LIPOPROTEINS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Sometimes the answers in medicine are not as simple, direct, and straight forward as we would like them to be. Such is the case with the relationship between lipoproteins (LP's) and chronic obstructive pulmonary disease (COPD). Scientists have known for some time that there is a relationship between lipoproteins and coronary heart disease (CHD). Since the heart and lungs work closely together, and in fact, rely on each other; it would seem that there may be a similar relationship between LP's and COPD, but is there? Since we are familiar with COPD, let's first get a better understanding of lipoproteins before we look for a relationship.

Cholesterol by itself is insoluble in water and thus makes it very difficult to get around in the body. The solution for cholesterol was to combine itself with a protein molecule, thus becoming a lipoprotein water-soluble complex! It turns out that cholesterol is made up of a number of sub-fractions. The sub-fractions each vary in the amount of lipid and protein that they contain. The larger lipoprotein particles contain more lipid relative to protein and are, therefore, lighter in density. The different lipoprotein particles were discovered by ultracentrifugation in which heavier LP's traveled farther in a glucose gradient than did lighter LP's. The various sub-fractions are known as chylomicrons, very low-density lipoproteins (VLDL), low-density lipoproteins (LDL), high-density lipoproteins (HDL).

Are there any studies that show a relationship between lipoproteins HDL, LDL and COPD?

Apolipoproteins are primarily located on the surface of lipoprotein particles. These proteins help maintain the structural integrity of the lipoprotein particles and in addition serve as ligands for cell receptors and as activators and inhibitors of the various enzymes that modify lipoprotein particles. There are ten apolipoproteins based on their molecular weight, plasma concentration, major lipoprotein location, and function. The are labeled Apo A-I, Apo A-II, Apo A-IV, Apo B-100, Apo B-48, Apo C-1, Apo C-II, Apo C-III, Apo E and Apo(a). As an example, Apo B-48 is found only in chylomicrons, Apo A-I and Apo A-II are found exclusively in HDL's.

There are four major pathways involved in the movement of lipids around in the body. The lipid absorption pathway, exogenous pathway, and endogenous pathway all depend on Apo B-containing lipoprotein particles (chylomicrons, VLDL, LDL). As a group they are responsible for transporting dietary lipid and hepatic-derived lipid to peripheral cells. Lipid is removed from the tissues and carried by to the liver for break-down and elimination from the body by Apo A-1 and A-II containing lipoprotein containing particles (HDL).

The lipid absorption occurs from the eating of fatty foods. The average person ingests, absorbs, and transports about 60-130 grams of fat a day, mostly in the form of triglycerides (three fatty acid molecules attached to one molecule of glycerol). The terms cis- and trans- fatty acids comes from the relationship of the bonding in the molecules. Saturated fatty acids (no double bonds) tend to pack closer together and form solids, whereas cis-fatty acids (have one or more double bonds) cannot be packed as close together and tend to be oils.

The exogenous pathway uses chylomicrons, which are synthesized in the gut to carry fats initially in the lymphatic ducts and eventually the circulation by way of the thoracic duct on to the tissues.

In the endogenous pathway most triglycerides in the liver are packed into VLDL and derived from the diet after recirculation from adipose tissue. Only a small amount of fat is synthesized in the liver from dietary carbohydrate. After a number of biochemical steps about half of the VLDL is converted to LDL. LDL are the major lipoproteins responsible for delivery of exogenous cholesterol to the tissues.

The previous three pathways all involved getting fats and cholesterol into tissues. These pathways involve both ingested and internally made (by the liver) fats. Thus, the storage of fat can become a problem!

The final pathway is a reverse cholesterol pathway. HDL acts as a sink for removal of small amounts of cholesterol and deliver it (cholesterol) directly to the liver for breakdown. Another mechanism in the reverse pathway involves the ABCA1 tranporter. This transporter can pump various ligands across the plasma membrane to assist in removal of fats and cholesterol from the cell. A defect in the gene for the ABCA1 transporter can lead to Tangier disease, a disorder associated with low HDL and a predisposition to premature coronary heart disease.

From the previous discussion you can easily see that a person's lipoprotein make-up can be used as a predictor of cardiovascular disease. High HDL and low LDL, VLDL would

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indicate a lower risk for heart disease; whereas, a low HDL and high LDL, VLDL would be a high risk for heart disease.

The following chart will give you a good example of commonly accepted lipoprotein values:

LDL cholesterol Levels

< 100	Optimal
100-129	Near Optimal/Above Optimal
130-159	Borderline High
160-189	High
>/= 190	Very High

Total Cholesterol Levels

< 200	Desirable
200-239	Borderline High
>/= 240	High

HDL Cholesterol Levels

< 40	Low
>/= 60	High

To date, many studies have been done to show this inverse relationship between high HDL and lower incidence of heart disease, as well as the direct relationship between high LDL and high incidence of heart disease. But are there any studies that show a relationship between lipoproteins HDL, LDL and COPD?

Ulubas and colleagues (2003) showed in a study involving 20 COPD patients and 20 healthy controls that there was an increase in HDL among the COPD patients. Another study by Uzuner and associates (2002) showed that long term treatment with theophylline in asthmatic children adversely affected lipoprotein levels and may be a potential increased risk factor for atherosclerotic heart disease in children. Fekete and Mosler (1987) in a study of 29 COPD patients that triglyceride levels were significantly lower in COPD females only. Other studies have not shown any statistically significant change in lipoprotein levels in COPD patients.

Current thinking on the relationship between lipoproteins and COPD is that the disease specifically (COPD) is not the agent that is bringing about a consistent pattern of benefit or risk in terms of lipoprotein patterns. It is speculated that certain drugs can bring about an alteration in lipoprotein patterns; however, since COPD patients generally are on multiple medications at any one time, it is hard to say which, if any of the medications is causing the changes noted by some researchers. Research in this area is still in it's infancy and much has yet to be done.

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"You're not speaking to the department director, you're speaking to his parole officer..."