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Other Blood Tests

Factor VIII

Factor VIII, which is also known as antihemophilic factor (AHF) or fibrin stabilizing factor, is a plasma coagulation protein, and is a critical cofactor in the clotting process.

Data from clinical trials have shown that persons with high levels of factor VIII are at increased risk of cardiovascular disease and recurrent venous thromboembolism. Furthermore, high levels of factor VIII were determined to be the cause, rather than a consequence, of venous thromboembolism.

Other recent investigations support the hypothesis that there is a physiological basis to the geriatric syndrome of frailty, which is characterized as a wasting syndrome and physiological state of vulnerability to increased morbidity and mortality. Data show a significant increase in markers of inflammation (factor VIII, fibrinogen, and CRP) in the presence or absence of two prevalent chronic diseases: diabetes and cardiovascular disease. Investigators surmise that these specific physiological abnormalities “may make frail older adults more vulnerable to disease processes, functional decline, and mortality.”⁴⁴

BNP (brain natriuretic peptide)

BNP is released at continuously low levels by the heart, though the rate of release may be increased by various physiological and neuroendocrine factors that regulate cardiac function. Increased levels of BNP have been associated with hypertension, congestive heart failure (CHF),⁴⁵ HIV-related cardiomyopathy,⁴⁶ and atherosclerosis, and is a powerful predictor of left ventricular function and prognosis.^{47,48}

Measurement of BNP involves a relatively simple, inexpensive blood test that is able to diagnose CHF in 15 minutes. CHF is the fourth leading cause of hospitalization in the U.S., and the leading cause of hospitalization among people over age 65. Its diagnosis is sometimes difficult, with symptoms such as shortness of breath and edema (fluid retention) that are diagnostic of several conditions, and physical examinations prone to error. Although markers such as cytokines and catecholamines (stress hormones) are elevated in CHF, they are hard to measure quickly and often are not elevated until the disease becomes severe.

In a study of 250 patients with shortness of breath who were admitted to urgent care and emergency rooms, BNP measurements of 80 pg/ml were 95% accurate in diagnosing CHF, and lower values were 98% accurate in ruling out the condition. Furthermore, urgent care physicians missed 30 cases of CHF diagnosed by the

cardiologists; a BNP test could have brought this figure down to one.⁴⁹ One of this study's co-authors remarked that the test has greater diagnostic accuracy than the PSA for prostate cancer, the mammogram for breast cancer, or a PAP smear for cervical cancer. Given that one study estimated that up to 20% of all CHF cases are misdiagnosed, the new test will enable urgent care physicians to provide a more rapid, accurate diagnosis for this group of patients.⁵⁰

Millions of people worldwide with elevated blood glucose levels/Type II diabetes are taking either Avandia™ or Actos™ (thiazolidinediones) to control hyperglycemia. Patients with Type II diabetes are at increased risk of developing or exacerbating CHF, and treatment with thiazolidinediones such as Avandia™ or Actos™ further increases the risk.^{51,52}

Until very recently, no way existed to identify those most likely to suffer from this devastating side effect. In a recent study, however, data showed that BNP levels were a good marker of left ventricular dysfunction (LVD)/CHF induced by pioglitazone (actos). The investigators concluded that Type II diabetes patients treated with pioglitazone (Actos™) who had elevated BNP levels prior to the start of treatment should be carefully monitored using regular BNP testing to avoid the adverse effects of CHF.⁵³

Dietary

Selenium

The selenium test is used to monitor occupational exposure to selenium and detect deficiencies in the serum.

An essential trace mineral, selenium is necessary for normal functioning of the immune system and thyroid gland, and helps protect cells against free radicals that can damage cells, contribute to chronic diseases, and promote cancers. The amount of selenium contained in plant foods is determined by soil content (e.g., high in the Dakotas, very low in some parts of China and Russia). Brazil nuts, walnuts, and bread (in the U.S.) are high in selenium, as is meat from animals that eat grains or plants grown in selenium-rich soils. The current RDA is 55 mcg for men and women, 60 mcg for pregnant women, and 70 mcg for women who are lactating. One ounce of brazil nuts supply 840 mcg of selenium.

Selenium deficiency, common in areas with selenium-deficient soil, may lead to Keshan Disease (enlarged heart and poor heart function). Low levels are also seen in patients on TPN (total parenteral nutrition) and patients with malabsorption problems (severe gastrointestinal disorders). Deficiencies can also affect thyroid function.

Studies indicated that the incidence of death from cancers (lung, colorectal and prostate) is lower among people with higher blood levels of selenium.⁵⁴⁻⁶⁰ Furthermore, areas of the US with selenium-deficient soils have higher rates of nonmelanoma skin cancer.⁶¹

Low levels of selenium may also be associated with an increased risk of heart disease, rheumatoid arthritis, and HIV/AIDS.

Selenium levels should be tested in anyone who suspects occupational exposure (toxic levels) and monitored in those living in areas of selenium-deficient soil, as well as anyone with risk of (or who already has) heart disease, cancer, or arthritis.

Vitamin B12 and Folate

Vitamin B12, found only in animal source foods, is necessary for the formation and regeneration of red blood cells. It also promotes growth and increases appetite in children, increases energy, and helps maintain a healthy nervous system. Elderly

people suffering from neurological impairment find that B12 supplementation improves their cognitive function.

Folic acid helps protect against chromosomal (genetic) damage; prevents atherosclerosis caused by excess homocysteine; in high doses has been shown to decrease risk of cardiovascular disease; is needed for the utilization of sugar and amino acids; may prevent some types of cancer; promotes healthier skin; and helps protect against intestinal parasites and food poisoning. It has also been established that folic acid can prevent spina bifida; therefore, women of childbearing age should increase their RDA of folic acid.

Vitamin B12 and folate deficiencies are most commonly due to problems of malabsorption (B12: gastrointestinal disorders, pancreatitis, tapeworm, and alcoholism; folate: drug interference and jejunal mucosal disease) or inadequate dietary intake (B12 in rare cases of strict vegetarian diets and folate in general malnutrition or alcoholism),

Low levels of B12 are also seen in patients with multiple myeloma and iron deficiency, in those who smoke, and the elderly; in patients with cancer, aplastic anemia, and folate deficiency; in patients on hemodialysis; and in those who ingest high doses of vitamin C. High levels may be increased in acute and myelogenous leukemia, polycythemia vera, leukocytosis and liver disease.

Folic acid levels may be decreased in alcoholics; those with a chronic disease, undergoing hemodialysis, or having anorexia nervosa; and in premature infants and the elderly. Besides pregnancy, increased doses of folic acid may be indicated in hyperthyroidism, neoplasia, hemolytic anemias, and psoriasis.

Endocrine

DHT (5 α -Dihydrotestosterone)

DHT is synthesized from free (noncomplexed) testosterone by the enzyme cholestanone 5 α -reductase, which is found in the prostate, various adrenal glands, and hair follicles. It is responsible for the development of the male genitals and prostate, the physical changes that accompany male maturation, and growth of muscle tissue. Only a small portion of DHT is found in the blood, primarily complexed to sex hormone-binding globulin (SHBG).

Low levels of DHT may be associated with decreased sex drive, erectile dysfunction, male pseudohermaphroditism, or pseudovaginal perineoscrotal hypospadias. Increased levels of DHT may be implicated in male-pattern baldness (alopecia), hirsutism (excessive hair growth in women), benign prostatic hyperplasia, and acne.

Drugs that block 5-alpha-reductase, such as Propecia (finasteride) for male-pattern baldness, interfere with the production of DHT with possible consequential erectile dysfunction and hindrance of muscle growth.

Fasting Insulin and HOMAIR

Fasting serum insulin is used as an index of insulin sensitivity and resistance. Insulin resistance, estimated by homeostasis model assessment (HOMAIR), has been shown to increase accuracy over the traditional test.⁶² HOMAIR is determined by multiplying fasting blood glucose level by fasting insulin level and then dividing by 22.5. The lower the number, the better.

Insulin resistance (where the body does not respond to the insulin that it produces) is a common finding in metabolic disorders, including glucose intolerance, dyslipidemia, hyperuricemia, and hypertension,⁶² and is associated with an increased risk of

symptomatic coronary artery disease.⁶³ Furthermore, approximately 25% of persons with insulin resistance will go on to develop diabetes Type II.

According to Bonora et al, the prevalence of insulin resistance estimated by HOMA is 65.9% in patients with impaired glucose tolerance, 83.9% in NIDDM (non-insulin-dependent diabetes mellitus) subjects, 53.5% in persons with hypercholesterolemia, 84.2% in hypertriglyceridemia patients, 88.1% in patients with low HDL cholesterol, 62.8% in patients with hyperuricemia, and 58% in hypertensive patients. In patients with a combination of glucose intolerance, dyslipidemia and/or hypertension, the prevalence of insulin resistance was 95.2%.⁶²

Data also show that HOMA-estimated insulin resistance is an independent predictor of cardiovascular disease in patients with Type II diabetes.⁶⁴

Insulin resistance may also be an indicator and likely cause of kidney disease in persons with diabetes Type I, according to a study at the University of Pittsburgh. Investigators also found that since insulin resistance predicts heart disease "it may explain the longstanding observation that in Type I diabetes, kidney disease predicts heart disease. In other words, insulin resistance may be the 'common ground' for both complications."⁶⁵

Early detection of insulin resistance may, therefore, help prevent potentially serious complications that may result from metabolic disorders, including diabetes type I and II, dyslipidemia, hyperuricemia, and hypertension.

Somatomedin-C (Insulin-like growth factor/IGF-1)

IGF-1 is the main effector of human growth hormone (HGH) activity and also affects glucose metabolism (insulin-like activity). Because it remains constant in the blood longer than HGH (which tends to fluctuate in response to various stimuli), it is a more accurate indicator of HGH deficiency, and is also more precise for monitoring HGH therapy than is testing HGH directly.

IGF-1 is critical in mediating the growth of muscle and other tissues, and normal levels steadily increase until 12-15 years of age, and then begin to decline. Up to one-third of skeletal muscle mass and strength is lost between the ages of 30 and 80.⁶⁶ A study by Barton-Davis et al showed that IGF-1 overexpression in the muscle cells of mice can preserve the characteristics (morphological and functional) of the skeletal muscles of old mice such that they are equivalent to those of young adult muscles.⁶⁶ Ruiz-Torres et al showed that when IGF-1 levels in older (>70 year-old) males were similar to levels in younger males (up to 39 years), the older males do not show age-dependent decreases in serum testosterone and lean body mass, nor increases in fat body mass.⁶⁷

Low levels of IGF-1 have been implicated in the development of atherosclerosis. Van den Beld et al found that free IGF-1 concentrations appeared to be linearly inversely related to atherosclerosis, suggesting that IGF-1 (along with endogenous testosterone and estrone) may play a protective role in the development of atherosclerosis in aging men.⁶⁸

A study by Carro et al suggests a role for IGF-1 as a neuroprotective hormone. Data show an inverse correlation between levels of IGF-1 (decreased) and amyloid-B (increased) accumulation in the brain of patients with Alzheimer's disease. In studies of mutant mice, high amyloid-B levels are seen when serum IGF-1 levels are low. Conversely, the amyloid-B burden can be decreased by increasing levels of serum IGF-1. Investigators suggested that "circulating IGF-1 is a physiological regulator of brain amyloid levels with therapeutic potential."⁶⁹

Elevated levels of IGF-1 may be indicative of acromegaly (gigantism) and diabetic retinopathy. Although it has been suspected that high levels of IGF-1 are associated with increased risk of prostate cancer, recent data suggest that IGF-1 may be serving as a tumor marker rather than an etiologic factor for the disease.⁷⁰ The IGF-1 test (decreased levels) may also be used to evaluate pituitary insufficiency and hypothalamic lesions in children (diagnosis of dwarfism and response to therapy). Low levels have also been found in patients with amyotrophic lateral sclerosis.⁷¹

A study on asymptomatic HIV-1-infected subjects tested the hypothesis that oral administration of 3 grams per day of acetyl-L-carnitine (ALCAR) could significantly affect IGF-1 levels. The researchers found that while ALCAR did not raise total IGF-1 levels, it significantly increased the levels of free IGF-1 (the bio-active component of total IGF-1) in treated patients. None of the subjects investigated reported any toxicity directly or indirectly related to ALCAR administration. Remarkably, all treated patients reported subjectively, without exception, an improved sense of well-being by the second/third week of ALCAR therapy.⁷²

Thyroid Hormones

Thyroid stimulating hormone (TSH) is secreted by the pituitary gland and serves to control thyroid hormone secretion in the thyroid. Thyroxine (T₄) and triiodothyronine (T₃, free) are hormones that are synthesized (from thyrotropin releasing hormone/TRH) and released from the thyroid. Iodine that is taken up by the thyroid is incorporated in T₃ and T₄ (so called because they have three and four iodine atoms, respectively), which serve to increase the body's basal metabolic rate, regulate growth and development, increase cardiac output, increase the metabolism of cholesterol, increase the number of LDL receptor sites in the liver, and inhibit TSH secretion.

Normally, a decrease in T₃ and T₄ stimulates TSH release from the pituitary that, in turn, stimulates T₃ and T₄ production and secretion, and growth of the thyroid gland. When T₃ and T₄ levels are increased, TSH production is shut down via negative feedback channels.

When TSH, T₃, and/or T₄ levels fall above or below normal, this is referred to as hypothyroidism (low thyroid activity) or hyperthyroidism (increased thyroid activity, also called thyrotoxicosis). Overt hyper- or hypothyroidism is generally easy to diagnose, but subclinical disease is a bit more elusive.

In a study by the National Health and Nutrition Examination Survey (NHANES III), hypothyroidism was found in 4.6% (4.3% mild and 0.3% clinical disease) of a cross-sectional population in the U.S. and hyperthyroidism in 1.3% (0.5% clinical and 0.7% mild) of the same study group. Because mild (or "subclinical") symptoms may be nonspecific (or absent) and progress slowly, and thyroid functions are not routinely screened, people with mild hyper- or hypothyroidism may go undiagnosed. Undiagnosed mild disease may progress to clinical disease states. People with hypothyroidism and elevated serum cholesterol and LDL have an increased risk of atherosclerosis.

Mild hypothyroidism (low thyroid gland function) may be associated with reversible hypercholesterolemia (high blood cholesterol) and cognitive dysfunction, as well as such nonspecific symptoms as fatigue, depression, cold intolerance, dry skin, constipation, and weight gain. Mild hyperthyroidism is often associated with atrial fibrillation and reduced bone mineral density and nonspecific symptoms such as fatigue, weight loss, heat intolerance, nervousness, insomnia, muscle weakness, dyspnea, and palpitations, among others.

Measurement of TSH is the best test for assessing thyroid function. Currently, the American Thyroid Association recommends TSH testing beginning at age 35, and every five years thereafter.⁷³ Comparing the ratios between TSH, T3, and T4 blood levels, though, may elucidate definitive diagnosis. This is extremely important, given that the majority of people with mild hypo- or hyperthyroidism are asymptomatic, and levels of thyroid hormones may be depressed or elevated only slightly.

Although the normally “accepted” upper range for TSH is 5.50 mIU/mL, investigations have shown that blood levels equal and greater than 2.0 mIU/mL may actually indicate adverse health effects:

TSH >2.0mIU/mL increased the 20-year risk of thyroid-induced autoimmune attack.⁷⁴

TSH >4.0mIU/mL increased the risk of heart attack.⁷⁵

On the positive side: when TSH levels are 2.0-4.0 mIU/mL, cholesterol levels decline in response to T4 therapy.

The table below summarizes characteristic thyroid panel results from persons with overt or mild hypo- or hyperthyroidism.

Free T3 is valuable in confirming the diagnosis of hyperthyroidism when an elevated free or total T4 level is found. Abnormal concentrations may be seen in T3 toxicosis in the presence of normal T4 levels.