The Great Plains Laboratory, Inc.

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Phospholipase A_2

Its Role in Inflammation and Chronic Disease

The Great Plains Laboratory, Inc. is excited about our recently developed phospholipase A_2 (PLA_2) test that measures the activity of PLA_2 in urine. We are the only commercial lab currently offering PLA2 level measurement as a urine test. PLA_2 is elevated in a wide range of inflammation-related disorders and is considered a good marker for increased risk of developing or worsening of inflammatory conditions. PLA_2 levels can easily be sampled along with the organic acid test (full or microbial), offering a powerful new combination of clinical insights.

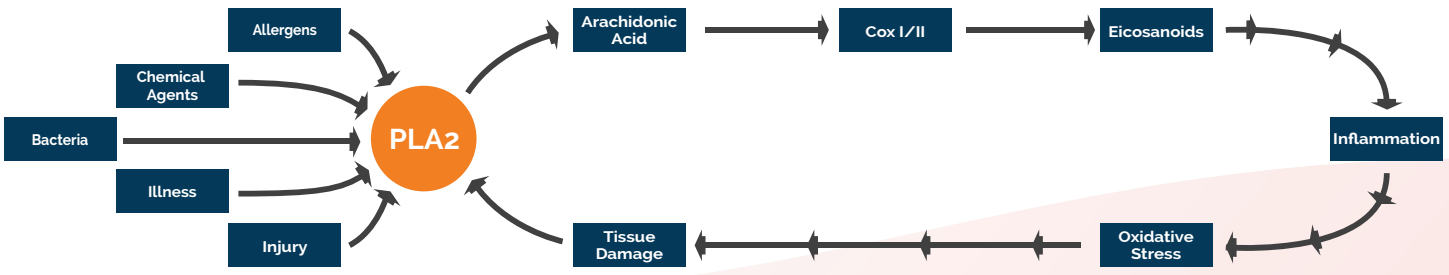
Specimen Requirement

10 mL of the first morning urine before food or drink is suggested.

Overview

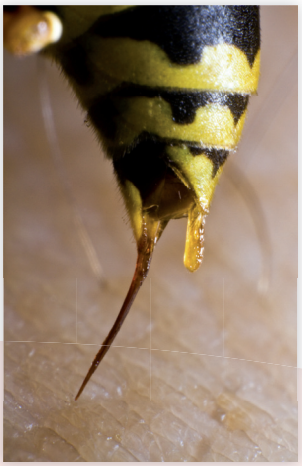
Bee stings and venomous snake bites cause immediate inflammation, resulting in pain and swelling. The enzyme in venom that triggers this immune response is phospholipase A_2. This enzyme is also present in human tissue. During infection, PLA_2 activates a cascade that results in the destruction of the cell membranes of invading microbes. The products of the PLA_2 reaction responsible for eliminating these organisms, lysolecithins and free fatty acids, are powerful detergents that damage cell membranes, denature proteins, and disrupt their function. However, this killing mechanism comes at a cost to the human host. Lysolecithin products are involved in the pain response and cause hemolysis of erythrocytes. The most common free fatty acid produced by PLA_2 is arachidonic acid, which can increase the production of powerful mediators of inflammation: prostaglandins, leukotrienes, and thromboxanes, collectively called eicosanoids. Release of these mediators initiates the pain, swelling, and other unpleasant symptoms we experience as part of an inflammatory response.

Excess PLA_2 not only causes local damage, but can be transported by the blood vessels to other parts of the body, causing widespread tissue damage. Normal amounts of PLA_2 are involved in remodeling cell membranes and changing cell architecture, but sustained release of PLA_2 and the resulting inflammation is implicated in the development of chronic conditions including multiple sclerosis, cardiovascular disease, rheumatoid arthritis, gastrointestinal disorders, allergies, and neuropsychiatric disorders.



PLA2 testing is recomended for the following disorders:

- **Multiple sclerosis**
- **Rheumatoid arthritis**
- **Crohn's disease**
- **Pancreatitis**
- **Ulcerative colitis**
- **Allergies**
- **Cardiovascular disease including atherosclerosis**
- **Neurodegenerative diseases**
- **Schizophrenia**
- **Bipolar depression, subtype with psychosis**
- **Candida infection**
- **Sepsis**
- **Long term depression**
- **Asthma**
- **Chronic obstructive pulmonary disease (COPD)**



What Causes Elevated PLA_2?

A large dose of PLA_2 is delivered in venom from snakes, spiders, and bees (experienced as pain and stinging) and is responsible for much of the toxicity of these venoms. Microorganisms such as Candida albicans and certain Clostridia species produce PLA_2, which increases the ability of the microorganism to infect the host. This same enzyme is produced in the body as a response to invading microorganisms and foreign proteins such as allergens, particularly house dust and cats. Physical trauma may also cause significant increases in PLA_2, contributing to tissue damage and brain injury.

Phospholipase A_2 is in fact a family of enzymes that are categorized by location and function. They have strong antibacterial and antiviral properties as part of the innate immune system, but also participate in many other biochemical processes that include cell signaling, cell proliferation and differentiation, cell migration and apoptosis, and modulation of inflammatory response. PLA_2 is not only released in tissues and cells of the immune system, it is also produced by the pancreas and released into the small intestine following a fatty meal, to assist in the digestion and absorption of phospholipids. Additionally, PLA_2 is expressed in neuronal tissue and is involved in the degranulation process that releases neurotransmitters from neurons. Research efforts have focused on the role that derangement of normal PLA_2 activity plays in the etiology of many chronic illnesses. The specific roles, interactions, and interdependencies of PLA_2 have been a major area of interest as it relates to chronic inflammatory conditions, cardiovascular disease, and cancer.

PLA_2 and Inflammatory Disease

Research has implicated PLA_2 in the pathophysiology of neurodegenerative diseases such as multiple sclerosis (MS) and Alzheimer's disease (AD). Multiple sclerosis involves both antigen-specific mechanisms and components of the innate immune system that result in inflammatory response. Elevated PLA_2 activity was found to be ongoing among MS patients, with the highest levels measured in patients with progressive disease. In the development of Alzheimer's disease, the abnormal PLA_2 levels appear to be related to oxidative signaling pathways involving NADPH oxidase and production of ROS species that lead to impairment and destruction of neurons and inflammation of glial cells.

Inflammation is the hallmark of rheumatoid arthritis (RA), a joint-destructive autoimmune disease. PLA_2 is found in synovial fluid of RA-affected individuals and in the cartilage of RA patients as compared to cartilage from osteoarthritic and normal individuals.

Measurement of PLA_2 is emerging as an important tool for evaluating the chance of cardiovascular disease (CVD), including future stroke, myocardial infarction, heart failure, and other vascular events. PLA_2 appears to be more specific than hsCRP for CVD risk and may also have a pivotal role as a mediator of cardiovascular pathology. In atherosclerosis, PLA_2 not only activates macrophages and formation of foam cells, but it also hydrolyzes LDL and HDL, spawning increased numbers of pro-atherogenic small LDL particles, and impairing anti-atherogenic HDL. PLA_2 activity may even precipitate bleeding from atherosclerotic plaques.

PLA_2 is expressed normally in pancreatic, gall bladder, and GI epithelial cells, but is significantly increased in inflammatory gastrointestinal disorders. In ulcerative colitis and Crohn's disease, all intestinal cell types increase expression of PLA_2, which increases gut permeability and may actually contribute to infectivity.

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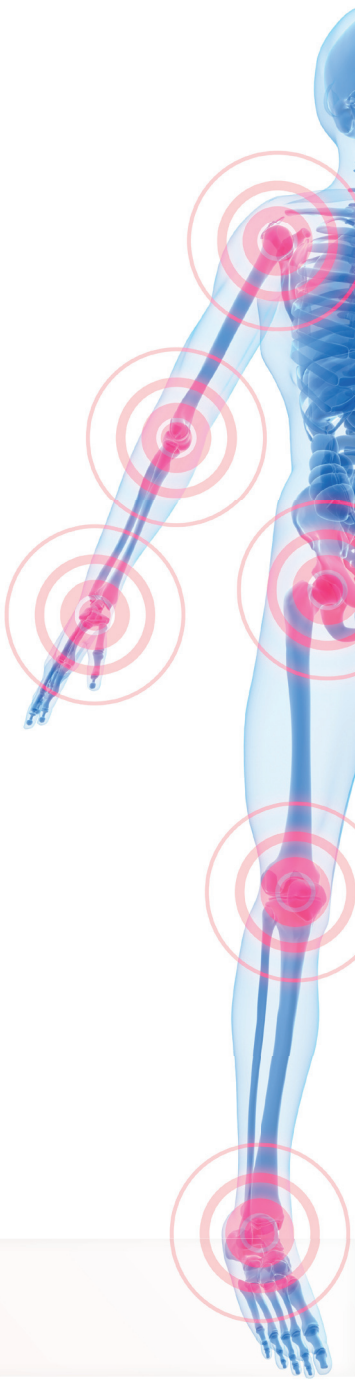

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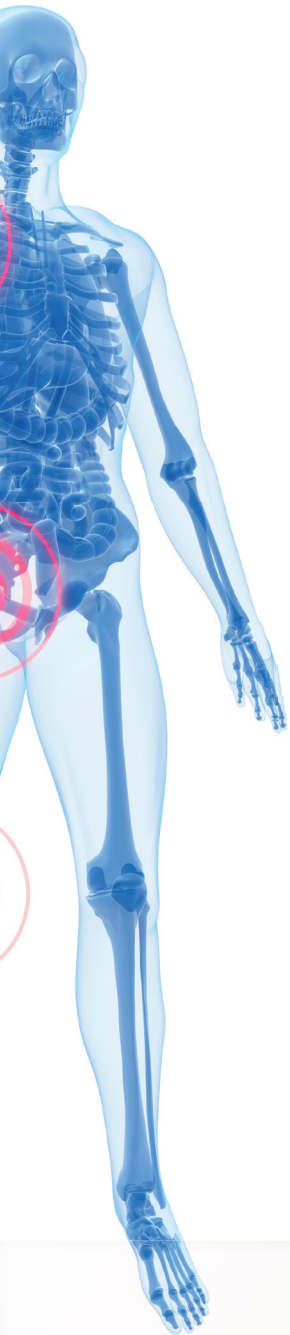
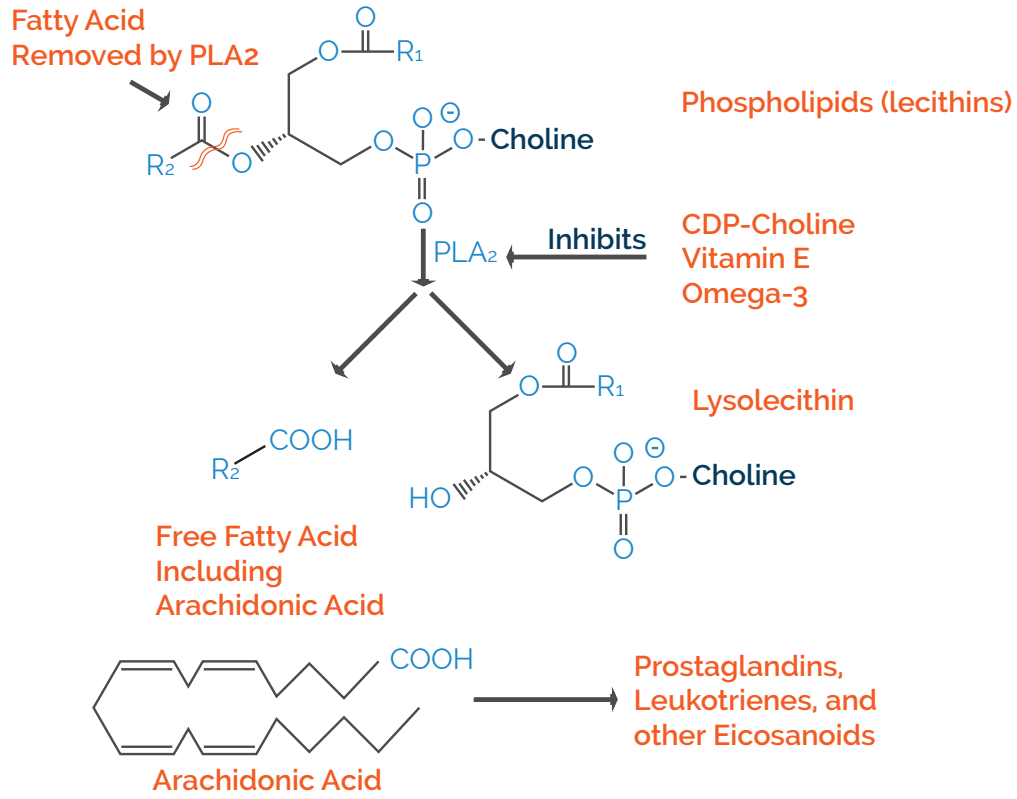


PLA_2 and Cancer

Elevations of PLA_2 have been found in gastrointestinal cancers including colonic adenomas and carcinomas and pancreatic ductogenic carcinomas, among others. Patients with lung tumors positive for PLA_2 had a greatly increased tumor growth rate and a markedly reduced survival rate. Patients with lung cancer also had higher plasma levels of PLA_2 than patients with benign nodules. A similar pattern has been observed in prostate cancer, although metastatic tumors expressed lower PLA_2 than primary tumors. As PLA_2 releases arachidonic acid and other fatty acids from cell membranes, they initiate downstream production of tumor-promoting eicosanoids. In cancer, the spread of tumor cells from a primary tumor to the secondary sites within the body is a complicated process involving cell proliferation and migration, degradation of basement membranes, invasion, adhesion, and angiogenesis. Continued research on PLA_2 expression in cancer will certainly reveal valuable new insights.



What Lowers PLA_2?

Glucocorticoids such as the natural hormone cortisol and pharmaceutical agents such as dexamethasone inhibit the production of phospholipase, decreasing harm caused by the enzyme but also decreasing the benefits of the enzyme in killing harmful microorganisms. Thus, excess glucocorticoids can reduce inflammation in a patient with tuberculosis while reducing the effects of PLA_2 against the bacteria resulting in spread of the illness. Lithium at pharmacological doses, carbamazepine, and the antimalarial drug chloroquine are all PLA_2 inhibitors. Vitamin E is also an inhibitor of PLA_2. In addition, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) (belonging to the omega-3 class of fatty acids) inhibit PLA_2.

Cytidine 5-diphospho-choline (CDP-choline), a precursor in the formation of phospholipids, is a potent inhibitor of PLA_2 that has been used as a nutritional supplement at doses ranging from 500-4000 mg per day in the treatment of patients with a variety of disorders including Parkinson's disease, memory disorders, vascular cognitive impairment, vascular dementia, senile dementia, schizophrenia, Alzheimer's disease (especially effective in those with the epsilon-4 apolipoprotein E genotype), head trauma, and ischemic stroke. A trial in patients with Alzheimer's disease indicated that citicoline (1,000 mg/day) is well tolerated and improves cognitive performance, cerebral blood perfusion, and the brain bioelectrical activity pattern. No side effects were noticed at the lower doses of CDP-choline and only some mild gastrointestinal symptoms were found using higher doses. No abnormal blood chemistry or hematology values were found after the use of CDP-choline.

Testing for PLA_2

Because PLA_2 is a relatively small enzyme (about 14 KD), it is able to be excreted in urine. 10 mL of the first morning urine before food or drink is suggested for testing. There are no dietary restrictions. This test is convenient to include with other urine tests such as organic acids, amino acids, and peptides. Since chelating agents might interfere with the test, they should not be used for at least 48 hours prior to testing.

Easy to Understand Results

A free phone consultation with our nutritional consultant is available to practitioners and patients with physician approval.

References

For a list of accessed references please visit:
www.http://www.greatplainslaboratory.com/home/eng/pla2.asp.com

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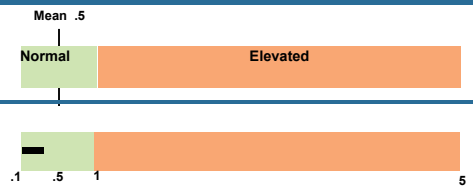
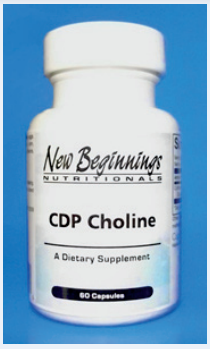
Requisition #:	800348	*Physician Name:*	
Patient Name:		*Date of Collection:*	12/30/1899
Patient Age:	43	*Time of Collection:*	Not Given
Sex:	M	*Print Date:*	2/2/2015

Phospholipase A2

Test	Patient Value PLA2 Activity / Creatinine
Phospholipase A2	0.345



CDP Choline from New Beginnings Nutritionals



www.NBNUS.com

Cytidine Diphosphate Choline (CDP Choline) is an active lipotrope of choline that restores brain levels of Phosphatidylserine, Phosphatidylcholine and Sphingomyelin which are crucial to the function of neurons and the myelin sheath that protects them. It also increases brain levels of key neurotransmitters like acetylcholine (for memory), dopamine (for fine motor control and mood), and norepinephrine (for mental energy). CDP Choline has also been shown to inhibit the ability of Phospholipase A_2 (PLA_2) to promote inflammation in the body. With all of the above modulating activities, it isn't surprising that CDP Choline has so many beneficial effects on the brain and body, helping to maintain optimal function and balance.

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