SydPath
ST VINCENT'S PATHOLOGY

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LIPOPROTEIN (a) INFORMATION SHEET

SUMMARY

Lipoprotein (a), which is expressed verbally as "lipoprotein little a" and abbreviated as Lp(a), is an LDL-like particle found in the circulation of all individuals. Like all lipoproteins it is made up of cholesterol, triglycerides, protein and phospholipids. The size and composition of this particle are very similar to LDL with the exception that it contains an additional protein which is known as apolipoprotein (a) ("apolipoprotein little a", abbreviated Apo(a)). The levels of Lp(a) in the circulation are largely genetically determined and higher levels are associated with an increased risk of cardiovascular disease.

STRUCTURE

Lipoprotein (a) consists of a Low Density Lipoprotein (LDL) particle with a single molecule of the protein Apo (a) linked covalently to the apolipoprotein B-100 (Apo B) molecule which is the only protein found in LDL. The Apo(a) molecule itself exists in a range of sizes due to variability in the number of repeats of the "kringle" sequences, so named because of a similarity with a Danish cake of the same name. The number of kringles, and therefore the molecular weight of the Apo(a) is determined genetically. The size of the protein is between 400 and 700 kilodaltons with over 40 different isoforms detected.

PHYSIOLOGY

Lp(a) is made directly by the liver without using VLDL as a precursor. The physiological roles of Lp(a) are unknown although possibilities include lipid transport and involvement in the coagulation process. The latter possibility is supported by homology between Apo(a) and plasminogen. The concentration of Lp(a) is inversely related to the size of the Apo(a) molecule and is highly genetically determined with about 90% of the inter-individual variation being under genetic control.

CIRCULATING CONCENTRATIONS

Lp(a) is distributed in the population in a skewed manner, meaning that the spread of values cannot be described by a mean and standard deviation. Levels may vary between <1 and >1000 mg/L. Reference intervals are usually expressed as less than the 80th percentile of values from the population as concentrations above this level are associated with increased risk of cardiovascular disease.

Levels rise during early childhood reaching a plateau throughout adult life. Further rises may be seen in post-menopausal women. Apo(a) is an acute phase reactant and therefore may rise after such events as surgery, myocardial infarction, stroke or other cause of tissue damage. The measurement should therefore be left for at least one month after these events. Apo(a) may also fall with hyperthyroidism and return to usual values with appropriate treatment. Increased circulating levels are seen in chronic renal failure and in transplant patients receiving cyclosporin as an anti-rejection medication.

PATHOLOGY AND CLINICAL USE

The relative risk of myocardial infarction is reported to be 1.75 time higher for individuals with Apo(a) values greater than 300 mg/L compared to those with Apo(a) below this figure. Alternatively patients with vascular disease on average have an Lp(a) level 1.4 times that of healthy controls. Higher re-stenosis rates after coronary bypass rates are also associated with higher levels of Apo(a). The mechanism for the atherogenic effects of Apo(a) are unknown but may include direct effects on the vessel wall or interference with coagulation or fibrinolysis.

Although there is a statistical association between Apo(a) concentrations and risk of cardiovascular disease, the association is insufficient to be useful for screening purposes. Testing should be restricted to those with a family history of ischaemic heart disease or with existing disease. In response to elevated levels of Lp(a), more aggressive reduction in LDL cholesterol levels may be indicated than would otherwise be recommended. The level of Apo (a) in the blood is resistant to most common lipid-lowering therapeutic measures including diet, weight-loss and statin therapy. Some response has been seen with nicotinic acid and hormone replacement therapy but the role of these interventions on the basis of Lp(a) levels is currently uncertain.

TESTING

Requests for Apo(a) measurement at SydPath are referred to the laboratories at ICPMR, Westmead hospital. As with all lipid testing, collection after an overnight fast is recommended. No special preparations are required.

REFERENCES

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