مختبرات البرج الطبية
Al Borg Medical Laboratories

Newsletter

HOMOCYSTEINE

LITHIUM

OSMOLALITY AT A GLANCE

CELIAC DISEASE

ANTIPHOSPHOLIPID SYNDROME

CHROMOSOME ANALYSIS

Newsletter

Home

Al Borg Medical Laboratories 1st Newsletter

Homocysteine

❖ **What is homocysteine?**

Homocysteine is an amino acid that your body makes from another amino acid called methionine. You obtain methionine from many of the protein-dense foods that you eat on a regular basis, such as meat, eggs, and fish.

❖ **Clinical significance:**

Elevated level of homocysteine in blood is an independent risk factor for atherosclerotic vascular disease affecting the coronary (arteries supplying the heart), cerebral (arteries supplying the brain) and peripheral arteries (supplying the rest of the body).

❖ **Factors which can result in increased SERUM Homocysteine**:

- **Genetics:** altered enzyme activity of HCy related pathways
- **Sex:** men higher than women
- **Diet:** low intake of B6, B12, Folate, and/or methionine
- **Renal (kidney) disease:** increases with serum creatinine
- **Transplantation**
- **Post stroke**
- **Severe psoriasis**
- **Corticosteroid therapy**
- **Cyclosporine**
- **Smoking**

❖ **Homocysteine & Cardiovascular Risk**

- Injures the inner lining of blood vessel walls.
- Oxidizes LDL cholesterol, making it more likely to stick to injured blood vessels.
- Accelerates the growth of smooth muscle cells, narrowing blood vessels.
- Induces oxidative stress and impairs the ability of blood vessels to expand and contract.
- Increases blood clot formation, which can lead to a heart attack or stroke

Newsletter

❖ **How is the homocysteine level measured?**

Homocysteine is measured using a simple blood test. It can be measured at any time of day. You don't have to prepare in any special way for the blood test.

❖ **What do the results mean?**

A healthy homocysteine level is less than 12 µmol per L. A level greater than 12 µmol per L is considered high. If your homocysteine level is greater than 12 µmol per L and you have blockages in any blood vessel, you need to lower your homocysteine. If you have no other major risk factors for cardiovascular disease and you do not have atherosclerosis, it may be okay for you to have a modestly high homocysteine level (12 to 15 µmol per L).

❖ **Who should have their Homocysteine level tested?**

Homocysteine testing may be most useful in checking the overall risk of heart disease for people who have a strong personal or family history of heart disease but who do not have other risk factors that can be controlled, such as smoking or high blood pressure. Homocysteine testing also may be useful for people who have early heart disease but who do not have known risk factors and for people who have had unexplained deep vein thrombosis or stroke.

❖ **How can I lower a high homocysteine level?**

Dietary supplementation with folic acid can reduce elevated homocysteine levels in most patients. The usual therapeutic dose is 1 mg/day. When this is not effective, vitamins B6 and/or B12 can be added to the regimen, which should be continued permanently.

Newsletter

Al Borg Medical Laboratories 2nd Newsletter

Lithium

Advancing treatment of bipolar disorder

1. What is lithium?

Lithium is a metallic element that was discovered in 1818. Because it was found in a mineral, it was called ‘lithium’, which is derived from the Greek word lithos, stone. Lithium is identified by the symbol Li on the periodic table at the position number 3 with an atomic mass of 6.94. Lithium is used in a range of industries, typically in the form of alloys and compounds, since it is extremely reactive. Well known lithium applications include the lithium-ion battery and lithium carbonate tablet for treatment of bipolar disorder and mood stabilization.

Lithium is administered as lithium carbonate, it is completely absorbed by the gastro-intestinal tract; peak serum levels occur 2 to 4 hours after an oral dose. The half life in serum is 48 to 72 hours and it is cleared through the kidneys (excretion parallels that of sodium). Reduced renal function can prolong clearance time. Lithium acts by enhancing the uptake of neurotransmitters, which produces a sedative effect on the central nervous system. Serum lithium concentrations are measured essentially to ensure compliance and to avoid toxicity.

In the diagnostic laboratory, lithium has traditionally been measured using flame emission photometry, atomic absorption spectrometry, or ion selective electrodes. Alborg laboratory is currently using a colorimetric method to measure serum lithium.

2. what is the Medical use of lithium?

Lithium is used as a therapeutic agent mainly for treating the following disorders:

1. Bipolar (manic depression) disorder
2. As mood stabilizing agent
3. Schizophrenia and Alzheimer’s Disease

Lithium is the first modern recognized treatment for bipolar disorder and has served a unique role for this and other conditions for over 35 years. It became U.S. FDA-approved for treating acute manic episodes in 1970, and approved for maintenance therapy for patients of manic symptoms in 1974. All

clinical practice guidelines recommend lithium as the choice for acute and prophylactic treatment of manic and mixed states, bipolar depression, and rapid cycling.

3. What are the Side effects of lithium therapy?

Early symptoms of intoxication include apathy, sluggishness, drowsiness, lethargy, speech difficulties, irregular tremors, myoclonic twitchings, and muscle weakness
These symptoms usually settle as the patient's body adapts to the medication.
However, lithium, when existing in excessive amounts in the blood, can be dangerously toxic. Excess lithium can slow or stop breathing, cause seizures, coma and even death. This is because lithium has a very narrow therapeutic window and its effective dose is uncomfortably close to its toxic dose. To avoid lithium toxicity, patients must have their blood levels monitored regularly to assure that they remain within an acceptable therapeutic range. Blood lithium levels need to be monitored more frequently during the early stages of treatment. As the treatment stabilizes, monitoring can occur every two to three months.

4. Why and when are lithium blood levels tested?

Lithium has a narrow therapeutic range (0.4-1.4 mM), and too low of a dosage leads to ineffectiveness and too high leads to severe toxicity. Therefore regular monitoring of the patient's clinical state and serum lithium levels is required to:

(1) identify and /or prevent potential toxicity associated with high levels .

(2) assure ongoing efficacy and effectiveness .

(3) monitor the patient's adherence to the prescribed regimen .

The lithium test may be ordered frequently (every few days) when a patient first begins taking lithium or if a patient is returning to its use after an absence. This is done to help adjust the dose to the desired blood level. The test may be ordered at regular intervals or as needed to monitor blood concentrations. One or more lithium tests may be ordered if a patient starts taking additional medications (to judge their effect, if any, on lithium levels) and may be ordered if the doctor suspects toxicity.

Once stable blood concentrations in the therapeutic range have been achieved, lithium may then be monitored at regular intervals to ensure that it remains in this range.
The test may also be ordered when a patient's condition does not appear to be responding to initial lithium dosage levels in order to determine whether concentrations are too low, the medication is ineffective, and/or to determine if the patient is complying with therapy. It may also be ordered when

a patient experiences a troublesome level of side effects and/or exhibits symptoms that the doctor suspects may be due to toxicity.
Lithium blood levels are generally performed 12-18 hours after the last dose. Since dosage timing varies and some formulations are time released, collection specifics may vary.

5. Lithium measurement in Alborg medical laboratories

Lithium, Serum or Plasma : test code 259

Test principle: colorimetric method

Lithium present in the sample reacts with a substituted porphyrin compound at an alkaline pH, resulting in a change in absorbance which is directly proportional to the concentration of lithium in the sample

Performed:	Daily
Reported:	Within 24 hours
Specimen Required:	Patient Prep: Specimens are commonly drawn approximately 12 hours after last dose of lithium taken. Collect: Serum Plasma: K_2-EDTA and Na-heparin plasma. Specimen Preparation: Allow serum to clot completely at room temperature. Separate serum from cells ASAP or within 2 hours of collection. Storage/Transport Temperature: Frozen. Unacceptable Conditions: Specimens collected in lithium heparin or sodium fluoride/potassium oxalate. Grossly hemolyzed specimens. Stability (collection to initiation of testing): After separation from cells: Ambient: 1 day; Refrigerated: 7 days; Frozen: 6 months

Reference Interval:

Therapeutic.: 0.6-1.2 mmol/L

Toxic: 2.0 or greater mmol/L

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Newsletter

Al Borg Medical Laboratories 3rd Newsletter

Home

OSMOLALITY at a glance

Osmolality of body fluid is a measure of its solute/water ratio. The osmolality of serum, urine, or other body fluids depends on the number of osmotically active ions and molecules dissolved in a kilogram of body water. Sodium, potassium, chloride, bicarbonate, glucose and urea are the osmotically important body fluid solutes. The osmolality of a body fluid increases as the ratio of solute to water molecules increases.

Water balance in the body is a dynamic process that is regulated by controlling the amount of water excreted in the urine and by increasing or decreasing water drinking by regulating "thirst. Osmoreceptors perceive and react to increases and decreases in the amount of water and particles in the bloodstream. When blood osmolality increases, indicating either a decrease in the amount of water in the blood or an increase in the number of particles, the hypothalamus secretes antidiuretic hormone (ADH), the kidneys will conserve water. This results in a more concentrated urine with a higher urine osmolality and a more dilute blood with lower osmolality. As blood osmolality decreases, ADH secretion is suppressed, the kidneys excrete increased amounts of dilute urine, the amount of water in the body decreases, and blood osmolality returns to normal.

Osmolality is expressed as "so many" milliosmoles per kilogram of water (mOsm/kg water).

Serum osmolality: Osmolality be measured by an osmometer. It can also be calculated by adding the values of its constituent solutes.

Osmolal gap is the difference between the calculated value and measured value

Urine osmolality: is a more accurate measurement of urine concentration than specific gravity. In addition urine osmolality can be compared with the serum osmolality to obtain a more accurate picture of a patient's fluid homeostasis.

Patients may get tested for osmolality to evaluate the body's water and electrolyte balance; to investigate hyponatremia and increased or decreased urine production; to detect the ingestion of toxins such as methanol; to monitor the effectiveness of treatment for conditions affecting osmolality.

Serum osmolality may be increased with:

- Dehydration
- Diabetes mellitus

- Hyperglycemia
- Hypernatremia
- Ingestion of ethanol, methanol, or ethylene glycol
- Kidney damage
- Mannitol therapy
- Shock

Serum osmolality may be decreased with:

- excess hydration
- hyponatremia
- inappropriate ADH secretion

Urine osmolality may be increased with:

- congestive heart failure
- hypernatremia
- inappropriate ADH secretion
- liver damage
- shock

Urine osmolality may be decreased with:

- Diabetes insipidus
- Excess fluid intake
- Hypercalcemia
- Hypokalemia

Newsletter

- Kidney tubular damage

Osmolality measurement at Alborg laboratories

Al Borg laboratory uses the OSMOMAT 030, which is the standard system for the determination of the total osmolality in aqueous solutions.

This system is very reliable and provides extremely rapid sample handling.

Osmolality, Urine : 297

Methodology:	Freezing Point
Performed:	Daily
Reported:	Within 24 hours
Specimen Required:	Collect: Random urine. Specimen Preparation: 1 mL aliquot from a well-mixed random urine (Min: 0.5 mL) Unacceptable Conditions: Urine collected with preservatives. Stability (collection to initiation of testing): Ambient: 24 hours; Refrigerated: 1 week; Frozen: 6 months

Reference Interval:

0-30 days: 50-645 mOsm/kg

1 month-16 years: 50-1500 mOsm/kg

17 years and older: 50-800 mOsm/kg

Newsletter

Osmolality, Serum or Plasma : 284

Methodology:	Freezing Point
Performed:	Daily
Reported:	Within 24 hours
Specimen Required:	Collect: Serum separator tube or plasma separator tube. Specimen Preparation: Separate serum or plasma from cells within 2 hours of collection. 0.5 mL serum or plasma (Min: 0.5 mL) Stability (collection to initiation of testing): After separation from cells: Ambient: 24 hours; Refrigerated: 1 week; Frozen: 6 months

Reference Interval:
0-16 years: 271-296 mOsm/kg
17 years and older: 280-303 mOsm/kg

Newsletter

Al Borg Medical Laboratories 4th Newsletter

Home

CELIAC DISEASE

UNDER-DIAGNOSED AND UNDER-TREATED

Celiac disease (CD) is an autoimmune disease that is characterized by a genetically-mediated, non-allergic, immunological response to the ingestion of gluten.

Celiac disease has emerged as an increasingly recognized Global health problem over the last half-century. Once considered a Western epidemic, It is now acknowledged as a common disease among Middle Eastern and North African populations.

Gluten is found in cereal grains such as wheat and barley. It is a protein mixture, composed largely of glutenin and gliadin.
Symptoms of CD are triggered when the grains are consumed. Currently, the only treatment is to maintain a strict gluten-free diet.
Undiagnosed and untreated, celiac disease can lead to the development of other autoimmune disorders, as well as osteoporosis, infertility, neurological conditions and in rare cases, cancer.

Populations at risk for CD

Prevalence is much higher in:

- First-degree (ten folds) and second -degree relatives of patients with CD
- Diabetes Mellitus (type 1)
- Down syndrome
- Turner syndrome
- Williams syndrome
- Selective IgA deficiency and other autoimmune disorders.

It is not uncommon for patients to be misdiagnosed or to experience a delay in the diagnosis of CD. It is estimated that only 3-15% of those with CD are diagnosed.

It is important for clinicians to be aware of high-risk groups susceptible to developing CD as these should be screened for the disease using serological tests.

Pathogenesis

Patients genetically susceptible to CD have human leukocyte antigens (HLAs) that recognize and bind gliadins. Bound gliadin stimulates the production of anti-gliadin antibodies. Certain gliadin polypeptides are resistant to gastric, pancreatic and intestinal peptidases and remain intact in the intestinal lumen. In individuals who are genetically-susceptible to CD, increased intestinal permeability allows additional gliadin polypeptides to enter the intestinal submucosa. Gliadin polypeptides deamidated by the intestinal

enzyme tissue transglutaminases (tTG) initiate an immune response that creates anti-tissue transglutaminase autoantibodies (anti-tTG). These antibodies cause inflammation and damage the intestinal lining, restricting absorption of vital nutrients.

Anti-tTG antibodies also deposit in skin and brain as well as other tissues that contain tTG. CD patients can therefore have a spectrum of medical conditions other than malabsorption.

There are many factors which may trigger the onset of CD. In children, recurring gastrointestinal infections may play a role in the development of CD. In genetically susceptible adults who consume gluten, additional factors such as stress, surgery, pregnancy, or infections can result in acute CD symptoms.

Classification of CD

Recognition of the different clinical presentations of CD is important in order to accurately diagnose and decrease the risk of long-term complications.

Classical CD is dominated by symptoms of gastrointestinal malabsorption.

Atypical CD is characterized by non-prominent gastrointestinal manifestations with little or no symptoms. This may be the most common form of CD. Patients may present with chronic fatigue, anemia, dental enamel hypoplasia, reflux, bloating, migraines, osteoporosis, short stature, constipation, infertility, muscle weakness and/or depression.

Silent CD is described as asymptomatic patients with positive serological tests and villous atrophy on biopsy. This form of CD is usually diagnosed by screening high-risk individuals.

Latent CD is defined by positive serological tests, but with a normal small bowel biopsy. Patients are asymptomatic, but often develop symptoms and/or histological changes at a later date.

Diagnosis of CD

Who to test?

Serological testing is recommended for patients with:

- GI symptoms including chronic diarrhea, malabsorption, weight loss, and abdominal distension
- Unexplained persistent elevations of transaminases, short stature, delayed puberty, iron-deficiency anemia, recurrent miscarriages and infertility
- Irritable bowel syndrome
- Persistent aphthous stomatitis
- Other autoimmune diseases
- Peripheral neuropathy
- Cerebellar ataxia

- Dental enamel hypoplasia
- Those at higher risk of CD, *e.g.*, patients with type 1 diabetes mellitus, Down syndrome, Turner syndrome, Williams syndrome, or first or second degree relative with a confirmed diagnosis of CD.

Initial testing

Serological tests are the first steps to diagnosing CD in symptomatic patients. Confirmatory biopsy should be performed in positive cases. It is recommended to use multiple serological markers to achieve better clinical sensitivity and specificity.

Available tests include:

Serological tests

- Tissue Transglutaminase (tTG) IgA/IgG or endomysial antibody (EMA) has the highest sensitivity which varies between 84 and 88% and specificity greater than 90%. tTG is considered to be the most useful screening tool in adults
- IgG and IgA gliadins have poorer positive and negative predictive values for CD, but may be useful in screening children under the age of 18 months.
- 3-5% of celiacs are IgA deficient and 10 % of IgA deficient patients have CD. That's why Immunoglobulin IgA test should be started with to determine whether to use IgA or IgG tTG.

Intestinal biopsy

- To confirm a diagnosis of celiac disease, a biopsy of the small intestine is examined to detect damage to the intestinal villi. However, given the invasive nature and cost of a biopsy, antibody tests are often used to identify those individuals with high probability of having celiac disease.

Genetic testing

- 20-30% of the general population can have the genes, but only 0.1-1% may actually develop the disease.
- Due to their low positive predictive value, HLA-DQ2 and HLA-DQ8 testing is recommended mostly for exclusion when diagnostic and biopsy results are equivocal

Post diagnosis and monitoring

- Patients should have dietary instruction to recover from symptoms and avoid complications. Symptoms should disappear within 6-12 months of a strict gluten-free diet and blood tests should become negative.
- tTG IgA and IgG assays(based on IgA levels) every 3-6 months. Decline in antibody levels may correlate with normalization of the intestinal villi
- Patients should be assessed for deficiencies in vitamins and minerals, including fat-soluble vitamins, iron and calcium.

- Patients should undergo screening for osteoporosis.
- Children should have on-going evaluations to monitor growth and development.

Recommendations for Celiac Disease (CD) Testing in Children and Adolescents (ESPGHAN 2012)

European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommends testing for CD in children and adolescents

- **With unexplained**
  - Gastroenterological symptoms
  - Poor growth
  - Delayed puberty
  - Iron deficiency anemia
  - Abnormal liver testing
- **In the presence of the following risks for CD (even if asymptomatic)**
  - Autoimmune disorders – DM type 1, autoimmune thyroiditis, autoimmune liver disease
  - Genetic syndromes –Down syndrome, Turner syndrome, Williams syndrome
  - First degree relatives with CD
  - Selective IgA deficiency

Newsletter

Home

Al Borg Medical Laboratories 5th Newsletter

DIAGNOSING A COMPLEX CONDITION

Antiphospholipid syndrome (APS) is an autoimmune disease with serious consequence including venous/arterial thrombosis, and pregnancy complications such as recurrent fetal loss and severe preeclampsia. Sera taken from patients with APS often contain antibodies to cardiolipin, an acidic phospholipid - hence its original name “antiphospholipid syndrome”. To this day, APS remains a complex illness that is inherently difficult to diagnose.

APS is a major women’s health issue, as 75–90% affected are women. It is estimated that APS is the cause of 15–20% of all thrombotic events, 10–25% of recurrent miscarriages, and one-third of the strokes in patients under the age of 50. The syndrome is also thought to be present in 40–50% of patients with systemic lupus erythematosus (SLE).

Pathogenesis of APS

Thrombosis has a key role in the clinical manifestations of APS. Several mechanisms have been proposed for APS-related thrombosis; however, it is most probably multifactorial in etiology. The thrombotic tendency may be caused by antiphospholid antibodies through the following mechanisms:

- Inhibition of the factors of the anticoagulant system, affecting thrombin formation and antithrombin activity.
- Impairment of fibrinolytic activity.
- Interference with coagulation factors and complement, particularly the intrinsic and protein C pathway.
- Direct effect of antiphospholipid antibodies on cell function, such as platelets, endothelial cells and vascular cells.

There is growing evidence that phospholipid antibodies are present in patients months to years before the onset of any clinical symptoms of APS. Many individuals with APS may never experience a thrombotic event or pregnancy loss. Secondary risk factors, co-morbidities, and other factors influence whether a patient actually experiences the clinical manifestations of APS. Thrombosis may be initiated by trigger events, such as surgery, pregnancy, or the use of oral contraceptives.Thrombotic events can affect arteries and veins of all sizes, including the microvascular system. The thrombosis can also be recurrent.The most frequent thrombotic events are deep-vein thrombosis (DVT) and ischemic stroke. An accelerated form of this syndrome that results in multiple organ failure is a very rare variant.

Diagnosis

It was proposed that a patient must have at least one clinical criterion and one positive laboratory criterion to be diagnosed with APS.

Clinical criteria

- Vascular thrombosis:
  - At least one confirmed clinical episode in an arterial, venous, or small vessel in any tissue or organ that has been confirmed.
- Pregnancy morbidity:
  - One or more unexplained deaths of a normal fetus at or beyond the 10^{th} week of gestation.
  - Three or more unexplained consecutive spontaneous abortions before the 10thweek of gestation.
  - One or more premature births of a normal neonate delivered prematurely before the 34thweek of gestation due to severe pre-eclampsia, eclampsia, or severe placental insufficiency (where other causes are excluded).

Laboratory criteria

- Positive results on two or more occasions at least 12 weeks apart for at least one of the following tests:
  - Lupus anticoagulant (LA);
  - Cardiolipin antibodies (aCL) of IgG and/or IgM isotype in medium or high titre, > 40 units;
  - ß2-glycoprotein I (ß2GPI) antibodies of IgG and/or IgM isotype.
- The elapsed time of 12 weeks between the initial and confirmatory test is to increase the probability of excluding temporary infection-associated antibodies.
- If there are fewer than 12 weeks, or more than 5 years between a positive APS test and the clinical manifestations, the classification criteria should not be used.

Although the pathophysiology of APS is now relatively well understood, difficulties still persist with making a definitive diagnosis based solely on clinical criteria. The prevalence of the clinical symptoms is high and the differentials for vascular thrombosis and pregnancy morbidity are relatively broad. Laboratory testing can therefore be very helpful in providing definitive diagnosis.

APS laboratory testing

Laboratory testing for APS includes both functional coagulation assays and immunology testing.

1. Lupus anticoagulant (LAC) testing a functional assay detecting the effect of phospholipid antibodies on the coagulation cascade. Phospholipid antibody tests are a direct measure of the presence or absence of the antibodies themselves.
2. There are two main classes of antiphospholipid antibodies assays available

- Cardiolipin antibodies detect antibodies binding to ß2-glycoprotein within context of a protein/phospholipid complex,
- ß2-glycoprotein I antibodies detect antibodies binding to ß2-glycoprotein in absence of phospholipids.

1.Lupus anticoagulants (LAC)

The term “lupus anticoagulant” was first used in 1972 to describe an inhibitor directed against the coagulation cascade phospholipids.The name is a misnomer as most people testing positive for “lupus anticoagulant” (LAC) do not have SLE and it has a procoagulant effect in vivo, however the name persists despite attempts to modify.The LAC test detects various APA’s on the basis of their interference with the phospholipid dependent steps in the coagulation cascade. Testing for the presence of LAC is performed following strict guidelines set up by International Society of Thrombosis and Haemostasis (ISTH) which include the preparation of platelet-poor plasma, and utilizing screening, mixing and confirmation tests.The ISTH guidelines state that laboratories are to perform two different screening tests.They recommend to perform (a) the dilute Russell’s Viper Venom Time (dRVVT) and (b) the activated partialthromboplastin time (aPTT) using a reagent with low phospholipid content.If either test is positive, the results are to be confirmed using a bilayer or hexagonal-phase phospholipid based reagent.

Interpreting LAC test results

- It has been shown that LAC is more consistent with the clinical manifestations of APS than phospholipid antibodies.
- Testing should not be performed while patients are on anticoagulant therapy. Heparin and vitamin K antagonist treatments may impair the detection of the lupus anticoagulant.

2.Phospholipid antibodies

The challenge with the laboratory tests for phospholipid antibodies (APA) is that there is no diagnostic “gold standard”. The presence of APA is a necessary inclusion criterion to make the diagnosis, but is not diagnostic of APS. The antibodies may also be found in children with viral infection, other autoimmune disorders, patients with infections, malignancy and even in healthy individuals.

a.Cardiolipin (aCL) antibodies

The real limitation of the aCL assay is inter-assay variability. The results for different assays on the market particularly differ in the lower measuring range for the test.

Interpreting aCL antibodies test results

- Only medium and high levels, > 40 units of aCL antibodies (IgG or IgM) are included in the diagnostic criteria which improve the specificity.
- At lower concentrations, aCL-IgM tends to give false-positive results for APS, particularly in the presence of rheumatoid factor or cryoglobulins.

- aCL IgA is of little diagnostic value; it has more use in classifying patients into diagnostic subgroups for risk since IgA aCL may also be associated with thrombocytopenia, skin ulcers and vasculitis.

b.ß2-glycoprotein I (ß2GPI) antibodies

ß2GPI antibodies have been incorporated into the 2006 updated criteria and are considered to be the most clinically significant antibodies. The assay shows higher specificity than the aCL assay and can be the only positive test in 3–10% of the APS patients.

Interpreting ß2GPI antibodies test results

- High titres of ß2GPI antibodies are associated with a high risk of thrombosis.
- Interferences by cryoglobulins or rheumatoid factor may cause a false positive in interpretation of IgM ß2GPI antibodies.

Predicting future APS-associated events

Several studies have been done on the use of these laboratory tests in identifying patients at risk for thrombotic events or severe pregnancy complications:

- Positive antiphospholipid lab tests, in the absence of clinical criteria, should only be considered to be risk factors rather than diagnostic criteria for APS. Patients should be assessed for additional thromboembolic risk factors (e.g., smoking, obesity, hypertension) for risk reduction.
- Clinical studies have shown that testing for the antibody profile is more useful in identifying thrombotic risk than the result of any individual test.
- The presence of both aCL–IgG antibodies and ß2GPI antibodies is believed to identify patients at higher risk for APS.
- The presence of LAC has been observed more frequently in patients without clinical events, and may be false positive in the elderly.
- ß2GPI antibodies have been correlated with thrombosis, pre-eclampsia, and eclampsia as well as having a role in young women with ischemic stroke.

Tests to Order in Cases of Suspected APS

Patients presenting with clinical symptoms suggestive of APS should have the following tests ordered, particularly those without other common risk factors:

- Lupus anticoagulant
- Cardiolipin antibodies, IgG and/or IgM
- ß2GPI glycoprotein I antibodies, IgG and/or IgM

Results of these tests will be adjunctive to the clinical findings and should be not be considered diagnostic of, but rather as risk factors for thrombosis, pregnancy loss and clinical manifestations of APS.If positive, confirmatory tests should be repeated within 6 to 12 weeks.

Newsletter

Test	Sample Collection	Specimen preparation	Storage/transport temprature	Perfomed (Run Days)	reported
Lupus Anticoagulant	Light blue-capped tube (Na citrate)	1 ml frozen platelet poor plasma in plain plastic Wassermann tube with no additives	Critical Frozen (separate tube	Saturdays & Tuesdays	Same day
Anti-Cardiolipin Antibodies (IgG & IgM)	Red-capped tube (Plain)	1 ml refrigerated serum	refrigerated		Same day
Anti-Beta 2 Glycoprotein 1 Antibodies (IgG & IgM)	Red-capped tube (Plain)	1 ml refrigerated serum	refrigerated		Same day

Newsletter

Al Borg Medical Laboratories 6th Newsletter

Home

CHROMOSOME ANALYSIS

Chromosomes contain the thousands of genes in the human genome that direct cellular processes controlling growth, development, and functioning of the human body. Gains or losses in chromosome content lead to alterations in gene function and disrupt these vital cellular processes. This can result in mental retardation or other developmental abnormalities, birth defects, and many well-characterized genetic syndromes.

This test will detect abnormalities in chromosome number (aneuploidy) e.g. Down Syndrome with an extra chromosome 21 , Edward Syndrome with an extra chromosome 18 , Patau Syndrome with an extra chromosome 13 , Klinefelters Syndrome in males with an extra chromosome X or Turner Syndrome in females with a single X. Not only will this test detect numerical aberrations but structural aberrations as well can be detected in the form of translocations (Reciprocal or Robertsonian) , deletions , duplications , or isochromosomes.

When should a Karyotype be ordered ?

Problems of early growth & development : failure to thrive , developmental delay , dystrophic fancies , multiple malformations , short stature , ambiguous genitalia , & mental retardation.

Stillbirth & Neonatal death : the incidence of chromosome abnormalities is much higher among stillbirths & early neonatal deaths.

Fertility problems : women with amenorrhea or recurrent miscarriages & men with infertility may have a chromosomal aberration leading to infertility & hence may be offered a different mode of Assisted Reproductive Techniques combined with Pre Implantation Genetic Diagnosis.

Family History : a known or suspected chromosome abnormality in a first degree relative is an indication for chromosome analysis under some circumstances.

Neoplasia : Virtually all cancers are associated with one or more chromosome

abnormalities. Chromosome analysis in the appropriate tissue , the tumor itself or the bone marrow , can provide useful diagnostic & prognostic information.

Pregnancy in woman of advanced age : There is an increased risk of chromosome abnormality in fetuses conceived by women older than about 35 years. Fetal chromosome analysis should be offered as a routine part of prenatal care in such pregnancies.