

Professor Chris J. Packard
Professor of Vascular Biochemistry, University of Glasgow,
10 Alexandra Parade, Glasgow, G31 2ER

chris.packard@clinmed.gla.ac.uk

Horizons in vascular disease prevention and treatment

Coronary heart disease is still the major cause of morbidity and mortality in developed countries and will continue to be so as populations age. Likewise, for the many developing nations it is predicted that in the near future CHD will replace infection as the principal health problem. Social, economic and demographic changes, therefore require that we monitor constantly our strategy for CHD prevention and treatment so that its impact on healthcare delivery and costs is manageable.

As understanding of the disease process grows the intervention paradigm alters. Previous focus on the prime role of low density lipoprotein (LDL) has been replaced by a broader view on the impact of all lipoprotein classes on atherogenesis and the contribution of other pathways such as the innate immune system and matrix metalloproteinases. It is now dogma that LDL levels need to be lowered in those at risk for CHD and the remarkable success of statins in clinical trials has indicated that the lower LDL levels fall, the greater the benefit. It can, therefore, be safely assumed that statin therapy will be the universal first step in any treatment algorithm.

What next is the question that researchers in atherosclerosis focus upon. Do we raise high density lipoprotein (HDL, lower triglyceride levels, improve insulin sensitivity, perturb inflammatory pathways or alter matrix metabolism? Can we develop direct anti-atherosclerotic agents and how should these be tested?

By common assent, it is now held that the next step is to raise HDL levels since this lipoprotein is established as a cardio protective agent. This can be done in a number of ways e.g. by fibrates, by inhibitors of cholesteryl ester transfer protein or by inducing cellular export of cholesterol. HDL structure, function and metabolism are more complex than that of LDL and the outcome of interventions cannot be predicted readily. At the present time, we await the results of proof of concept clinical trials. If new modalities can be combined successfully with statin therapy then a virtual "cure" for atherosclerosis and its clinical consequences may lie on the horizon (for those able to access it!).