

“Unlike clinical practitioners, underwriters don't use lab test results to diagnosis or treat disease. Instead, they interpret what the results mean in terms of mortality risk.”

Laboratory testing is an integral part of the risk selection process for life insurance. Test results are interpreted in order to categorize mortality risks rather than diagnose and treat disease. Consequently, what is considered abnormal for insurance risk selection may differ from the evaluations made in a clinical practice. The following descriptions pertain to laboratory tests reviewed at Legal and General America for risk selection.

Analysis of blood lipids is the cornerstone of coronary artery disease (CAD) risk management and treatment. Total serum cholesterol, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol are routinely measured in this process. **LDL or “bad cholesterol”** is a major risk factor for CAD; any value above 130 mg/dl is considered abnormal. Recommended treatment of CAD and diabetes includes lowering LDL cholesterol to levels lower than 100 mg/dl. Mainstays of treatment are a diet low in unsaturated fats and drug therapy.

HDL cholesterol, or “good cholesterol”, removes cholesterol from atherosclerotic plaques; normal values are 40 mg/dl or higher in men and 50 mg/dl or higher in women. HDL values are increased by weight loss, cessation of smoking and exercise. Drug therapy currently available for raising HDL is not well tolerated and produces less than satisfactory results. Levels above 70 mg/dl may be an indicator of excessive alcohol use.

The cholesterol/HDL ratio, which is obtained by dividing the total cholesterol by the HDL cholesterol level, is one of the best predictors for the risk of cardiovascular disease. The normal value is 5 or lower (lower values are favorable).

An elevated **triglyceride** level is one of the components of metabolic syndrome and increases the risk of cardiovascular disease. Very high levels are associated with an increased risk of pancreatitis.

Inflammation appears to contribute to the rupture of atherosclerotic plaque. In most cases rupture of the plaque is the triggering event that leads to blockage of the coronary arteries and myocardial infarction (heart attack). **C-reactive protein (CRP)** is a marker for inflammation and correlates with increased cardiovascular mortality when it is elevated. CRP values between 1 mcg/mL and 10 mcg/mL are predictive of increased risk of myocardial infarction.

Brain Natriuretic Peptide - BNP (most laboratories measure **ProBNP** as it is more stable) is a peptide produced by the ventricle of the heart in response to stress and usually indicates systolic or diastolic left ventricular dysfunction. Atrial fibrillation and kidney failure are also causes of elevation. The highest levels of BNP are seen in congestive heart failure. Elevated BNP correlates with higher mortality in individuals with coronary artery disease.

Blood glucose, fructosamine and hemoglobin A1c are screening tests for diabetes and are also used for classifying diabetes cases into appropriate risk classes (see UW Dialogue, issue #1, “Diabetes”).

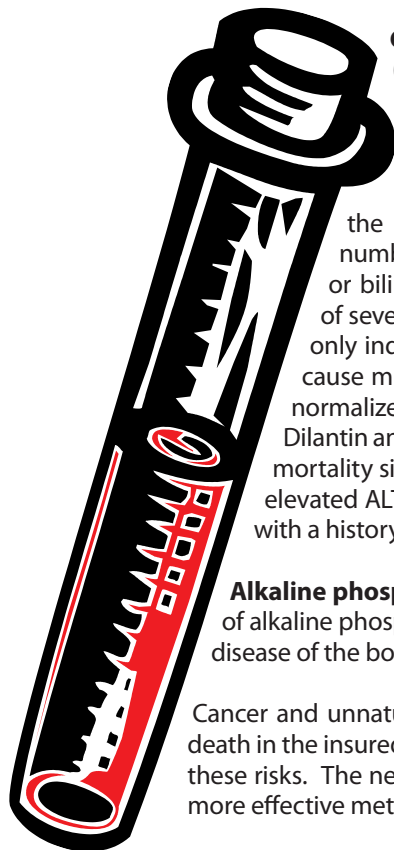
Blood urea nitrogen (BUN), serum creatinine and glomerular filtration rate (GFR) are measures of kidney function. Elevated serum creatinine and decreased GFR are very reliable



indicators of decreased kidney function. The serum creatinine value depends on the muscle mass of the individual; thus normal values are lower in women, men of smaller build and the elderly. GFR is a calculated value. The formula to calculate GFR uses serum creatinine, height, weight, age and sex to arrive at a value that is a superior indicator of kidney function for that individual. The serum creatinine is occasionally falsely elevated due to errors in processing of the specimen prior to arrival in the laboratory. As the GFR calculation is based on serum creatinine, it also would be falsely abnormal in these situations.

Serum proteins are mostly composed of albumin and globulin. **Serum albumin** is synthesized by the liver and is essential to holding the fluid inside blood vessels. It transports a multitude of essential components that perform vital functions. A decreased albumin level is nearly always significant and could be an indication of liver, kidney or bowel disease. It is also decreased in pregnancy because of hemodilution (increased body water). Low serum albumin is a marker for chronic diseases and increased mortality in the elderly. **Globulins** are mostly antibodies and are synthesized by plasma cells. An elevated globulin level is seen in many chronic disorders that cause inflammation such as collagen vascular disorders. It also may be an indicator of more serious disease such as multiple myeloma or lymphoma. The combination of low albumin and elevated globulin is usually an indicator of advanced liver disease.

Serum bilirubin is a break down product of red cells and is processed by the liver. The most frequent cause of bilirubin elevation is a common benign condition, Gilbert's Syndrome, caused by deficiency of an enzyme **glucuronyltransferase**. Other causes of elevation are increased blood cell destruction and all forms of liver diseases including obstruction of the bile duct by gallstones.



Gamma-glutamyl transpeptidase (GGT), Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) are enzymes familiar to most underwriters as elevation of these enzymes is frequently encountered in the insurance testing. Abnormalities of these enzymes may be transient or persistent and may be indicators of significant liver disease, chronic excessive alcohol use or a benign disorder. In general, the significance of these enzymes increases with increasing levels and the number of enzymes involved. The presence of elevated alkaline phosphatase or bilirubin in combination with GGT, AST or ALT indicates a higher likelihood of severe liver disease. However an isolated minimal elevation of ALT may be the only indicator of liver disease in chronic hepatitis C. Prescription drugs may also cause mild elevations of GGT, AST and ALT. In these situations the enzyme levels normalize with discontinuation of the medicine. Antiepileptic medications such as Dilantin and phenobarbital can cause significant isolated elevation of GGT that has no mortality significance. **Hepatitis B and C testing** is performed on all applicants with elevated ALT, abnormal blood alcohol or those who test positive for marijuana. Those with a history of alcohol or drug abuse are also tested for hepatitis.

Alkaline phosphatase is an enzyme that is produced by both liver and bone. Elevation of alkaline phosphatase in combination with GGT indicates probable liver disease. Paget's disease of the bone and cancer metastatic to bone are additional causes of elevation.

Cancer and unnatural causes (homicide, suicide and accidents) are leading causes of early death in the insured population. Current underwriting practices do not screen adequately for these risks. The need to maintain aggressive pricing of term insurance requires that we find more effective methods of screening for cancer and unnatural causes of death.

Cancer markers vary in their reliability, as they may also be elevated in benign conditions. Because of this we use cancer markers with higher cutoff values to improve their accuracy as screening tests for cancer. When these are abnormal, an evaluation would be required before the applicant is considered for insurance.

Prostate specific antigen (PSA) is used as a screening test for prostate cancer in clinical practice. Values that are considered normal increase with age. Benign prostatic hypertrophy is the most frequent cause of elevation. Prostate cancer causes PSA elevation disproportionate to

the size of the prostate. A PSA value that fluctuates is usually due to prostatitis. Determination of free or unbound PSA is useful in separating benign from malignant prostate disease. **Free PSA** is expressed as a percentage of the total; low values suggest cancer and high values benign disease.

Carcinoembryonic antigen (CEA) is a broad-spectrum cancer marker used in clinical practice to monitor progress or relapse of cancer patients. The normal value is less than 2.5 mg/dl for nonsmokers and less than 5.0 mg/dl for smokers. Mild elevation of CEA may be seen in benign disease; moderate to high levels or rising values increase the likelihood of cancer. Cases with significant elevation or history of cancer require an evaluation by a physician before they can be considered for insurance.

Alpha-fetoprotein is a cancer marker utilized in the diagnosis and monitoring of germ cell tumors and hepatocellular cancers. This test may also be abnormal in other cancers. Those with values higher than 100 ng/ml are postponed for evaluation.

Alcohol related deaths contribute significantly to early mortality in the insured population. Evaluation of inappropriate or excessive alcohol use is part of the underwriting process. This



includes evaluation of medical records, liver function tests, motor vehicle reports and inspection reports. **Blood alcohol** testing is performed as a screening test on applicants; 10 mg/dl (0.01g/dl) is used as the detection limit; 80 mg/dl (0.08g/dl) is the legal limit for DUI or DWI charges in most states. It is assumed that most applicants will not consume alcohol or food before the insurance examination. Moderate alcohol consumption the evening prior to the examination would not be detected using this screening test, even though it could produce abnormal lipid results. **Carbohydrate deficient transferrin (CDT)** is widely accepted as an alcohol marker. At Legal & General America, a CDT test is performed in selected situations where there are other indicators of excessive alcohol use. An abnormal test is considered in combination with other factors to make a risk classification decision.

HIV screening is performed on all applicants. Those with a positive or indeterminate (borderline abnormal) test are notified of the abnormality and are advised of the need for evaluation by their physicians before they can be considered for insurance.

Urine testing has been an essential part of risk selection for life insurance for decades. With advances in technology more tests on urine are able to be performed. The urine sample is routinely tested for **protein** and **red cells** to evaluate for the presence of kidney disorders. Testing for **microalbumin** is performed if protein is present, when there is an admitted history of diabetes, or diabetes is suspected based on laboratory testing. **Screening** for the presence of drugs of abuse such as **cocaine** and **marijuana** is also performed on the urine sample.

Protein in the urine (**proteinuria**) is an indicator of protein leakage in some part of the urinary tract and is not always an indicator of kidney disease. Microalbumin (**microalbuminuria**) in the urine indicates the presence of kidney disease and future risk of kidney failure as well as cardiovascular disease. Protein/creatinine ratio and microalbumin/creatinine ratio provide a more precise indication of risk as these values are adjusted for the concentration of urine.

Presence of red cells (**hematuria**) in the urine is always a significant finding, except in women during their reproductive years. In those under age 40 it indicates glomerular disease; in others it may be a symptom of cancer of the kidney or bladder. When further evaluation is required, younger (< age 40) applicants should consult a nephrologist (medical kidney specialist) and older applicants a urologist (surgical kidney specialist).

Legal & General America sends the results of lab testing to all applicants. Applicants are encouraged to consult their physicians for evaluation of results and appropriate follow-up.