TABLE OF CONTENTS

CARDIAC FUNCTION
Elevated Ultra Sensitive Cardiac Troponin (cTnI)..............................1
Elevated N-Terminal pro-B-type Natriuretic Peptide (NT-proBNP)..........2

INFLAMMATION
Elevated Ultra Sensitive Endothelin (ET) ........................................ 3
Elevated Ultra Sensitive Interleukin-6 (IL-6) ..................................... 4
Elevated Ultra Sensitive Interleukin-17A (IL-17A).............................. 5
Elevated Ultra Sensitive Tumor Necrosis Factor-Alpha (TNF-α) .......... 6
Elevated Lipoprotein-associated Phospholipase A2 (Lp-PLA₂) Activity 7
Elevated High Sensitivity C-Reactive Protein (hs-CRP) ....................... 8
Elevated Homocysteine .............................................................. 9
Elevated Uric Acid (UA) ............................................................ 10

LIPID MANAGEMENT
Elevated Triglycerides (TG) ....................................................... 11
Low High Density Lipoprotein-cholesterol (HDL-C).......................... 12
Low High-Density Lipoprotein 2b (HDL-2b).................................. 13
Elevated Low Density Lipoprotein Cholesterol (LDL-C).................... 14
Elevated Small Dense LDL (sdLDL) ........................................... 15
Low Apolipoprotein A1 (Apo A1).................................................. 16
Elevated Apolipoprotein B (Apo B) ............................................. 17
ApoB/ApoA1 Ratio .................................................................... 18
Elevated Lipoprotein (a) (Lp[a]) .................................................. 19

DIABETES & WEIGHT MANAGEMENT
Elevated Fasting Glucose ........................................................... 20
Elevated Fasting Insulin .............................................................. 21
Elevated Hemoglobin A1c (HbA1c) ............................................... 22
Abnormal Cortisol ................................................................. 23
Abnormal Adiponectin .............................................................. 24
Abnormal Leptin ..................................................................... 25
Elevated Ferritin ..................................................................... 26

CALCIUM, BONE & MINERAL HEALTH
Elevated Parathyroid Hormone (PTH) .......................................... 27
Insufficient Vitamin D ................................................................ 28

RENAL
Elevated Cystatin C ................................................................. 29

HEPATIC
Elevated Gamma-Glutamyl Transferase (GGT) ............................... 30

THYROID
Abnormal Thyroid Tests: Thyroid Stimulating Hormone (TSH) .......... 31
Abnormal Thyroid Tests: T3 Total .............................................. 32
Abnormal Thyroid Tests: Free T3 .............................................. 33
Abnormal Thyroid Tests: T4 Total .............................................. 34
Abnormal Thyroid Tests: Free T4 .............................................. 35
Elevated Thyroid Peroxidase Antibody (TPOAb) ............................ 36
Elevated Thyroglobulin Antibodies (TgAb) .................................... 37
Table: Thyroid Antibodies ......................................................... 38

HORMONES
Abnormal Dehydroepiandrosterone Sulfate (DHEAS) ....................... 39
Abnormal Testosterone (male/female) ........................................... 40
Abnormal Sex Hormone Binding Globulin (SHBG) .......................... 41
Abnormal Estradiol .................................................................. 42
Abnormal Luteinizing Hormone (LH) ........................................ 43
Abnormal Follicle Stimulating Hormone (FSH) ............................. 44
Abnormal Prolactin ................................................................. 45
Abnormal Progesterone ........................................................... 46

ONCOLOGY
Total PSA, Free PSA ................................................................ 47
Table: Probability of Prostate Cancer ......................................... 48

REFERENCES
References .............................................................................. 49-53
### CARDIAC FUNCTION

**Elevated Ultra Sensitive Cardiac Troponin (cTnl)**

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac troponin-I</strong> is a contractile protein found in cardiomyocytes. In the primary prevention setting, even slight elevations indicate risk for incident heart failure (HF), and cardiovascular (CV) death. In secondary prevention patients, elevations are risk for future non-fatal myocardial infarction, HF, or CV death.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In the Minnesota Heart Survey, Singulex hs-cTnl levels > 10 pg/mL were associated with an 8.5x increase in CV death compared to levels ≤ 10 pg/mL in an asymptomatic population.

In Merlin TIMI 36, patients with non-ST elevation ACS and Singulex SMC hs-cTnl levels between 4.84-10.05 pg/mL, were associated with 2.19x increase in CV death or myocardial infarction (MI) by one year, as compared to those with cTnl levels < 4.84 pg/mL.

Elevations of cTnl are seen in cardiomyocyte injury or death, cardiac and vascular disease, and infection. Causative factors for chronic cTnl elevations include hypertension (HTN), left ventricular hypertrophy and systolic dysfunction, type 2 diabetes, hypothyroidism, end-stage renal disease (ESRD), and cardiac inflammation.

Evaluate baseline cardiac function to determine ischemic versus non-ischemic pathology. Consider therapies that have been shown to improve cardiac function (e.g., decrease cardiac workload and control blood pressure).
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elevated N-Terminal pro-B-type Natriuretic Peptide (NT-proBNP)</strong></td>
<td>Peptide released in response to cardiac wall stress or stretch. Elevations in NT-proBNP may indicate risk for developing atherosclerosis, cardiac dysfunction and heart failure, and are independently associated with cardiac events in both primary and secondary prevention patient populations.(^1,2,3) OR up to 4.1 for heart failure, CV events and all-cause mortality in a general population.(^3) In the PROTECT study with heart failure patients, increasing NT-proBNP concentrations over time, were associated with 2x increased occurrence of CV events, compared to stable or decreasing NT-proBNP concentrations below 1000 pg/mL.(^4)</td>
<td>NT-proBNP is elevated in medical conditions that impart stress on heart muscle or stretch on cardiac chambers, such as congestive heart failure, ischemic heart disease, atrial fibrillation and valvular disease.(^1,2,3) Elevated levels are also seen in patients of advanced age, and in the presence of hyperthyroidism, sleep apnea, renal failure, cirrhosis of the liver and chronic lung disease.(^2,5)</td>
<td>Evaluate underlying causes of cardiac dysfunction. Exercise has been shown to reduce NT-proBNP levels.(^5,6)</td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>INFLAMMATION</td>
<td>Endothelin is a pro-inflammatory peptide, secreted by vascular endothelial cells and vascular smooth muscle cells, that regulates arterial vasomotor tone and thus blood pressure. In addition, it is secreted by and exerts its effects on renal, pulmonary, cardiac, hepatic, and adipose cells. ET promotes the development of atherosclerotic vascular disease by stimulating inflammatory cytokine release, platelet aggregation, cell adhesion molecule expression, and vascular smooth muscle cell proliferation. In a study including patients with chronic stable angina, only endothelin was found to be an independent predictor of rapid disease progression (OR 6.6).</td>
<td>The renal vasculature is much more sensitive to ET than other vascular beds, and in such, elevations are associated with an upregulation of the renin-angiotensin-aldosterone system (RAAS), hypertension, and renal dysfunction. Excess endothelin production is also associated with pulmonary hypertension, chronic heart failure, cancer, obesity, insulin resistance, type 2 diabetes, and allograft rejection.</td>
<td>Endothelin elevations reflect advanced disease and a worsening prognosis. Due to its multisystem effects, endothelin elevations should be considered in conjunction with other biomarker abnormalities to determine the cause or causes of the increased endothelin levels. In general, therapies for elevated endothelin levels are targeted at improving vasomotor tone and the endothelial health of the organ or organ systems affected. Multiple treatment options exist, including dietary flavonoids, hormone replacement therapy, fenofibrate therapy in type 2 diabetics, and endothelin receptor blockers.</td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>INFLAMMATION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated Ultra Sensitive Interleukin-6 (IL-6)</td>
<td>Elevated pro-inflammatory cytokine that may increase platelet aggregation and synthesis of C-reactive protein (CRP), and is associated with increased severity of cardiovascular disease (CVD). IL-6 is involved in the pathogenesis of atherosclerosis, as elevated IL-6 concentrations are found in atheromatous arterial plaques. There is a strong independent association between elevated IL-6 levels and the presence of clinical and subclinical CVD, including heart failure and mortality in the elderly. In the EPIC-Potsdam study, an adjusted OR of 2.6 for developing type 2 diabetes was found in those with elevated IL-6. Severe sleep apnea associated with elevated IL-6 after sleep (OR=3.82). Elevations in IL-6 may be due to hyperlipidemia, cardiovascular disease, hypertension, heart failure, diabetes, sleep apnea, central adiposity, periodontal disease, smoking, active inflammation/infection and autoimmune disease (e.g. rheumatoid arthritis, thyroid dysfunction). Current research shows IL-6 as a prognostic marker in cancer and is most commonly elevated in patients with endometrial, lung, colorectal, breast, ovarian cancer, and renal cell carcinoma.</td>
<td>Lifestyle habits that have been shown to reduce IL-6 and other markers of inflammation include maintaining a healthy weight and dietary habits, a regular exercise routine that incorporates aerobic and strength training, adequate sleep, and stress management.</td>
<td></td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>------------------</td>
<td>---------------</td>
</tr>
<tr>
<td><strong>INFLAMMATION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated Ultra Sensitive Interleukin-17A (IL-17A)</td>
<td>IL-17A is a T-cell derived cytokine that stimulates stromal cells and macrophages to secrete pro-inflammatory cytokines. It is responsible for inducing and mediating immune and inflammatory responses. Elevations are seen in cardiovascular disease and it has been shown that IL-17A plays a role in atherosclerosis and plaque instability.</td>
<td>Elevations are associated with cardiovascular disease, periodontal disease, inflammatory bowel disease, systemic lupus erythematosus, osteoporosis, and other autoimmune diseases such as rheumatoid arthritis, and thyroid diseases. Expression of IL 17-A is associated with the pathology of a variety of tumors, has been linked to the pathogenesis of RA and psoriasis, and has been found in endometriotic lesions of women with endometriosis correlating to disease severity and infertility of patients.</td>
<td>Lifestyle habits that decrease inflammation include maintaining a healthy weight and dietary habits, a regular exercise routine that incorporates aerobic and strength training, adequate sleep, and stress management.</td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
## INFLAMMATION

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Ultra Sensitive Tumor Necrosis Factor-Alpha (TNF-α)</td>
<td>TNF-α is a pro-inflammatory cytokine secreted by macrophages. Elevated levels may contribute to insulin resistance and endothelial dysfunction.\textsuperscript{1,2} There is a strong independent association between elevated TNF-α levels and the presence of clinical and subclinical cardiovascular disease, and heart failure (HF).\textsuperscript{3,4,5}</td>
<td>Elevated TNF-α levels are often due to increased body fat, specifically visceral fat. Elevated levels may also be seen in dyslipidemia, atherosclerosis, HF, rheumatoid arthritis, Cushing’s disease, kidney disease, insulin resistance, type 2 diabetes, obstructive sleep apnea, and in those who smoke.\textsuperscript{2,7,8}</td>
<td>Reduction of body fat (particularly visceral fat) to optimal levels, strict weight management, regular exercise, smoking cessation, and healthy dietary habits have been shown to reduce circulating TNF-α levels.\textsuperscript{2,7}</td>
</tr>
</tbody>
</table>

1. TNF-α is a pro-inflammatory cytokine secreted by macrophages. Elevated levels may contribute to insulin resistance and endothelial dysfunction.\textsuperscript{1,2} 
2. There is a strong independent association between elevated TNF-α levels and the presence of clinical and subclinical cardiovascular disease, and heart failure (HF).\textsuperscript{3,4,5} 
3. In the Health Aging and Body Composition study, IL-6 and TNF-α were independently associated with incident heart failure, in a multi-variable adjusted model.\textsuperscript{4} 
4. Increased TNF-α concentration is associated with peripheral insulin resistance and increased plasma glucose and insulin levels prior to onset of type 2 diabetes.\textsuperscript{6}
**DISORDER** | **PATHOLOGY** | **CAUSATIVE FACTORS** | **CONSIDERATIONS**
---|---|---|---
**INFLAMMATION** | Elevated Lipoprotein-associated Phospholipase A2 (Lp-PLA₂) Activity | Vascular specific inflammatory enzyme that is associated with the formation of rupture-prone plaque.¹  
Lp-PLA₂ activity is an independent predictor of coronary heart disease and stroke in the general population.²,³,⁴  
*In the REGARDS study, Lp-PLA₂ Activity levels above 225 nmol/min/ml activity units, showed a significant increase in CHD events in patients without known CHD (HR 1.54).*⁵ | Primarily related to LDL, with increased Lp-PLA₂ enzyme activity present in small dense LDL (sdLDL). Values increase with plaque progression, particularly that of rupture-prone plaque.¹  
Medications that have been shown to reduce Lp-PLA₂ levels include niacin, statins, fibrates, ezetimibe, and fish oil.⁶,⁷  
Healthy dietary habits with reduced carbohydrate consumption, moderate alcohol intake, maintenance of a healthy weight and regular physical activity have also demonstrated a Lp-PLA₂ lowering effect. Smoking cessation should also be advised.⁸,⁹ |
### INFLAMMATION

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
</table>
| Elevated High Sensitivity C-Reactive Protein (hs-CRP)                    | Primarily an acute phase reactant produced in the liver that is associated with generalized inflammatory response and atherogenesis. Elevated concentrations are predictive of recurrent ischemia, myocardial infarction, and stroke.¹  
  **In high-functioning older persons, a measure of inflammation can identify those at risk of mortality and functional decline.**  
  OR up to 6.6 with elevations of IL-6 > 3.8pg/mL, hs-CRP > 2.65 mg/l, low albumin <3.8 g/dl, and low cholesterol <170mg/dl.² | hs-CRP is released from activated leukocytes in response to infection or trauma, and from vascular smooth muscle cells in response to atherosclerosis.  
  Elevations are also seen in overweight individuals, those with insulin resistance, type 2 diabetes, periodontal disease, sleep-disordered breathing, autoimmune disorders, women on birth control pills and smokers.³⁴⁵ | Treat underlying causes of inflammation with lifestyle modification: weight loss, glucose and insulin control, and smoking cessation.³⁶  
  Medications to consider include those that target inflammation and/or the underlying causes of inflammation, such as aspirin, lipid-lowering and anti-diabetic agents.⁷ |
### INFLAMMATION

**Elevated Homocysteine**

Homocysteine is the by-product of methionine metabolism, a process that requires vitamin B6, vitamin B9 (folic acid), and vitamin B12. Elevated levels are an independent cardiovascular risk factor, and may contribute to cardiovascular disease by damaging endothelial cells, altering platelet aggregation, inhibiting vasodilation, and increasing oxidation of low-density lipoprotein (LDL) cholesterol.¹,²

**Each increase of 5 umol/L in homocysteine level increases the CHD events by 20%, independently of traditional risk factors.³**

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFLAMMATION</td>
<td>Elevated Homocysteine</td>
<td>Elevations in homocysteine may be seen with deficiencies of folic acid, B6 and B12, renal failure, pernicious anemia, hypothyroidism, acute lymphoblastic leukemia, psoriasis, Alzheimer’s disease, vascular dementia, cognitive impairment, coronary artery disease, stroke, pregnancy complications, bone loss, older age and menopause.⁴,⁵,⁶ Excess alcohol, caffeine, or nicotine intake as well as lack of exercise or a diet deficient in fruits and vegetables may contribute to increases in homocysteine.²</td>
<td>Treatment of homocysteine is controversial, but treatment of associated causes of endothelial dysfunction is prudent. Identify and treat underlying abnormalities such as renal insufficiency, vitamin deficiency and pernicious anemia with folic acid (L-methylfolate), vitamin B12, and vitamin B6 supplements. Consider diet high in green, leafy vegetables.⁴,⁷ Increased physical activity and moderate alcohol intake have shown to decrease levels.⁶</td>
</tr>
</tbody>
</table>

---

¹,²,³,⁴,⁵,⁶,⁷ The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
### Inflammation

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Pathology</th>
<th>Causative Factors</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Uric Acid (UA)</td>
<td>Uric acid is a product of purine metabolism.</td>
<td>Possible causes of elevations of uric acid include hypoparathyroidism, gout, alcoholism, type 2 diabetes, and kidney disease.</td>
<td>Treat underlying cause and consider using medications to lower the uric acid levels to prevent gouty attacks.</td>
</tr>
<tr>
<td></td>
<td>Risk factors associated with elevated UA include hypertension, metabolic syndrome, obstructive sleep apnea, vascular disease, endothelial dysfunction, and stroke. Elevated UA is a negative prognostic marker for stroke, and is associated with inflammatory markers such as CRP, IL-6 and TNF-α.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>In the NHANES-III study the prevalence of metabolic syndrome was very high among individuals with gout. Age and sex adjusted (OR 3.05).</td>
<td></td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>-------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>LIPID MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Elevated Triglycerides (TG)</strong></td>
<td>Triglycerides are an important biological marker of cardiovascular disease risk, due to their association with remnant particles (such as very low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL)) and impaired reverse cholesterol transport. Elevated triglycerides are an independent cardiovascular risk, especially in those at risk for or diagnosed with type 2 diabetes.(^1)</td>
<td>Causes of elevated triglycerides include genetic tendency, obesity, insulin resistance, type 2 diabetes, high-carbohydrate and/or high-fat diet, excessive alcohol consumption, sedentary lifestyle, hypothyroidism, renal disease, and medications such as beta blockers, thiazide diuretics, glucocorticosteroids, anabolic steroids and some HIV medications.(^1)</td>
<td>Dietary strategies to reduce triglycerides include adoption of a Mediterranean-style diet (increased intake of monounsaturated fats and omega-3 fatty acids, elimination of trans fats, reduction of total carbohydrate to less than 50% of calories, emphasis on low glycemic-load foods and reduction of fructose).(^1,3) Decreases in alcohol intake, weight loss and regular exercise have been shown to reduce triglycerides.(^1,4)</td>
</tr>
</tbody>
</table>

In a meta-analysis, an OR of 1.72 was found for incident coronary heart disease.\(^2\) |
### LIPID MANAGEMENT

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low High Density Lipoprotein-cholesterol (HDL-C)</td>
<td>HDL particles contain close to equal amounts of lipid and protein. The function of HDL is to mediate reverse cholesterol transport, in which cholesterol from the peripheral tissues is returned to the liver for excretion as bile.</td>
<td>Low HDL may be due to genetics, excess weight, inactivity, smoking, high carbohydrate intake, elevated triglycerides, insulin resistance, type 2 diabetes, liver, renal, or thyroid disease, and certain medications (e.g., beta blockers, anabolic steroids, and progestational agents).</td>
<td>Dietary strategies to improve HDL include adequate intake of monounsaturated fats and omega-3 fatty acids, and moderate alcohol intake. Treat insulin resistance and type 2 diabetes. Encourage weight loss, regular exercise, and smoking cessation when appropriate. Medications that have been shown to increase HDL include statins, niacin, omega-3 fatty acids, thiazolidinediones, and fibrates.</td>
</tr>
</tbody>
</table>

HDL is additionally cardioprotective, due to its anti-inflammatory, anti-oxidative, and anti-thrombotic characteristics.

Low HDL is an independent risk factor for cardiovascular disease, while high HDL has been shown to be protective against the development of cardiovascular disease.

In a meta-analysis, CHD risk decreases by 2-3% for every 1-mg/dL increase in HDL-C level.
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIPID MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low High-Density Lipoprotein 2b (HDL-2b)</td>
<td>The cardioprotective function and inverse relationship with cardiovascular disease seen in HDL comes mostly from the subclass HDL-2b.(^1) Low HDL-2b is associated with adverse cardiovascular events.(^1,2)</td>
<td>Low HDL-2b may be due to genetic tendency, elevated triglycerides, a high-carbohydrate diet, visceral obesity, insulin resistance, type 2 diabetes, smoking, liver and thyroid disease, renal failure and certain medications.(^3,4)</td>
<td>Lifestyle modifications include a healthy, low-to-moderate carbohydrate diet, moderate alcohol consumption, regular physical activity, weight management and smoking cessation.(^5)</td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>LIPID MANAGEMENT</td>
<td></td>
<td></td>
<td>A diet emphasizing monounsaturated fats, omega-3 fatty acids and moderate total carbohydrate consumption, combined with a regimen of regular moderate-to-intense physical activity, has been shown to reduce LDL.⁴,⁵</td>
</tr>
<tr>
<td>Elevated Low Density Lipoprotein Cholesterol (LDL-C)</td>
<td>LDL-C is a measure of the cholesterol content of LDL particles. Elevated LDL-C may promote atherosclerosis, particularly when the LDL is oxidized.¹</td>
<td>Elevated LDL-C may be found in inactive and/or obese individuals, and in those with an excessive intake of saturated fats, trans-fats, and carbohydrates.³ Elevations may also be due to genetic factors, advancing age, and the presence of other diseases, including hypothyroidism.³</td>
<td>Lipid-lowering therapies include statins, fibrates, niacin, fish oil, and cholesterol-absorption inhibitors.⁶</td>
</tr>
<tr>
<td></td>
<td>LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²
² LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²
³ LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²
⁴ LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²
⁵ LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²
⁶ LDL-C was associated with an overall incident cardiovascular disease HR of 1.20.²
### LIPID MANAGEMENT

#### Elevated Small Dense LDL (sdLDL)

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
</table>
| **Elevated Small Dense LDL (sdLDL)** | • The atherogenicity of sdLDL is related to its extended time in circulation, ability to more easily enter the arterial wall, and susceptibility to oxidation. Elevated sdLDL is independently associated with incident cardiovascular disease (CV), as well as disease progression and severity.  
  
  **Elevations show up to 3.6x increased risk of incident ischemic heart disease in men.**  
  
  **In the ARIC study, a HR of 1.61 was found with elevated sdLDL even in individuals considered to be at low CV risk based on LDL-C levels.** | • Elevations in sdLDL are often seen with insulin resistance, metabolic syndrome, elevated triglycerides, type 2 diabetes, fatty liver, lack of physical activity and a high carbohydrate diet.  
  
  Medications that have demonstrated a shift in particle size from small dense to larger LDL particles include pioglitazone, fibrates and niacin. Statins will lower total particle number, but have a variable effect on shifting LDL particle size.  
  
  Lifestyle strategies to reduce sdLDL include moderation of carbohydrate intake, emphasis on monounsaturated fats and oils, regular physical activity, and stress management. |
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIPID MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Apolipoprotein A-1 (Apo A-1)</td>
<td>Apo A-1 is the major protein of high-density lipoprotein (HDL). Apo A-1 containing particles mediate reverse cholesterol transport by returning excess cholesterol from peripheral tissues to the liver. Low levels indicate suboptimal reverse cholesterol transport.¹</td>
<td>Causes of low apo A-1 include genetic tendency, high-fat/high-carbohydrate diet, visceral obesity, insulin resistance, type 2 diabetes, inactive lifestyle, smoking, familial hypoalphalipoproteinemia, and liver, renal, and thyroid disease.²⁻⁹</td>
<td>Strategies to improve HDL include adequate intake of monounsaturated fats and omega-3 fatty acids, and moderate alcohol intake. Treat insulin resistance and type 2 diabetes; encourage weight loss, regular exercise, and smoking cessation when appropriate. Medications that have been shown to increase HDL include statins, niacin, omega-3 fatty acids, thiazolidinediones, and fibrates.¹⁰,¹¹</td>
</tr>
<tr>
<td></td>
<td><strong>In a meta-analysis, a RR of 1.62 for incident CHD was found with low apo A-1.³</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>Elevated Apolipoprotein B (Apo B)</strong></td>
<td>Apo B is the primary protein component in very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), lipoprotein(a) [Lp(a)], chylomicrons and chylomicron remnants. Apo B is associated with each particle in a 1:1 ratio; it is considered a direct measure of atherogenic lipoproteins.¹</td>
<td>Genetic tendency, obesity, high carbohydrate/fat diet, sedentary lifestyle, other illness (e.g., hypothyroidism, kidney disease, cystic fibrosis), certain medications (e.g., beta blockers, estrogen, androgen, and glucocorticoids).³</td>
<td>A cardioprotective diet emphasizing a reduction in saturated fats, trans fats and carbohydrates (especially in the presence of elevated triglycerides), weight loss as appropriate, and regular aerobic exercise have been shown to reduce apo B.³ Lipid-lowering medications including statins, niacin, fibrates, cholesterol absorption inhibitors, bile acid sequestrants, and omega-3 fatty acids, may also be beneficial.³,⁴</td>
</tr>
<tr>
<td></td>
<td>Elevated apo B is associated with the presence of carotid atherosclerosis, cardiovascular events, the metabolic syndrome and type 2 diabetes.¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>In a meta-analysis, a 1.99 RR for CHD was found in individuals in the top third versus those in the bottom third tertile.²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## DISORDER | PATHOLOGY | CAUSATIVE FACTORS | CONSIDERATIONS
---|---|---|---
### LIPID MANAGEMENT

#### Apo B/Apo A-1 Ratio

| The apo B/apo A-1 ratio has been shown to be a strong and independent predictor of myocardial (MI) infarction and cardiovascular disease (CVD) as well as a target for lipid lowering therapy. The lower the apo B/apo A-1 ratio, the lower the CVD risk.¹  
The INTERHEART study found that the apo B/apo A-1 ratio was among the most significant risk factors for MI, with an odds ratio of 4.73 for the highest vs. lowest decile.²  
In individuals taking lipid lowering medications, the apo B/apo A-1 ratio was a stronger predictor of risk for major CV events (hazard ratio 1.24; <.001) than either the LDL-C to HDL-C ratio or the total cholesterol to HDL-C ratio.³  
Anything that causes an increase in apo B and/or the lowering of apo A-1 will result in an elevated ratio of atherogenic particles relative to antiatherogenic particle; and thus increase the risk for major CV events. See pages for apo B and apo A-1 in this guide for additional information. | See pages for apo B and apo A-1 in this guide for additional information. |
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIPID MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated Lipoprotein(a) (Lp[a])</td>
<td>Lp(a) is the most powerful genetic risk factor for cardiovascular disease.(^1) Structurally similar to plasminogen, it competes for plasminogen receptor sites, which results in increased coagulability and reduced fibrinolysis.(^2) Lp(a) is a stable risk factor for coronary artery disease, peripheral vascular disease, ischemic stroke and abdominal aortic aneurysm.(^3) <strong>For each 10 mg/dL increase in Lp(a), there was a significant 6%-9% increase in relative risk of CHD.</strong>(^4)</td>
<td>Elevations in Lp(a) are largely due to genetic factors and, to a lesser extent, to diseases of the liver and kidney. In addition, hormonal factors such as hypothyroidism, pregnancy, menopause and steroids can elevate levels.(^2,5,6)</td>
<td>Because Lp(a) is very resistant to treatment, it is important to aggressively treat all associated atherogenic lipoprotein abnormalities.(^2) Lifestyle changes have no impact on Lp(a) levels.(^2,3,5) Niacin is the primary Lp(a)-lowering treatment, but therapeutic response may be gradual.(^1) Other agents reported to decrease Lp(a) to a minor degree include aspirin, L-carnitine, ascorbic acid combined with L-lysine, calcium antagonists, ACE inhibitors and hormones (e.g. estrogen and levothyroxine).(^1)</td>
</tr>
</tbody>
</table>
## DISORDER

### DIABETES & WEIGHT MANAGEMENT

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
</table>
| Elevated Fasting Glucose                                                 | Elevated glucose is a risk for both microvascular and macrovascular disease, and contributes to endothelial dysfunction and cardiovascular disease (CVD). Elevated fasting levels above 100 mg/dL are associated with an increased risk of developing type 2 diabetes and future CVD.¹  
Impaired fasting glucose is associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension.²  
**Impaired fasting glucose carried a 6.02 RR for the development of diabetes mellitus.³** | Risk factors for elevated glucose include genetics, physical inactivity, poor diet, overweight status, and polycystic ovary syndrome (PCOS) with a high BMI > 25 kg/m² in women.¹ | Weight management, regular exercise, and a carbohydrate-controlled diet have all been shown to reduce elevated glucose. Medications used in the management of diabetes and to maintain glucose control include biguanides, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, and insulin.¹⁴ |

¹ [Reference 1]  
² [Reference 2]  
³ [Reference 3]  
⁴ [Reference 4]

**The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).**
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DIABETES &amp; WEIGHT MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated Fasting Insulin</td>
<td>Elevated fasting insulin levels are associated with pre-diabetes, type 2 diabetes, and future cardiovascular events. Generally, elevated insulin levels are detected before changes in glucose levels. Elevations in both insulin and apo B were found to have an OR of 11.0 for ischemic heart disease risk.</td>
<td>Elevations in fasting insulin are multifactorial and include excess weight, increases in visceral fat, metabolic syndrome, insulin resistance, stress, illness, type 2 diabetes, polycystic ovary syndrome (PCOS), and Cushing's disease. Some medications, including corticosteroids, levodopa, and oral contraceptives, may also increase fasting insulin levels.</td>
<td>Weight management, regular exercise, and a carbohydrate-controlled diet have all been shown to reduce the risk of type 2 diabetes. Medications used in the management of diabetes and to maintain glucose control include biguanides, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, and insulin.</td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>-------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>DIABETES &amp; WEIGHT MANAGEMENT</td>
<td>Elevated Hemoglobin A1c (HbA1c)</td>
<td>HbA1c represents the average level of blood glucose over the previous 3 months, and demonstrates the degree of glucose control.(^1) A 1% increase in HbA1c concentrations is associated with a 20–30% increase in cardiovascular events and all-cause mortality.(^2)</td>
<td>HbA1c is elevated in any condition where glucose control may be compromised; this includes metabolic syndrome and insulin resistance, type 1 and type 2 diabetes, and undiagnosed diabetes. Levels may also be acutely elevated during periods of illness or as a result of some medications.(^3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weight management, regular exercise, and a carbohydrate-controlled diet have all been shown to reduce elevated HbA1c.(^4) Medications used in the management of diabetes include biguanides, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, and insulin.(^5)</td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DIABETES &amp; WEIGHT MANAGEMENT</strong></td>
<td>Abnormal Cortisol</td>
<td>Cortisol elevations may occur in response to physiologic (sepsis, trauma) and psychological stress, and are seen in Cushing’s Syndrome, type 2 diabetes, and obstructive sleep apnea (OSA).&lt;sup&gt;1,4,5,6&lt;/sup&gt; Low levels of cortisol are associated with Addison’s disease, secondary adrenal insufficiency due to pituitary or hypothalamic insufficiency, and congenital adrenal hyperplasia.&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Weight loss achieved through improved dietary intake and regular exercise has been shown to reduce cortisol in overweight individuals.&lt;sup&gt;9&lt;/sup&gt; Adequate sleep, stress management, and continuous positive airway pressure (CPAP) in those with OSA also reduce cortisol levels.&lt;sup&gt;9,10,11,12,13&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Cortisol is a hormone responsible for regulating blood sugar, energy production, inflammation, and immune response. Cortisol levels may elevate in a response to physical, mental, or environmental stress.&lt;sup&gt;1&lt;/sup&gt; Cortisol directly affects the heart and blood vessels, influencing vascular function, atherogenesis, and vascular remodeling.&lt;sup&gt;1,2&lt;/sup&gt; Elevations may also affect glucose and lipid metabolism, as well as blood pressure.&lt;sup&gt;1&lt;/sup&gt;</td>
<td>5x increased risk of cardiovascular death.&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
### Abnormal Adiponectin

Adiponectin is a protein hormone secreted primarily by adipocytes. It has anti-inflammatory, anti-atherogenic, and insulin-sensitizing effects on the heart and blood vessels. Serum levels of adiponectin are **reduced** in patients with type 2 diabetes, insulin resistance, obesity, and coronary artery disease.<sup>1</sup>

Paradoxically, **elevated** levels may be seen in post acute coronary syndrome and chronic heart failure patients, and are predictive for mortality.<sup>2</sup>

Longitudinal studies have shown that circulating levels of adiponectin are a marker for all-cause mortality, heart failure, CAD and type 2 diabetes.<sup>3</sup>

**In a meta-analysis, higher levels of adiponectin were associated with lower risk of type 2 diabetes across diverse populations, consistent with a dose-response relationship.**<sup>4</sup>

**Low** levels of adiponectin may be caused by obesity (increased body fat, waist-to-hip ratio, and intra-abdominal fat) and are associated with insulin resistance.<sup>1,5</sup> This may be due to transcriptional suppression or decreased secretion caused by inflammatory cytokines, or genetic factors.<sup>1</sup>

**Elevated** adiponectin may be seen in chronic inflammatory conditions such as heart failure, type 1 diabetes, systemic lupus erythematosus, rheumatoid arthritis, and irritable bowel syndrome.<sup>1,6</sup> It is also theorized to be the result of compensatory response to stress, aberrant expression of receptors, or adiponectin resistance.<sup>7</sup>

Drug therapies that have been shown to increase adiponectin include pioglitazone, fenofibrates, beta blockers, certain angiotension receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors.<sup>1,7</sup>

Lifestyle modifications that have been shown to increase low adiponectin include a reduction in body weight of >10%, consumption of a Mediterranean-type diet, increased physical activity, and moderate alcohol intake.<sup>7</sup>
### DIABETES & WEIGHT MANAGEMENT

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
</table>
| **Abnormal Leptin** | Leptin is an adipokine that helps regulate appetite by signaling satiety to receptors in the hypothalamus. It also has peripheral actions that stimulate vascular inflammation, oxidative stress, and vascular smooth muscle hypertrophy. These actions may contribute to the pathogenesis of type 2 diabetes, hypertension, and cardiovascular disease (CVD).

**Elevated leptin and high blood pressure is associated with OR 4.89 in men and OR 4.10 in women for ischemic stroke.**

**Higher levels of leptin have been associated with increased risk of breast cancer in postmenopausal women (OR 1.94).** |

Elevations in leptin are associated with insulin resistance, increased risk for type 2 diabetes, CVD, and stroke. Leptin deficiency and resistance are associated with metabolically-reduced energy expenditure, and may be affected by inadequate sleep duration.

Weight loss via a low-glycemic index diet, regular exercise, short-term fasting, and adequate sleep have been shown to decrease leptin levels. |
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DIABETES &amp; WEIGHT MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Elevated Ferritin</strong></td>
<td>Ferritin is an iron-containing protein produced in the liver. Elevated iron stores may enhance the oxidation of lipids through the production of free radicals via the Fenton Reaction.(^1) Additionally, iron deposits in the liver, beta cells, and peripheral muscle tissue may contribute to insulin resistance by interfering with the ability of insulin to suppress hepatic glucose production, and disrupting glucose metabolism in muscle.(^2) <strong>In the EPIC-Norfolk study, elevated ferritin was found to have an OR of 3.2 for incident type 2 diabetes.</strong>(^3)</td>
<td>Elevated ferritin is associated with abdominal obesity, inflammation, hemochromatosis, hepatic disease, inappropriate iron therapy, and lead poisoning.(^4,5,6)</td>
<td>As elevated serum ferritin is often associated with obesity and the metabolic syndrome, weight loss to maintain a body mass index (BMI) of &lt;25, achieved through a cardioprotective diet and exercise is recommended. Limit or eliminate iron-rich foods and supplements, if warranted, to reduce iron intake; consider phlebotomy to reduce iron levels.(^1,7)</td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Calcium, Bone &amp; Mineral Health</td>
<td><strong>Elevated Parathyroid Hormone (PTH)</strong>: Primary hyperparathyroidism is the unregulated overproduction of PTH associated with abnormal parathyroid function, resulting in abnormal calcium homeostasis. The catabolic effect of primary hyperparathyroidism promotes osteoclast activity and bone resorption and is considered a cause of secondary osteoporosis.¹ In secondary hyperparathyroidism, chronic vitamin D deficiency leads to a decrease in blood calcium, which stimulates increased PTH secretion. Excessive PTH levels have a pro-inflammatory effect, stimulating the release of cytokines by vascular smooth muscle cells, promoting cardiomyocyte hypertrophy and vascular remodeling.²,³ <strong>Elevations showed a HR of 1.47 for increased risk of death, coronary artery disease, myocardial infarction and stroke, independent of vitamin D levels.⁴</strong></td>
<td>Causes of elevated PTH include renal disease, low vitamin D status, and adenomas.⁴,⁵ PTH elevations have been associated with insulin resistance, type 2 diabetes, hypertension and vascular inflammation.⁴,⁶</td>
<td>Distinguish between primary and secondary hyperparathyroidism. In secondary hyperparathyroidism, vitamin D supplementation may be considered, as well as treatment for kidney disease.⁷</td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CALCIUM, BONE &amp; MINERAL HEALTH</strong></td>
<td><strong>Insufficient Vitamin D</strong></td>
<td>Low levels of vitamin D are caused by inadequate dietary intake of vitamin D, low sun exposure, a dark-skinned complexion, kidney and liver disease, impaired absorption (such as in Crohn's disease, celiac disease, and cystic fibrosis), obesity, smoking, and medications such as anticonvulsants, glucocorticoids, and HIV medications.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>The primary function of vitamin D is the regulation of intestinal calcium absorption and the maintenance of serum calcium concentration via the stimulation of bone resorption. Most Americans do not achieve adequate vitamin D levels. An estimated 90% of adults between 51 and 70 years of age do not obtain adequate vitamin D from their diet. Low levels of vitamin D are associated with endothelial dysfunction, inflammation, hypertension and left ventricular hypertrophy, elevated parathyroid hormone (PTH), osteoporosis, cancer, insulin resistance and type 2 diabetes, and risk for cardiovascular events. For every 10 ng/mL decline in vitamin D, there is a 9% greater relative hazard of mortality, and a 25% greater relative hazard of myocardial infarction.</td>
<td>Adequate sun exposure, high vitamin D containing foods (such as wild-caught salmon or fortified milk), and vitamin D supplementation have all been shown to increase vitamin D levels. The combination of supplemental calcium and vitamin D can reduce the risk of fracture in older populations.</td>
<td></td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
### RENAL

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Cystatin C</td>
<td>Cystatin C is a serum protein produced at a steady rate by all nucleated cells. It is cleared only via glomerular filtration and is less influenced by age, gender, race, and muscle mass than creatinine, making it an ideal marker for assessing kidney function. Studies have shown cystatin C to be a marker for early detection of kidney disease, and a superior risk marker to creatinine-based eGFR for cardiovascular morbidity and mortality. A combined creatinine-cystatin C equation is superior to equations based on either marker alone and may be useful for detecting and confirming chronic kidney disease (CKD). In addition, Cystatin C distinguishes between “higher risk” and “lower risk” individuals for CKD complications with creatinine-based eGFR &lt;60 ml/min. <strong>HR 3.87 for cardiovascular mortality in a secondary prevention population with elevated cystatin C.</strong></td>
<td>Increases in cystatin C are seen with impaired renal function.</td>
<td>Therapies for elevated cystatin C should target improving or protecting kidney function; this includes blood pressure control, cardioprotective diet, regular exercise, maintaining a healthy body weight, and smoking cessation.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEPATIC</td>
<td>GGT is an enzyme primarily produced by the liver. It is associated with diseases that cause damage to the liver or bile ducts, such as cancer and viral hepatitis.¹ An increased GGT level over time may predict onset of metabolic syndrome, incident CVD and death and is associated with insulin resistance and incident type 2 diabetes in both men and women.²,³ OR 2.49 and 2.53 in middle aged men and women, respectively, for type 2 diabetes.² HR up to 1.67 for incident CVD in the Framingham Heart Study.³</td>
<td>Elevated levels may be associated with hepatitis, cirrhosis, cardiovascular disease, congestive heart failure, hypertension, diabetes, pancreatitis, bone disease, smoking, alcohol abuse, and metabolic syndrome.¹,⁴ Nonalcoholic fatty liver disease is a common condition associated with metabolic syndrome and it is the most common cause of elevated liver enzymes including GGT.⁴ Drugs that may increase GGT levels include: phenytoin, carbamazepine, and barbiturates such as phenobarbital, NSAIDs, lipid-lowering drugs, antibiotics, histamine receptor blockers, antifungal agents, antidepressants, and testosterone.¹</td>
<td>Treatment should aim at diagnosing the cause of elevated liver enzymes. Gradual weight loss, exercise, and appropriate treatment of risk factors for CVD, dyslipidemia, and diabetes is the primary treatment for obese patients with nonalcoholic liver disease. Medications used to treat insulin resistance, hyperlipidemia, and obesity have been shown to improve levels.⁴</td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>THYROID</strong></td>
<td><strong>Abnormal Thyroid Tests:</strong> Thyroid Stimulating Hormone (TSH)</td>
<td>Both hyperthyroidism and hypothyroidism produce changes in cardiac contractility, myocardial oxygen consumption, cardiac output, blood pressure, and vascular resistance.¹ Hyperthyroidism and hypothyroidism may lead to cardiac arrhythmias, and hypothyroidism may contribute to hypercholesterolemia.¹ The risk of CHF was higher among those with high TSH of 7.0-9.9 mIU/L (HR 2.58) and those with TSH of 10.0 mIU/L (HR 3.26).² TSH may be increased with primary hypothyroidism, Hashimoto’s thyroiditis, TSH antibodies, thyrotoxicosis, thyrotropin-producing tumors, and hypothyroid patients not receiving sufficient replacement hormone. Increases may also occur during treatment with lithium or dopamine.₄,⁵ TSH may be decreased with hyperthyroidism, secondary pituitary or hypothalamic hypothyroidism, euthyroid sick patients, treated Graves’ disease, and over-replacement of thyroid hormone in treatment of hypothyroidism. TSH may decrease when treated with T3, aspirin, corticosteroids, and heparin.₅,⁶</td>
<td>Determine the underlying cause of hypo/hyperthyroidism. Thyroid hormone replacement may be considered for hypothyroidism.₄,⁶ Restoration of thyroid function often reverses the abnormal cardiovascular hemodynamics and lipids.¹,⁷</td>
</tr>
</tbody>
</table>

¹, ², ₄, ⁵, ⁶, ⁷

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
### THYROID

#### Abnormal Thyroid Tests: T3 Total

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>THYROID</td>
<td>T3 concentration in serum is more a reflection of the functional state of the peripheral tissue than the secretory performance of the thyroid gland. T3 works directly on the cardiomyocyte and systemic vasculature, affecting systemic vasculature resistance, blood volume, cardiac contractility, heart rate, and cardiac output.¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>~30% of patients with congestive heart failure have low T3;¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reduced T3 is a predictor of all-cause and cardiovascular mortality.¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Increased</strong> T3 values are associated with hyperthyroidism, T3 thyrotoxicosis, daily dosage of 25 µg or more of T3, or 300 µg or more of T4, acute thyroiditis, and thyroxine binding globulin (TBG) elevation from any cause.¹²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Decreased</strong> T3 levels are associated with hypothyroidism (however, some will have normal levels), starvation and state of nutrition, acute illness, TBG decrease from any cause, and drugs such as glucocorticoids, androgens, large doses of aspirin, propranolol, phenytoin, and amiodarone.¹²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treat underlying cause and consider further diagnostic testing.
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>THYROID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal Thyroid Tests: Free T3</td>
<td>Free T3 is the physiologically active form of T3.</td>
<td>Free T3 may be elevated with hyperthyroidism and lowered with hypothyroidism, starvation, and acute illness.</td>
<td>Determine and treat underlying cause.</td>
</tr>
</tbody>
</table>

1,2,3

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>THYROID</strong></td>
<td><strong>Abnormal Thyroid Tests: T4 Total</strong></td>
<td>T4 total may <strong>increase</strong> in hyperthyroidism, acute thyroiditis (first stage), and liver disease (hepatitis).&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
<td>Treat underlying cause (e.g., hyperthyroidism, primary and secondary hyperthyroidism) and adjust TSH suppression therapy if indicated.</td>
</tr>
<tr>
<td></td>
<td>The determination of T4, which measures both bound, unbound and free thyroxine, can be utilized for detection of hyperthyroidism, primary and secondary hypothyroidism, and monitoring of thyroid stimulating hormone (TSH) suppression therapy.&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
<td>T4 total may <strong>decrease</strong> in hypothyroidism, hypoproteinemia and treatment with triiodothyronine.&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

1. Reference numbers indicate sources for the information provided.
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>THYROID</td>
<td>Abnormal Thyroid Tests: Free T4</td>
<td>Lower free thyroxine (T4) levels have been associated with increased cardiovascular risk, insulin resistance, hyperlipidemia, and metabolic syndrome.¹,²,³</td>
<td>Determine and treat underlying cause.</td>
</tr>
<tr>
<td></td>
<td>Increased free T4 levels are associated with Graves’ disease (hyperthyroidism), hypothyroidism treated with thyroxine or radioactive iodine and euthyroid sick syndrome.¹,²,³</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreased free T4 levels are associated with primary hypothyroidism, secondary hypothyroidism (pituitary), tertiary hypothyroidism (hypothalamic), and hypothyroidism treated with triiodothyronine.¹,²,³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>----------</td>
<td>---------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>THYROID</td>
<td>Thyroid antibodies develop when the immune system mistakenly targets components of the thyroid gland or thyroid proteins leading to chronic inflammation of the thyroid (thyroiditis), tissue damage and/or disruption of thyroid function. TPOAb is the most common test for autoimmune thyroiditis disease (sensitive and specific); it can be detected in both Hashimoto’s thyroiditis and Graves’ disease.¹,²</td>
<td>Elevations may be due to chronic autoimmune disease of the thyroid such as Hashimoto’s thyroiditis and Graves’ disease, which result from complex interactions between genetic and environmental factors.¹</td>
<td>Treat underlying cause. Consider thyroid hormone therapy for Hashimoto thyroiditis (dosage may change over time).³ Monitor closely and treat subclinical or clinical hypothyroidism in women trying to get pregnant or who are pregnant or at risk for miscarriages related to hypothyroidism.³</td>
</tr>
</tbody>
</table>

Elevated Thyroid Peroxidase Antibody (TPOAb)

¹,²

¹

³
## THYROID

### Elevated Thyroglobulin Antibodies (TgAb)

This antibody targets thyroglobulin, the storage form of thyroid hormones. Thyroglobulin (Tg) may leak into the bloodstream when there is follicular destruction through inflammation (i.e. Hashimoto's thyroiditis) or rapid disordered growth of thyroid tissue (i.e. Graves' disease). This may result in the development of autoantibodies to Tg (+TgAb) in some individuals.¹

Patients with Hashimoto thyroiditis frequently have TgAb elevations and may have a higher risk for papillary thyroid cancer. TgAb trends can be used as a surrogate differentiated thyroid cancer (DTC) tumor marker in preference to Tg IMA, provided that the same method is used over time.²

Treat underlying disease state (autoimmune hypo/hyperthyroid, thyroid CA). If patient is being followed for DTC tumor, it is very important to utilize same lab methodology to follow trends over time. If patient has Graves' disease or Hashimoto's thyroiditis, see considerations in TPOAb section.²
## Thyroid Antibodies

The following table summarizes some examples of typical thyroid test results and their potential meaning.\(^1\)\(^2\)

<table>
<thead>
<tr>
<th>TSH</th>
<th>FREE T4</th>
<th>FREE OR TOTAL T3</th>
<th>TPOAb and TgAb</th>
<th>PROBABLE INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Normal</td>
<td>Normal</td>
<td>May be present (+Hashimoto thyroiditis)</td>
<td>Mild (subclinical) hypothyroidism</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
<td>Low or normal</td>
<td>May be present (+Hashimoto thyroiditis)</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Low</td>
<td>Normal</td>
<td>Normal</td>
<td>May be present (+Graves’ disease)</td>
<td>Mild (subclinical) hyperthyroidism</td>
</tr>
<tr>
<td>Low</td>
<td>High or normal</td>
<td>High or normal</td>
<td>May be present (+Graves’ disease)</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Low</td>
<td>Low or normal</td>
<td>Low or normal</td>
<td>Not present</td>
<td>Non-thyroidal illness; pituitary (secondary) hypothyroidism</td>
</tr>
<tr>
<td>Normal</td>
<td>High</td>
<td>High</td>
<td>Not present</td>
<td>Thyroid hormone resistance syndrome (a mutation in the thyroid hormone receptor decreases thyroid hormone function)</td>
</tr>
</tbody>
</table>

1. \(^1\)\(^2\)
### HORMONES

#### Abnormal Dehydroepiandrosterone Sulfate (DHEAS)

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DHEAS</strong> is an adrenal androgen with weak intrinsic effect and a precursor to testosterone and dihydrotestosterone as well as estrogen. DHEAS is used to help evaluate adrenal function, detect adrenal tumors or cancers and determine the cause of virilization in girls and women and early puberty in boys.¹ In women, DHEAS is associated with polycystic ovarian syndrome (PCOS), hirsutism, acne, amenorrhea and/or infertility.¹</td>
<td><strong>An elevated</strong> DHEAS may indicate an adrenocortical tumor, Cushing disease, adrenal cancer, adrenal hyperplasia, or rarely a DHEAS-producing ovarian tumor.¹ DHEAS may be elevated in people taking DHEA supplements and specific drugs: metformin, troglitazone, prolactin, danazol, and calcium channel blockers. Nicotine may also increase DHEAS levels.¹</td>
<td><strong>Determine and treat underlying cause.</strong> DHEAS is typically evaluated with other hormones such as FSH, LH, prolactin, estrogen, and testosterone.¹</td>
<td></td>
</tr>
</tbody>
</table>

¹ DHEAS may be elevated in people taking DHEA supplements and specific drugs: metformin, troglitazone, prolactin, danazol, and calcium channel blockers. Nicotine may also increase DHEAS levels.¹

¹ A low level of DHEAS may be due to adrenal insufficiency, adrenal dysfunction, Addison disease, or hypopituitarism.¹

¹ **Low** levels of DHEAS may also be associated with drugs or hormones such as insulin, oral contraceptives, corticosteroids, dopamine, hepatic enzyme inducers (carbamazepine, imipramine, phenytoin), fish oil, and vitamin E.¹
### HORMONES

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Testosterone</strong></td>
<td>Low testosterone in men is frequently accompanied by adverse health consequences, including decreased muscle mass, increased abdominal fat, insulin resistance, dyslipidemia, and hypertension. Studies in men have also shown that low testosterone levels are associated with increased risk of mortality, cardiovascular events and future type 2 diabetes.</td>
<td>Low testosterone in males may be due to genetic predisposition, injury, infection, cancer treatment, pituitary disorders, obesity, and aging.</td>
<td>Treat underlying cause of low testosterone. Exercise and weight loss have been shown to increase testosterone in males, and supplementation may be considered for significant declines in testosterone.</td>
</tr>
<tr>
<td>(male)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Elevated Testosterone</strong></td>
<td>Elevated testosterone levels in women are associated with adverse metabolic features, including insulin resistance and type 2 diabetes, abdominal obesity, dyslipidemia, chronic inflammation, cardiovascular disease, and polycystic ovary syndrome (PCOS).</td>
<td>Many premenopausal women with PCOS have hyperandrogenism.</td>
<td>For women with PCOS, treatments include lifestyle modification and hormone-influencing medications, blood sugar regulation agents including insulin and metformin.</td>
</tr>
<tr>
<td>(female)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Abnormal Sex Hormone Binding Globulin (SHBG)

Testosterone and estradiol circulate in the bloodstream, bound mostly to SHBG. SHBG is a sex hormone transport protein that affects the circulating levels of bioavailable testosterone, and has emerged as one of many factors associated with type 2 diabetes, metabolic syndrome, sleep apnea, and cardiovascular disease (especially in women).\(^1\)\(^2\)\(^3\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)

Total testosterone and SHBG tests are ordered to evaluate free androgens by calculating the Free Testosterone Index (FTI), a method of quantifying the amount of testosterone, not bound to SHBG.

SHBG concentrations are affected by a number of different diseases, **high** values being found in hyperthyroidism, hypogonadism, androgen insensitivity and hepatic cirrhosis in men. **Low** concentrations are found in myxoedema, hyperprolactinaemia and syndromes of excessive androgen activity. Concentrations are also affected by drugs such as androgens, estrogens, thyroid hormones and anticonvulsants. Measurement of SHBG enables identification of those women with hirsutism who are more likely to respond to estrogen therapy.\(^1\)

SHBG assessment is particularly useful when the total testosterone value is inconsistent with clinical signs, or when monitoring testosterone replacement therapy.\(^9\)

Exercise and weight loss has been shown to increase SHBG in men and women but long term impact needs further evaluation.\(^10\)\(^11\)
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Estradiol</td>
<td>Primarily produced in the ovaries in pre-menopausal women and in the testicles in men. It is used to evaluate ovarian function. In women, estradiol is associated with assessing hormonal imbalances such as infertility, menopause, and abnormal menstrual periods but also monitor pregnancy, bone metabolism and metabolic conditions. Abnormal estradiol levels are associated with increased risk of developing atherosclerosis in premenopausal women. Abnormal estradiol levels are associated with increased risk for CVD, atherosclerosis, ischemic heart disease and bone loss in menopausal women. High blood pressure (hypertension), anemia, and impaired liver and kidney function can affect estrogen levels. Drugs that may increase levels include glucocorticoids, ampicillin, estrogen-containing drugs, phenothiazines, and tetracyclines. Drugs that may decrease levels include clomiphene and oral contraceptives. In women, elevated levels are associated with tumors of the ovary or adrenal glands, hyperthyroidism and cirrhosis. Decreased levels are associated with Turner syndrome, hypopituitarism, dysfunction of the ovaries, failing pregnancy, eating disorders such as anorexia nervosa, menopause, PCOS, and extreme endurance exercise. In men, elevated estrogen levels may be associated with gynecomastia, testosterone or androgen deficiency and estrogen-producing tumors. Lifestyle approaches, including smoking avoidance, proper nutrition, and regular exercise may influence estradiol levels. Hormone replacement therapy for premenopausal and post-menopausal women may be beneficial.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
**DISORDER** | **PATHOLOGY** | **CAUSATIVE FACTORS** | **CONSIDERATIONS**
---|---|---|---
**HORMONES** | **Abnormal Luteinizing Hormone (LH)** | LH is a hormone associated with reproduction and the stimulation of the release of an egg from the ovary (ovulation) in women and testosterone production in men. It is used to evaluate the function of ovaries or testicles. It is associated with pituitary disorders or hypothalamic disorders. In women abnormal levels are associated with infertility, abnormal menstrual cycles and menopause. In men, abnormal levels are associated with testosterone production, infertility, low sperm count, low muscle mass and decreased sex drive. | Drugs that can increase LH include anticonvulsants, clomiphene, and naloxone. Drugs that can lower LH include digoxin, oral contraceptives, and hormone treatments.

LH is typically evaluated in conjunction with other tests such as FSH, testosterone, estradiol and progesterone. **Low** levels are associated with hypothalamic or pituitary disorders in both men and women.

In women, **elevated** levels are associated with ovarian failure related to ovarian agenesis, ovarian tumors, PCOS, menopause, Turner syndrome, defects in steroid production, radiation, chemotherapy, autoimmune disease, adrenal disease and thyroid disease.

In men, **elevated** levels may be associated with gonadal agenesis, Klinefelter syndrome, viral infections, trauma, radiation, chemotherapy, autoimmune disease and germ cell tumors.
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HORMONES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal Follicle Stimulating Hormone (FSH)</td>
<td>FSH is a hormone associated with reproduction and the stimulation of the release of an egg from the ovary (ovulation) in women and testosterone production in men. It is used to evaluate the function of ovaries or testicles. It is associated with pituitary disorder or hypothalamic disorder. ¹</td>
<td>FSH is typically evaluated in conjunction with other hormones such as LH, testosterone, estradiol, and progesterone. <strong>Low</strong> levels are associated with hypothalamic or pituitary disorders in both men and women. It may also be low in pregnancy. ¹</td>
<td>FSH can be increased with use of certain drugs, including cimetidine, clomiphene, digitalis, and levodopa. ¹</td>
</tr>
<tr>
<td></td>
<td>In women, abnormal levels are associated with infertility, abnormal menstrual cycles and menopause. ¹</td>
<td>In women, <strong>elevated</strong> levels are associated with ovarian failure related to ovarian agenesis, ovarian tumors, PCOS, menopause, Turner syndrome, defects in steroid production, radiation, chemotherapy, autoimmune disease, Adrenal disease and Thyroid disease. ¹</td>
<td>FSH can be decreased with oral contraceptives, phenothiazines, and hormone treatments. ¹</td>
</tr>
<tr>
<td></td>
<td>In men, abnormal levels are associated with testosterone production, infertility, low sperm count, low muscle mass and decreased sex drive. ¹</td>
<td>In men, <strong>elevated</strong> levels may be associated with gonadal agenesis, Klinefelter syndrome, viral infections, trauma, radiation, chemotherapy, autoimmune disease and Germ cell tumors. ¹</td>
<td></td>
</tr>
<tr>
<td>DISORDER</td>
<td>PATHOLOGY</td>
<td>CAUSATIVE FACTORS</td>
<td>CONSIDERATIONS</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>HORMONES</td>
<td><strong>Abnormal Prolactin</strong></td>
<td>Elevated levels in men and non-pregnant women are associated with tumors, anorexia nervosa, hypothyroidism, kidney disease, liver disease, PCOS, pituitary and hypothalamic disorders. Stress from illness, chest wall trauma, seizures, lung cancer, and use of marijuana can cause moderate increases in prolactin. Drugs that can elevate prolactin include: estrogens, tricyclic antidepressants, risperidone, opiates, amphetamines, reserpine, verapamil, methyldopa and cimetidine. Low prolactin levels may be caused by drugs such as dopamine, levodopa, and ergot alkaloid derivatives.</td>
<td>Treatments are aimed at reducing hyperprolactinemia. Prolactinomas are often identified with MRI of the brain to locate and determine the size of the tumor as well as the size of the pituitary gland.</td>
</tr>
<tr>
<td></td>
<td>Prolactin is a hormone responsible for the production of breast milk, galactorrhea and prolactinoma. Hyperprolactinemia is associated with an increased risk of overall cancer. Prolactinomas are associated with optic nerve disorders, headaches and visual disturbances. In women, abnormal levels are associated with infertility and absence of menstrual periods. In men, abnormal levels are associated with erectile dysfunction, reduced libido, nipple discharge, infertility and low testosterone. Severe hyperprolactinemia is associated with sexual dysfunction in men. Elevated prolactin was associated with hypoactive sexual desire (HR 8.60) in men.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Progesterone</td>
<td>Progesterone is a hormone used to help determine the causes of infertility, track ovulation, help diagnose an ectopic or failing pregnancy, monitor the health of a pregnancy, monitor progesterone replacement therapy, or help diagnose the cause of abnormal uterine bleeding in women. In men, progesterone is associated with the development of sperm.</td>
<td>Progesterone levels may be affected by estrogen and progesterone supplementation.³</td>
<td>Treat underlying cause.</td>
</tr>
</tbody>
</table>

- **Elevated** levels of progesterone in women may be associated with molar pregnancies, ovarian cysts, ovarian cancer, and adrenal disorders.³
- **Low** levels of progesterone in women may be associated with ectopic pregnancy, miscarriage, amenorrhea, dysfunction of the ovaries, and toxemia in pregnancy.³

Progesterone levels may be affected by estrogen and progesterone supplementation.³
<table>
<thead>
<tr>
<th>DISORDER</th>
<th>PATHOLOGY</th>
<th>CAUSATIVE FACTORS</th>
<th>CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ONCOLOGY</strong></td>
<td><strong>Elevated Total Prostate Specific Antigen (PSA), Free PSA</strong></td>
<td></td>
<td>Measurement of PSA levels can be used for staging of prostate cancer and to predict response to specific therapy, surgery, etc.⁵</td>
</tr>
<tr>
<td></td>
<td><strong>Total PSA:</strong> Prostate Specific Antigen (PSA) is a glycoprotein produced by cells of the prostate gland and absorbed into the bloodstream. Increases in glandular size and tissue damage may increase circulating PSA levels. PSA, in combination with a digital rectal examination (DRE) substantially enhances prostate cancer detection rate.¹ Prostate cancer screening is controversial; any man who is considering getting tested should first be informed in detail about the potential harms and benefits.²</td>
<td>Elevated total PSA may be seen in: prostate cancer, benign prostatic hyperplasia, prostatitis, urinary tract infection, sexual activity, competitive-level cycling, aging.⁴</td>
<td>In patients previously treated for prostate cancer, PSA testing is used to detect disease recurrence.⁶ Free PSA may be used to help decide if a prostate biopsy is needed when PSA results are in the borderline range (between 4 and 10 ng/mL).³</td>
</tr>
<tr>
<td></td>
<td><strong>Free PSA:</strong> Most PSA in the blood is bound to serum proteins. Free PSA is not protein bound. The risk of cancer increases if the free to total ratio is less than 25%.³</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The above statements are meant only for clinical guidance. Medication treatment and lifestyle management is solely determined by the physician(s).
Probability of finding prostate cancer on needle biopsy by age in years (95% confidence interval)\(^7\)

<table>
<thead>
<tr>
<th>% Free PSA ratio</th>
<th>50-59</th>
<th>60-69</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>49.2 (12.4-86.9)</td>
<td>57.5 (17.9-89.3)</td>
<td>64.5 (30.4-88.3)</td>
</tr>
<tr>
<td>11-18</td>
<td>26.9 (5.7-68.9)</td>
<td>33.9 (8.6-73.7)</td>
<td>40.8 (15.8-71.7)</td>
</tr>
<tr>
<td>19-25</td>
<td>18.3 (3.5-57.9)</td>
<td>23.9 (5.4-63.4)</td>
<td>29.7 (10.1-61.1)</td>
</tr>
<tr>
<td>&gt; 25</td>
<td>9.1 (3.1-23.7)</td>
<td>12.2 (4.7-28.1)</td>
<td>15.8 (9.0-26.1)</td>
</tr>
</tbody>
</table>

**IL-6**


**IL-17A**

References

Homocysteine

Uric Acid

LIPID MANAGEMENT

Triglycerides

HDL-C

HDL-2b

LDL-C

sdLDL

Apo A1


Apo B

ApoB/ApoA1 Ratio

Lp(a)
**DIABETES & WEIGHT MANAGEMENT**

**Glucose**

**Insulin**

**HbA1c**

**Cortisol**

**Adiponectin**

**Leptin**

**Ferritin**
6. Fischbach F and Dunn ing M. *Nurses’ Quick Reference to Common Laboratory & Diagnostic Tests, 4th ed. (PA : Lippincott Williams & Wilkins, 2006).*

**CALCIUM, BONE & MINERAL HEALTH**

**PTH**

**Vitamin D**

97-0041-08
**References**

**RENAAL**

Cystatin C


**HEPATIC**

GGT


**THYROID**

TSH

2. Fischbach F and Dunning M. *Nurses’ Quick Reference to Common Laboratory & Diagnostic Tests*, 4th ed. (PA : Lippincott Williams & Wilkins, 2006).

**HORMONES**

DHEAS


**TPOAb**


**TgAb**


**Table: Thyroid Antibodies**

Testosterone

SHBG

Estradiol

Luteinizing Hormone (LH)

Follicle Stimulating Hormone (FSH)

Prolactin

Progesterone

ONCOLOGY
Total PSA, Free PSA

SHBG

Estradiol

Luteinizing Hormone (LH)

Follicle Stimulating Hormone (FSH)

Prolactin

Progesterone