Metabolic Syndrome:

The metabolic syndrome comprises a clustering of cardiovascular risk factors including abdominal obesity, insulin resistance, elevated triglycerides, low HDL-C and hypertension. The presence of metabolic syndrome increases cardiovascular risk by 1.6-2.6 fold. The greater risk occurs in patients with type 2 diabetes mellitus or elevated hs-CRP. Criteria for metabolic syndrome include ≥ 3 of the following parameters:

- Abdominal obesity (waist circumference in males >102 cm or 40 inches or in females >88 cm or 34.6 inches).
- Triglycerides ≥ 1.7 mmol/L
- HDL <1 mmol/L in males or < 1. 3 mmol/L in females
- BP ≥ 130/85
- FBG 6.2-7 mmol/L

The prevalence of metabolic syndrome in North America is approximately 25% and this reflects the rising prevalence of obesity and inactivity. Metabolic syndrome is associated with production of a variety inflammatory proteins including CRP. The presence of metabolic syndrome is a strong predictor of new onset of diabetes. In addition metabolic syndrome is associated with the presence of more atherogenic small dense LDL particles and elevated apoliprotein B levels which reflects the total number of atherogenic lipid particles.

The battle against metabolic syndrome is intricately linked to the battle against obesity and diabetes and includes:

- Weight reduction ≥ 5% body weight.
- Regular physical activity≥ 30 minutes 5 times/week
- Targeted therapy of dyslipidemia to lower LDL, raise HDL, lower triglycerides and optimize TC/HDL (<4/1) and LDL/HDL (<3/1) ratios
- Tight BP control optimally including use of an ACE inhibitor
- Tight BS control to achieve euglycemia ASAP with oral hypoglycemic therapy and insulin sensitizers as per CDA Guidelines

Lipoprotein (a):

Lipoprotein (a) is a newly recognized risk factor for heart disease. Lipoprotein (a) is a type of LDL which is particularly atherogenic (causes cholesterol deposits in arteries) and also appear to increase the risk of blood clot formation in already narrowed arteries leading to heart attacks or strokes. Lipoprotein (a) is dependent on genetic factors and hence levels are often found to be elevated in families with a history of early heart disease. A normal lipoprotein (a) level is about 15 mg/dl. Heart disease risk increases with levels above 30 mg/dl. The only effective medication for ipoprotein (a) is Niacin, but the risk associated with lipoprotein (a) decreases if LDL cholesterol is lowered by diet or other medications. Lipoprotein (a) is measured in specialized laboratories.

Apolipoprotein B

Apolipoprotein B is a protein which associates with atherogenic lipid particles including VLDL, intermediate density lipoprotein, LDL and lipoprotein (a). Apolipoprotein B has been shown to be a better estimate of cardiovascular events than the LDL-C level and in conjunction with TG > 1.5 mmol/L, an apolipoprotein B of > 1.2 g/L imparts the highest risk and is associated with the

presence of smaller denser more atherogenic LDL particles. Measurement of apolipoprotein B is independent of TG levels and levels may be of value in assessing adequacy of statin therapy. Optimal level of apolipoprotein B in patients at high risk for cardiovascular events is < 0.9 g/L.

Homocyst(e)ine

Homocysteine is an amino acid in the blood. Amino acids are the building blocks of proteins. Build-up of homocysteine in the blood may be due to vitamin deficiencies or hereditary deficiencies of enzymes that normally break down homocysteine. An excess of homocysteine in the blood has been linked to premature vascular disease (hardening of the arteries) and early development of stroke, heart attack or peripheral vascular disease. There is as yet, no proof that treating homocysteine excess with vitamins know to work with certain enzymes to increase the breakdown of homocysteine, has any effect on clinical outcome. Nevertheless, in patients with premature atherosclerosis or in patients with no obvious risk factors who develop CAD, it is reasonable to test for homocysteine and to treat with appropriate doses of Vitamins B6, B 12 and folic acid (Folic acid 1-5 mg, B6 10-50 mg, B12 250-500 mcg). The target level for homocysteine is < 10 μmol/L.

CRP (C-reactive protein)

Atherosclerosis is an inflammatory disease. Inflammatory cells are active within the cholesterol plaque ingesting cholesterol to aide in its removal. CRP or C-reactive protein is a marker of vascular inflammation. CRP has been shown to be a strong predictor of future cardiovascular events. An increased CRP at admission has been shown to be a marker for worse short and long term prognosis in patients with unstable angina. In one recent trial CRP was superior to an elevated LDL as a predictor of primary cardiovascular events. CRP and LDL are independent, thus the use of both markers has been shown to be superior to the use of either marker alone. Almost 50% of cardiovascular events occur in patients with normal LDL levels. The measurement of CRP in these patients helps to identify those patients at greater risk. Low risk is defined as hs-CRP (high sensitivity-CRP) <1 mg/ml; average risk as hs-CRP 1.0 - 3.0 mg/L and high risk as hs-CRP 3.0-10 mg/L. If hs-CRP is >10 mg/L, the test should be repeated and patient examined for sources of infection or inflammation. Risk estimates based on hs-CRP levels are not affected by the use of HRT (hormone replacement therapy).

Unfortunately high sensitivity CRP (hs-CRP) assays are not yet widely available. When they are, CRP will become a useful test to predict cardiovascular risk, particularly in those patients with low LDL levels and the absence of other traditional cardiac risk factors.