By Dr. Duane Graveline, M.D., M.P.H.

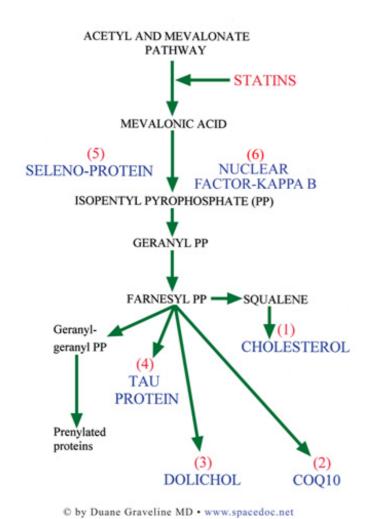
The reasons for statin drug side effects are better appreciated by using this figure of the mevalonate pathway (also known as the HMG-CoA reductase pathway) adapted from any medical school biochemistry book.

All statins are reductase inhibitors and therefore exert their effect at the very beginning of the mevalonate pathway, the location of this key reductase step.

When statin drug manufacturers make the claim of reduction of cholesterol synthesis, it is based upon inhibition of the mevalonate pathway, shared by the other major elements such as CoQ10 and dolichols.

Statins act by inhibiting HMG-CoA reductase as indicated in this figure.

All metabolic functions further down the pathway are consequently affected.



Acetyl and Mevalonate Pathway

Not only is glial cell cholesterol synthesis in our brains vital for memory function and cognition, cholesterol also is the substrate for our most important homones: aldosterone, cortisone, estrogen, progesterone and testosterone as well as the quasi-hormone, vitamin D (calcitrol). Cholesterol's vital role in membrane structure and function and lipid raft formation, makes it of critical importance in cell identification, cell communication and immunodefense.

Glial Cell Inhibition Potential Side Effects:

Amnesia
Forgetfulness
Confusion
Disorientation
Increased Senility

Hormone Lack Potential Side Effects:

Loss of Libido (sexual desire) Erectile Dysfunction (ED) Osteoporosis Hair Loss

2.) CoQ10 (Ubiquinone) Inhibition

Coenzyme Q10 (CoQ10) is important for structural integrity of cells, anti-oxidation and, as part of the mitochondria, the production of Adenosine Triphosphate (ATP) energy. Part of its extreme importance in anti-oxidation is because of its location within the mitochondria, protecting the delicate components of the mitochondria from excess oxidative change and mutation.

Lack of Energy Potential Side Effects:

Chronic Fatigue Syndrome Congestive Heart Failure Fluid Retention Shortness of breath

Loss of Cell Wall Integrity Potential Side Effects:

Hepatitis

Pancreatitis

Myopathy (muscle pain and weakness, cramps)

Peripheral Neuropathy (numbness, tingling or burning sensations particularly in hands and feet) Rhabdomyolysis (rapid breakdown of skeletal muscle tissue)

Excessive Oxidation Potential Side Effects:

Mitochondrial Damage Permanent Neuropathy Permanent Myopathy Neurodegeneration

3.) Dolichol Inhibition

Dolichols are vital to the process of glycoprotein formation in the endoplasmic reticula of cells. In this capacity it is critical to the formation of the glycoproteins involved in neuropeptides, cell identification, cell messaging and immunodefense. Reduced bioavailability of dolichols can affect every cellular process in the body.

Neuropeptide Dysfunction *Potential Side Effects:*

Aggressiveness
Hostility
Irritability
Road Rage
Homicidal Behavior
Depression

Altered Glycoprotein Synthesis Potential Side Effects:

Impairment of DNA error correction
Dysfunction of almost any cellular process
Altered cell identification
Altered cell messaging
Altered immunodefense

4.) Tau Protein Synthesis

When normal phosphorylation is interfered with by mevalonate blockade, our cells increase the production of Tau protein. Tau is the protein substance of the neurofibrilatory tangles common to Alzheimer's and other neurodegenerative diseases.

Neuro-Degenerative Diseases Include:

Parkinson's Disease Alzheimer's Disease Amyotrophic Lateral Sclerosis (ALS) Primary Lateral Sclerosis (PLS) Multiple Sclerosis (MS) Multiple System Atrophy (MSA) Frontal Lobe Dementia

5.) Selenoprotein

Only recently discovered were selenoproteins and the effect of statin blockade of the mevalonate pathway on their role in human physiology. Deficiency of selenoproteins has been proven to result in various types of myopathies formerly seen only in areas known to be deficient in this trace element. Additionally cognitive dysfunction is known to be associated with selenium lack.

6.) Nuclear Factor - kappa B (NF-kB)

The benefit of statin drugs in cardiovascular disease control is in their ability to inhibit this vital transcriptase. The entire anti-inflammatory and immunomodulatory effect of statins is mediated by statin inhibition of nuclear factor-kappa B. Improvement in atherosclerosis results from the inhibition of the key inflammatory elements: smooth muscle migration. lymphocyte adhesion, macrophage attraction and platelet activation associated with inhibition of NF-kB. The immunodefense system is also keyed to NF-kB, explaining the changing patterns of certain infections and cancers. The rise in cancers of all kinds secondary to statin use is of major concern.

Duane Graveline MD MPH

Former USAF Flight Surgeon Former NASA Astronaut Retired Family Doctor Updated July 2011