Low-Density Lipoprotein, Non–High-Density Lipoprotein, and Apolipoprotein B as Targets of Lipid-Lowering Therapy

To the Editor:

Grundy discusses the virtues of low-density lipoprotein (LDL)-cholesterol, non–high-density lipoprotein-cholesterol, and apolipoprotein B as targets of lipid-lowering therapy.1 However, the only valid reason to treat any lipid disorders (other than markedly lowering elevated triglycerides to prevent pancreatitis) is the prevention of atherothrombotic disease (ATD) or, if ATD is extant, then its stabilization/regression. I have published a risk factor graph utilizing the cholesterol retention fraction (CRF, or [LDL−HDL]/LDL) on the ordinate and systolic blood pressure (SBP) on the abscissa.2 On this graph exists a threshold line (angiographic stabilization/regression line, or ASRL) defined by (CRF-SBP) loci (0.74, 100) and (0.49, 140) (Figure). This graph and its threshold line were derived from my age-sex database of 908 patients who developed some form of ATD in northwest Ohio during the 1974 to 2001 timeframe. From an epidemiological viewpoint, ATD events are common above the ASRL and uncommon (rare, if cigarette smoking is excluded) below the ASRL. In an analysis of 8 published angiographic regression trials (about 2500 angiograms), I showed that any therapy that brought the patient’s CRF-SBP plot below the ASRL resulted in angiographic plaque stabilization/regression in a minimum of 75% of cases.3 One of the angiographic regression studies (POSCH, or Program in the Surgical Control of Hyperlipidemia) was not structured to control blood pressure, with the result that many POSCH CRF-SBP plots lay beyond the ASRL. Had antihypertensive therapy been given, virtually all those plots would have been brought below the ASRL, and the percentage of plaque stabilization/regression cases could have been in the nineties.

This graph, coupled with cigarette smoking, fulfills Dr Grundy’s requirement for a multi-factoral risk factor tool that predicts the population at risk of ATD and guides therapy to maximally stabilize/reverse extant ATD. This graph brings together various lipidologic views relating to LDL and HDL.

Triglycerides (TG) are not substantially present in the arterial plaque. TG, however, do track with the CRF (Feeman, unpublished data, 2002). Moreover, when TG are elevated, ATD events are more frequent and occur at a younger age than when TG levels are normal (≤149 mg/dL).4 The reasons for this, in my opinion, are that elevated TG are associated with small, dense LDL-cholesterol (which is more atherogenic), low HDL levels (which is a pro-atherogenic state), and elevated plasminogen activator inhibitor-1 levels (which are thrombogenic). In conclusion, the graph has the virtue of being simple, so that any physician anywhere in his/her office can readily use this tool in the fight against ATD.

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