

# Healthspan Assessment Panel

## Interpretive Guide

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# Healthspan Assessment Panel - Clinical Utility

The Healthspan Assessment panel provides a baseline health assessment for cardiovascular, endocrine, hepatic, renal, immune, and metabolic health, along with markers of inflammation, autoimmunity, and nutrient status. By assessing various body systems, this comprehensive approach helps determine overall health and wellness and positions you for optimal health and longevity. Testing various body systems enables a holistic understanding of health status, detects potential imbalances or abnormalities, and guides further diagnostic and treatment decisions.

For more information, please visit

[https://www.vibrant-wellness.com/test/HealthspanAssessmentPanel.](https://www.vibrant-wellness.com/test/HealthspanAssessmentPanel)



Please be aware that the low and high considerations are not exhaustive but represent common factors. When interpreting laboratory results, please consult the patient's age- and/or gender-matched reference range to determine whether their values are low, high, or within normal limits.

Anemia		
Marker	Low	High
<p><b>Ferritin</b></p> <p>The main storage form of iron in the body.</p>	<p><b>Disease associations:</b> Iron deficiency anemia</p>	<p><b>Disease associations:</b> Hemochromatosis, hemosiderosis, iron overload, inflammation, liver dysfunction, oxidative stress, megaloblastic/B12/folate deficiency anemia, hemolytic anemia, chronic hepatitis, chronic renal disease</p> <p><b>Diet:</b> Excess iron consumption (e.g., drinking water, iron cookware, especially with acidic foods, supplements)</p> <p><b>Other:</b> Blood transfusion</p>
<p><b>Iron</b></p> <p>70% of iron in the body is in the form of hemoglobin. The remaining 30% is found in the storage form in the liver, spleen, and bone marrow.</p>	<p><b>Disease associations:</b> Iron deficiency anemia, hypochlorhydria, internal bleeding, internal microscopic bleeding, incretion, increased blood loss during menses, renal dysfunction, chronic renal failure, hypothyroidism, and liver dysfunction.</p> <p><b>Diet:</b> Vitamin C deficiency.</p>	<p><b>Disease associations:</b> Liver dysfunction, hemochromatosis, hemosiderosis, iron overload, thalassemia, viral infection, lead poisoning, renal dysfunction, hemolytic anemia, pernicious anemia</p> <p><b>Diet:</b> Excess iron consumption (e.g., drinking water, iron cookware, especially with acidic foods, supplements)</p> <p><b>Other:</b> Iron conversion issues from serum iron (inorganic iron) to hemoglobin (organic iron) may require b12, folic acid, b6, and/or copper. May falsely increase levels with estrogens, oral contraceptives, and alcohol consumption. It has also been noted that there are diurnal variations in serum iron levels where the peak value occurs most often in the morning.</p>
<p><b>UIBC</b></p> <p>Unsaturated iron-binding capacity (UIBC) determines the reserve capacity of transferrin, i.e., the portion not yet saturated with iron. UIBC is used to calculate TIBC. <math>TIBC = UIBC + iron</math></p>	<p><b>Disease associations:</b> Hemochromatosis, iron overload, chronic infection or illness, hemolytic anemia, sideroblastic anemia, or iron toxicity.</p>	<p><b>Disease associations:</b> Iron deficiency, malabsorption of iron</p> <p><b>Diet:</b> Poor iron intake</p>

<p><b>TIBC</b></p> <p>Primary iron-binding protein. This marker approximates the amount of transferrin available to bind to iron.</p>	<p><b>Disease associations:</b> Hemochromatosis, hemosiderosis, iron overload, microscopic bleeding</p> <p><b>Diet:</b> Low protein, e.g., malnutrition, starvation, nephrotic syndrome, and cancer.</p>	<p><b>Disease associations:</b> Iron deficiency anemia, internal bleeding, blood loss, liver dysfunction, hepatitis</p> <p><b>Other:</b> Late pregnancy, falsely increased levels with oral contraceptives</p>
<p><b>Transferrin<sup>1</sup></b></p> <p>Protein that carries most of the iron in the blood.</p>	<p><b>Disease associations:</b> Liver damage, kidney insult or injury, infection, and malignancy. Atransferrinemia (a genetic mutation resulting in the absence of transferrin, which leads to hemosiderosis in the heart and liver, which can lead to heart and liver failure. This condition is treated by plasma infusion).</p>	<p><b>Disease associations:</b> Low iron, which means there is less iron bound to transferrin, allowing for a high circulation of non-bound iron transferrin in the body, revealing a possible iron deficiency anemia.</p>
<p><b>Transferrin Saturation</b></p> <p>A value that is a better index of iron saturation than transferrin levels.</p> <p>(Serum iron x 100) / TIBC</p>	<p><b>Disease associations:</b> Iron deficiency anemia, chronic infection</p> <p><b>Diet:</b> B12 or folate deficiency</p> <p><b>Other:</b> Pregnancy in 3<sup>rd</sup> trimester</p>	<p><b>Disease associations:</b> Hemochromatosis, hemosiderosis, iron overload, hemolytic anemia, megaloblastic anemia, thalassemia, cirrhosis, lead poisoning</p> <p><b>Diet:</b> Low protein, e.g., malnutrition, deficiencies in vitamins B12, B6, and/ or folate</p>

**Nutrition**

Marker	Low	High
<p><b>Folate</b></p> <p>Folate (Vitamin B9) is the naturally occurring form found in foods; folic acid is the supplement/ synthetic form of B9.</p>	<p><b>Disease associations:</b> Malabsorption (digestive disorders affecting the digestive tract, such as celiac disease, Crohn's disease, and certain gastrointestinal surgeries, can impair folate absorption), alcoholism, anemia, hemolytic anemia, excessive stress, infection</p> <p><b>Diet:</b> Folate deficiency</p> <p><b>Medications:</b> Methotrexate, anticonvulsants, antacids, and oral contraceptives can interfere with folate metabolism and cause deficiency</p> <p><b>Other:</b> Pregnancy and breastfeeding, increased requirements for growth phases, e.g., adolescence, hemodialysis, MTHFR gene mutations, aging</p>	<p><b>Disease associations:</b> Kidney dysfunction, impaired renal function, cancer, especially leukemias and cancers of the digestive tract, epilepsy, vitamin B12 deficiency or anemia masking B12 deficiency- Excessive folate supplementation can mask symptoms of vitamin B12 deficiency or pernicious anemia, as it can correct the anemia without treating the underlying B12 deficiency.</p> <p><b>Diet:</b> High or excess folate-rich foods or fortified foods, high-dose folate supplements</p> <p><b>Other:</b> Intestinal microbiota- Certain individuals may have gut bacteria that produce excessive folate, contributing to elevated levels.</p>
<p><b>Vitamin D, 25-OH</b></p> <p>Synthesized in the liver from both vitamin D3 and D2.</p> <p>Vitamin D, 25-OH, is the inactive precursor to 1,25-OH-D3, the active form of vitamin D (calcitriol).</p> <p>It is important to note that it does not reflect overall active D3 levels but rather what is available for conversion if cofactors are sufficient.</p>	<p><b>Disease associations:</b> Malabsorption disorders (celiac disease, short bowel syndrome, gastric bypass, inflammatory bowel disease, chronic pancreatic insufficiency, and cystic fibrosis may lead to vitamin D deficiency), decreased endogenous synthesis due to chronic liver disease, e.g., cirrhosis, end-organ resistance (seen in hereditary vitamin D resistant rickets)<sup>2</sup></p> <p><b>Diet:</b> Low vitamin D intake</p> <p><b>Medications:</b> Phenobarbital, carbamazepine, dexamethasone, nifedipine, spironolactone, clotrimazole, and rifampin induce hepatic p450 enzymes, which activate the degradation of vitamin D.</p> <p><b>Other:</b> Aging, decreased sun exposure- About 50% to 90% of vitamin D is absorbed through the skin via sunlight, while the rest comes from the diet. Twenty minutes of sunshine daily with over 40% of skin exposed is required to prevent vitamin D deficiency.</p>	<p><b>Diet:</b> Excessive vitamin D supplement intake.</p> <p><b>Medications:</b> Less commonly, poisoning from exposure to rodenticides containing cholecalciferol can also lead to vitamin D toxicity.<sup>3</sup></p> <p><b>Other:</b> Vitamin D toxicity (hypervitaminosis D) has not been observed to result from sun exposure.<sup>4</sup></p>

### Vitamin B12

Vitamin B12 (cobalamin) plays an essential role in red blood cell formation, cell metabolism, nerve function, and the production of DNA, the molecules inside cells that carry genetic information.<sup>5</sup>

**Disease associations:** Pernicious anemia, Celiac disease, atrophic gastritis, chronic inflammation and thinning of the stomach lining, hypochlorhydria,<sup>6</sup> oral contraceptive pill,<sup>7</sup> chronic alcohol dependence, obesity, preeclampsia, and eclampsia<sup>8</sup>

**Medications:** Proton pump inhibitors (PPIs) and H2 blockers, Metformin

**Diet:** Vegetarian or vegan diet

**Other:** Pregnancy, bariatric surgery, and gastric bypass

**Disease associations:** Polycythemia vera, critically ill patients, high or supraphysiological serum B12 levels without supplementation have been associated with many pathological conditions, including renal failure, hematological disorders, cancer, autoimmune diseases, and liver disease. Thus, a high or supraphysiological serum B12 concentration without supplementation could be helpful as a diagnostic marker for a severe underlying disease.<sup>9</sup>

**Diet:** Excessive supplement intake. No toxic or adverse effects have been associated with large intakes of vitamin B12 from food or supplements in healthy people.<sup>10</sup>

**Other:** Elevated serum B12 levels may also be associated with a functional deficiency of the vitamin, which is due to a failure of cellular uptake or intracellular processing, trafficking, or utilization.

## Hormones

### Estradiol

Commonly known as E2 or 17 $\beta$ -Estradiol, it is the predominant and most biologically active estrogen in circulation in males and females.

**Disease associations:** Ovariectomy, hypogonadism, hypothyroidism, genetic disorders/17 $\alpha$ -hydroxylase/17,20-lyase deficiency

**Medications:** Aromatase inhibitors, anti-androgens, immunosuppressive drugs, antidepressants, antipsychotics, anticonvulsants, anti-hypertensives, H2 receptor antagonists, opiates, antimalarials, herbicides, agricultural antifungals<sup>11</sup>

**Other:** Menopause, aging, anti-Mullerian hormone, cigarette smoke<sup>12</sup>

**Disease associations:** Chronic liver disease, hyperthyroidism, dysregulated gut microbiome/elevated beta-glucuronidase,<sup>13</sup> cancer, inflammation,<sup>12</sup> age, obesity, genetic causes /CYP19A1 rearrangement.<sup>14</sup>

**Medications:** Exogenous estrogen use, insulin, gonadotropin use

**Other:** Excess aromatase activity, alcohol

### FSH (Follicle Stimulating Hormone)

In females, FSH stimulates follicles on the ovary to grow and mature in preparation for ovulation. As the follicles increase in size, they begin to release estrogen and a low level of progesterone into your blood.<sup>17</sup>

**Disease association:** Being very underweight or having had recent rapid weight loss, not producing eggs (not ovulating), parts of the brain (the pituitary gland or hypothalamus) not producing normal amounts of some or all its hormones<sup>16</sup>

**Other:** Pregnancy

**Disease associations:** Pituitary tumor, Turner syndrome<sup>16</sup>

**Medications:** Hormone therapy

**Other:** Occurs during or after menopause, including premature menopause

### DHEA-S

Dehydroepiandrosterone sulfate (DHEAS) is a male sex hormone found in both men and women. It plays a vital role in making the male sex hormone testosterone and the female sex hormone estrogen and is involved in the development of male sexual characteristics at puberty.<sup>17</sup>

**Disease association:** Adrenal gland disorders (e.g., adrenal insufficiency, Addison disease), pituitary gland not producing normal amounts of its hormones (hypopituitarism)<sup>18</sup>

**Medications:** Glucocorticoids

**Other:** DHEA sulfate levels typically decline with age in both men and women<sup>18</sup>

**Disease association:** Tumor of the adrenal gland (can be benign or malignant), polycystic ovary syndrome (PCOS)

**Other:** Congenital adrenal hyperplasia, precocious puberty<sup>17</sup>

<p><b>LH (Luteinizing Hormone)</b></p> <p>LH plays a role in sexual development in children and fertility in adults. In women, LH triggers the release of an egg from the ovary and is highest before ovulation. In men, LH causes testicles to make the testosterone needed to produce sperm. Typically, levels in men do not change much. In children, LH levels are low, but in girls, LH signals ovaries to make estrogen and is involved in the growth of breasts, body hair, and the start of menstruation. In boys, LH signals testicles to produce testosterone involved in facial and body hair development, changes in one's voice, and sperm production.<sup>19</sup></p>	<p><b>Disease association:</b> Hypopituitarism<sup>19</sup></p>	<p><b>Disease association:</b> Autoimmune disease, for women it may be due to anovulation in those of child-bearing age, ovarian hypofunction, primary ovarian insufficiency (POI), polycystic ovary syndrome (PCOS), thyroid disease, adrenal gland disorders, or Turner Syndrome. For men, it may be due to anorchia, testes that have not developed or don't function normally, mumps, Klinefelter syndrome, overactive endocrine glands, or a tumor (multiple endocrine neoplasia). Higher-than-normal LH levels are seen in early (precocious) puberty in children.<sup>20</sup></p> <p><b>Other:</b> During or after menopause, radiation therapy, chemotherapy</p>
<p><b>SHBG (Sex Hormone Binding Globulin)</b></p> <p>SHBG helps control the amount of sex hormones that are actively working in the body. When the SHBG protein binds to sex hormones, they are bound and unavailable for tissues to use. Tissues can only use sex hormones that are "free," which means they aren't attached to proteins, such as SHBG.<sup>21</sup></p>	<p>When SHBG is low, more total testosterone will likely be available for the body to use.</p> <p><b>Disease association:</b> Hypothyroidism, type 2 diabetes, overweight, obesity, Cushing's syndrome, polycystic ovary syndrome (PCOS)<sup>22</sup></p> <p><b>Medications:</b> Anabolic steroids, steroid medications (general)</p> <p><b>Other:</b> Older age</p>	<p>When SHBG is high, less total testosterone is available for tissues. Thus, tissues may not get enough testosterone.</p> <p><b>Disease association:</b> Liver disease, hyperthyroidism, eating disorders. In males, reduced production of sex hormones<sup>22</sup></p> <p><b>Medications:</b> In females, estrogen medications (hormone replacement therapy, birth control pills)</p>
<p><b>Cortisol</b></p> <p>Known as "the stress hormone," cortisol plays a significant role in maintaining glucose and protein homeostasis, mediating the stress and immune response, and suppressing inflammation.</p>	<p><b>Disease associations:</b> Primary adrenal insufficiency due to Addison's disease, primary adrenal insufficiency due to adrenal destruction from other causes (malignancy, surgery, etc.), primary adrenal insufficiency due to genetic conditions (i.e., congenital adrenal hyperplasia), secondary adrenal insufficiency (i.e., withdrawal from glucocorticoid therapy), postpartum pituitary necrosis, liver disease, pituitary adenoma, craniopharyngioma/ hypophysectomy, hypopituitarism, rheumatoid arthritis, early traumatic experiences, chronic stress, post-traumatic stress disorder (PTSD), hypothyroidism, recurrent infectious processes, Waterhouse-Friderichsen syndrome</p> <p><b>Medications:</b> Long-term use or recent withdrawal from corticosteroid therapy</p>	<p><b>Disease associations:</b> Cushing's disease, ACTH-secreting neoplasm, hyperpituitarism, hyperthyroidism, severe hepatic disease, anorexia, hypoglycemia, diabetes mellitus (uncontrolled), adrenal neoplastic disease, eclampsia, shock, glucocorticoid resistance, infectious disease, burns, virilism, HIV, Crohn's disease, chronic renal disease, hypertension, depression, neuropsychiatric disease, psychological stress, obesity, opioid withdrawal, alcoholism, alcohol withdrawal</p> <p><b>Other:</b> Pregnancy, surgery/post-op recovery, stress from heat, cold, trauma, or pain, night shift work/circadian disruption, exercise or chronic overexercise, cigarette smoking</p>

<p><b>Testosterone, Total</b></p> <p>Measures free testosterone and testosterone that are attached to proteins.</p>	<p><b>Disease association:</b> In males, liver disease, kidney disease, pituitary gland disorder, benign tumors, or Klinefelter syndrome. In females, low testosterone levels are normal. Still, extremely low levels may be a sign of an adrenal gland disorder, a pituitary gland disorder, an ovarian disorder, or an alcohol use disorder.<sup>22</sup></p> <p><b>Medications:</b> Neuropharmacological agents (central nervous system (CNS) inhibitors, e.g., analgesics, anesthetics, sedatives, tranquilizers, or CNS stimulants, e.g., antidepressants, stimulants, hallucinogens), narcotic drugs, marijuana, and marijuana derivatives, anti-hypertensives, chemotherapeutic agents (especially anticancer drugs), phencyclidine<sup>23</sup></p> <p><b>Other:</b> Older age, testicular injury</p>	<p><b>Disease association:</b> Adrenal gland disorder (e.g., congenital adrenal hyperplasia, testicular tumor, PCOS, ovarian cancer), disorder of the pituitary gland (hyperpituitarism and gonadotroph adenomas)<sup>23</sup></p> <p><b>Medications:</b> Steroids</p>
<p><b>Testosterone, Free</b></p> <p>It measures only the "active" form of testosterone, which is not attached to proteins.</p>	<p>Refer to high <b>SHBG</b> and low <b>testosterone in total</b>.</p>	<p>Refer to low <b>SHBG</b> and high <b>testosterone in total</b>.</p>
<p><b>Progesterone</b></p> <p>Progesterone is the precursor to critical steroid hormones such as aldosterone, cortisol, testosterone, and estradiol. It also has essential cardiovascular, renal, and musculoskeletal functions.</p>	<p><b>Disease associations:</b> Irregular or anovulatory cycles (including during breastfeeding), PCOS, thyroid disorders, obesity, hyperprolactinemia, anorexia, endometriosis.</p> <p><b>Pregnancy:</b> Low progesterone in pregnancy can be caused by ectopic pregnancy or complications or failure with the fetus or placenta. Later in pregnancy, low progesterone can be caused by toxemia or preeclampsia of pregnancy.</p> <p>In males: While sudden dramatic reductions in progesterone are uncommon, waning progesterone can occur as a sequelae of reduced androgens that occur gradually over time after the 4th decade in men.<sup>24</sup></p> <p><b>Medications:</b> Long-term use of NSAIDs,<sup>25</sup> oral contraceptives<sup>26</sup></p> <p><b>Other:</b> Over exercise, aging, menopause, environmental toxicants (e.g., phthalates, pesticides, herbicides show pre-clinical evidence of reduced steroidogenesis, including progesterone)<sup>27</sup></p>	<p><b>Disease associations:</b> Ovarian cysts, ovarian tumors, testicular tumors, adrenal hyperplasia from congenital or oncologic origin</p> <p><b>Diet:</b> Caffeine</p> <p><b>Medications:</b> exogenous progesterone supplementation or exposure.</p> <p><b>Other:</b> Elevated beyond luteal phase values in pregnancy, stress</p>
<p><b>Parathyroid Hormone</b></p> <p>Parathyroid Hormone (PTH) is released from the parathyroid glands to control calcium levels in your blood. It also controls phosphorus and vitamin D levels.</p>	<p><b>Disease association:</b> Injury to the parathyroid glands during thyroid or neck surgery, autoimmune attack on the parathyroid glands, very low magnesium level in the blood, familial hypoparathyroidism, DiGeorge syndrome</p> <p><b>Medications:</b> Radioactive iodine treatment for hyperthyroidism<sup>28</sup></p>	<p><b>Disease association:</b> Adenomas, hyperplasia, cancer (parathyroid carcinomas, multiple endocrine neoplasia (MEN) types 1 and 2), kidney disease<sup>29</sup></p> <p><b>Diet:</b> Low vitamin D levels (from lack of sun or malnutrition)</p>

<p><b>Prolactin</b></p> <p>Hormone responsible for lactation, certain breast tissue development, and milk production.</p>	<p><b>Other:</b> Prolactin levels are usually low unless pregnant or breastfeeding, so the only sign of having lower-than-normal levels of prolactin is a lack of breast milk production after giving birth. In these cases, hypopituitarism is often the cause.</p> <p><b>Hypopituitarism</b> is a rare condition in which there's a lack (deficiency) of one, multiple, or all the hormones the pituitary gland makes. It's usually caused by abnormal pressure on the pituitary gland or damage to the pituitary gland.<sup>31</sup></p>	<p><b>Disease association:</b> Pituitary tumors (e.g., prolactinoma), chest wall injury or irritation, presence of nipple rings, hypothalamus disorder, hypothyroidism, kidney disease, abnormal clearance of prolactin molecules (macro prolactin)<sup>32</sup>, shingles (especially if rash or blisters are on chest)<sup>30</sup></p> <p><b>Diet:</b> High-protein meals (temporary increase)</p> <p><b>Medications:</b> Antidepressants, butyrophenones, estrogens, H2 blockers, methyl dopa, metoclopramide, opioids, phenothiazines, reserpine, risperidone, verapamil, marijuana products</p> <p><b>Other:</b> A temporary increase in prolactin levels may be due to intense emotional or physical stress, intense breast stimulation, a recent breast exam, or recent exercise.<sup>31</sup></p>
<p><b>Dihydrotestosterone</b></p> <p>DHT plays a vital role in the sexual development of males. During embryonic life, DHT is involved primarily in the sexual differentiation of organs. Through adolescence and adulthood, DHT promotes prostate growth, sebaceous gland activity, male pattern baldness, and body, facial, and pubic hair growth. This hormone, however, does not seem to play any significant role in normal female physiology.<sup>32</sup></p>	<p><b>Disease association:</b> 5-alpha reductase deficiency, low testosterone (male hypogonadism)</p> <p>Dihydrotestosterone is thought to have fewer effects in women, and, as a result, it is believed they are relatively unaffected by having too little dihydrotestosterone. It is possible, however, that the start of puberty may be delayed in girls with too little dihydrotestosterone, and the amount of pubic and body hair present in adult females may also be reduced.</p> <p>In contrast, low levels of dihydrotestosterone in men can have dramatic effects. If there is too little dihydrotestosterone while male fetuses are still in the womb, for example, they may not be "masculinized," and their genitalia may seem similar to that seen in girls of the same age. Later, boys with too little dihydrotestosterone may undergo some of the changes usually seen in puberty (such as muscle growth and production of sperm) but will not develop normal body hair growth and genital development.</p>	<p><b>Disease association:</b> Excess testosterone production, benign prostatic hyperplasia, prostate cancer, androgenic alopecia (male pattern hair loss), PCOS.</p>
<p><b>Pregnenolone</b></p> <p>A precursor to various steroid hormones, including cortisol, progesterone, estrogen, and testosterone. Sometimes measured to assess adrenal function and hormonal balance.</p>	<p><b>Disease association:</b> Congenital lipid adrenal hyperplasia (CLAH)<sup>33</sup></p> <p><b>Other:</b> Mutations in the genes encoding both the cholesterol side-chain cleavage enzyme (P450scc) and the steroidogenic acute regulatory protein (StAR)<sup>34</sup></p>	<p><b>Disease association:</b> Congenital adrenal hyperplasia<sup>34</sup></p>



## Rheumatoid Arthritis

Marker	Low	High
<p><b>RF (Rheumatoid Factor), IgM</b></p> <p>Rheumatoid factor (RF) is an autoantibody that can be associated with various autoimmune diseases, particularly rheumatoid arthritis (RA). RF IgM refers to the immunoglobulin M class of rheumatoid factor.</p>	<p>Lower levels of RF are generally considered beneficial and not clinically significant.</p>	<p>RF IgM is often found in the blood of individuals with rheumatoid arthritis. However, it's important to note that not all individuals with RA have detectable levels of RF, and RF can also be found in people without RA or other autoimmune diseases. Therefore, while RF IgM is a useful diagnostic marker, it is not definitive for RA.</p> <p>Rheumatoid arthritis is an autoimmune disease characterized by chronic inflammation of the joints. The presence of RF IgM suggests that the immune system is producing antibodies that target the body's own tissues, leading to joint inflammation and damage.</p> <p>RF IgM is one of the laboratory tests used to diagnose rheumatoid arthritis. However, other tests, such as anti-cyclic citrullinated peptide (anti-CCP) antibodies, are also used in conjunction with RF to improve diagnostic accuracy.</p> <p>It's important to interpret RF IgM results in the context of a patient's overall clinical picture, including symptoms, physical examination, and other laboratory tests. The diagnosis of rheumatoid arthritis is typically based on a combination of clinical and laboratory findings.</p>
<p><b>Anti-CCP3, IgG and IgA</b></p> <p>Anti-cyclic citrullinated peptide (anti-CCP) antibodies are autoantibodies associated with RA.</p>	<p>Lower levels of anti-CCP are generally considered beneficial and not clinically significant.</p>	<p>Like RF IgM, the presence of anti-CCP antibodies, including Anti-CCP3, is strongly associated with rheumatoid arthritis. Testing for these antibodies is commonly used in the diagnosis of RA and can aid in differentiating RA from other forms of arthritis.</p> <p>Anti-CCP antibodies, including Anti-CCP3, are considered highly specific for rheumatoid arthritis. Their presence is often detected in the early stages of the disease, and they are included in the classification criteria for RA.</p> <p>High levels of anti-CCP antibodies, particularly Anti-CCP3, are associated with more severe and erosive forms of rheumatoid arthritis. Therefore, measuring these antibodies can also provide prognostic information about the potential course of the disease.</p> <p>It's important to note that while anti-CCP antibodies are strongly associated with RA, not all individuals with RA will test positive for these antibodies.</p>
<p><b>hs-CRP</b></p> <p>High sensitivity C-reactive protein measures C-reactive protein levels, a marker of systemic inflammation and cardiovascular risk.</p>	<p>Lower levels of hs-CRP are generally considered beneficial and not clinically significant.</p> <p>Values that are <math>\leq 0.9</math> mg/L can be considered a normal level in most healthy adults.</p> <p><b>Medications:</b> NSAIDs and statins will decrease hs-CRP levels.<sup>101</sup></p>	<p><b>Disease associations:</b> Obesity, depression, diabetes, common cold, gingivitis, periodontitis, genetic polymorphisms, systemic inflammation such as rheumatoid arthritis, systemic lupus erythematosus, other autoimmune diseases, malignancies, myocardial infarction, pancreatitis, bronchitis, acute bacterial infections, viral infections, systemic vasculitis, major trauma</p> <p>Recent injury or illness can falsely elevate levels. A more than 50 mg/dl CRP test result is generally considered severe elevation. Results over 50 mg/L are associated with acute bacterial infections about 90% of the time.<sup>34</sup></p> <p><b>Other:</b> Being female or elderly, pregnancy, sedentary lifestyle, insomnia, cigarette smoking.<sup>102</sup></p>

<p><b>ANA IFA Panel</b></p> <p>Antinuclear Antibody (ANA) by IFA is a test that refers to ANA detection by indirect fluorescent antibody (IFA) assay to detect the presence of ANA in blood.</p> <p>If ANA test results are positive, it is often reported in two parts: the pattern and titer.</p> <p>Please note that the ANA IFA Panel is measured by looking at patterns and titers, not “Low” or “High” as indicated by the column header.</p>	<p><b><u>PATTERNS</u></b></p> <p><b>Homogenous</b> (diffuse) is associated with systemic lupus erythematosus.</p> <p><b>Speckled</b> is associated with systemic lupus erythematosus, Sjogren syndrome, scleroderma, polymyositis, rheumatoid arthritis, and mixed connective tissue disease.</p> <p><b>Nucleolar</b> is associated with scleroderma and polymyositis.</p> <p><b>RIM</b> is associated with systemic lupus erythematosus and Sjogren syndrome.</p> <p><b>Cytoplasmic</b> is associated with polymyositis/dermatomyositis, systemic lupus erythematosus, and scleroderma.</p> <p><b>Centromere</b> is associated with scleroderma and calcinosis, Raynaud disease, esophageal motility disorder, sclerodactyly, and telangiectasia (CREST).</p>	<p><b><u>TITERS</u></b></p> <p>Titers are reported in ratios, most often 1:40, 1:80, 1:160, 1:320, and 1:640.</p> <p>The higher the ANA titer, the more likely it will be clinically significant.</p>
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Thyroid		
Marker	Low	High
<p><b>T3 (Triiodothyronine)</b></p> <p>T3 is the most active thyroid hormone and is primarily produced from the conversion of thyroxine (T4) in the peripheral tissue. Total T3 measures the T3 that is both attached to proteins and floating free in the blood.</p>	<p><b>Disease associations:</b> Primary hypothyroidism, selenium deficiency, severe liver disease</p> <p><b>Diet:</b> Low selenium-rich foods</p> <p><b>Medications:</b> Thyroid drug</p> <p><b>Other:</b> Pregnancy, radiation therapy to the thyroid, and severe illness may lead to decreased levels</p>	<p><b>Disease associations:</b> Hyperthyroidism, iodine deficiency, renal disease, liver disease, iatrogenic hyperthyroidism</p> <p><b>Diet:</b> Protein malnutrition</p> <p><b>Medications:</b> Falsely elevated levels may be from following desiccated thyroid medications (several hours)</p>
<p><b>T4 (Thyroxine)</b></p> <p>Total T4 measures the T4 that is both attached to proteins and floating free in the blood.</p>	<p><b>Disease associations:</b> Primary hypothyroidism, iodine deficiency</p> <p><b>Diet:</b> Poor iodine intake</p> <p><b>Medications:</b> Exogenous T3, anabolic steroids, exogenous androgens, anticonvulsant, salicylates, anti-coagulants</p>	<p><b>Disease associations:</b> Hyperthyroidism, liver disease, adrenal fatigue</p> <p><b>Medications:</b> Thyroid hormone replacement, oral contraceptives, exogenous estrogen use, contrast radiopaque substances used for x-ray, heroin, methadone, propranolol</p> <p><b>Other:</b> Elevated metabolic activity, pregnancy (particularly during the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters due to increased estrogen)</p>
<p><b>Free T3</b></p> <p>Free T3 measures only the T3 that is floating free in the blood.</p>	<p>See section on low <b>T3 (Triiodothyronine)</b>.</p>	<p>See section on high <b>T3 (Triiodothyronine)</b>.</p>
<p><b>Free T4</b></p> <p>Free T4 measures only the T4 that is floating free in the blood.</p>	<p>See section on low <b>T4 (Thyroxine)</b>.</p>	<p>See section on high <b>T4 (Thyroxine)</b>.</p>

<p><b>TSH (Thyroid Stimulating Hormone)</b></p> <p>It indicates thyroid function and is often included in assessing thyroid health and screening for thyroid disorders.</p>	<p><b>Disease associations:</b> Hyperthyroidism, secondary hypothyroidism (anterior pituitary hypofunction), tertiary hypothyroidism (hypothalamus hypofunction), Hashimoto's thyroiditis, subacute thyroiditis</p> <p><b>Diet:</b> Protein malnutrition</p> <p><b>Medications:</b> T3 treatment, aspirin, corticosteroids, heparin, dopamine</p> <p><b>Other:</b> Heavy metals (lead, aluminum, cadmium, and other toxic metals), pregnancy</p>	<p><b>Disease associations:</b> Primary hypothyroidism, Hashimoto's thyroiditis, subacute thyroiditis, liver/biliary dysfunction due to conjugation problems, severe debilitating illness, thyrotoxicosis, thyrotropin-producing tumor</p> <p><b>Medications:</b> Prescription lithium therapy, potassium iodide, TSH injections</p> <p>Per the American Thyroid Association, "Biotin has no effect on thyroid hormone levels or thyroid function in the body. However, biotin can interfere with the measurement of hormone levels in the laboratory, making them inaccurate. This is because biotin is added as a reagent during some of the laboratory methods. The hormone measurements that can be affected are thyroxine, triiodothyronine, TSH, and thyroglobulin."<sup>35</sup></p>
<p><b>Anti-TPO (Thyroid Peroxidase)</b></p> <p>Thyroid antibodies arise when the immune system erroneously identifies components of the thyroid gland or proteins as threats. This autoimmune reaction, characterized by the immune system mistakenly attacking body tissues, can result in persistent thyroid inflammation, tissue injury, and/or interference with thyroid function.</p>	<p>Lower levels of anti-TPO are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> The presence of TPO antibodies in your blood suggests that the cause of thyroid disease is an autoimmune disorder, such as Hashimoto's or Graves' disease. Some people with TPO antibodies may not have thyroid disease. However, TPO antibodies may increase the risk of future thyroid disorders.<sup>36</sup></p> <p><b>Other:</b> Pregnancy</p>
<p><b>Reverse T3</b></p> <p>Reverse Triiodothyronine (reverse T3, rT3) is a metabolically inactive form of thyroid hormone and is a product of T4 degradation.</p>	<p><b>Disease associations:</b> Untreated hypothyroidism<sup>37</sup>, central hypothyroidism<sup>38</sup>, X-linked monocarboxylate transporter 8 deficiency<sup>39</sup></p> <p><b>Medications:</b> Low doses of levothyroxine<sup>40</sup>, growth hormone<sup>41</sup>, glucocorticoids</p>	<p><b>Disease associations:</b> With only a few exceptions, notably uremia and human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), total serum rT3 concentrations are elevated in all circumstances that cause low serum T3 levels in the absence of obvious clinical signs of hypothyroidism. These conditions include, in addition to the newborn period, a variety of acute and chronic nonthyroidal illnesses, calorie deprivation, and thyrotoxicosis.<sup>38</sup> Other considerations are hypothyroidism and euthyroid sick syndrome (ESS).<sup>42</sup></p> <p><b>Medications:</b> Amiodarone, glucocorticoids, ipodate, propranolol (high doses), PTU (antithyroid drug), thyroxine<sup>38</sup></p>
<p><b>Anti-TG (Thyroglobulin)</b></p> <p>Measures antibodies against thyroglobulin and is used to diagnose autoimmune thyroid disease (AITD).</p>	<p>Lower levels of anti-TG are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Graves' disease or overactive thyroid, Hashimoto thyroiditis, underactive thyroid, subacute thyroiditis systemic lupus erythematosus, type 1 diabetes<sup>43</sup></p>

## CBC w/ Differential Platelets

Marker	Low	High
<p><b>WBC (White Blood Cells)</b></p> <p>Assesses immune system function and screens for infections or inflammatory conditions.</p>	<p><b>Disease associations:</b> Chronic viral infection, chronic bacterial infection, pancreatic insufficiency, systemic lupus erythematosus, bone marrow depression (caused by certain drugs, chemotherapeutic agents, radiation, heavy metals), hepatitis, free radical diseases (neoplasm), anemia (related to vitamin B12, vitamin B6, and folic acid), anterior pituitary dysfunction, adrenal dysfunction, parathyroid hyperfunction, intestinal parasites (chronic), rheumatoid arthritis, multiple food allergies</p> <p><b>Diet:</b> Raw food diet</p> <p><b>Other:</b> Hourly rhythm (early morning tends to be low and peaks in late afternoon), hormonal influences in females over age 40 may cause lower than normal total WBC count</p>	<p><b>Disease associations:</b> Childhood diseases (measles, mumps, chicken pox, rubella, etc.), acute viral infection, acute bacterial infection, intestinal parasites, free radical pathology (neoplasm), adrenal dysfunction, asthma, emphysema, polycythemia, influenza with secondary bacterial infection, observed when there's a large number of nucleated RBCs.</p> <p><b>Diet:</b> Highly refined foods</p> <p><b>Other:</b> Stressful situations, late pregnancy, age (newborns and infants have higher counts, and it gradually tapers until about age 21).</p>
<p><b>RBC (Red Blood Cells)</b></p> <p>Evaluates oxygen-carrying capacity and screens for anemia or other blood disorders.</p>	<p><b>Disease associations:</b> Anemia (due to deficiencies in iron, B12, folic acid, and/or copper), internal bleeding, liver dysfunction, renal dysfunction</p> <p><b>Diet:</b> Low vitamin B6 intake</p> <p><b>Other:</b> Free radical pathology, falsely decreased levels can be due to posture, pregnancy (RBCs get diluted in increased fluid volume), and drugs</p>	<p><b>Disease associations:</b> Decrease in blood volume (e.g., dehydration from decreased fluid intake, vomiting, diarrhea), respiratory distress, vitamin C deficiency, polycythemia vera, adrenal hyperfunction, cystic fibrosis</p> <p><b>Medications:</b> Tobacco use, overuse of diuretics, gentamicin, methyl dopa</p> <p><b>Other:</b> Stress, age (a newborn has higher RBC than adults; normal levels reached by age 14), high altitude</p>
<p><b>Hemoglobin</b></p> <p>Oxygen-carrying molecule in red blood cells.</p>	<p><b>Disease associations:</b> Anemia (deficiencies in iron, B12, folate, B6, copper), blood loss, decreased hemoglobin is associated with vitamin C need, digestive inflammation, internal bleeding, chronic intestinal parasites, adrenal hypofunction, thiamine deficiency, liver, renal dysfunction</p> <p><b>Diet:</b> Excessive fluid intake</p> <p><b>Medications:</b> NSAID, anti-hypertensives (ACE inhibitors, angiotensin receptor blockers), cephalosporins, dapson, levodopa, and levofloxacin. Methyl dopa, nitrofurantoin, penicillin, and its derivatives</p> <p><b>Other:</b> Pregnancy</p>	<p><b>Disease associations:</b> Asthma and emphysema, polycythemia (relative or primary), dehydration, vitamin B6 anemia, diarrhea, adrenal dysfunction</p> <p><b>Medications:</b> Gentamicin, methyl dopa</p> <p><b>Other:</b> Falsely increased levels due to high altitude and infant age</p>

<p><b>Hematocrit</b></p> <p>Expressed as a percentage of the volume of RBCs in a known volume of centrifuged blood.</p>	<p><b>Disease associations:</b> Anemia (deficiencies in iron, B12, folate, B6, copper), blood loss, internal bleeding, digestive inflammation, thymus hypofunction, a decreased hematocrit is associated with vitamin C need, chronic intestinal parasites, adrenal hypofunction, thiamine deficiency, liver, and renal dysfunction</p> <p><b>Other:</b> Females have lower hematocrit than males; those aged 60+ tend to have lower hematocrit</p>	<p><b>Disease associations:</b> Asthma and emphysema, polycythemia (relative or primary), dehydration, spleen hyperfunction, vitamin B6 anemia, diarrhea, adrenal dysfunction</p> <p><b>Other:</b> Falsely increased levels due to high altitude, infant age</p>
<p><b>MCV (Mean Corpuscular Volume)</b></p> <p>One of the RBC indices to differentiate anemia. Can help determine the type of anemia.</p>	<p><b>Disease association:</b> Iron deficiency anemia, iron anemia secondary to digestive inflammation or hypochlorhydria, B6 deficiency, internal bleeding, intestinal parasites</p> <p><b>Other:</b> Heavy metal body burden</p>	<p><b>Disease association:</b> Macrocytosis, anemia (B12 and/or folic acid deficiency), hypochlorhydria, increased MCV associated with vitamin C need</p> <p><b>Other:</b> Falsely increased levels may be due to high WBC count, high reticulocyte count, newborn age, autoagglutination (clumping of red blood cells)</p>
<p><b>MCH (Mean Corpuscular Hemoglobin)</b></p> <p>Average weight of hemoglobin per red blood cell. Can help determine the cause of anemia.</p>	<p><b>Disease association:</b> Iron deficiency anemia, B6 anemia, internal bleeding, a decreased MCH is associated with vitamin C need, intestinal parasites, rheumatoid arthritis</p> <p><b>Other:</b> Heavy metal body burden</p>	<p><b>Disease association:</b> Anemia (B12 and/or folic acid deficiency), hypochlorhydria</p> <p><b>Other:</b> Falsely increased levels may be due to hyperlipidemia, WBC &gt; 50,000, high heparin</p>
<p><b>MCHC (Mean Corpuscular Hemoglobin Concentration)</b></p> <p>Average concentration of hemoglobin in RBC. Can help monitor anemia therapy.</p>	<p><b>Disease association:</b> Iron deficiency anemia, B6 anemia, a decreased MCHC is associated with vitamin C need, internal bleeding, thalassemia</p> <p><b>Other:</b> Heavy metal body burden</p>	<p><b>Disease association:</b> Anemia (B12 and/or folic acid deficiency), hypochlorhydria</p> <p><b>Other:</b> Falsely increased levels may be due to hyperlipidemia, rouleaux formation in blood, high heparin</p>
<p><b>RDW-SD (Red Cell Distribution Width - Standard Deviation)</b></p> <p>Measures the variation in size of red blood cells, used to diagnose and monitor various types of anemia and other blood disorders.</p>	<p><b>Disease association:</b> Iron deficiency anemia, thalassemia, bone marrow disorders, chronic diseases (e.g., chronic kidney disease, chronic liver disease – less common than high RDW-SD in these conditions)</p> <p><b>Other:</b> Blood transfusions that provide a more uniform population of RBCs, especially if from a single donor or source</p>	<p><b>Disease association:</b> Anemia, hemolysis, bone marrow disorders, chronic diseases (e.g., rheumatoid arthritis, chronic kidney disease, chronic liver disease)</p> <p>Nutritional deficiencies in iron, vitamin B12, and folate can lead to abnormal RBC production.</p>
<p><b>Platelet Count</b></p> <p>Measures blood clotting ability and screens for bleeding disorders or thrombocytopenia.</p>	<p><b>Disease association:</b> Decreased production of platelets (leukemia and other cancers, anemia, viral infections, such as hepatitis C or HIV) or increased breakdown of platelets (immune thrombocytopenia, bacteremia, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome)<sup>45</sup></p> <p><b>Medications:</b> Chemotherapy drugs, heparin, quinine, sulfa-containing antibiotics, anticonvulsants<sup>45</sup></p> <p><b>Other:</b> Radiation therapy, heavy alcohol consumption, pregnancy<sup>44</sup></p>	<p><b>Disease association:</b> Reactive thrombocytosis (can be caused by blood loss, cancer, infections, iron deficiency, removal of your spleen, hemolytic anemia, inflammatory disorders, such as rheumatoid arthritis, sarcoidosis or inflammatory bowel disease, surgery, other types of traumas), essential thrombocythemia<sup>45</sup></p>

<p><b>Neutrophils</b></p> <p>WBCs are used to combat bacterial or pyrogenic infections. The body's most numerous and significant WBC in the body's reaction to inflammation.</p>	<p><b>Disease association:</b> Neutropenia from any decrease in bone marrow output (e.g., aplastic anemia, pernicious anemia, acute lymphoblastic leukemia), chronic viral infection, hepatitis, anemia (deficiency in B12, B6, and/or folic acid), anterior pituitary dysfunction, adrenal dysfunction, parathyroid hyperfunction, chronic intestinal parasites, rheumatoid arthritis, multiple food allergies.</p> <p><b>Other:</b> Falsely decreased levels may be due to extreme cold or heat, age (elderly or the weak may not respond to an infection), and myelosuppressive chemotherapy.</p>	<p><b>Disease association:</b> Childhood diseases (measles, mumps, chicken pox, rubella, etc.), bacterial infections (acute/localized, and general), acute viral infection, chronic viral infection, chronic bacterial infection, inflammation, intestinal parasites, adrenal hypofunction, asthma, emphysema, polycythemia, influenza with secondary bacterial infection</p> <p><b>Medications:</b> Steroids (neutrophilia peaks in 4-6 hours)</p> <p><b>Other:</b> Late pregnancy. Falsely elevated levels may be due to stress, excitement, exercise, age (children respond to infection with a more significant rise than adults), or extreme cold or heat.</p>
<p><b>Lymphocytes</b></p> <p>Made in the bone marrow, and are used by the body to destroy and get rid of toxic byproducts of protein metabolism.</p>	<p><b>Disease association:</b> Lymphopenia, chronic viral or bacterial infection, active infection, oxidative stress, free radical activity, suppressed bone marrow production, hepatitis, anemia (deficiencies in vitamin B12, B6, and/or folic acid), anterior pituitary dysfunction, adrenal dysfunction, intestinal parasites (chronic), rheumatoid arthritis, multiple food allergies</p>	<p><b>Disease association:</b> Childhood diseases (measles, mumps, chicken pox, rubella, etc.), acute and chronic viral infection, infectious mononucleosis, acute bacterial infection, inflammation, systemic toxicity, poor detoxification, intestinal parasites, neoplasm, adrenal dysfunction (hypoadrenalism), hypothyroidism, asthma, emphysema, polycythemia, influenza with secondary bacterial infection</p> <p><b>Other:</b> Late pregnancy</p>
<p><b>Monocytes</b></p> <p>The body's second line of defense against infection. They are phagocytic cells that remove dead cells, microorganisms, and particulate matter from the circulating blood</p>	<p><b>Disease association:</b> Not usually associated with any specific disease or disorder</p> <p><b>Medications:</b> Corticosteroid therapy</p>	<p><b>Disease association:</b> Recovery phase of acute infection, liver dysfunction, intestinal parasites, in males it may be due to urinary tract congestion, e.g., benign prostatic hypertrophy (BPH)</p>
<p><b>Eosinophils</b></p> <p>Type of white blood cell involved in allergic reactions and parasitic infections; elevated levels may indicate allergies, asthma, or parasitic infections.</p>	<p><b>Other:</b> Alcohol intoxication, overproduction of certain steroids in the body (such as cortisol)<sup>46</sup></p>	<p><b>Disease association:</b> Adrenal gland deficiency, allergic disease, including hay fever, asthma, autoimmune diseases, eczema, fungal infections, hypereosinophilic syndrome, leukemia, and other blood disorders, lymphoma, parasite infection, such as worms<sup>47</sup></p>
<p><b>Basophils</b></p> <p>Type of white blood cell involved in allergic reactions and inflammatory responses; elevated levels may indicate allergies or certain inflammatory conditions.</p>	<p><b>Disease association:</b> Infection, allergic reaction, hyperthyroidism<sup>47</sup></p>	<p><b>Disease association:</b> Leukemia, polycythemia vera, myelofibrosis, hypothyroidism, inflammatory bowel disease, autoimmune disease, allergic reaction, infection</p> <p><b>Medications:</b> NSAIDs<sup>48</sup></p>

<p><b>Immature Granulocytes</b></p> <p>Refers to immature forms of white blood cells (neutrophils, eosinophils, and basophils); elevated levels may indicate infection, inflammation, or bone marrow disorders.</p>	<p><b>Disease association:</b> Blood or bone marrow condition (aplastic anemia, leukemia)<sup>49</sup></p> <p><b>Other:</b> Side effect of cancer treatment</p>	<p><b>Disease association:</b> Infection, blood cell cancer, autoimmune disease, chronic myelogenous, leukemia (CML), primary thrombocythemia, polycythemia vera, primary myelofibrosis<sup>50</sup></p>
<p><b>Neutrophil Count</b></p> <p>Measures the number of neutrophils, the most abundant type of white blood cell, involved in fighting bacterial infections; elevated levels may indicate bacterial infections or inflammation.</p>	<p>See section on low <b>Neutrophils</b>.</p>	<p>See section on high <b>Neutrophils</b>.</p>
<p><b>Lymphocyte Count</b></p> <p>Measures the number of lymphocytes, which are white blood cells involved in immune responses; alterations may indicate viral infections, immune system disorders, or certain cancers.</p>	<p>See section on low <b>Lymphocytes</b>.</p>	<p>See section on high <b>Lymphocytes</b>.</p>
<p><b>Monocyte Count</b></p> <p>Measures the number of monocytes, a type of white blood cell involved in immune defense and inflammation; elevated levels may indicate chronic infections, autoimmune diseases, or inflammatory conditions.</p>	<p>See section on low <b>Monocytes</b>.</p>	<p>See section on high <b>Monocytes</b>.</p>
<p><b>Eosinophil Count</b></p> <p>Measures the number of eosinophils, a type of white blood cell involved in allergic reactions, parasitic infections, and certain inflammatory conditions.</p>	<p>See section on low <b>Eosinophils</b>.</p>	<p>See section on high <b>Eosinophils</b>.</p>
<p><b>Basophil Count</b></p> <p>Measures the number of basophils, a type of white blood cell involved in allergic reactions and inflammation, particularly in response to parasitic infections and allergic conditions.</p>	<p>See section on low <b>Basophils</b>.</p>	<p>See section on high <b>Basophils</b>.</p>
<p><b>Immature Granulocyte Count</b></p> <p>Measures the number of immature forms of granulocytes (including neutrophils, eosinophils, and basophils), which may increase in response to infections, inflammation, or bone marrow disorders.</p>	<p>See section on low <b>Immature Granulocytes</b>.</p>	<p>See section on high <b>Immature Granulocytes</b>.</p>
<p><b>MPV (Mean Platelet Volume)</b></p> <p>Measures the average size of platelets and may help diagnose certain platelet disorders or assess the risk of cardiovascular events.</p>	<p><b>Disease association:</b> Aplastic anemia, lupus, marrow hypoplasia, Wiskott-Aldrich syndrome, primary or secondary thrombocytosis<sup>50</sup></p>	<p><b>Disease association:</b> Cancer, diabetes, cardiovascular disease, preeclampsia, Crohn's disease, hyperthyroidism, immune thrombocytopenia, myeloproliferative disease, vitamin deficiency (B12, D, or folate), macrothrombocytopenia<sup>51</sup></p>

<p><b>Nucleated RBC Count</b></p> <p>NRBCs are immature RBC precursors that are usually not present in the circulation of healthy adults. This marker measures the number of RBCs with nuclei present in the bloodstream, which typically indicates increased erythropoiesis (red blood cell production) in response to various conditions such as hypoxia, bone marrow disorders, or certain infections.</p>	<p>Lower levels of NRBCs are generally considered beneficial and not clinically significant.</p>	<p><b>Disease association:</b> Anemia, myelofibrosis, thalassemia, miliary tuberculosis, malignancies of the bone marrow (myelomas, leukemias, lymphomas), prolonged hypoxemia<sup>51</sup></p> <p>Brisk hemolysis or rapid blood loss can cause NRBCs to be released into the blood as erythropoiesis increases to compensate for acute anemia.<sup>52</sup></p>
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<p><b>Nucleated RBC %</b></p> <p>Represents the percentage of nucleated red blood cells in the total red blood cell population, providing insight into the degree of erythropoiesis occurring in the body.</p>	<p>Low NRBC % are generally considered beneficial and not clinically significant.</p>	<p>See section on high <b>Nucleated RBC Count</b>.</p>
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### Reticulocytes

Marker	Low	High
<p><b>Reticulocyte Count</b></p> <p>Must be viewed in relation to the total red blood cell count.</p>	<p><b>Disease association:</b> Anemia (related to vitamin B12, vitamin B6, and/or folic acid), adrenal hypofunction, anterior pituitary hypofunction</p> <p><b>Other:</b> Falsely decreased levels may be due to recently transfused patients</p>	<p><b>Disease association:</b> Presence of an occult or unknown disease, e.g., microscopic internal bleeding or hemolysis, hemolytic anemia, severe iron deficiency anemia, vitamin C anemia, renal dysfunction, liver dysfunction</p> <p><b>Other:</b> Heavy metal body burden. Falsely increased levels may be due to infant age, pregnancy, or presence of Howell-Jolly bodies (asplenia)</p>
<p><b>Reticulocyte %</b></p> <p>A young, immature red blood cell.</p>	<p>See section on low <b>Reticulocyte Count</b>.</p>	<p>See section on high <b>Reticulocyte Count</b>.</p>
<p><b>IRF (Immature Reticulocyte Fraction)</b></p> <p>Measures the percentage of immature RBCs (reticulocytes) in the bloodstream, indicating the rate of erythropoiesis and the bone marrow's response to anemia or other conditions affecting RBC production.</p>	<p><b>Disease association:</b> Bone marrow disorder, kidney disease, hypothyroidism</p> <p><b>Diet:</b> Nutrition deficiency (iron, vitamin B12, or folate)</p> <p><b>Medications:</b> Chemotherapy drugs</p>	<p><b>Disease association:</b> The body is making more young RBC than usual, which may be due to blood loss or anemia.</p> <p><b>Other:</b> High altitude area with less oxygen, intense exercise, dehydration (may temporarily raise IRF)</p>
<p><b>Retic-Hemoglobin</b></p> <p>The reticulocyte hemoglobin content (CHr or Ret-He) provides an indirect measure of the functional iron available for new RBC production over the previous 3-4 days.<sup>53</sup></p>	<p><b>Disease association:</b> Iron deficiency, iron deficiency anemia, low ferritin.<sup>54</sup></p>	<p><b>Other:</b> Iron treatment, e.g., IV iron therapy<sup>55</sup></p>



## Complete Metabolic Panel

Marker	Low	High
<p><b>Sodium</b></p> <p>An electrolyte essential for maintaining fluid balance, nerve function, and muscle contraction.</p>	<p><b>Disease associations:</b> Diarrhea, vomiting, excess perspiration, renal dysfunction, congestive heart failure, edema, adrenal hypofunction/Addison's</p> <p><b>Medications:</b> Diuretics, heparin, laxatives, sulfates</p> <p><b>Diet:</b> Low salt intake</p>	<p><b>Disease associations:</b> Dehydration, renal insufficiency, primary aldosteronism, adrenal hyperfunction/Cushing's, diabetes insipidus</p> <p><b>Medications:</b> Steroids, aspirin, NSAIDs, anti-hypertensives, laxatives</p> <p><b>Diet and supplements:</b> High salt intake, licorice, calcium, fluoride, iron</p> <p><b>Other:</b> Water softener use</p>
<p><b>Potassium</b></p> <p>Electrolytes crucial for nerve and muscle function, including heart rhythm regulation.</p>	<p><b>Disease associations:</b> Adrenal hyperfunction/Cushing's disease, hypertension, diarrhea, diuretic use, anemia</p> <p><b>Diet:</b> Excess refined carbohydrates</p>	<p><b>Disease associations:</b> Adrenal hypofunction/Addison's disease, dehydration, tissue destruction (damaged cells release K+), metabolic acidosis, respiratory distress, renal insufficiency/renal failure, bradycardia, diabetes</p> <p><b>Other:</b> Falsely increased in hemolyzed samples</p>
<p><b>Chloride</b></p> <p>A general marker for acidity that tends towards an inverse relationship with CO2 levels and a positive relationship with sodium levels</p>	<p><b>Disease associations:</b> Hyperhydration, metabolic alkalosis (particularly if CO2 is high, and calcium and potassium are low), respiratory distress disorders (e.g., COPD and/or CHF), renal dysfunction, hypochlorhydria (particularly if low serum iron and/or ferritin, high BUN, low serum phosphorus, and low B12. Hypochlorhydria may also be associated with H. pylori infection, which may lead to reduced HCl secretion), adrenal hypofunction/Addison's disease (which decreases corticosteroid and mineralocorticoid hormones e.g., cortisol and aldosterone), diabetes, or persistent vomiting.</p> <p><b>Medications:</b> Steroids, laxatives, diuretics, bicarbonate, theophylline</p>	<p><b>Disease associations:</b> Dehydration, metabolic acidosis, particularly if CO2 is high, respiratory alkalosis/hyperventilation (e.g., rapid shallow breathing due to pulmonary disorders, anxiety, stress, fever, high altitude, or liver disease), renal tubular acidosis, adrenal hyperfunction/Cushing's disease, particularly if sodium is high and potassium is low, diabetes insipidus</p> <p><b>Medications:</b> Salicylate (aspirin) excess</p>
<p><b>Carbon Dioxide</b></p> <p>Essential for maintaining blood pH balance</p>	<p><b>Disease associations:</b> Dehydration, renal dysfunction (e.g., renal acidosis), diabetes, metabolic acidosis (particularly if chloride is high), respiratory alkalosis (e.g., hypotension, high altitude, hyperventilation)</p> <p><b>Medications:</b> Diuretics (e.g., HCTZ), aspirin, salicylates</p>	<p><b>Disease associations:</b> fever, persistent vomiting, metabolic alkalosis (particularly if chloride, calcium, and potassium are low), respiratory acidosis (e.g., COPD, emphysema, pneumonia), adrenal hyperfunction/Cushing's disease, hypochlorhydria</p> <p><b>Medications:</b> Diuretics</p>

<p><b>Glucose (Renal)</b></p> <p>Reflects the level of glucose filtered and reabsorbed by the kidneys, providing insight into kidney function.</p>	<p><b>Disease associations:</b> Hyperthyroidism, fever</p> <p><b>Other:</b> Pregnancy, exercise<sup>56</sup></p> <p><b>Medications:</b> Iatrogenic hypoglycemia due to excess insulin administration or excessive dose of oral hypoglycemic medication</p>	<p><b>Disease associations:</b> The causes of glucosuria can be grouped under two classes: the inability of the proximal convoluted tubule (PCT) to reabsorb glucose and an increase in glucose concentration in the circulating blood. Defects in the PCT, either primary or secondary, can result in glucosuria. Examples include Fanconi syndrome and acute tubular necrosis. A mutation in SGLT1 is associated with glucose-galactose malabsorption, a mutation in SGLT2 is associated with familial renal glucosuria (FRG), and a mutation in GLUT2 is associated with Fanconi-Bickel syndrome. Diabetes, renal disease (diabetic glomerulosclerosis), heart failure, chronic hyperglycemia, lack of oxygenation of the PCT.</p> <p><b>Diet:</b> Excess carbohydrate intake</p> <p><b>Medications:</b> Chloride, iodide, bromide, and nitrate of sodium</p> <p><b>Other:</b> Pregnancy, older age<sup>55</sup></p>
<p><b>BUN (Blood Urea Nitrogen)</b></p> <p>Measures the concentration of urea nitrogen in the blood, serving as an indicator of kidney function and hydration status.</p>	<p><b>Diet:</b> Low-protein diet, overhydration, liver disease</p> <p><b>Other:</b> Aging (infants and children have lower BUN levels), small body type<sup>56</sup></p>	<p><b>Disease associations:</b> Dehydration, burns, blockage in the urinary system that prevents one from urinating, stress, heart attack, gastrointestinal bleeding</p> <p><b>Diet:</b> High-protein diet</p> <p><b>Medications:</b> Carbamazepine, methotrexate, tetracycline<sup>57</sup></p>
<p><b>Creatinine</b></p> <p>Indicates the level of creatinine, a waste product of muscle metabolism, in the blood; used to assess kidney function.</p>	<p><b>Disease associations:</b> History of an amputation, muscle wasting disease, severe liver disease (cirrhosis)</p> <p><b>Diet:</b> Vegan or vegetarian diet</p> <p><b>Other:</b> Low muscle mass, pregnancy<sup>58</sup></p>	<p><b>Disease associations:</b> Kidney disease or injury, infection, poor blood flow to kidneys, blockage in the urinary system, kidney failure. Note that high blood creatinine levels don't always indicate kidney disease.<sup>57</sup></p> <p><b>Diet:</b> Eating large amounts of cooked meats or creatine supplements</p> <p><b>Medications:</b> Cimetidine, cobicistat, dolutegravir, fenofibrate, ritonavir, or trimethoprim</p> <p><b>Other:</b> Recent high-intensity exercise, high muscle mass (very muscular body frame, bodybuilder)<sup>58</sup></p>
<p><b>eGFR</b></p> <p>An estimate of the kidney's filtration rate, calculated based on serum creatinine levels, age, sex, and other factors, is a key indicator of kidney function.</p>	<p><b>Disease associations:</b> Severe dehydration, kidney damage, chronic kidney disease often caused by diabetes and hypertension, kidney failure, malnutrition, chronic illnesses, cirrhosis, nephrotic syndrome caused by having too much protein in urine</p> <p><b>Diet:</b> High protein diet<sup>59</sup></p> <p><b>Medications:</b> Statins, NSAIDs, antimicrobials, diabetes medication, antacid medications<sup>60</sup></p> <p><b>Other:</b> Unusual muscle mass affecting weight of muscles, pregnancy, being over the age of 70, solid organ transplant<sup>61</sup></p>	<p>Higher levels of eGFR are generally considered beneficial.</p>

<p><b>eGFR (African American)</b></p> <p>Similar to eGFR but adjusted for individuals of African American descent. Please note the National Kidney Foundation (NKF) has stated that the U.S. now mandates all transplant hospitals adopt a new race-free eGFR equation.<sup>62</sup></p>	<p>See section on low <b>eGFR</b>.</p>	<p>Higher levels of eGFR (African American) are generally considered beneficial.</p>
<p><b>BUN/Creatinine Ratio</b></p> <p>Provides additional information about kidney function and hydration status.</p>	<p><b>Disease associations:</b> Malnutrition, starvation, impaired metabolic activity in the liver due to parenchymal liver disease or, rarely, to congenital deficiency of urea cycle enzymes, reduced urea synthesis as in advanced liver disease, supernormal excretion of urea as in sickle cell anemia, increased creatinine production as in rhabdomyolysis, effective removal of urea than creatinine during dialysis</p> <p><b>Diet:</b> Inadequate protein intake</p> <p><b>Medications:</b> Salicylates, cimetidine, and trimethoprim interfere with tubular secretion of creatinine and cause a spuriously low creatinine<sup>63</sup></p>	<p><b>Disease associations:</b> Gastrointestinal bleeding, catabolic processes such as fever or infection</p> <p><b>Medications:</b> Antianabolic drugs such as tetracyclines (except doxycycline), glucocorticoids</p> <p><b>Diet:</b> High-protein diet<sup>63</sup></p>
<p><b>Calcium</b></p> <p>Essential for bone health, muscle function, nerve transmission, and various biochemical processes in the body.</p>	<p><b>Disease associations:</b> The causes of hypocalcemia can be divided into three broad categories: PTH deficiency, high PTH, and other causes.</p> <p><b>PTH Deficiency:</b> Postsurgical (thyroidectomy, parathyroidectomy, or radical neck surgery), autoimmune hyperparathyroidism, autoimmune polyglandular syndrome type I, also called autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome (APECED), abnormal parathyroid gland development, parathyroid gland destruction</p> <p><b>High PTH Levels:</b> Absolute or relative vitamin D deficiency, chronic kidney disease (CKD), pseudohypoparathyroidism (PHP, a genetic disorder that causes end-organ resistance to the action of PTH concentration)</p> <p><b>Other Causes:</b> Pseudohypocalcemia, acidosis/alkalosis, acute pancreatitis, severe sepsis/critical illness/trauma, blood transfusions containing citrate, which binds to calcium, hypomagnesemia/hypermagnesemia, acute hyperphosphatemia, osteoblastic metastasis, pregnancy</p> <p><b>Medications:</b> Bisphosphonates, denosumab, cinacalcet, cisplatin, foscarnet, massive blood transfusion<sup>64</sup></p>	<p><b>Disease Associations:</b> Excess parathyroid hormone (PTH), PTH-mediated causes (adenoma/hyperplasia of the gland, familial hypocalciuric hypercalcemia, and multiple endocrine neoplasia syndromes (type 1, 2A)), renal carcinomas, leukemias, lymphomas, rhabdomyosarcoma, hypervitaminosis D, sarcoidosis, tuberculosis, fungal infections, thyrotoxicosis, hypoadrenalism, pheochromocytomas, Williams-Beuren syndrome, Murk Jansen syndrome, hypophosphatasia, hypervitaminosis A, acute/chronic renal failure, milk-alkali syndrome, subcutaneous fat necrosis</p> <p><b>Diet:</b> Excessive vitamin D intake</p> <p><b>Medications:</b> Thiazide diuretics, lithium</p> <p><b>Other:</b> Prolonged immobilization</p>
<p><b>Albumin</b></p> <p>The most abundant protein in the blood plasma that plays a critical role in maintaining oncotic pressure, transporting various substances, and regulating fluid balance.</p>	<p><b>Disease Associations:</b> Infection, inflammation due to sepsis, inflammatory bowel disease (IBD), kidney disease, liver disease (cirrhosis, fatty liver disease, liver cancer or hepatitis A, B or C), malnutrition, thyroid disease<sup>65</sup></p> <p><b>Other:</b> Surgery, hospitalized, critically ill, elderly patients<sup>66</sup></p>	<p><b>Disease Associations:</b> Dehydration, severe diarrhea<sup>65</sup></p>

<p><b>ALT</b></p> <p>ALT (Alanine Aminotransferase) is an enzyme primarily found in the liver.</p>	<p>Lower levels of ALT are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Acute or chronic viral hepatitis, alcoholic hepatitis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), chronic hepatitis B or C, autoimmune hepatitis, alpha-1 antitrypsin deficiency, hemochromatosis, Wilson disease, celiac disease, ischemic hepatitis, Budd-Chiari syndrome, vascular disease, genetically related conditions affecting the liver, drug-associated, occupational exposure, or herbal supplement-induced liver injury</p> <p><b>Other:</b> Extreme physical exertion, diurnal variation (nadir value at 4:00 hr, peak value is at 16:00 hr), gender (higher in males compared to females), ethnicity (Mexican Americans have a higher ALT elevation prevalence than other ethnicities)<sup>67</sup></p>
<p><b>AST</b></p> <p>Aspartate Aminotransferase is an enzyme found in various tissues, including the liver, heart, muscles, and kidneys.</p>	<p>Lower levels of AST are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Alcohol-related, steatohepatitis, cirrhosis, hemolysis, myopathy, thyroid disease</p> <p><b>Other:</b> Extreme physical exertion<sup>68</sup></p>
<p><b>Bili, Total</b></p> <p>Measures the total amount of bilirubin in the blood, a waste product from the breakdown of red blood cells.</p>	<p>Lower levels of bilirubin are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Hemolytic disease, sickle cell disease, adverse reaction to a blood transfusion, biliary disease or gallstone disease (gallstones, cholecystitis, cholangitis), infections (viral hepatitis, mononucleosis), Gilbert's syndrome, Wilson disease, Crigler-Najjar syndrome, toxic hepatitis (alcohol-induced or drug-induced), cirrhosis, chronic liver failure<sup>69</sup></p>
<p><b>Protein, Total</b></p> <p>Measures the total amount of protein in the blood, including albumin and globulins.</p>	<p><b>Disease associations:</b> Liver or kidney problem, maldigestion or malabsorption of protein<sup>70</sup></p>	<p><b>Disease associations:</b> Amyloidosis, dehydration, hepatitis B, hepatitis C, HIV/AIDS, monoclonal gammopathy of undetermined significance (MGUS), multiple myeloma</p> <p><b>Diet:</b> A high-protein diet doesn't cause high blood protein.<sup>71</sup></p>
<p><b>Alkaline Phosphatase</b></p> <p>Enzymes found in various tissues, including the liver, bones, kidneys, and intestines.</p>	<p><b>Disease associations:</b> Wilson disease, malnutrition, magnesium deficiency, zinc deficiency, pernicious anemia, hypothyroidism, congenital hypophosphatasia, mononucleosis, bone metastasis<sup>72</sup></p>	<p><b>Disease associations:</b> Cholestasis (intrahepatic, extrahepatic), biliary obstruction due to cancer (cholangiocarcinoma, pancreatic head adenocarcinoma, ampullary adenocarcinoma), choledocholithiasis, biliary stricture, sclerosing cholangitis, primary biliary cholangitis (PBC), drug-induced liver injury, chronic rejection of liver allografts, infiltrative liver diseases (sarcoidosis, amyloidosis, tuberculosis, and liver metastasis), severe alcoholic hepatitis leading to steatonecrosis, AIDS, opportunistic infections (cytomegalovirus, cryptosporidiosis), granulomatous liver involvement from tuberculosis, cirrhosis, chronic hepatitis, viral hepatitis, congestive heart failure, ischemic cholangiopathy, intra-abdominal infections, cholestasis of sepsis, myeloid metaplasia, osteomyelitis, local bile duct obstruction, augmented leakage of the liver isoenzymes (Hodgkin's lymphoma, Stauffer syndrome), biliary atresia, osteitis deformans, osteogenic sarcoma, hyperparathyroidism, hyperthyroidism, osteomalacia, untreated celiac disease<sup>71 73</sup></p>

<p><b>Serum Osmolality</b></p> <p>Measures the concentration of solutes in the blood plasma, reflecting the body's hydration status and electrolyte balance.</p>	<p><b>Disease associations:</b> Psychogenic polydipsia, syndrome of inappropriate antidiuretic hormone (SIADH), nephrotic syndrome (proteinuria over 3 grams/day), hypertriglyceridemia, hypoalbuminemia, and a hypercoagulable state), liver cirrhosis<sup>74</sup></p>	<p><b>Disease associations:</b> Dehydration, diabetes insipidus<sup>73</sup></p>
Lipids		
Marker	Low	High
<p><b>Cholesterol, Total</b></p> <p>Represents the total amount of cholesterol in the blood, including both LDL (low-density lipoprotein) and HDL (high-density lipoprotein) cholesterol.</p>	<p><b>Disease associations:</b> Having a low lipid level rarely causes a problem, but it may indicate the presence of another disorder. For example, a low cholesterol level may indicate a genetic disorder (abetalipoproteinemia, chylomicron retention disease (Anderson disease), hypoalphalipoproteinemia), anemia, cancer, chronic infection such as hepatitis C, malabsorption, hyperthyroidism, or undernutrition.<sup>75</sup></p>	<p><b>Disease associations:</b> Familial hypercholesterolemia, chronic kidney disease, diabetes, HIV infection, hypothyroidism, lupus erythematosus, overweight, obesity, PCOS, sleep apnea[i]</p> <p><b>Diet:</b> Excessive saturated or trans fats and alcohol</p> <p><b>Medications:</b> Cholesterol levels can also be worsened by some types of medications for other health problems, such as acne, cancer, high blood pressure, HIV/AIDS, irregular heart rhythms, and organ transplant medications.</p> <p><b>Other:</b> Stress, lack of exercise, smoking, age<sup>77</sup></p>
<p><b>LDL Calculation</b></p> <p>Estimates LDL cholesterol based on the Friedewald formula (FF): total cholesterol (TC) minus HDL cholesterol minus triglycerides (TGs)/5 in mg/dl). Used to assess cardiovascular risk.</p> <p>The FF is not valid for patients with TGs &gt;400 and those with type 3 dyslipoproteinemia.<sup>78</sup></p>	<p>There is no consensus on defining very low LDL cholesterol, but LDL would be considered very low if it is less than 40 milligrams per deciliter of blood.</p> <p><b>Disease associations:</b> Although the risks are rare, very low levels of LDL cholesterol may be associated with an increased risk of cancer, hemorrhagic stroke, depression, anxiety, preterm birth, and low birth weight if cholesterol is low while pregnant.<sup>79</sup></p>	<p><b>Disease associations:</b> Overweight, obesity, diabetes, chronic kidney disease, HIV, familial hypercholesterolemia</p> <p><b>Diet:</b> Excessive intake of fatty meats (red/processed meats), fried foods, full-fat dairy products, bakery goods, fast food</p> <p><b>Medications:</b> Blood pressure and HIV drugs</p> <p><b>Other:</b> Smoking, tobacco products, age, post-menopausal stage<sup>80</sup></p>
<p><b>HDL Direct</b></p> <p>Measures the level of HDL cholesterol, often referred to as "good" cholesterol due to its protective effects against cardiovascular disease.</p>	<p><b>Disease associations:</b> Tangier disease, apoA1 deficiency, familial combined hyperlipidemia (FCH), fish-eye syndrome, metabolic syndrome atherogenic lipid phenotype (features include insulin resistance, type 2 diabetes mellitus, obesity, hypertension, borderline high LDL, elevations of triglyceride enriched remnants)<sup>81</sup></p> <p><b>Medications:</b> Beta blockers, thiazide diuretics, androgens, progestogens, anabolic steroids</p> <p><b>Other:</b> Smoking<sup>82</sup></p>	<p><b>Disease associations:</b> usually, high HDL cholesterol (the "good" cholesterol) may decrease the risk of heart attacks and strokes. However, HDL cholesterol levels may be increased in some genetic disorders. In these disorders, the high HDL level may not protect against heart attacks or strokes, probably because the disease also causes other changes in lipid levels and other abnormalities in the way the body breaks down food</p> <p><b>Genetics:</b> Cholesteryl ester transfer protein (CETP) deficiency, familial hyperalphalipoproteinemia), alcohol use disorder without cirrhosis, hyperthyroidism, primary biliary cirrhosis</p> <p><b>Medications:</b> Corticosteroids, insulin, phenytoin<sup>83</sup></p>

<p><b>Cholesterol/ HDL Ratio</b></p> <p>This ratio is calculated by dividing the total cholesterol by the HDL level. An ideal ratio is 5:1, with an even more favorable ratio at 3.5:1</p>	<p>A lower ratio is generally associated with better cardiovascular health.<sup>84</sup></p>	<p>A higher ratio is generally associated with a higher risk of heart disease<sup>85</sup></p>
<p><b>Triglycerides</b></p> <p>They function as carriers for fatty acids, provide a source of energy, insulate and protect organs, and help transport fat-soluble vitamins.</p>	<p>Exceedingly low results are rare and may be attributed to certain genetic, infectious, or autoimmune conditions and analytical interference.<sup>86</sup></p> <p><b>Disease associations:</b> Strenuous exercise (endurance or resistance), autoimmune disease, immune system hyperreactivity<sup>87 88</sup></p> <p><b>Diet:</b> Fish oils rich in n-3 fatty acids<sup>89</sup></p> <p><b>Medications:</b> IV insulin infusion, fibrates, therapeutic doses of niacin, statins<sup>84</sup></p>	<p><b>Disease associations:</b> Hypertriglyceridemia is usually multifactorial. A combination of genetic factors, increased production, and or impaired clearance of triglyceride-rich lipoproteins (TRLP) are known to play a role in hypertriglyceridemia.</p> <p><b>Genetics:</b> Familial hypertriglyceridemia (excess Very Low-Density Lipoprotein but normal Total Cholesterol), familial combined hyperlipidemia, apolipoprotein C-III, lipoprotein lipase deficiency, apolipoprotein C-II deficiency, apolipoprotein AV deficiency, dysbetalipoproteinemia), obesity, metabolic syndrome, diabetes mellitus type 2, hypothyroidism, Cushing's syndrome, chronic kidney disease, human immunodeficiency virus, some autoimmune conditions (e.g., systemic lupus erythematosus)</p> <p><b>Diet:</b> Excessive alcohol intake, foods rich in saturated fat or with a high glycemic index</p> <p><b>Medications:</b> Thiazides, beta-blockers, oral estrogens, tamoxifen, Oral contraceptive pills (OCP), antiretroviral protease inhibitors, atypical antipsychotics, isotretinoin, corticosteroids, bile acid-binding resins, immunosuppressive agents (sirolimus)</p> <p><b>Other:</b> Pregnancy<sup>90</sup></p>
<p><b>LDL Direct</b></p> <p>Directly measures LDL cholesterol level rather than using an equation to estimate LDL levels.</p> <p>Direct measurement of LDL cholesterol is not a routine cholesterol test. Instead, it is often used if high triglycerides are implicated.</p> <p>High triglycerides can invalidate the formula used to calculate LDL cholesterol. As a result, a direct LDL cholesterol test may be recommended if high triglycerides were on a prior test or if there are risk factors for high triglycerides.</p>	<p>See section on low <b>LDL Calculation.</b></p>	<p>See section on high <b>LDL Calculation.</b></p>

Apolipoproteins		
Marker	Low	High
<p><b>Apo A-1</b></p> <p>Apolipoprotein A1, the main protein component of HDL cholesterol; higher levels are associated with decreased cardiovascular risk.</p>	<p><b>Disease associations:</b> Familial hypoalphalipoproteinemia, Tangier disease, Hepatocellular disorders, poorly controlled diabetes, nephritic syndrome, chronic kidney failure, coronary artery disease, cholestasis</p> <p><b>Medications:</b> Diuretics, androgens</p> <p><b>Other:</b> Smoking cigarettes<sup>91</sup></p>	<p><b>Disease associations:</b> Familial hyperalphalipoproteinemia, familial cholesteryl ester transfer protein deficiency</p> <p><b>Medications:</b> Estrogens, niacin, statin</p> <p><b>Other:</b> Weight loss<sup>90</sup></p>
<p><b>Apo B</b></p> <p>Apolipoprotein B, the main protein component of LDL cholesterol; higher levels are associated with increased cardiovascular risk.</p>	<p><b>Disease associations:</b> Sepsis, liver disease</p> <p><b>Medications:</b> Estrogens<sup>92</sup></p>	<p><b>Disease associations:</b> Hypercholesterolemia, nephrotic syndrome</p> <p><b>Other:</b> Pregnancy<sup>91</sup></p>
<p><b>Apo B: Apo A-1</b></p> <p>The ratio of Apo B to Apo A-1 that is considered a sensitive marker of atherogenic risk.</p>	<p>Lower Apo B: Apo A-1 ratio indicates higher levels of Apo A-1, and thus HDL cholesterol, which are associated with a reduced cardiovascular risk<sup>93</sup></p>	<p>Higher Apo B: Apo A-1 ratio indicates a higher cardiovascular risk, such that the cut-off value of 0.9 has been proposed to define a risk of developing cardiovascular disease.<sup>94</sup></p>
Inflammation		
Marker	Low	High
<p><b>PLAC</b></p> <p>Measures lipoprotein-associated phospholipase A2, a marker of vascular inflammation and atherosclerosis.</p>	<p>Lower levels of PLAC are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Inflammation, hypertension, hypercholesterolemia<sup>95</sup></p> <p><b>Diet:</b> Binge eating</p> <p><b>Medications:</b> Beta-blockers, steroids<sup>96</sup></p>
<p><b>Homocysteine</b></p> <p>Amino acid associated with an increased risk of cardiovascular disease when elevated; may indicate deficiencies in B vitamins or genetic factors.</p>	<p>Lower levels of homocysteine are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Genetic defect in the enzyme Methylene Tetrahydrofolate Reductase (MTHFR), vitamin B12, B6, and folate deficiency, cognitive decline, osteoporosis, chronic kidney disease, hypothyroidism, Alzheimer's disease, schizophrenia</p> <p><b>Medications:</b> Proton pump inhibitors</p> <p><b>Other:</b> Hip fracture, alcohol use<sup>97</sup></p>

<p><b>ox-LDL</b></p> <p>Oxidized LDL is LDL cholesterol that has undergone oxidation, contributing to atherosclerosis and cardiovascular disease.</p>	<p>Lower levels of ox-LDL are generally considered beneficial and not clinically significant.</p>	<p><b>Disease associations:</b> Metabolic syndrome (obesity, dyslipidemia, hypertension, and insulin resistance), low-grade inflammation, high oxidative stress, infection, diabetes/hyperglycemia, hyperuricemia, hyperhomocysteinemia<sup>98 99</sup></p> <p><b>Diet:</b> excessive intake of unhealthy fats and sugar</p> <p><b>Other:</b> Smoking, irradiation, environmental pollution (i.e., PM2.5), physical inactivity<sup>97</sup></p>
<p><b>MPO</b></p> <p>Myeloperoxidase is an enzyme released by white blood cells and is associated with oxidative stress, inflammation, and increased cardiovascular risk. It is abundantly expressed in immune cells (neutrophils, lymphocytes, monocytes, macrophages) and other body cells</p>	<p>Generally, low MPO indicates low cardiovascular risk; however, lack of functional myeloperoxidase leads to less efficient killing of intracellular pathogens.</p> <p><b>Disease associations:</b> MPO deficiency (autosomal recessive disorder caused by mutations in the MPO gene on chromosome 17), diabetes mellitus, pregnancy, iron deficiency, renal transplantation, thrombotic diseases, lead poisoning, obstructive jaundice, disseminated cancers, hematologic disorders, and neoplasms such as acute and chronic myeloid leukemia, myelodysplastic syndrome, polycythemia vera, Hodgkin's lymphoma, severe infections, cytotoxic agents</p> <p><b>Medications:</b> Anti-inflammatory drugs like sulfapyridine<sup>100</sup></p>	<p><b>Disease associations:</b> Tissue injury, rheumatoid arthritis, cardiovascular diseases, liver diseases, diabetes, cancer.<sup>101</sup> Systemic myeloperoxidase levels are significantly elevated in patients with acute coronary syndrome presenting with eroded culprit plaque compared with patients presenting with ruptured culprit plaque<sup>102</sup></p>
<p><b>High-sensitivity C-reactive protein (hs-CRP)</b></p> <p>Hs-CRP measures levels of C-reactive protein, a marker of systemic inflammation and cardiovascular risk.</p>	<p>See low hs-CRP under <b>Rheumatoid Arthritis Panel</b>.</p>	<p>See high hs-CRP under <b>Rheumatoid Arthritis Panel</b>.</p>

### Lipoprotein Markers

Marker	Low	High
<p><b>sdLDL</b></p> <p>Small Dense LDL is a subtype of LDL cholesterol associated with increased cardiovascular risk due to its ability to penetrate arterial walls more easily.</p>	<p><b>Disease associations:</b> Fasting triglycerides less than 70 mg/dL.</p> <p><b>Medications:</b> Alpha-blockers, niacin, and fibric acid derivatives<sup>106</sup></p>	<p><b>Disease associations:</b> Metabolic syndrome (MetS), fasting triglycerides greater than 250 mg/dL, HDL below 35, dyslipidemia, diabetes, insulin resistance, chronic kidney disease (CKD), genetic predisposition<sup>103 104 105</sup></p> <p><b>Diet:</b> Excessive saturated fats</p> <p><b>Medications:</b> Beta-blockers<sup>103</sup></p> <p><b>Other:</b> Sedentary lifestyle</p>



<p><b>Lp(a)</b></p> <p>Genetic variation of LDL cholesterol associated with increased risk of cardiovascular disease and atherosclerosis.</p>	<p>Lower levels of Lp(a) are generally considered beneficial and not clinically significant.</p> <p><b>Disease associations:</b> Hyperthyroidism, liver disease depending on the cause (mixed results for non-alcoholic fatty liver disease)</p> <p><b>Diet:</b> Low-carb diet high in saturated fat</p> <p><b>Medication:</b> Hormone replacement therapy<sup>106</sup></p>	<p><b>Disease associations:</b> Genetic factors play a major role in Lp(a) concentrations. In fact, Lp(a) levels are 70% to 90% genetically determined. Non-genetic influences include hypothyroidism, kidney disease (chronic kidney disease and hemodialysis, peritoneal dialysis, nephrotic syndrome, kidney transplantation)</p> <p><b>Diet:</b> Saturated fat reduction</p> <p><b>Medication:</b> Growth hormones</p> <p><b>Other:</b> Menopause<sup>106</sup></p>
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### Glycemic Control

Marker	Low	High
<p><b>Glucose (Diabetes)</b></p> <p>Measures the concentration of glucose in the blood, used for diagnosing and monitoring diabetes mellitus and assessing glycemic control.</p>	<p>See low Glucose (Renal) under <b>Complete Metabolic Panel (CMP)</b></p>	<p>See high Glucose (Renal) under <b>Complete Metabolic Panel (CMP)</b></p>
<p><b>Hemoglobin A1C</b></p> <p>Reflects average blood glucose levels over the past three months, providing a long-term indicator of glycemic control.</p> <p>The amount of glucose that is present in the blood will attach to the hemoglobin protein, and increased glucose levels will reflect on the surface of the hemoglobin protein, thereby rendering a higher A1c level</p>	<p><b>Disease associations:</b> Reticulocytosis, chronic liver disease, genetic or chemical alterations in hemoglobin (hemoglobinopathies, fetal hemoglobin, methemoglobin), decreased erythrocyte life span (splenomegaly, rheumatoid arthritis), increased intraerythrocyte pH.</p> <p>A falsely low HbA1c value can result from high altitude, pregnancy, hemorrhage, blood transfusion, erythropoietin administration, iron supplementation, hemolytic anemia, chronic kidney failure, liver cirrhosis, alcoholism, sickle cell anemia, and spherocytosis. Vitamin C supplementation can either increase or decrease the HbA1c level depending on the method used for its measurement.<sup>107</sup></p> <p><b>Medications:</b> Vitamin B12, aspirin, vitamin E, ribavirin, dapsone, anti-retrovirals.<sup>108</sup></p>	<p><b>Disease associations:</b> deficiency in iron or vitamin B12, decreased erythropoiesis, genetic or chemical alterations in hemoglobin (hemoglobinopathies, fetal hemoglobin, methemoglobin), alcoholism, chronic renal failure, decreased intraerythrocyte pH.</p> <p>A falsely high HbA1c may be due to a lack of available iron in the blood (iron deficiency anemia, infection-induced anemia, tumor-induced anemia), hemoglobinopathies (thalassemia, B12 deficiency), hypertriglyceridemia, organ transplantation, hyperglycation in certain ethnic groups).</p> <p>People diagnosed with sickle cell anemia, thalassemia, anemia, kidney failure, liver disease, or patients receiving blood transfusions can experience altered results due to the longevity of the red blood cell.<sup>107</sup></p> <p><b>Medications:</b> Immunosuppressants and protease inhibitors can sometimes lead to a falsely high HbA1c.<sup>107</sup></p> <p><b>Other:</b> Increased erythrocyte life span via splenectomy<sup>108</sup>, age (HbA1c concentrations increase by 0.1% per decade after 30 years of age)<sup>110</sup></p>

<p><b>Glycated Serum Protein (GSP)</b></p> <p>Reflects the percentage of serum proteins, e.g., fructosamine and glycated albumin that are glycated (bound to glucose molecules) and provides an alternative marker for assessing glycemic control.</p> <p>GSP level is relatively stable and can reflect the blood glucose level in the human body within 2–3 weeks.<sup>109</sup></p>	<p>Lower levels of GSP are generally considered beneficial and not clinically significant.</p> <p>However, consistently low levels of GSP could potentially indicate a higher risk of hypoglycemia.</p>	<p><b>Disease associations:</b> Diabetes, hyperglycemia, elevated HbA1c, elevated glycated albumin<sup>109</sup></p> <p>Glycated albumin represents 90% of the glycated serum proteins.<sup>110</sup> Factors that influence albumin metabolism may alter glycated albumin independent of glycemia (nephrotic syndrome, cirrhosis, thyroid disease, hyperuricemia, hypertriglyceridemia, smoking).<sup>111</sup></p> <p>Fructosamine levels may also affect glycated serum proteins. Serum uric acid may also interfere with fructosamine measurements by nitroblue tetrazolium, leading to falsely higher fructosamine concentrations.<sup>110</sup></p>
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**Insulin Resistance**

Marker	Low	High
<p><b>Adiponectin</b></p> <p>Adipokine hormone secreted by adipose tissue, plays a role in regulating glucose levels, fatty acid oxidation, and inflammation.</p>	<p><b>Disease associations:</b> Obesity, overweight, insulin resistance, atherosclerosis, lipodystrophy<sup>112</sup></p>	<p>Higher levels of adiponectin are generally considered beneficial and not clinically significant.</p> <p>Higher adiponectin is associated with better metabolic health in both nonobese and obese white individuals.<sup>113</sup></p>
<p><b>Ferritin</b></p> <p>Protein that stores iron in cells, reflecting the body's iron stores; used to assess iron status and diagnose iron deficiency or iron overload disorders.</p>	<p><b>Disease associations:</b> Low iron stores, low gastrointestinal absorption of iron due to post-bariatric surgery, Crohn's disease, ulcerative colitis, celiac disease, hemorrhoids, colon cancer, peptic ulcer, menorrhagia, hematuria</p> <p>Rarely, hypoferritinemia may be due to disorders of iron metabolism.<sup>114</sup></p> <p><b>Diet:</b> Decreased iron intake, poor diet</p>	<p><b>Disease associations:</b> Iron overload, hemochromatosis, liver or renal disease, malignancy, metabolic syndrome, obesity, inflammation, diabetes, liver disease, malignancy, infection<sup>115 116</sup></p> <p><b>Diet:</b> Excessive alcohol consumption</p>

**Beta Cell Function**

Marker	Low	High
<p><b>Insulin</b></p> <p>Hormone produced by the pancreas that regulates blood glucose levels by promoting glucose uptake by cells.</p>	<p><b>Disease associations:</b> Advanced liver disease, renal failure, malnutrition, anorexia nervosa</p> <p><b>Diet:</b> Excess intake of carbohydrates may cause hyperinsulinemia initially, subsequently progressing to failure of beta cells of the pancreas and hypoinsulinemia.</p> <p><b>Other:</b> Surgical stress</p>	<p><b>Disease associations:</b> Obesity is the most common reason for insulin resistance with consequent hyperinsulinemia. Other reasons for hyperinsulinemia are type II diabetes mellitus, genetic predisposition with a family history of hypertension,<sup>117</sup> metabolic syndrome, higher childhood body mass index (BMI), and tumors of the pancreatic <math>\beta</math> cells.</p> <p><b>Diet:</b> Excessive free fatty acids in high-fat diet</p> <p><b>Other:</b> Increase in reactive oxygen species, air pollution, bisphenol A exposure, puberty<sup>118</sup></p>

## Other Markers

Marker	Low	High
<p><b>Total IgG</b></p> <p>Measures the total level of immunoglobulin G antibodies in the blood, providing information about the overall immune response and antibody-mediated immunity. In normal serum, about 80% is IgG.<sup>119</sup></p>	<p><b>Disease associations:</b> Congenital deficiencies, primary or secondary immune deficiencies, chronic lymphocytic leukemia (CLL), hyper-IgM syndrome (characterized by normal to elevated IgM levels and decreased levels of IgG, IgA, and IgE immunoglobulins), prolonged infections<sup>119</sup></p> <p><b>Medications:</b> Corticosteroids, immunosuppressants</p> <p><b>Other:</b> Hazardous environmental conditions<sup>120 122</sup></p>	<p><b>Disease associations:</b> Liver disease, autoimmune disease, vasculitis, infection, hematological disease, IgG4-related disease, immunodeficiency, and iatrogenic (from intravenous immunoglobulin administration)<sup>121</sup></p>
<p><b>Total IgM</b></p> <p>Measures the total level of immunoglobulin M antibodies in the blood, serving as an indicator of recent or current infection, particularly with certain bacteria or viruses, as IgM is the first antibody produced in response to an infection.</p>	<p><b>Disease associations:</b> Immunodeficiencies resulting from genetic disorders and/or chromosomal anomalies during the development of the immune system, nutritional disorders, infections, chemotherapy, malignancy, nephrotic syndrome, metabolic diseases<sup>120</sup></p>	<p><b>Disease associations:</b> Impaired B cell immunoglobulin class switching, acute infection, hyper-IgM syndrome<sup>121</sup></p>
<p><b>Total CK</b></p> <p>Creatine kinase is an enzyme found predominantly in muscle tissue, released into the bloodstream following muscle damage; it is used to diagnose and monitor muscle injury or disease.</p>	<p><b>Disease associations:</b> Low muscle mass, autoimmune disease (e.g., lupus, rheumatoid arthritis)<sup>122 123</sup></p> <p><b>Other:</b> Pregnancy (CK levels may be reduced in the second trimester of pregnancy).<sup>124</sup></p>	<p><b>Disease associations:</b> Endocrine disorders (e.g., hyperthyroidism, hypothyroidism, hyperparathyroidism, acromegaly, Cushing syndrome), metabolic disturbances (e.g., hyponatremia, hypokalemia, hypophosphatemia), muscle trauma (e.g., strenuous exercise, intramuscular injections, needle electromyography, seizures), celiac disease, malignancy, macro CK, cardiac disease, acute kidney disease, viral illness, predisposition to malignant hyperthermia</p> <p><b>Medications:</b> Statins, fibrates, antiretrovirals, beta-blockers, clozapine, angiotensin II receptor blockers, hydroxychloroquine, isotretinoin, colchicine</p> <p><b>Other:</b> Surgery, pregnancy, transient rise after exercise, or heavy manual labor. Total CK may increase to as much as 30 times the upper limit of normal within 24 hours of strenuous physical activity, then slowly decline over the next seven days. The degree of CK elevation depends on the type and duration of exercise, with greater elevation in those who are untrained.<sup>125</sup></p>

<p><b>Uric Acid</b></p> <p>Uric acid is a waste product created when the body breaks down purines. This marker determines how well the body produces and removes uric acid.</p>	<p><b>Disease associations:</b> Hereditary xanthinuria, hereditary renal hypouricemia, multiple sclerosis, Parkinson's disease, Alzheimer's disease, optic neuritis<sup>126 129</sup></p> <p><b>Medications:</b> Uric acid inhibitors (allopurinol and tisopurine), uric acid excretors (probenecid, benzbromarone), uric acid lyser (urate-oxidase), losartan, fenofibrate, NSAIDs<sup>127 128</sup></p>	<p><b>Disease associations:</b> Gout, hypertension, cardiovascular disease, renal disease, genetics, leukemia, metabolic syndrome, obesity, polycythemia vera, psoriasis, tumor lysis syndrome (rapid release of cells into the blood caused by certain cancers or by chemotherapy for those cancers)<sup>129</sup></p> <p><b>Diet:</b> Purine-rich diet (high in foods such as liver, game meat, anchovies, sardines), excessive intake of alcohol, soda, fructose</p> <p><b>Medications:</b> Diuretics, immune-suppressing drugs, niacin (vitamin B3)<sup>130</sup></p>
<p><b>Human IGF-1</b></p> <p>Insulin-like Growth Factor 1 is a hormone primarily produced in the liver in response to growth hormone stimulation, playing a role in cell growth, development, and metabolism; levels may be altered in growth disorders, acromegaly, or metabolic</p>	<p><b>Disease associations:</b> Laron Syndrome, liver cirrhosis, aging including age-related-cardiovascular and neurological diseases, intrauterine growth restriction, malnutrition, diabetes, hypothyroidism, liver disease<sup>131 132</sup></p> <p><b>Diet:</b> High consumption of butter, eggs, and egg products<sup>133</sup></p>	<p><b>Disease associations:</b> Pituitary tumors that lead to acromegaly, malnutrition, obesity, eating disorders, poorly controlled diabetes, cystic fibrosis, hepatic and renal disease, hypothyroidism, severe infection</p> <p><b>Diet:</b> High consumption of dairy products including milk, cheese and yogurt, margarine, high protein, high glycemic-index diet<sup>132 134</sup></p> <p><b>Medications:</b> Supraphysiological testosterone replacement, oral estrogen use</p> <p><b>Other:</b> Pregnancy, adolescence stages</p>
<p><b>Cystatin C</b></p> <p>Protein produced by all nucleated cells, is used as a marker of kidney function and to estimate glomerular filtration rate (GFR).</p>	<p><b>Disease associations:</b> Hypothyroidism, neuromyelitis optica spectrum disorders, bladder cancer, genetics<sup>135 136 137 138</sup></p> <p><b>Other:</b> Prolonged broadband noise exposure (e.g., from jet engines)<sup>139</sup></p>	<p><b>Disease associations:</b> Kidney condition (e.g., chronic kidney disease, low eGFR), cancer, HIV, hyperthyroidism, hypothyroidism, diabetes, higher C-reactive protein, white blood cell count, and lower serum albumin<sup>140 141</sup></p>
<p><b>GGT</b></p> <p>Gamma-glutamyl transferase is an enzyme found in liver cells and other tissues, used as a marker of liver function and to detect liver disease or bile duct obstruction.</p>	<p>Lower levels of GGT are generally considered beneficial and not clinically significant.</p> <p><b>Medications:</b> Birth control pills, clofibrate<sup>142</sup></p>	<p><b>Disease associations:</b> Oxidative stress, cholestasis, liver diseases (e.g., hepatitis, cirrhosis, cholestasis, non-alcoholic fatty liver, liver ischemia, liver tumor, liver cancer), alcohol use disorder, pancreatitis, pancreatic cancer, diabetes, metabolic syndrome, cardiovascular mortality, atrial fibrillation, exacerbation of congestive heart failure, sleep apnea<sup>143 144 145 148</sup></p> <p><b>Diet:</b> High alcohol consumption</p> <p><b>Medications:</b> Acetaminophen, carbamazepine, phenytoin, phenobarbital, and the use of any enzyme-inducing drugs can lead to increased free radical production and the threat of glutathione depletion.<sup>146</sup></p> <p><b>Other:</b> Smoking</p>

## LDH

Lactate Dehydrogenase is an enzyme present in many body tissues, particularly in the heart, liver, muscles, and red blood cells; elevated levels may indicate tissue damage or disease.

Lower LDH levels are not as common and usually aren't considered to be a health problem.

**Disease associations:** Lactate dehydrogenase deficiency (rare)

**Diet:** Excessive intake of vitamin C or E<sup>147</sup>

**Disease associations:** Liver diseases, kidney diseases, muscle injury, trauma, heart attack, certain infectious diseases, pancreatitis, cancer, anemia, metastatic cancer, hematologic malignancies, and infection<sup>148 150</sup>

**Medications:** Anesthetics, aspirin, alcohol, certain narcotics, and procainamide may falsely increase LDH.

**Other:** Strenuous exercise, age (infants and young children usually have much higher normal levels of LDH levels as compared to older children and adults<sup>149</sup>

## Leptin

Hormone produced by adipose tissue; play a key role in regulating energy balance, appetite, and metabolism.

**Disease associations:** Dysregulation of cytokine production, autoimmune disorders, malnutrition, inflammatory responses, congenital leptin deficiencies, acquired hyperleptinemia (lipodystrophy syndromes, hypothalamic amenorrhea), severe obesity, impaired satiety, chronic starvation, eating disorders (anorexia, intensive hyperphagia, constant food-seeking behavior), recurrent bacterial infections, hyperinsulinemia, liver steatosis, dyslipidemia, hypogonadotropic hypogonadism, neuroendocrine dysfunction, glucose intolerance, insulin resistance<sup>150 151</sup>

**Other:** Exercise-induced energy deficiency

**Disease associations:** Leptin resistance, common obesity, non-alcoholic fatty liver disease, Rabson-Mendenhall syndrome, neurodegenerative disorders, depression, food addiction, Cushing's syndrome<sup>151 152</sup>

**Medications:** Glucocorticoids



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