HDL$_2$ OF HEAVY ALCOHOL DRINKERS INCREASE CHOLESTEROL EFFLUX

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Background: Protective effect of alcohol consumption on atherosclerosis is mediated partly through lipopoteins, e.g. by increase in HDL cholesterol and phospholipid levels in plasma. These anti-atherogenic changes can also be seen in HDL of alcohol abusers. There are two main subclasses of HDL: larger, less dense HDL2 and smaller, denser HDL3. Very little is known about the effects of chemical composition of HDL subclasses on cholesterol efflux, the first important step in the reverse cholesterol transport process whereby peripheral cell cholesterol is transported to the liver for excretion.

Hypothesis: HDL isolated from heavy alcohol drinkers promote reverse cholesterol transport by increasing cholesterol efflux from macrophages. We also hypothesize that cholesterol efflux is not affected to the same extent by HDL2 and HDL3 due to different alcohol-induced changes in the chemical composition of these subclasses.

Methods: Total HDL, HDL2 and HDL3 were isolated from heavy alcohol drinkers (n=6) and controls (social drinkers and teetotallers) (n=6). Chemical composition (phospholipids, cholesterol, triglycerides and proteins) of HDL particles isolated from study subjects was determined by standard methods. HDL size was determined on a 4-30% native gradient gel electrophoresis. Cholesterol efflux to HDL was measured from ^{3}H-cholesterol-loaded RAW 264.7 macrophages. PLTP and CETP activities in serum of study subjects were analysed.

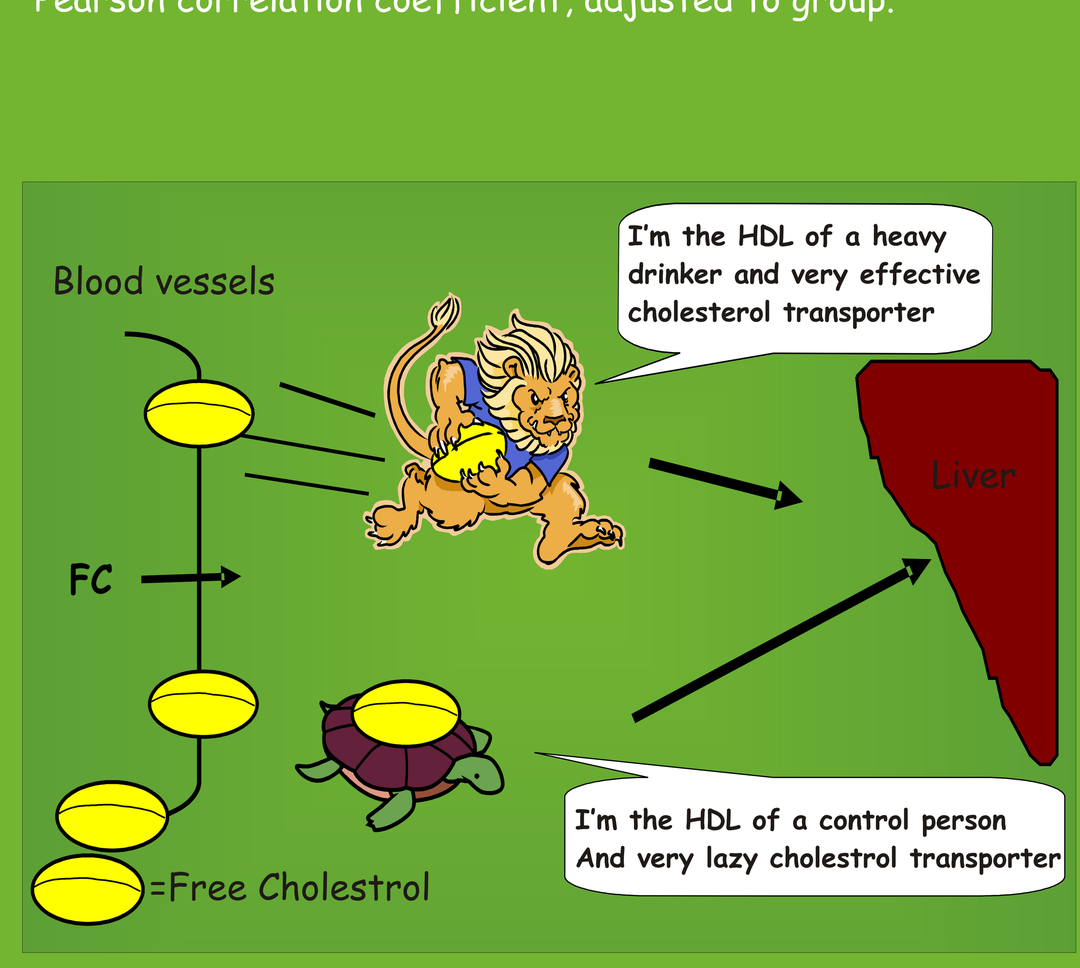

Figure 2. Correlation between HDL2 size and HDL2 cholesterol efflux. Controls are social drinkers and teetotallers (n=6). *Pearson correlation coefficient, adjusted to group.

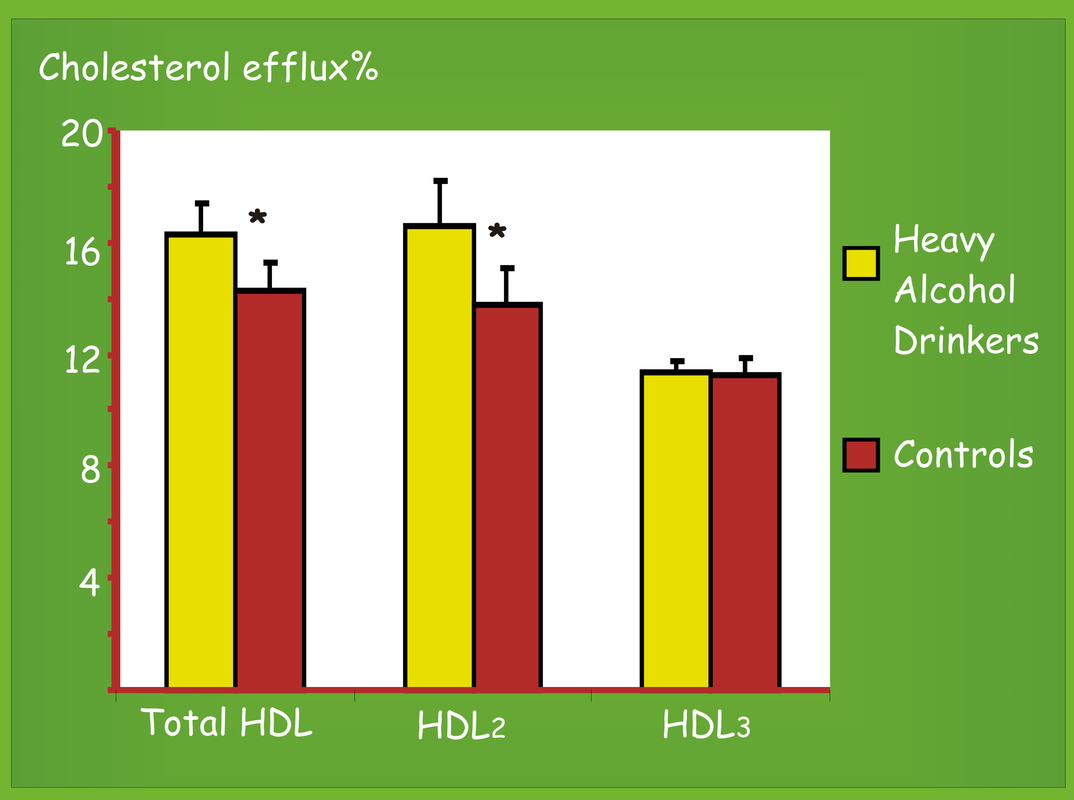

Figure 1. HDL2 of heavy alcohol drinkers increases cholesterol efflux. * p<0.05, mann whitney U -test.

Results: Total HDL and HDL2 of heavy alcohol drinkers incresed cholesterol efflux but cholesterol efflux to HDL3 was similar between the groups (figure 1). Increased efflux was correlated positively with HDL2 particle size (figure 2) and phospholipid/protein ratio. Serum CETP activity was lower and PLTP activity higher in heavy alcohol drinkers.

Conclusions: This is the first study to show that HDL of heavy alcohol drinkers has increased potential to facilitate cholesterol efflux specifically to HDL2. The increase in efflux is associated with alcohol-iduced changes in HDL2 composition , which may be partly due to lower activity of CETP and higher activity of PLTP.