HDL and Small HDL Particles Predict Cardio Problems in HIV

February 18, 2009 By Tim Horn

Interrupting antiretroviral (ARV) therapy has a rapid unfavorable effect on “good” HDL cholesterol levels, significantly increasing the risk of cardiovascular disease (CVD). This was an additional finding from the SMART trial, reported by Daniel Duprez, MD, of the University of Minnesota and his colleagues at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) last week in Montreal. According to the researchers, HIV-positive people not on treatment experienced a high rate of serious coronary-related problems.

Previous data from SMART indicated that treatment interruption is associated with drops in both HDL cholesterol and “bad” LDL cholesterol. But even with a decrease in LDL levels—typically a favorable outcome—there were still disproportionately more CVD problems in the treatment interruption group, compared with those who remained on treatment throughout the study.

By way of background information, Duprez explained that HDL is one of the five major groups of lipoproteins—the other four are chylomicrons, VLDL, IDL and LDL—that help fats such as cholesterol and triglycerides move through the water-based bloodstream. Because HDL removes cholesterol from fatty deposits in artery walls (atheromas), it is widely considered “good” cholesterol. When HDL levels fall below 40 milligrams per decaliter (mg/dL), the risk of CVD increases, as there isn’t enough of the lipoprotein to halt or reverse thickening of the arteries.

Duprez also noted that not all HDL lipoproteins are created equal. For example, two individuals of similar ages and total HDL levels can have different amounts of small HDL particles—studies suggest these more accurately reflect protective action—in relation to medium and large HDL particles. (HDL particle concentrations are measured using sophisticated assays, such as electrophoresis and nuclear magnetic resonance spectroscopy).

To better understand the protective role of HDL, Duprez’s group measured lipoprotein concentrations in stored samples from 218 patients who discontinued treatment and 233 patients who remained on treatment in SMART. In addition, lipoprotein particles at study entry were measured in 248 SMART participants diagnosed with CVD and in 480 age-, region- and gender-matched SMART participants who remained free of coronary disease.

The average age of the patients included in the analysis was 49 years. About 19 percent in both groups were women, and nearly 40 percent were black.

Most lipoprotein levels—including total cholesterol, LDL and VLDL—were similar between those who developed CVD (cases) and those who did not while participating SMART (controls). Total HDL

levels, however, were significantly lower in the cases compared with controls at baseline: 38 mg/dL vs. 42 mg/dL, respectively. Total HDL particle concentrations were also lower among cases vs. controls—28.4 micromol/L vs. 30.2 micomol/L, respectively—suggesting that lipoprotein particle size is also directly related to the risk of CVD.

In the comparison between those off and on treatment in SMART, one month after entering the trial, both small and medium HDL particles fell significantly in the interruption group compared with those who remained on therapy. Concentrations of large HDL particles remained similar in both groups.

In concluding his talk, Duprez reiterated that lower total HDL levels—especially small HDL particles—can predict cardiovascular events in people living with HIV. Discontinued or intermittent therapy, he added, is associated with a decrease in HDL, when compared with continuous treatment. He recommends that additional studies, notably randomized clinical trials, be conducted to better understand the long-term effects of both ARV and lipid-altering therapies on HDL and HDL particles.
