



Cardiovascular Profiles

PRACTITIONER MANUAL

NutriPATH Pty. Ltd.

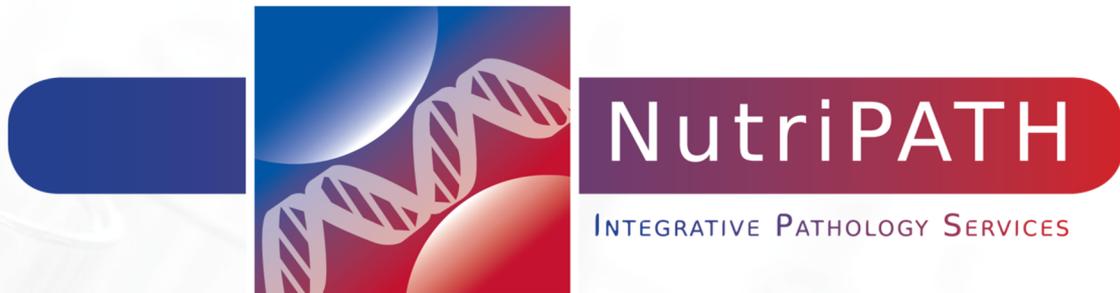
18a Harker Street, Burwood, VIC, 3125, Australia

Phone: 1300 688 522 (Australia)

+61 3 9880 2900 (International)

Fax: +61 3 9880 2999

Web: www.nutripath.com.au



v. 1.1

Contents

CARDIOVASCULAR DISEASE	5
Conventional Risk Factors for CVD	5
PREDICTING RISK WITH COMPREHENSIVE CARDIOVASCULAR PROFILES.....	6
Apolipoprotein A & Apolipoprotein B.....	6
Lipoprotein(a).....	7
Homocysteine.....	7
Fibrinogen.....	8
C-Reactive Protein (CRP).....	9
LDL Subfractions.....	10
Oxidised LDL cholesterol.....	10
LIPOSCREEN LDL-SUBFRACTIONS TEST	11
Benefits of the Liposcreen Profile.....	11
Clinical benefit.....	11
Indications.....	12
Clinical Indications.....	12
CARDIOVASCULAR DISEASES	13
Atherosclerosis.....	13
Risk factors.....	14
Prevention.....	15
Treatment.....	15
Statins.....	15
Diet.....	15
Coronary Heart Disease.....	16
Carotid Artery Disease.....	16
Peripheral Arterial Disease.....	16
Chronic Kidney Disease.....	16
OVERVIEW OF LIPID METABOLISM.....	17
Lipid Metabolism Disorders.....	18
Gaucher's Disease.....	18
Tay-Sachs Disease.....	18

Niemann-Pick Disease	18
Fabry's Disease	18
Fatty Acid Oxidation Disorders	19
MCAD Deficiency	19
Wolman's Disease	19
Refsum's Disease	19
NUTRIPATH CARDIOVASCULAR PROFILES	20
Analytes	20
Test Preparation	20
Specimen Collection Requirements.....	20
Result Turnaround Time.....	20
How to Order a Cardiovascular Profile Test Kit.....	20

CARDIOVASCULAR DISEASE

Cardiovascular disease (CVD) is one of the leading causes of death worldwide and accounts for 40% of all deaths in Australia. More years of potential life before the age of 75 are lost due to this disease than any other human condition. Fortunately, over the past thirty years significant progress has been made in the areas of diagnosis, prevention and treatment of CVD. One of the most critical advances has been the identification of the major risk factors for CVD, which arose from studies such as the Framingham Heart Study and the Seven Countries Study.

Conventional Risk Factors for CVD

The conventional risk factors for CVD include hypertension, smoking, diabetes mellitus, hypercholesterolaemia, hypertriglyceridaemia and low HDL cholesterol. However in a given individual the presence of only one of these factors has a low positive predictive value. Furthermore, a significant number of cardiovascular events still occur in individuals without these established risk indicators. At present the most advanced strategy for coronary risk assessment is therefore to combine the information of several risk factors. This 'multi-marker' approach can enhance risk stratification, identifying those individuals with a moderate baseline risk who might benefit from aggressive risk reduction strategies.

“High cholesterol is among the risk factors for heart disease, but is not the leading risk factor. The most prevalent risk factor is low HDL, along with small LDL particles. In fact, of every 100 people with coronary heart disease, 60-70% will have low HDL and small LDL particles, but fewer than 30% will have high LDL.” (Love Your Cholesterol. Dr Robert Buist, PhD. Integrative Therapies Pty Ltd, 2014)

http://www.amazon.com/Love-Your-Cholesterol-Robert-Buist/dp/0992525209/ref=sr_1_1?s=books&ie=UTF8&qid=1407201387&sr=1-1

See also The Cholesterol Myth: The New Healthy Heart Programme (1992), Dr Robert Buist.

PREDICTING RISK WITH COMPREHENSIVE CARDIOVASCULAR PROFILES

NutriPATH provides the most comprehensive cardiovascular profile available, reporting conventional risk factors and other state of the art CVD biomarkers such as lipoprotein (a), apolipoproteins A & B, homocysteine, fibrinogen and C-reactive protein (CRP). The **COMPREHENSIVE CARDIOVASCULAR PROFILE** also calculates a 5 year CVD risk, which illustrates the clinical relevance of the blood tests. Furthermore, the positive impact of potential treatment on the 5 year CVD risk is calculated; a powerful tool that practitioners can use to motivate their patients to action.

Apolipoprotein A & Apolipoprotein B

Lipoproteins are particles that transport lipids such as triglycerides and cholesterol esters through the plasma. Several types of these lipoproteins have been identified in plasma and are usually classified according to their hydrated density. The most common lipoproteins include high-density lipoprotein (HDL), low-density lipoprotein (LDL), intermediate-density lipoprotein, very-low-density lipoprotein (VLDL) 1 and 2, and chylomicrons. VLDL is secreted from the liver and is the precursor of LDL.

Apolipoproteins are the protein components of plasma lipoproteins. Apolipoprotein B-100 (apoB) is the chief protein constituent of the atherogenic very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL) and LDL particles. As there is only one apoB molecule on each lipoprotein particle, it can be used to estimate the total number of atherogenic particles (i.e. LDL, IDL, VLDL) present in plasma. In this aspect, apoB measurements are superior to standard LDL measurements, since the cholesterol content on the LDL and VLDL particles can vary considerably. In contrast, apolipoprotein A1 (apoA1) is the major apolipoprotein constituent of the anti-atherogenic high-density lipoproteins (HDL). Levels of apoA1 are strongly associated with those of HDL cholesterol. ApoA1 is critically involved in removing excess cholesterol from tissues and incorporating it into HDL for reverse transport, either directly or indirectly via LDL to the liver.

Epidemiological, observational and interventional studies of apoB and apoA1 in coronary heart disease (CHD), suggest that these markers are better predictors of cardiovascular risk than conventionally measured lipids. A recent meta-analysis of 23 prospective studies has shown a moderately strong association between baseline levels of each of apoA1 and apoB, and the risk of CHD. Furthermore, the ratio of the two apolipoproteins, apoB/apoA1, which determines the balance of the atherogenic (LDL, IDL, VLDL) versus the anti-atherogenic (HDL) particles, also correlated with disease. This simple ratio is an accurate index of CVD risk and evidence suggests that it is better than the conventional lipids as a risk marker and target for therapy.

Lipoprotein(a)

Lipoprotein(a) (Lp(a)) is another independent risk factor for vascular disease. Lp(a) has many properties in common with low-density lipoprotein (LDL) but contains a unique protein, apolipoprotein(a) (apo(a)), which is structurally different from other apolipoproteins. In numerous studies, mainly in white populations, increased plasma Lp(a) levels have been significantly correlated with future CHD. Furthermore, three meta-analyses have demonstrated an association of Lp(a) levels with cardiovascular disease in both retrospective and prospective studies. A meta-analysis of 5,436 subjects with CHD from 27 prospective studies concluded that individuals in the upper third of Lp(a) measurements were 70% more likely to develop CHD than those individuals in the bottom third. Although Lp(a) levels are only weakly correlated with known risk factors, there is evidence that the risk of developing CHD from an elevated Lp(a) level is exacerbated in the presence of other lipid risk factors such as high LDL cholesterol or low HDL cholesterol levels.

To date, the only major influence on Lp(a) levels is a size polymorphism in the apo(a) gene. Studies have shown Lp(a) levels to be hugely variable and under strict genetic control, largely by the (apo(a) gene. The protein molecular weight of apo(a) ranges from 300 to 800 kDa and impacts on the Lp(a) levels; there is a general inverse relationship. The smaller apo(a) sizes tend to correspond to higher Lp(a) levels. Differences in Lp(a) levels exist between populations, suggesting ethnic differences in the control of Lp(a) levels. For example, African populations have higher levels than Caucasians.

Apo(a) is a homologue of plasminogen. Because of this similarity, research into the effect of Lp(a) on fibrinolysis has been initiated. It is hypothesised that elevated levels of Lp(a) could interfere with plasminogen action and promote thrombosis. Indeed studies support these claims, with Lp(a) inhibiting plasminogen activity, increasing the plasminogen activator inhibitor-1 (PAI-1) and increasing platelet aggregation. Research also suggests that Lp(a) may promote atherosclerosis through its ability to increase the permeability of the endothelial cell layer, the expression of vascular adhesion molecules, foam cell formation and smooth muscle cell proliferation.

Homocysteine

Homocysteine, a sulphur-containing amino acid, is an intermediate product in the normal biosynthesis of the amino acids methionine and cysteine. Homocysteine is predominantly metabolised via two pathways. The enzyme methylenetetrahydrofolate reductase (MTHFR) converts homocysteine to methionine. The MTHFR is strongly dependent on the cofactors folate and vitamin B12. Homocysteine can also be converted to cysteine by cystathionine synthase (CS); an enzyme with pyridoxal-5-phosphate (P5P) as an essential cofactor. When a deficiency of these cofactors occurs, the activities of MTHFR and CS are decreased and homocysteine levels elevate.

The interest in mild hyperhomocysteinaemia as an important risk factor for cardiovascular disease was originally based on the observation that a rare inborn metabolic error, homocystinuria, leads to severe hyperhomocysteinaemia, atherosclerosis, and arterial or venous thromboembolic events by 30 years of age. It was then hypothesised that mild to moderate elevations of homocysteine in the general population would increase the risk of atherosclerosis in a manner similar to other classical risk factors. The evidence for this supposition has increased over the last 30 years, with hyperhomocysteinuria being shown to increase the risk of CVD mortality, coronary artery disease, chronic heart failure, cerebrovascular and peripheral vascular disease. Elevated levels of homocysteine have also been shown to be associated with stroke, cognitive deficit, Alzheimer's disease, bone fracture, osteoporosis and depression.

Whether homocysteine causes CVD or is only a marker for the condition is still under debate. Evidence for its involvement includes its prothrombotic properties, its proliferative effect on smooth muscle cells and its pro-oxidant activity. In addition, homocysteine can increase coagulability, cause endothelial dysfunction, induce the production of inflammatory factors and accelerate atherosclerosis in animal models.

Fibrinogen

Fibrinogen is a circulating glycoprotein that acts at the final step in the coagulation response to vascular and tissue injury. Cleavage by thrombin produces soluble fibrin fragments, which are the most abundant component of blood clots. In addition, fibrin is an acute-phase reactant, a platelet activator, a determinant of blood viscosity and a component of the atherosclerotic plaque.

Numerous epidemiological studies have established that fibrinogen is a strong, consistent, and independent cardiovascular risk marker. This has been confirmed in a recent individual participant meta-analysis which included 154,211 participants and 1.38 million person-years of follow-up, from 31 prospective studies. There was a log-linear association with fibrinogen for the risk of non-fatal or fatal coronary heart disease, nonfatal or fatal stroke, other vascular mortality, and total mortality. Other studies show that the concentration of plasma fibrinogen is positively correlated with the severity of the underlying coronary heart disease. Plasma fibrinogen levels are higher in patients with severe vasospastic angina or unstable than in patients with mild vasospastic or stable angina. It appears that fibrinogen concentration is at least as predictive of coronary events as are cholesterol concentration, diastolic blood pressure and body mass index.

It has also been demonstrated that extravascular fibrinogen that is deposited in tissues upon vascular rupture is not merely a marker, but a mediator of diseases with an inflammatory component. In addition to CVD, fibrinogen may play a role in rheumatoid arthritis, multiple sclerosis, sepsis and bacterial infection.

C-Reactive Protein (CRP)

C-reactive protein (CRP) is one of the most abundant acute phase proteins in humans. Its increased production by the liver is triggered by pro-inflammatory cytokines as a result of either trauma or infection. CRP is a biomarker of systemic inflammation, a process that is now widely accepted as central to every aspect of atherosclerotic development, from its initiation to its progression to plaque rupture.

Mendall *et al.* first showed that an increase of CRP was associated with coronary heart disease in 1996. Since then elevated levels of CRP have been confirmed to increase the risk of cardiovascular disease, myocardial infarction, and coronary artery disease deaths among individuals with angina pectoris; increase ischemic stroke for those with hypertension or peripheral artery disease; as well as predict future risk for age-related cataract, stroke, myocardial infarction, and peripheral artery disease. An elevated CRP level before percutaneous coronary intervention (angioplasty) also signifies a worse prognosis, as it does among patients undergoing coronary artery bypass grafting.

One of the most compelling studies on CRP has come from the Women's Health Study. Of the 12 markers investigated, high sensitivity-CRP was the strongest predictor of myocardial infarction, surgical re-vascularisation, or death from heart disease. Women who were in the highest quartile for this marker, as compared with the lowest quartile, were 4.4 times more likely to experience a cardiovascular event. Even in women with low cholesterol, hs-CRP still had a predictive effect, with women being 4.1 times more likely to experience an event if they were in the highest quartile of hs-CRP levels. It was suggested that the measurement of CRP in addition to standard lipid tests would provide an improved method of identifying persons at risk for cardiovascular events.

Some investigators hypothesise that CRP plays a direct role in promoting vascular inflammation, vessel damage, and clinical CVD events, although this remains controversial. Histological staining of atherosclerotic lesions consistently places CRP within the lesion, where it may promote low-density lipoprotein (LDL) cholesterol uptake by macrophages, a key step in atherogenesis. CRP also induces the expression of adhesion molecules, modulates critical regulators of arterial vasodilatation, increases reactive oxygen species and initiates coagulation reactions.

In comparison to the moderate increases of CRP found in CVD (>3 mg/l), much larger elevations are associated with infections, trauma and other inflammatory conditions. Conditions such as rheumatoid arthritis, inflammatory bowel disease and cancer show high levels of this systemic inflammatory biomarker.

LDL Subfractions

Not all lipoprotein subclasses have the same atherogenic potential.

- Large buoyant LDL-1 and 2 are associated with average CAD risk.
- Presence of small dense LDL-3 through 7 are associated with 3 times greater risk for CAD independent of other risk factors.
- IDL levels above the normal reference range are also associated with increased CAD risk.
- Levels of small VLDL remnants above the normal reference range are also associated with increased CAD risk.
- Levels of HDL cholesterol below 1.0mmol/L are the equivalent of an additional risk factor while levels above 1.5mmol/L are equivalent to a negative risk factor.
- Small dense LDLs are oxidised faster than the larger LDL.

Liposcreen separates and quantifies all lipoprotein subfractions including the large, less atherogenic LDL-1 and LDL-2 and the small, highly atherogenic LDL-3 to LDL-7. It measures the cholesterol level in mmol/L in every lipoprotein sub-fraction from VLDL to HDL; in all 14 parameters - total cholesterol, total LDL, HDL, VLDL, 3 IDL fractions, 7 LDL fractions. The test also measures VLDL and IDL cholesterol linked with type III dyslipidaemia and associated hyperlipoproteinaemias.

Oxidised LDL cholesterol

It is mainly the so-called oxidised LDL that forms deposits on the vascular walls. The oxidation of plasma lipoproteins, in particular of LDL cholesterol, induced by oxygen radicals constitutes the main factor of arteriosclerosis.

Oxidised LDL can no longer bind to the LDL-receptors and cannot be cleaved, resulting in distinct cytotoxic effects and an increased transformation from monocytes into macrophages that can fix oxidised LDL by means of a special receptor (scavenger receptor).

Since this receptor is not inhibited by a high intracellular cholesterol level like the normal LDL receptor, cholesterol accumulates in the macrophages which then transform into so-called foam cells. The foam cells again promote connective tissue depositions that result in the formation of atherosclerotic plaques.

The recruitment of T-cells as well as the proliferation of smooth muscle cells provoke an inflammatory process at the vascular wall. This oxidative stress results in premature damaging and increased endothelial permeability. The fibrous cap of the plaques rich in lipid is weakened by the inflammatory process: the risk of plaque rupture is increasing; thrombus can take place which eventually causes myocardial infarction.

The analytical determination of oxidised LDL provides information about the progress of endothelial damage and what kind of therapeutic measure needs to be taken.

LIPOSCREEN LDL-SUBFRACTIONS TEST

Liposcreen is an in-vitro diagnostic test for separating and measuring cholesterol in lipoprotein fractions and lipoprotein subfractions.

It is a new procedure that determines the actual heart attack risk by means of a differentiated analysis of HDL and LDL subfractions.

It can:

- Identify and differentiates all cholesterol particles quantitatively by their size for the first time.
- Differentiate the highly atherogenic, small, dense LDL and IDL from the large, less atherogenic LDL and VLDL and the protective HDL.
- Determine IDL fractions.

Benefits of the Liposcreen Profile

- Measures the amount of cholesterol in mmol/L in each lipoprotein fraction and sub-fraction from VLDL to HDL (14 parameters in total).
- Values outside the reference range flagged in red.
- Easy to interpret colour coded profile differentiates normal, Type A lipid profile from an abnormal, non-Type A profile.
- Identifies the highly atherogenic small dense LDL and IDL from the large, less atherogenic LDL and VLDL and the protective HDL.
- Clinical utility for screening, treatment decision and monitoring of lipid disorders associated with coronary artery disease (CAD) risk.

Clinical benefit

Clinical benefit for screening, treatment decisions and monitoring of lipid disorders associated with risks of coronary artery diseases:

- Conventional lipid tests do not convey the CAD risk associated with the small dense LDL or IDL subfractions, and therefore offers determination of the patient's true atherogenic risk.
- These risks could be present even when other lipid risk factor (total cholesterol, LDL and HDL cholesterol and triglycerides) are normal.
- Carefully targeted therapy.
- Reducing possibly counter-productive drugs.
- Therapy control: particularly important since sometimes, in case of administration of cholesterol-lowering drugs, the total cholesterol decreases, but the atherogenic LDL particles accumulate. In this case, a normal LDL control would suggest a therapy success.

Indications

The medical community recognises lipid testing as appropriate for evaluating atherosclerotic cardiovascular disease. Conditions in which lipid testing may be indicated include:

- Assessment of patients with atherosclerotic cardiovascular disease.
- Evaluation of primary dyslipidaemia.
- Any form of atherosclerotic disease, or any disease leading to the formation of atherosclerotic disease.
- Diagnostic evaluation of diseases associated with altered lipid metabolism, such as nephrotic syndrome, pancreatitis, hepatic disease, hypo and hyperthyroidism.
- Secondary dyslipidaemia, including diabetes mellitus, disorders of gastrointestinal absorption, chronic renal failure.
- Signs or symptoms of dyslipidaemias, such as skin lesions, as follow-up to the initial screen for coronary heart disease (total cholesterol + HDL cholesterol) when total cholesterol is determined to be high (>6.0 mmol/L) plus two or more coronary heart disease risk factors, or an HDL cholesterol < 0.9 mmol/L.

Clinical Indications

The LipoScreen test should be considered for anyone with two or more of the following risk factors.

Risk factors that cannot be changed:

- Increasing age - 84% of people who die of CHD are 65 or older.
- Gender - Men (45 years or older) have a greater risk of heart attack than women (55 years or older).
- Heredity (including race) - Family history of early heart disease (father or brother affected before age 55; mother or sister affected before age 65).

Risk factors that can be modified by lifestyle change or medications:

- Tobacco smoke - Smokers and non-smokers exposed to cigarette smoke are at increased risk of heart disease.
- High blood cholesterol and triglycerides
- Total blood cholesterol (> 5.5 mmol/L)
- High LDL cholesterol (> 3.5 mmol/L)
- Low HDL cholesterol (< 1.2 mmol/L)
- Triglycerides (> 2.0 mmol/L)
- Diet - less meat, more fish, vegetables and fruit.
- High blood pressure (BP > 140/90 mmHg)
- Physical inactivity - inactive lifestyle is a risk factor for CHD
- Obesity / overweight (BMI of > 25-29.9)
- Diabetes mellitus

CARDIOVASCULAR DISEASES

Atherosclerosis

Atherosclerosis is a specific form of arteriosclerosis in which an artery wall thickens as a result of invasion and accumulation of white blood cells (termed 'fatty streaks' early on because of appearance being similar to that of marbled steak) and containing both living active white blood cells (inflammation) and remnants of dead cells, including cholesterol and triglycerides, eventually calcium and other crystallised materials, within the outer-most and oldest plaque. These changes reduce the elasticity of the artery walls but do not affect blood flow for decades because the artery muscular wall enlarges at the locations of plaque. However, the wall stiffening may eventually increase pulse pressure; widened pulse pressure is one possible result of advanced disease within the major arteries. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response, i.e. white blood cells, in the walls of arteries, largely involving the accumulation of macrophages and white blood cells and promoted by low-density lipoproteins (LDL, plasma proteins that carry cholesterol and triglycerides) without adequate removal of fats and cholesterol from the macrophages by functional high-density lipoproteins (HDL). It is commonly referred to as a 'hardening' of the arteries. It is caused by the formation of multiple atheromatous plaques within the arteries.

The plaque is divided into three distinct components:

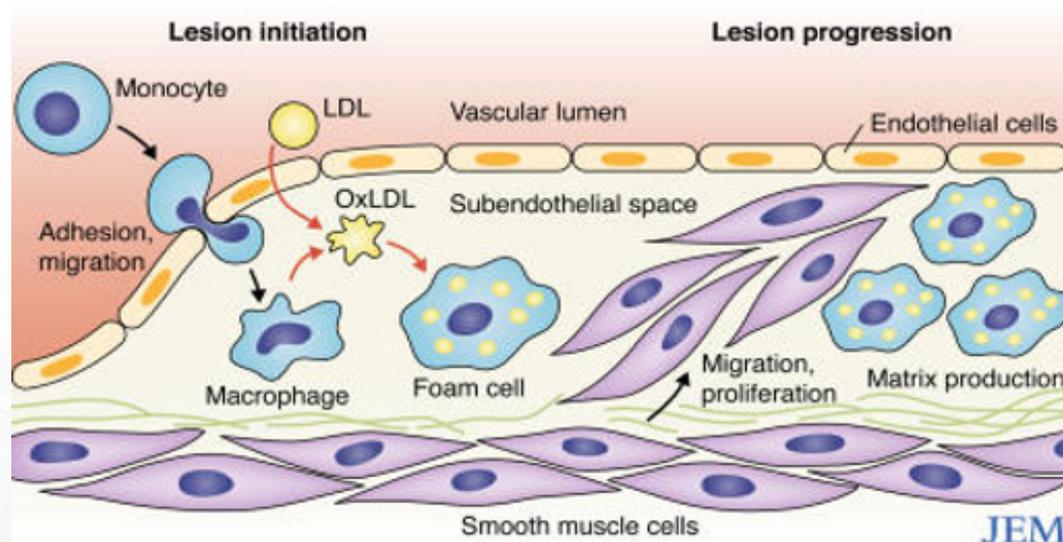
1. The atheroma which is the nodular accumulation of a soft, flaky, yellowish material at the centre of large plaques, composed of macrophages nearest the lumen of the artery.
2. Underlying areas of cholesterol crystals.
3. Calcification at the outer base of older or more advanced lesions.

Atherosclerosis is a chronic disease that remains asymptomatic for decades. Atherosclerotic lesions, or atherosclerotic plaques, are separated into two broad categories: Stable and unstable (also called vulnerable). Atherosclerosis is initiated by inflammatory processes in the endothelial cells of the vessel wall in response to retained low-density lipoprotein (LDL) particles.

Lipoproteins in the blood vary in size. Some data suggests that small dense LDL (sdLDL) particles are more prone to pass between the endothelial cells, going behind the cellular monolayer of endothelium. LDL particles and their content are susceptible to oxidation by free radicals and the risk is higher while the particles are in the wall than while in the bloodstream. However, LDL particles have a half-life of only a couple of days, and their content (LDL particles typically carry 3,000 to 6,000 fat molecules, including: cholesterol, phospholipids, cholesteryl esters, triglycerides and all other fats in the water outside cells, to the tissues of the body) changes with time.



Once inside the vessel wall, LDL particles can become more prone to oxidation. Endothelial cells respond by attracting monocyte white blood cells, causing them to leave the blood stream, penetrate into the arterial walls and transform into macrophages. The macrophages' ingestion of oxidised LDL particles triggers a cascade of immune responses which over time can produce an atheroma if HDL removal of fats from the macrophages does not keep up. The immune system's specialised white blood cells (macrophages and T-lymphocytes) absorb the oxidised LDL, forming specialised foam cells. If these foam cells are not able to process the oxidised LDL and recruit HDL particles to remove the fats, they grow and eventually rupture, leaving behind cellular membrane remnants, oxidised materials, and fats (including cholesterol) in the artery wall. This attracts more white blood cells, resulting in a snowballing progression that continues the cycle, inflaming the artery. The presence of the plaque induces the muscle cells of the blood vessel to stretch, compensating for the additional bulk, and the endothelial lining thickens, increasing the separation between the plaque and lumen. This somewhat offsets the narrowing caused by the growth of the plaque, but it causes the wall to stiffen and become less compliant to stretching with each heart beat.



Risk factors

- Diabetes;
- High serum concentration of low density lipoprotein (LDL, bad if elevated concentrations and small) and /or very low density lipoprotein (VLDL) particles. Refer to lipoprotein subclass analysis;
- Low serum concentration of functioning high density lipoprotein (HDL, protective if large and high enough particles);
- Elevated serum C-reactive protein concentrations;
- Vitamin B6 deficiency;
- Dietary iodine deficiency and hypothyroidism which can cause elevated serum cholesterol and lipid peroxidation.

Prevention

Medical management of atherosclerosis involves modification to risk factors like smoking cessation and diet restrictions. Additionally, a controlled exercise program combats atherosclerosis by improving circulation and functionality of the vessels. Exercise is also used to manage weight in patients who are either obese, lower blood pressure, and decrease cholesterol. Often lifestyle modification is combined with medication therapy. For example, statins help to lower cholesterol, antiplatelet medications like aspirin help to prevent clots, and a variety of antihypertensive medications are routinely used to control blood pressure. If the combined efforts of risk factor modification and medication therapy are not sufficient to control symptoms, or fight imminent threats of ischemic events, a physician may resort to interventional or surgical procedures to correct the obstruction.

Combinations of statins, niacin, intestinal cholesterol absorption-inhibiting supplements have been the most successful in changing common but sub-optimal lipoprotein patterns and group outcomes. In the many secondary prevention and several primary prevention trials, several classes of lipoprotein-expression-altering (less correctly termed 'cholesterol-lowering') agents have consistently reduced not only heart attack, stroke and hospitalization but also all-cause mortality rates.

Treatment

Medical treatments often focus on alleviating symptoms. However measures which focus on decreasing underlying atherosclerosis—as opposed to simply treating symptoms—are more effective. Non-pharmaceutical means are usually the first method of treatment, such as stopping smoking and practicing regular exercise. If these methods do not work, medicines are usually the next step in treating cardiovascular diseases, and, with improvements, have increasingly become the most effective method over the long term.

The key to the more effective approaches has been better understanding of the widespread and insidious nature of the disease and to combine multiple different treatment strategies, not rely on just one or a few approaches. In addition, for those approaches, such as lipoprotein transport behaviors, which have been shown to produce the most success, adopting more aggressive combination treatment strategies taken on a daily basis and indefinitely has generally produced better results, both before and especially after people are symptomatic.

Statins

The group of medications referred to as statins are widely prescribed for treating atherosclerosis. They shown benefit in reducing cardiovascular disease and mortality in those with high cholesterol with few side effects.

Diet

Changes in diet may help prevent the development of atherosclerosis.

RELATED DISEASES

Atherosclerosis can affect any artery in the body, including arteries in the heart, brain, arms, legs, pelvis, and kidneys. As a result, different diseases may develop based on which arteries are affected.

Coronary Heart Disease

Coronary heart disease (CHD), also called coronary artery disease, is the number one killer of both men and women in the Australia. CHD occurs if plaque builds up in the coronary arteries. These arteries supply oxygen-rich blood to the heart. Plaque narrows the coronary arteries and reduces blood flow to the heart muscle. Plaque buildup also makes it more likely that blood clots will form in arteries. Blood clots can partially or completely block blood flow. If blood flow to the heart muscle is reduced or blocked, this may result in angina (chest pain or discomfort) or a heart attack. Plaque also can form in the heart's smallest arteries - coronary microvascular disease (MVD). In coronary MVD, plaque doesn't cause blockages in the arteries as it does in CHD.

Carotid Artery Disease

Carotid artery disease occurs if plaque builds up in the arteries on each side of the neck in the carotid arteries. As these arteries supply oxygen-rich blood to the brain, if blood flow is reduced or blocked, a stroke or TIA may occur.

Peripheral Arterial Disease

Peripheral arterial disease (PAD) occurs if plaque builds up in the major arteries that supply oxygen-rich blood to the legs, arms and pelvis. If blood flow to these parts of the body is reduced or blocked, numbness, pain, and, sometimes, dangerous infections may occur.

Chronic Kidney Disease

Chronic kidney disease can occur if plaque builds up in the renal arteries. These arteries supply oxygen-rich blood to the kidneys and over time, chronic kidney disease causes a slow loss of kidney function.

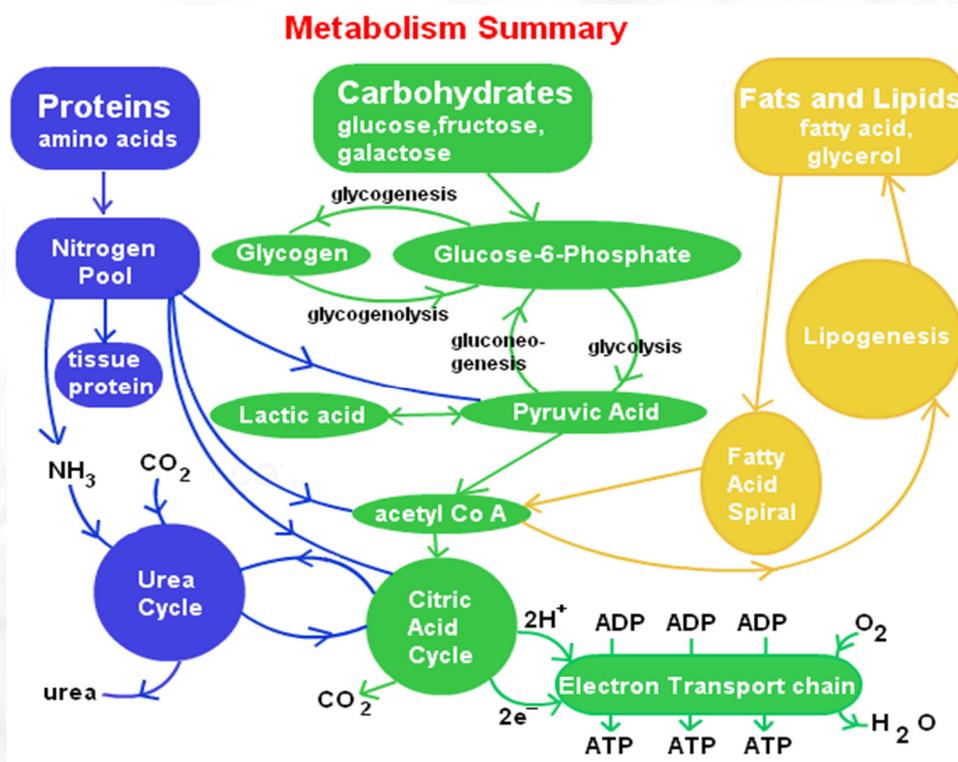
OVERVIEW OF LIPID METABOLISM

The major aspects of lipid metabolism are involved with fatty acid oxidation to produce energy or the synthesis of lipids which is called lipogenesis. Lipid metabolism is closely connected to the metabolism of carbohydrates which may be converted to fats. This can be seen in the diagram on the below. The metabolism of both is upset by diabetes mellitus.

The first step in lipid metabolism is the hydrolysis of the lipid in the cytoplasm to produce glycerol and fatty acids. Since glycerol is a three carbon alcohol, it is metabolised quite readily into an intermediate in glycolysis, dihydroxyacetone phosphate. The last reaction is readily reversible if glycerol is needed for the synthesis of a lipid.

The hydroxyacetone, obtained from glycerol is metabolised into one of two possible compounds. Dihydroxyacetone may be converted into pyruvic acid through the glycolysis pathway. In addition, the dihydroxyacetone may also be used in gluconeogenesis to make glucose-6-phosphate for glucose to the blood or glycogen depending upon what is required at that time.

Fatty acids are oxidised to acetyl CoA in the mitochondria using the fatty acid spiral. The acetyl CoA is then ultimately converted into ATP, CO₂ and H₂O using the citric acid cycle and the electron transport chain. Fatty acids are synthesised from carbohydrates and occasionally from proteins. The carbohydrates and proteins have first been catabolised into acetyl CoA. Depending upon the energy requirements, the acetyl CoA enters the citric acid cycle or is used to synthesise fatty acids in a process known as lipogenesis.



Lipid Metabolism Disorders

Fats (lipids) are an important source of energy for the body. The body's store of fat is constantly broken down and reassembled to balance the body's energy needs with the food available. Groups of specific enzymes help the body break down and process fats. Certain abnormalities in these enzymes can lead to the buildup of specific fatty substances that normally would have been broken down by the enzymes. Over time, accumulations of these substances can be harmful to many organs of the body. Disorders caused by the accumulation of lipids are called lipidoses. Other enzyme abnormalities prevent the body from converting fats into energy normally. These abnormalities are called fatty acid oxidation disorders.

Gaucher's Disease

Gaucher's disease is caused by a buildup of glucocerebrosides in tissues. Children who have the infantile form usually die within a year, but children and adults who develop the disease later in life may survive for many years. In Gaucher's disease, glucocerebrosides, which are a product of fat metabolism, accumulate in tissues. Gaucher's disease is the most common lipidosis. Gaucher's disease leads to an enlarged liver and spleen and a brownish pigmentation of the skin. Many people with Gaucher's disease can be treated with enzyme replacement therapy, in which enzymes are given by vein, usually every 2 weeks. Enzyme replacement therapy is most effective for people who do not have nervous system complications.

Tay-Sachs Disease

Tay-Sachs disease is caused by a buildup of gangliosides in the tissues. This disease results in early death. In Tay-Sachs disease, gangliosides, which are products of fat metabolism, accumulate in tissues. The disease is most common among families of Eastern European Jewish origin. At a very early age, children with this disease become progressively intellectually disabled and appear to have floppy muscle tone. Spasticity develops and is followed by paralysis, dementia, and blindness. The disease cannot be treated or cured.

Niemann-Pick Disease

Niemann-Pick disease is caused by a buildup of sphingomyelin or cholesterol in the tissues. This disease causes many neurologic problems. In Niemann-Pick disease, the deficiency of a specific enzyme results in the accumulation of sphingomyelin (a product of fat metabolism) or cholesterol. Niemann-Pick disease has several forms, depending on the severity of the enzyme deficiency, which determines how much sphingomyelin or cholesterol accumulates. In the most severe form (type A), children fail to grow normally and have several neurologic problems. These children usually die by age 3. Children with type B disease develop fatty growths in the skin, areas of dark pigmentation, and an enlarged liver, spleen, and lymph nodes. They may be intellectually disabled. Children with type C disease develop symptoms during childhood, with seizures and neurologic deterioration. Some forms of Niemann-Pick disease can be diagnosed in the fetus by chorionic villus sampling or amniocentesis.

Fabry's Disease

Fabry's disease is caused by a buildup of glycolipid in tissues. This disease causes skin growths, pain in the extremities, poor vision, recurrent episodes of fever and kidney or heart failure. In Fabry's disease, glycolipid, which is a product of fat metabolism, accumulates in tissues. The accumulation of glycolipid causes noncancerous (benign) skin growths (angiokeratomas) to form on the lower part of the trunk. The corneas become cloudy, resulting in poor vision. A burning pain may develop in the arms and legs, and children may have episodes of fever. Children with Fabry's disease eventually develop kidney failure and heart disease. Fabry's disease can be diagnosed in the fetus by chorionic villus sampling or amniocentesis. The disease cannot be cured or even treated directly, but researchers are investigating a treatment in which the deficient enzyme is replaced by transfusion. Treatment consists of taking analgesics to help relieve pain and fever or anticonvulsants.

Fatty Acid Oxidation Disorders

Fatty acid oxidation disorders are caused by a lack or deficiency of the enzymes needed to break down fats, resulting in delayed mental and physical development. Several enzymes help break down fats so that they may be turned into energy. An inherited defect or deficiency of one of these enzymes leaves the body short of energy and allows breakdown products, such as acyl-CoA, to accumulate. The enzyme most commonly deficient is medium chain acyl-CoA dehydrogenase (MCAD). Other enzyme deficiencies include short chain acyl-CoA-dehydrogenase deficiency (SCAD), long chain-3-hydroxyacyl-CoA-deficiency (LCHAD), and trifunctional protein deficiency (TFP).

MCAD Deficiency

This is one of the most common inherited disorders of metabolism, particularly among people of Northern European descent. Children are most likely to develop symptoms if they go without food for a period of time (which depletes other sources of energy) or have an increased need for calories because of exercise or illness. The level of sugar in the blood drops significantly, causing confusion or coma. Children become weak and may have vomiting or seizures. Over the long term, children have delayed mental and physical development, an enlarged liver, heart muscle weakness and an irregular heartbeat.

Wolman's Disease

Wolman's disease results when specific types of cholesterol and glycerides accumulate in tissues. This disease causes enlargement of the spleen and liver. Calcium deposits in the adrenal glands cause them to harden and fatty diarrhea also occurs.

Refsum's Disease

In Refsum's disease, phytanic acid, which is a product of fat metabolism, accumulates in tissues. A buildup of phytanic acid leads to nerve and retinal damage, spastic movements, and changes in the bone and skin. Treatment involves avoiding eating green fruits and vegetables that contain chlorophyll.

NUTRIPATH CARDIOVASCULAR PROFILES

Analytes

CARDIOVASCULAR PROFILE – COMPREHENSIVE [4001]

Cholesterol, Triglycerides, HDL, LDL, ratios, Fasting Glucose, Homocysteine, Apolipoproteins A & B, Lipoprotein (a), Fibrinogen, CRP

CARDIOVASCULAR PROFILE – COMPREHENSIVE 2 [4027]

Cholesterol, Triglycerides, HDL, LDL, ratios, Fasting Glucose, Homocysteine, Apolipoproteins A & B, Lipoprotein (a), Fibrinogen, CRP and LIPOSCREEN LDL-subfractions (x7)

LIPOSCREEN LDL-SUBFRACTIONS [4028]

Cholesterol, Triglycerides, HDL, LDL, VLDL, IDL, LDL-subfractions (x7)

OXIDISED LDLs [4029]- oxidised LDLs

Test Preparation

- This is a fasting test. Patient is not to eat any food 12 hours prior to the blood draw (i.e. fasting). Patient may consume water. Recommend patient takes morning medications after the blood draw if possible.
- Samples must be collected **Monday to Thursday** only.
- Be aware that this is a time sensitive test which needs to be processed efficiently.
- Your healthcare provider will tell you whether or not to discontinue any drugs or activities that may interfere with the test.

Specimen Collection Requirements

Blood samples collected in 1x Sodium Citrate, 1x EDTA, 1x Fluoride Oxalate and 1x SST Vacutainer tubes. All tubes must be sent by overnight express to NutriPATH.

Result Turnaround Time

One week after receipt of sample and test fee payment at NutriPATH.

How to order a Cardiovascular Profile Test Kit

Either order a test kit online (www.nutripath.com.au) or phone Customer Services on 1300 688 522. Please note these tests are not Medicare rebateable.