Sterols and Stanols (Part 2)

In part 1, I gave a brief overview of sterols and stanols and how they are absorbed in the intestine. I want to start this posting by talking about what happens when the sterols (cholesterol and noncholesterol sterols) are absorbed at the intestinal epithelium?

There is no doubt that the noncholesterol sterols are effective in reducing cholesterol levels by blocking absorption from the intestine. Evolution has gone to great lengths to keep noncholesterol sterols out of the human body so almost immediately after absorption some of the cholesterol and virtually all of the noncholesterol sterols are pumped back into the intestinal lumen (cavity) via something called ATP binding cassette transporters, ABCG5/G8. As I previously stated, only about 50-55% of ingested cholesterol makes it into chylomicrons in order to be transported to the liver for processing. These ATP binding cassette half-transporters G5 and G8, facilitate transport of sterols out of cells of both the intestine and liver into the intestinal lumen and into the bile. Any sterols that are not pumped back into the intestine become part of the contents of the intestinally produced chylomicron particle that transports lipids to the liver. 70% of the cholesterol in the body is transported as an ester, not as free cholesterol, and this is called cholesterol ester. Any noncholesterol sterols that were not sent back to the intestine via ABCG5/G8 also become part of the chylomicron and thus gain entry into the bloodstream. Noncholesterol sterols are not esterified as humans do not have the enzymes necessary for that. When these unesterified sterols get into an arterial wall, they are more atherogenic than cholesterol (an esterified sterol). This means they have a greater artery clogging potential than does cholesterol. If one lacks these transporters (homozygote), all sterols are absorbed and none are pumped back out: this is a very rare homozygous condition leading to the disease called sitosterolemia or phytosterolemia. It is associated with severe atherosclerosis, as noncholesterol sterols (which cannot be esterified) are more atherogenicthan cholesterol. Heterozygotes, people who have some transporter function, eliminate some but not all of these phytosterols. Stanols do not require these transporters to get back into these intestines. This is the reason that they are safe and effective to reduce cholesterol. Stanols are commercially available in the supermarket in a product called Benecol.
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We are now beginning to understand that not everyone has perfect functioning G5/G8 transporters and noncholesterol sterols get into some people: especially those with family history of CAD (coronary artery disease) and postmenopausal women. These sterols may contribute to their atherosclerosis. Such patients have slightly elevated sitosterol and campesterol levels (no where near what the homozygous patients have). As clinicians have no way of knowing which of our patients may be over absorbing sterols without measuring sitosterol levels. This is not routinely done in clinical practice.

Although sterols are artificially added to many foods and bay aspirin, it should be clear that in some people they may do more damage than does cholesterol. Prior to the introduction of eztemibe (Zetia), there was no way to effectively block the absorption of cholesterol and noncholesterol sterols. I have posted previously on this blog a paper called ezetimbe (Zetia). Zetia typically reduces the absorption of all sterols by 50%. It is FDA approved to lower cholesterol and noncholesterol sterols (sitosterolemia). Since the majority of cholesterol is produced in the liver, Zetia does not have a great effect in lowering ingested cholesterol. Statins are the first line therapy in treating high cholesterol. In was shown in a trial called the 4S trial that as a statin lowers cholesterol levels and block it's production, intestinal absorption of cholesterol and noncholesterol sterols increases. Using Zetia would eliminate this problem.