

HeartFacts

**SOUTHERN CALIFORNIA
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Lipids Made Simple – Part I

Hyperlipidemia is one of the



HYPERLIPIDEMIA

most common, complex and vexing problems in clinical practice. Various classification schemes have not made the problem any simpler for the practitioner. In addition to this, the patient gets an enormous amount of misinformation from TV, magazines, pharmacy leaflets, the Internet, and Aunt Molly. It's enough to drive one to the nearest In-and -Out store for a large greasy burger.

The following is a distillation of a 20-year effort to understand and treat dyslipidemia. It represents my own clinical practice. Some may see this as oversimplification. That is the idea.

Man is the only mammal on the planet with an LDL > 100 mg/dl.

In fact, the average U.S. LDL is currently about 130 mg/dl. We must remember however, that this number characterizes a population that is generating approximately 1.5 million new cases of coronary disease per year. Population studies have clearly shown that the risk is direct and progressive. It has been established that the higher the LDL in a given cohort, the higher the prevalence of CAD and stroke. Conversely, populations having an LDL < 100 have almost no incidence of CAD.

The other common dyslipidemia is an elevated triglyceride. Its clinical relevance historically has been as a recognized cause of acute pancreatitis. But now evidence is emerging that it too may be a risk factor for CAD.

With this as prelude, some simple statistics are useful. It is likely that only 30 percent of those eligible for lipid therapy are under treatment and of these only 10 percent are at

goal. This is an immense public health issue. Cost and misinformation seem to be the chief barriers to wider treatment.

We believe everyone above the age of 40 should have a lipid profile. That panel should consist of a total cholesterol, triglyceride, HDL, direct or calculated LDL and to estimate LDL size, apolipoprotein B. Now how to interpret the results? (Yes, we have to do that).

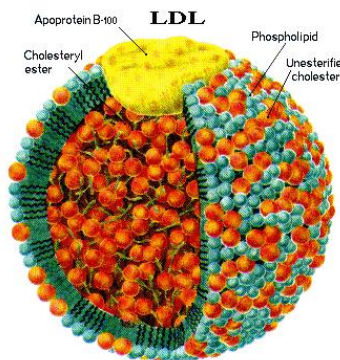
First of all forget the total cholesterol. It is useless. Yes, I know: patients obsess over it. But part of our job is to bring them (and us) into the new century. Since total cholesterol measures the aggregate of LDL, HDL, and cholesterol in the VLDL particle, it is probably only useful for population screening.

Triglyceride should be under 150. It mostly isn't because we Americans tend to gorge our-



selves on a cane-and grain-based nutrition (i.e. sugar and flour). Agriculture was invented about 10,000 years ago and it only took 1,000 years to figure out how to extract sugar and flour from the flesh of domesticated plants. For the 150,000 years prior to that our nutrition consisted of fruits, vegetables, nuts and lean sources of protein. This omnivorous habit provided our brains with a broad spectrum of amino acids. Not coincidentally and for better or worse we became the dominant species on the planet.

In the last 200 years we have become industrialized and civilized. Concomitant with this our diet has become laced with simple carbohydrates: sugar, flour, and starches. If this substrate is not burned in the hour after ingestion, the body has no choice but to cleave these 6-



Lipids Made Simple - Part I (continued)



carbon rings and remanufacture them as triglycerides. Overfed over years we gradually make the transition from lean children and adolescents to centripetally obese adults with all the consequences. Even our children have been affected.

Fifty percent of our children are now said to have the metabolic syndrome as a consequence of overfeeding and too little exercise. This syndrome includes obesity, insulin resistance, hypertriglyceridemia, hypertension, and diabetes. As triglyceride increases, HDL falls and LDL particle size shifts to the small, dense, atherogenic fraction. This metabolic domino effect is newly thought to be an additional risk factor for the premature development of CAD.

HDL should be > 45. HDL is responsible for reverse cholesterol transport. It removes excess cholesterol from cell membranes and is anti-atherogenic. Sedentary lifestyle and smoking lower HDL. Exercise, niacin, alcohol, and smoking cessation increase it. More HDL is better. The HDL of patients arriving in the emergency room with acute myocardial infarction is 35 or less.

LDL is the transport particle that delivers cholesterol to somatic cells to be used in the construction of cell membranes, bile acids and hormones. Some is good. More is not. This parti-

cle, when present in excess in the serum, infiltrates the subendothelium. It is oxidized there and ingested by macrophages. These latter become foam cells. As they accumulate they form fatty streaks and nascent atherosclerotic plaque. LDL should be less than 100. Period. But, how much less should it be?

Research conducted on Paleolithic peoples reveals total cholesterol levels that would suggest they had an LDL of 50-70. Thus in our hunter-gatherer incarnation man probably had an LDL half of what it is in our post lapsarian state (I put that word in to see if you are paying attention).

Moreover, two recent investigations appear to confirm this hypothesis that less is more. In the PROVE-IT trial maximum doses of Lipitor resulted in fewer cardiovascular events than Pravachol. Lipitor resulted in an LDL reduction to 62 mg/dl.



The REVERSAL trial pitted maximum doses of Lipitor against maximum doses of Pravachol. Plaque volume was measured in 502 patients with single vessel coronary disease at baseline and 18 months later. Plaque volume increased in the Pravachol group. It showed no increase and a trend to regression in the Lipitor group. LDL averaged 110 in the former cohort and 79 in the latter. Thus it seems that LDL between 60 and 80 may be the ideal goal for coronary patients.

Apolipoprotein B is used to estimate LDL particle size. One copy of this protein is present on each LDL particle. Thus, the larger the LDL species, the fewer particles present in the serum. ApoB > 120 identifies a small dense LDL population whereas apoB less than 90 is consistent with predominantly large particle LDL. Small particle LDL is atherogenic whereas large particle is not.

In our next issue we will discuss patterns and treatment. This too shall be made simple.

"Simple is as simple does."

Forrest Gump

"Simplicity is the ultimate sophistication."

Leonardo Da Vinci

(1452-1519)



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