when assessing your patients for inflammation and oxidation:

- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (quantitative)
- Ferritin
- Albumin
- Uric acid

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Iron

The iron-related biomarkers are helpful for assessing issues related to both iron deficiency and iron overload. Iron deficiency is the most common form of anemia worldwide, and the biomarkers on an iron panel are essential for assessing the degree of iron deficiency that is affecting your patient.

In addition to iron deficiency, the iron markers can be used to assess other disorders of iron metabolism including hemochromatosis, sideroblastic anemia, thalassemia, and anemia of chronic disease.

IRON — TOTAL

Serum iron reflects iron that is bound to serum proteins such as transferrin. Serum iron levels will begin to fall somewhere between the depletion of the iron stores and the development of anemia.

- **Increased** iron levels are associated with liver dysfunction, conditions of iron overload (hemochromatosis and hemosiderosis), and infections.
- **Decreased** iron levels are associated with iron deficiency anemia, hypochlorhydria, and internal bleeding. The degree of iron deficiency is best determined in the context of ferritin, TIBC, and % transferrin saturation levels.

FERRITIN

Ferritin is the main form of iron storage in the body.

- **Decreased** ferritin levels are strongly associated with iron deficiency where it is the most sensitive test to detect a growing trend towards iron deficiency.
- **Increased** ferritin levels are associated with iron overload, an increasing risk of cardiovascular disease, inflammation, and oxidative stress.

TOTAL IRON BINDING CAPACITY (TIBC)

Total iron binding capacity (TIBC) is an approximate estimation of the serum transferrin level. The transferrin protein carries most of the iron in the blood.

- **Elevated** TIBC levels are associated with iron deficiency anemia.
- **Decreased** TIBC levels are associated with possible iron overload or a protein deficiency.

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% TRANSFERRIN SATURATION

The % transferrin saturation index is a calculated value that tells how much serum iron is bound to the iron-carrying protein transferrin. A % transferrin saturation value of 15% means that 15% of iron-binding sites of transferrin is being occupied by iron.

- **Increased** % transferrin saturation levels function as a sign of too much iron in the blood or iron overload.
- **Decreased** % transferrin saturation levels serve as a sensitive screening test for iron deficiency anemia.

ADDITIONAL BIOMARKERS

These additional biomarkers may be useful when assessing the functional health of your patients:

- Transferrin
- Unsaturated iron-binding capacity (UIBC)

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Kidney & Prostate Health

Measure these biomarkers in order to assess the functional health of your patient's renal function and prostate. A decrease in renal function in your patient can be due factors such as dehydration, heavy metal toxicity, over the counter or prescription drugs, renal insufficiency, liver dysfunction, or renal disease.

Shifts in these biomarkers may also indicate that your patient's prostate function needs further assessment. Consider conditions such as benign prostatic hypertrophy, prostatitis, urinary tract infection, or early-stage prostate cancer.

A close review of prostate-specific antigen (PSA) levels and further testing for prostatic function may be required.

BLOOD UREA NITROGEN (BUN)

BUN, or blood urea nitrogen, is used predominantly to measure kidney function. BUN reflects the ratio between the production and clearance of urea in the body. Urea is formed almost entirely by the liver from both protein metabolism and protein digestion. The amount of urea excreted as BUN varies with the amount of dietary protein intake.

- **Increased** BUN levels are a sign of kidney dysfunction. An increased BUN level may be due to increased production of urea by the liver or decreased excretion by the kidney. Increased BUN levels are also associated with dehydration and hypochlorhydria.

- **Decreased** BUN levels are associated with malabsorption and a diet low in protein.

CREATININE

Creatinine is produced primarily from the contraction of muscles and is removed by the kidneys. A disorder of the kidney and/or urinary tract will reduce the excretion of creatinine and thus raise blood serum levels. Creatinine is traditionally used with BUN to assess for impaired renal function.

- **Increased** creatinine levels are associated with kidney dysfunction, kidney disease and a possible dysfunction in the prostate.

- **Decreased** creatinine levels are associated with muscle atrophy due to creatinine's connection to muscle metabolism.

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TOTAL PROSTATIC SPECIFIC ANTIGEN (PSA — TOTAL)

PSA is the most abundant protein synthesized in the prostate gland. Total PSA is used as a biological marker to detect diseases related to the prostate.

- **Increased** PSA levels are associated with an enlarged prostate (benign prostatic hyperplasia — BPH), prostate inflammation (prostatitis), and prostate cancer.

It's important to remember that elevated levels of total PSA may not necessarily signal prostate cancer, and prostate cancer may not always be accompanied by an expression of PSA.

ADDITIONAL BIOMARKERS

A more thorough analysis of the kidney and prostate can be made by assessing the optimal levels of the following biomarkers and biomarker ratios:

- BUN:creatinine ratio
- Estimated glomerular filtration rate (eGFR)
- Creatinine clearance

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Cardiometabolic Health

Measuring these biomarkers will be helpful for assessing your patient's risk for developing cardiovascular disease. Cardiovascular disease is still the number one killer of men and women in the world, and heart disease is a major cause of morbidity in our aging population.

Unfortunately, most heart disease is silent and asymptomatic, so a thorough assessment of the body's cardiometabolic system must include the following biomarkers as well as the additional biomarkers listed below.

TRIGLYCERIDES

Serum triglycerides are composed of fatty acid molecules that enter the bloodstream either from the liver or from the diet. Patients that are optimally metabolizing their fats and carbohydrates tend to have a triglyceride level at about one-half of the total cholesterol level.

- Levels will be **elevated** in patients with metabolic syndrome; fatty liver disease; and in patients with an increased risk of cardiovascular disease, hypothyroidism, and adrenal dysfunction.

- Levels will be **decreased** in patients with liver dysfunction, a diet deficient in fat, and inflammation.

CHOLESTEROL – TOTAL

Cholesterol is a steroid found in every cell of the body and in the plasma. It is an essential component in the structure of the cell membrane, where it controls membrane fluidity.

Additionally, it provides the structural backbone for every steroid hormone in the body, which includes adrenal and sex hormones and vitamin D. The myelin sheaths of nerve fibers are also derived from cholesterol, and the bile salts that emulsify fats are composed of cholesterol.

The liver, the intestines, and the skin produce between 60%–80% of the body's cholesterol. The remainder comes from diet.

- **Increased** cholesterol levels are just one of many independent risk factors for cardiovascular disease. It is also associated with metabolic syndrome, hypothyroidism, biliary stasis, and fatty liver disease.

- **Decreased** cholesterol levels are a strong indicator of gallbladder dysfunction, oxidative stress, inflammatory process, and low-fat diets.

It's important to remember that elevated levels of total PSA may not necessarily signal prostate cancer, and prostate cancer may not always be accompanied by an expression of PSA.

LOW-DENSITY LIPOPROTEIN (LDL)

LDL transports cholesterol and other fatty acids from the liver to the peripheral tissues for uptake and metabolism by the cells. It is known as "bad cholesterol" because it is thought that this process of bringing cholesterol from the liver to the peripheral tissue increases the risk for atherosclerosis.

Increased LDL levels are just one of many independent risk factors for cardiovascular disease. Increased levels are also associated with metabolic syndrome, oxidative stress, and fatty liver.

HIGH-DENSITY LIPOPROTEIN (HDL)

HDL transports cholesterol from the peripheral tissues and vessel walls to the liver for processing and metabolism into bile salts. Unlike LDL, HDL is often referred to as "good cholesterol" — it is thought that the process of bringing cholesterol from the peripheral tissue to the liver protects against atherosclerosis.

- **Decreased** HDL levels are considered atherogenic.

- **Increased** HDL levels are considered to protect against atherosclerosis.

LIPOPROTEIN (A)

Lipoprotein (a), or Lp(a), is a small, dense lipoprotein that carries cholesterol in the blood. **Increased** Lp(a) levels are considered an independent risk factor for atherosclerosis and may be a strong indicator of early cardiovascular disease.

There are no known negative effects of levels of Lp(a) at the lower end of the reference range. Some individuals may even have no detectable Lp(a) in their blood.

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ADDITIONAL BIOMARKERS

These additional biomarkers and biomarker ratios will allow you to conduct a more detailed analysis of your patient's cardiometabolic system:

- LDL:HDL ratio
- Cholesterol:HDL ratio
- Triglyceride:HDL ratio
- Very low density lipoprotein (VLDL)
- Apolipoprotein-A1
- Apolipoprotein B
- Apo B:Apo A-1 ratio
- Lipoprotein-associated phospholipase-A2 (LP pla2)
- Nuclear magnetic resonance (NMR) lipoprofile
- Vitamin D
- Glucose
- Insulin
- HsCRP
- Fibrinogen
- Ferritin
- Estradiol
- Testosterone
- Homocysteine

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Hepatobiliary Health

With these biomarkers, you can assess the functional health of your patient's liver and gallbladder. Factors affecting liver function include fatty liver disease (steatosis), hepatitis (inflammation of the hepatic cells from infections, toxins, etc.), liver cell damage (from cirrhosis, infection, alcohol, chemical damage, and hepatic necrosis), or a decrease in either the phase 1 or phase 2 liver detoxification pathways.

Factors affecting gallbladder function include problems in the liver itself that compromises the production of bile (biliary insufficiency), the progressive thickening of the bile within the gallbladder (biliary stasis), or biliary obstruction, which causes cholestasis, a condition characterized by impaired bile flow.

ALANINE TRANSAMINASE (ALT)

Alanine transaminase (ALT) is an enzyme present in high concentrations in the liver and, to a lesser extent, in the skeletal muscle, the heart, and kidney. ALT will be liberated into the bloodstream following cell damage or destruction.

Any condition or circumstance that causes damage to the hepatocytes will leak ALT into the bloodstream. These include exposure to chemicals, viruses (viral hepatitis, mononucleosis, cytomegalovirus, Epstein Barr, etc.), or alcoholic hepatitis.

- **Increased** ALT levels are associated with steatosis (fatty liver disease), cirrhosis, and hepatitis.
- **Decreased** ALT levels are associated with a B6 deficiency.

ASPARTATE AMINOTRANSFERASE (AST)

Aspartate Aminotransferase (AST) is an enzyme present in highly metabolic tissues such as skeletal muscle, the liver, the heart, kidney, and lungs. This enzyme is released into the bloodstream following cell damage or destruction.

- **Increased** AST levels occur when liver cells and/or heart muscle cells and/or skeletal muscle cells are damaged. The cause of the damage must be investigated.
- **Decreased** AST levels are associated with a B6 deficiency.

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GAMMA GLUTAMYL TRANSFERASE (GGT)

Gamma glutamyl transferase (GGT) is an enzyme that is present in the highest amounts in the liver cells and to a lesser extent the kidney, prostate, and pancreas. It is also found in the epithelial cells of the biliary tract.

- **Increased** GGT levels are associated with biliary insufficiency, biliary stasis and biliary obstruction. Levels can also be increased following chronic alcohol consumption.

- **Decreased** GGT levels are associated with vitamin B6 and magnesium deficiency.

BILIRUBIN — TOTAL

Total bilirubin is composed of two forms of bilirubin: indirect, or unconjugated bilirubin, which circulates in the blood on its way to the liver; and direct, or conjugated bilirubin, which is the form of bilirubin made water-soluble before it is excreted in the bile.

- **Increased** total biliirubin levels are associated with a dysfunction or blockage of the liver, gallbladder, or biliary tree, or red blood cell hemolysis.

- **Decreased** total bilirubin levels are associated with an increase in oxidative stress.

ADDITIONAL BIOMARKERS

These additional biomarkers and biomarker ratios allow you to do a more detailed analysis of your patient's hepatobiliary system:

- Bilirubin — Direct
- Bilirubin — Indirect
- AST:ALT ratio
- Alkaline phosphatase (Alk phos)
- Lactate dehydrogenase (LDH)

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Mineral Status

These biomarkers can provide us with a general indication of the balance of certain minerals in the body.

Mineral levels in the body are closely regulated, and deficiencies in one or more minerals may be due to a number of factors, such as the amount of a given mineral in the diet; a patient's ability to digest and break down individual minerals from food or supplements; and how well those minerals are absorbed, transported, and ultimately taken up by the cells themselves.

MAGNESIUM — SERUM AND RED BLOOD CELL

Magnesium is important for many different enzymatic reactions, including carbohydrate metabolism, protein synthesis, nucleic acid synthesis, and muscular contraction. Magnesium is also needed for energy production and is used by the body in blood clotting.

- **Increased** serum or red blood cell magnesium levels are mainly associated with kidney dysfunction and renal failure.
- **Decreased** serum or red blood cell magnesium levels are a sign of magnesium deficiency and is a common finding with muscle cramps.

CALCIUM

Serum calcium levels, which the body tightly regulates within a narrow range, are principally regulated by parathyroid hormone (PTH) and vitamin D.

- **Increased** calcium levels are associated with parathyroid hyperfunction. If calcium is significantly elevated, check serum PTH levels and refer to an endocrinologist.
- **Decreased** calcium calcium levels indicate that calcium regulation is out of balance and not necessarily that the body is deficient of calcium and needs supplementation. Before supplementing with calcium, check vitamins A, B, C, and D levels; rule out hypochlorhydria; and the need for magnesium, phosphorus, unsaturated fatty acids, and iodine as some of the reasons for a calcium "need" before supplementing with calcium.

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ZINC – SERUM

Zinc is a trace mineral that participates in a significant number of metabolic functions and is found throughout the body's tissues and fluids.

- **Increased** zinc levels are often seen in people supplementing with zinc.
- **Decreased** zinc levels are associated with zinc deficiency. Zinc deficiency will negatively affect the multitude of metabolic functions that depend on zinc, including wound healing, immune function, protein synthesis, carbohydrate and lipid metabolism, antioxidant activity, and the production of insulin and thyroid hormone.

ADDITIONAL BIOMARKERS

These additional biomarkers and biomarker ratios will allow you to do a more detailed analysis of your patient's mineral status:

- Calcium:albumin ratio
- Calcium:phosphorous ratio
- Selenium — serum
- Copper — serum
- Zinc — red blood cell
- Ceruloplasmin
- Chromium

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Vitamin Status

Vitamin levels are constantly fluctuating based on a number of factors, such as the amount a patient receives from their diet, a patient's ability to digest and break down individual vitamins from the food or supplements you consume, and the ability of those vitamins to be absorbed, transported and taken up into the cells.

VITAMIN D (25-OH)

Testing for levels of 25-OH vitamin D is an exceptionally effective way to assess vitamin D status. An increased serum vitamin D is usually seen with patients that are supplementing with too much vitamin D. A decreased serum vitamin D is extremely common and is a sign of vitamin D deficiency. Vitamin D deficiency has been associated with many disorders including:

- Several forms of cancer
- Hypertension
- Cardiovascular disease
- Chronic inflammation
- Chronic pain
- Mental illness, including depression
- Diabetes
- Multiple sclerosis
- And more

VITAMIN B12

Vitamin B12 is an essential nutrient for DNA synthesis and red blood cell maturation. Additionally, B12 is necessary for myelin sheath formation and the maintenance of nerves in the body.

- **Decreased** serum B12 levels are associated with a deficiency of B12, insufficient B12 intake in the diet, or malabsorption.

- **Paradoxically,** increased serum B12 levels may be accompanied by signs of B12 deficiency and may indicate a functional deficiency marked by inadequate uptake at the tissue level.

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ADDITIONAL BIOMARKERS

These additional biomarkers allow you to do a more detailed analysis of your patient's vitamin status:

- Vitamin A
- Vitamin C
- Vitamin E
- Active B12
- Folate — serum
- Folate — red blood cell
- Methylmalonic acid

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Gastrointestinal Function

Measuring these biomarkers can help you assess the functional status of your patient's gastrointestinal (GI) system. Factors affecting GI function include inadequate chewing, eating when stressed or in a hurry, hypochlorhydria, gastritis, pancreatic insufficiency, dysbiosis, and/or intestinal hyperpermeability.

PROTEIN — TOTAL

Total serum protein is made up of the levels of albumin and total globulin in the blood. Conditions that affect albumin and total globulin readings will impact the total protein value.

- **Decreased** total protein levels can be an indication of malnutrition, digestive dysfunction due to a need for hydrochloride, or liver dysfunction. Malnutrition leads to a decreased total protein level in the serum primarily from lack of available essential amino acids.

- **Increased** total protein levels are most often due to dehydration.

ALBUMIN

Albumin is one of the major blood proteins. Produced primarily in the liver, albumin plays a major role in water distribution and serves as a transport protein for hormones and various drugs.

- **Decreased** albumin levels can be an indication of malnutrition, digestive dysfunction due to HCl need (hypochlorhydria), or liver dysfunction. Malnutrition leads to a decreased albumin level in the serum primarily from lack of available essential amino acids. Decreased albumin can also be a strong indicator of liver dysfunction, oxidative stress, and excess free radical activity.

- **Increased** albumin levels are a strong indicator of dehydration.

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GLOBULIN — TOTAL

Total globulin is composed of individual globulin fractions known as the alpha 1, alpha 2, beta, and gamma fractions. Total globulin levels are greatly impacted by concomitant increases or decreases in one or more of these fractions.

Globulins constitute the body's antibody system, and the total serum globulin is a measurement of all the individual globulin fractions in the blood.

- **Increased** total globulin levels are associated with hypochlorhydria, liver dysfunction, immune activation, oxidative stress, and inflammation.
- **Decreased** levels are associated with inflammation in the digestive system and immune insufficiency.

ADDITIONAL BIOMARKERS

These additional biomarkers and biomarker ratios may be helpful when assessing your patients' functional gastrointestinal health:

- Gastrin
- Albumin:globulin ratio

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Thyroid

Changes in these biomarkers may indicate that there is dysfunction in your patient's thyroid and a need for further assessment and treatment.

Consider that the dysfunction might be a hyperactive thyroid, primary hypothyroidism (a dysfunction in the thyroid itself, often caused by autoimmune thyroiditis), secondary hypothyroidism (a dysfunction in the anterior pituitary), or thyroid conversion syndrome.

THYROID-STIMULATING HORMONE (TSH)

TSH, or thyroid-stimulating hormone, is a hormone produced by the anterior pituitary to control the thyroid gland's production of thyroxine (T4), to store T4, and to release it into the bloodstream. TSH synthesis and secretion is regulated by the release of TRH (thyroid releasing hormone) from the hypothalamus.

TSH levels represent the body's need for more thyroid hormone (T4 or triiodothyronine — T3), which relates to the body's need for energy.

- **High** TSH levels indicate that the body needs more thyroid hormone.
- **Low** TSH levels reflect the body's low need for thyroid hormone.
- **Optimal** TSH levels in a normally functioning pituitary can tell us that the amount of T4 in the blood matches the body's current need and/or ability to utilize the energy necessary for optimal cell function.

FREE THRYOXINE (T4)

T4 is the major hormone secreted by the thyroid gland. T4 production and secretion from the thyroid gland are stimulated by TSH. Deficiencies of zinc; copper; and vitamins A, B2, B3, B6, and C will cause a decrease in the production of T4 by the follicles of the thyroid gland. Free T4 is the unbound form of T4 in the body.

Only about 0.03%–0.05% of circulating T4 is in its free form. Free T4 will be elevated in hyperthyroidism and decreased in hypothyroidism.

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FREE TRIDOTHYRONINE (T3)

T3 is the most active thyroid hormone and is primarily produced from the conversion of T4 in the peripheral tissue. Free T3 is the unbound form of T3 measured in the blood. Free T3 represents approximately 8%–10% of circulating T3 in the blood. Free T3 levels may be elevated with hyperthyroidism and decreased with hypothyroidism.

ADDITIONAL BIOMARKERS

These additional biomarkers and biomarker ratios allow you to perform a more detailed analysis of your patient's thyroid health:

- Total T4
- Total T3
- T3 uptake
- Free thyroxine index
- Reverse T3
- Free T3:reverse T3 ratio
- Thyroid-binding globulin
- Thyroglobulin antibodies
- Anti-thyroid peroxidase (anti-TPO) antibodies
- Thyrotropin receptor antibodies
- Thyroid-stimulating immunoglobulin

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Immune Health

When the immune system is in a state of balance, we can cope with infections with little or no lasting negative side-effects. The following biomarkers and the additional biomarkers listed below allow you to determine whether your patient's immune system is in a state of balance or not.

Some of the factors to consider include immune insufficiency, bacterial or viral infections, or GI dysfunction associated with decreased immune function. These include abnormal immunity in the gut lining, a decrease in immune cell function in the gut, or an increase in abnormal bacteria in the gut.

TOTAL WHITE BLOOD CELL COUNT

A total white blood cell (WBC) count measures the sum of all the WBCs in the peripheral blood. WBCs fight infection; defend the body through a process called phagocytosis; and produce, transport, and distribute antibodies as part of the immune process.

It is important to look at the WBC differential count (which counts the different varieties of WBCs: neutrophils, lymphocytes, etc.) to identify the source of an increased or decreased WBC count.

- **Decreased** total WBC levels are associated with chronic bacterial or viral infections, immune insufficiency, and may be seen in people eating a raw food diet.

- **Increased** total WBC levels are associated with acute bacterial or viral infections and may be seen in people who eat a diet of highly refined foods.

NEUTROPHILS

Neutrophils are WBCs used by the body to combat bacterial infections and are the most numerous and important white cell in the body's reaction to inflammation.

- **Increased** neutrophil levels will be seen in bacterial infections.

- **Decreased** neutrophil levels are often seen in chronic viral infections.

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LYMPHOCYTES

Lymphocytes are WBCs that are part of the adaptive immune system. They are able to recognize invading organisms using specific cellular receptors and are the source of immunoglobulins, which function as antibodies.

- **Increased** lymphocyte levels are usually a sign of a viral infection but can also be a sign of increased toxicity in the body or inflammation.
- **Decreased** lymphocyte levels are often seen in a chronic viral infection, for which the body can use up a large number of lymphocytes and undergo significant oxidative stress. A decreased lymphocyte count may also indicate the presence of a fatigued immune response, especially with a low total WBC count.

MONOCYTES

Monocytes are WBCs that represent the body's second line of defense against infection. They are phagocytic cells that are capable of movement and remove dead cells, microorganisms, and particulate matter from circulating blood. Levels tend to rise during the recovery phase of an infection or with chronic infection.

ADDITIONAL BIOMARKERS

These biomarkers and biomarker ratios can also be useful in assessing your patients' immune health:

- Eosinophils
- Basophils
- Bands
- Neutrophil:lymphocyte ratio

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CRITICAL TRAINING

In an annual training hosted by **Dr. Dicken Weatherby**, we dive into the nature of the biomarkers listed in this guide and more, as well as the body's functional physiology, which biomarkers to run on your patients' blood panels, and the discrete patterns that signify dysfunction.

Here's what students have to say:

> [The training helped me] think through and **understand the causes** behind dysfunctions and diseases so much more clearly.

> [The training helped me] **connect the dots** of client symptomology with lab results.

> [The training translated] a very complex subject and [made] it understandable, accessible, and **relevant to clinical practice.**

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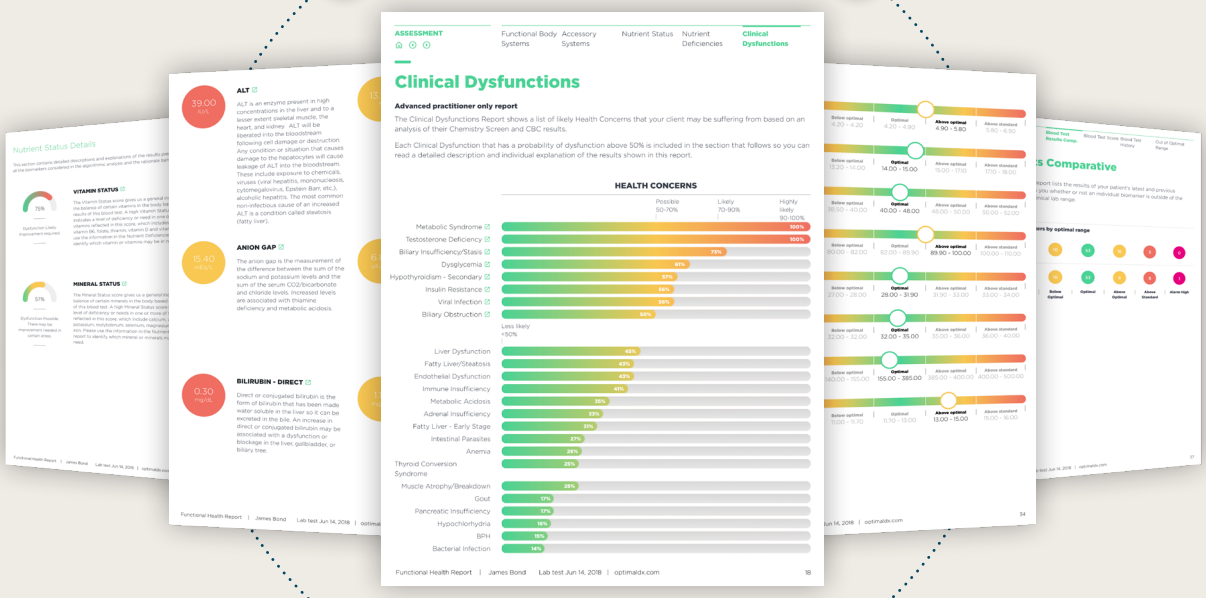

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