CLINICAL PRACTICE

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The not so good and the not so bad

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Today's question: How good is the good cholesterol?

Since before med school we knew that is a bad cholesterol and a good one. And like old days vigilantes we fight the bad one and support the good. But, like the characters in the novels, the bad one seems to have a bright side and the good one has dark secrets.

First let's talk about the LDL. It's involvement in atherosclerosis it's a fact and it's a silent killer. The cardiologists are fighting it since 1987 when the introduction of lovastatin in ischemic cardiac disease.

Figure 1: The good and the bad cholesterol [5].

Now let's talk about the sheriff, HDL cholesterol. The one that protect us in the front of vascular aggressors. We know that the bigger is the better and we are very sad when our patient have low levels of it. But 500 years ago we knew that the earth is flat, so what is the truth?

Recently 4 Big Pharma firms developed a new class of lowering cholesterol drugs – Cholesteryl Ester Transfer Protein Inhibitors (CETPi) that were announced to be the new milestone in the treatment of dyslipidemia. Preliminary studies showed a spectacular HDL levels rise.

First to go first to fall – torcetrapib – shortly the mortality increased from an unknown cause.

Next dalcetrapib and evacetrapib – HDL levels reached the top. Well tolerated, few side effects, no increased mortality.

Then the bomb dropped: the studies were shutdown prematurely. Why? Headmaster of the late ACCELERATE study, Steve Nissen declared for Forbes magazine that "the drug didn't work". I don't think that was the accurate response. In my opinion the drug worked because patients achieved incredible was a real breakthrough. But what the neurologists have to say? After the initial enthusiasm was tempered they started to ask: our patients have a LDL cholesterol level way below 70 mg/dl. They are safe. But they look dumber. Why? The statin lead to a mental decline or the low LDL level is to blame? In my opinion is the LDL level. I noticed that in several of my patients with very low LDL levels: they develop very fast dementia symptoms that regress dramatically when their LDL levels rise above 70 mg/ml. Is it a coincidence? Maybe. But what if the bad has good side?

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high HDL levels. The problem was that despite these very high HDL levels the cardiovascular events were not different from the placebo group. So I would say that drug proved to be effective in what it was made to do but high HDL levels were useless.

Here comes the question: is the HDL as protective as we used to believe or just handsome good-for-nothing cholesterol as suggested by those studies?

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