

The Safety of Lipid Lowering Medications:
The Effects of Statins on the Muscles
By Michael Richman M.D.

I have spent the last 2 weeks answering questions about Vytorin and Zetia after the media caused an inexcusable hysteria that in some way Zetia or any combination which included it was bad. One well known expert from the Cleveland Clinic always seems to weigh in on every cholesterol issue and gives the thumbs up if he was involved in the study and the thumbs down if he was not. I can tell you that those of us who practice full time clinical medicine and see patients daily have not altered our prescribing practice on the basis of the ENHANCE study which was strictly an imaging study with no outcome data regarding what the findings actually mean in the patients. It is a shame that the ASTEROID and METEOR studies involving Crestor, which were also imaging studies but showed a decrease in the plaque burden in the heart arteries (ASTEROID) and a regression in some patients and no progression in others (METEOR) of the same thing that was measured in the ENHANCE study (CIMT or Carotid Intimal Medial Thickness) and generated all the confusion, were not mentioned in the media. The point is that all of these studies are imaging studies and there is no outcome data so I really do not know what any of them mean in a practical sense.

Now let's move on to the topic at hand. I am asked most frequently by patients if statins are bad for the muscles? Once again I will present the evidence based data. First, I will give you some definitions. Myalgia is a non-specific common complaint of muscle ache and there are no abnormalities of the muscle enzyme CPK or CK on a blood test. Myalgia has rarely been examined in clinical trials and it is thought that some type of muscle aches can occur in up to 30% of patients on statins. Unfortunately, many of these patients start a vigorous exercise program at the time they start their statin because they decide it is to "get in shape" and one doesn't know where the origin of the muscle ache is from. There are many other causes of myalgias too. Statin muscle pain typically occurs in the proximal muscle groups (closer to the trunk of the body) and also lower back. Statin induced myalgias have occurred up to 3 years after starting a statin. Myopathy has been used to refer to all muscle complaints or CK elevations > 10 times the upper limits of normal with or without associated muscle symptoms. Myositis has been defined as muscle symptoms with increased CK levels. This term implies muscle inflammation but this appears to be a secondary event associated with the healing process. Rhabdomyolysis, by strict definition exists whenever there is evidence of muscle damage, such as a mildly elevated CK level but is used clinically to refer to severe muscle damage and is usually associated with kidney dysfunction. The Muscle Expert Panel of the Statin Safety Task Force believes that due to all this confusion about terms, a new format should be made as follows. Myopathy should be used as a general term for all muscle problems. Symptomatic Myopathy should be used to refer to muscle pain (myalgias), weakness, and cramps. Asymptomatic Myopathy should be used to refer to CK elevations without any symptoms. Finally, Rhabdomyolysis should be used to refer to any evidence of muscle cell destruction with resulting change of renal function. What does all this mean? First of all, muscle problems do occur with all statins. Muscle

complaints have been documented to increase with increasing blood levels of the statin. There are 2 different classes of statins. Fat soluble and water soluble statins. The fat soluble statins include Lipitor and Zocor and the water soluble include Pravachol and Crestor. Since fat soluble statins can easily enter the inside of the muscle cells, theoretically muscle damage should be increased with their use, as water soluble statins do not easily get into the muscle cells. This hypothesis has not been confirmed and cases of Rhabdomyolysis, while rare, occurring about 1 time for every 15 million prescriptions written, has occurred with all statins. My practice is to obtain a baseline CK level before starting statins to see if it is elevated. When a patient on a statin develops myalgia symptoms, I closely monitor them and if severe, I will get a CK level to see if there is any muscle damage. The problem exists : however, that frequent inquires may prompt symptoms in suggestible patients. Based on clinical experience, statin-related myalgias resolve when stopping the medicine. There is insufficient evidence to conclude whether myalgia that persists after stopping the statin is caused by the medications. All patients who are symptomatic on statin therapy should have thyroid function tests done as hypothyroidism can exacerbate symptoms. Also, other medications or nutraceuticals that slow down statin metabolism should be known such as red yeast rice(which may contain a statin and produce myopathy) and grapefruit juice consumption impedes the breakdown of fat soluble statins mostly affecting patients on Lipitor. Regardless of the CK level, if the pain is severe, the statin should be stopped until all the symptoms resolve. Once this occurs, the same statin could be started at the same dose to see if symptoms recur or started at a lower dose. Alternatively, a different statin can be tried. There is no direct comparison of tolerability among statins and therefore no definitive evidence to recommend a given statin. In my practice: however, I will change a patient from a fat soluble statin to a water soluble statin if myalgias start and this has been successful for me in reducing muscle problems. As I said earlier; however, there is no direct evidence that water soluble statins produce less muscle problems as compared to fat soluble statins. If the muscle pains are tolerable with or without a CK elevation < 10 times the upper limit of normal, the Muscle Panel recommends that statin therapy be continued at the same dose or a reduced dose. Generally it is my experience that muscle aches do go away or become tolerable to the patients if the statin is continued. Many physicians are too quick to stop statins with any muscle aches. The risks vs benefits of statins need to be weighed. One must remember that statins have reduced Cardiovascular Morbidity and Mortality by approximately 40%. While there is no definitive clinical evidence of any strategies that can be used to prevent or reduce muscle injury, there is some evidence that coenzyme Q10 may cause a significant reduction in statin-induced pain. Since the response has been variable, the use of coenzyme Q 10 cannot be recommended with any degree of confidence.