LIPIDS & CARDIOVASCULAR DISEASE

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INTRODUCTION
Cardiovascular disease is the dominant single cause of premature mortality in Australia. In men and women dying before 70 years of age in 1993, 17.8% of deaths were due to coronary heart disease (CHD) and 4.1% of deaths to stroke. Cardiovascular mortality has fallen by around 60% since 1968, principally because of a decline in coronary deaths. The MONICA Study has demonstrated that this declining death rate is driven more by a falling incidence of disease than by a falling case fatality rate (Lancet 1999;353:1547-1557).

CLINICAL & PATHOLOGICAL PICTURE
Cardiovascular disease in its various manifestations (coronary disease, cerebrovascular disease, peripheral vascular disease, etc) has a long pre-symptomatic or incubation period, possibly 30-50 years in duration.   This indicates that "outwardly healthy" citizens might propose insurance, yet they will be at increased risk of a vascular event.

The underlying pathological process in CHD (and occlusive disease elsewhere) is atherosclerosis. This may give rise to a gradual obstruction of vessels and diminution in blood flow. Alternatively, a small coronary artery plaque, perhaps blocking only 30% of blood flow, may be unstable and fracture. This leads to coronary thrombosis which becomes a myocardial infarction (i.e. a heart attack).

RISK FACTORS
A number of risk factors have been identified. They are more properly called "causal factors". A short list of these factors might include: cholesterol and other lipid abnormalities, elevated blood pressure, cigarette smoking, diabetes, obesity, blood coagulation abnormalities, male gender, family history of premature CHD, increasing age. Three important points must be made:

1.   Risk factor knowledge can predict 50-80% of first coronary events (the proportion depends on the cutpoint used to define normal values).
2.   Not all subjects with risk factors will develop premature vascular disease.
3.   Some subjects with vascular disease will not manifest known risk factors.

The balance of this presentation is related to lipid factors in cardiovascular disease. Although there is some relationship of lipid abnormalities to ischaemic stroke, the comments that follow will be devoted mainly to CHD issues.

LIPIDS & LIPOPROTEINS
Fats such as cholesterol and triglycerides are transported in the bloodstream as part of lipoprotein particles. The classes include Low Density Lipoprotein (LDL, which carries most of the blood cholesterol), Very Low Density Lipoprotein (VLDL, which carry most of the blood triglycerides), High Density Lipoprotein (HDL cholesterol) and Chylomicrons (recently absorbed fat).

Excess LDL cholesterol (say a total serum cholesterol > 4-5mmol/L) is the most widely accepted risk factor for heart disease. Excess triglycerides (say >1.8mmol/L) are probably important in CHD but this is controversial. A low concentration of HDL cholesterol (say <1.0mmol/L) is also accepted as a major risk factor. Excess triglycerides may be more important when HDL cholesterol is low. The balance of total to HDL cholesterol is interesting and there are some who examine the ratio of total cholesterol/HDL. Values >4-5 for this ratio may be adverse, but use of the ratio is controversial.

Serum cholesterol (and hence LDL cholesterol) has consistently been shown to be a significant risk factor for CHD and other major cardiovascular diseases as well. The relationship is continuous, graded, strong, independent of other risk factors, predictive and generally assessed as causally related. This judgement is reinforced by results of many randomised, placebo-controlled trials to lower serum cholesterol in middle-aged and older persons with average or elevated readings. These trials demonstrate that effective, sustained reduction of serum cholesterol by dietary measures, by drug therapy, or by both will reduce (but not eliminate) future CHD and cardiovascular risk (JAMA 2000;284:311-318).

The impact of cholesterol on CHD risk is increased if other risk factors are simultaneously present. Cholesterol is a risk factor for a first coronary event. It appears to be highly predictive of a recurrent event.

LIFETIME CORONARY DISEASE RISK
The Framingham investigators have evaluated the lifetime risk of a coronary event in someone now free of CHD (Lancet 1999;353:89-92). The lifetime risk to 94 years at age 40 is one in two for men and one in three for women. Even at age 70 years, this risk is one in three for men and one in four for women.

CHOLESTEROL PREDICTS ALL-CAUSES MORTALITY
Serum cholesterol predicts all-causes mortality in men under 40 years followed for 16-34 years (JAMA 2000;284:311-318). The risk of dying is increased 10-25% with every 1 mmol/L increase in serum cholesterol.

CHOLESTEROL AND CORONARY DISEASE RISK
Cholesterol significantly predicts the risk of CHD death in young men (under 40 years) and older men. The risk of CHD death in young men increases by 40-80% for every 1 mmol/L increase in serum cholesterol. In older men the gradient is a 10-30% increase in CHD risk. It is clear that serum cholesterol "wanes" as a

predictor of CHD with increasing age. In the Dubbo Study of the Elderly, it is not predictive beyond 70 years.

CHOLESTEROL & LIFE EXPECTANCY
In men under 40 years it is now possible to compute the impact of a lower cholesterol level on longevity (JAMA 2000;284:311-318). One can calculate the increase in life expectancy for a given follow-up period. If cholesterol is under 5.2mmol/L compared with a reading >6.2mmol/L, the increase in life expectancy in three studies was: 6.1 years in 25 years follow-up, 8.7 years in 34 years, 3.8 years in 16 years.

CONCLUSIONS
Serum cholesterol is related to all-causes mortality and CHD, and its impact on longevity can be computed. Clinical trials have confirmed that cholesterol-lowering will reduce the future risk of coronary disease. Risk reduction is not back to zero, but to that risk predicted by the resulting cholesterol level.

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