

New Knowledge about Cholesterol Drugs and Muscle Problems

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Statin drugs are one of the great health breakthroughs of the 20th century, dramatically lowering cholesterol and helping to prevent heart attacks and strokes. Taken by millions of people, statins are one of the most effective and widely prescribed medications ever. But they're not risk free. The most common problem reported is muscle pain. PHI asked polio survivor Edward A. Bollenbach, a retired professor of microbiology and chemistry, to explain why this occurs and to discuss how it may relate to post-polio people.

PHI: *What is this new knowledge about muscle problems, and which cholesterol drugs are involved?*

EB: There have been studies at Harvard and Beth Israel in Boston with statins, such as Lipitor and Crestor, which were published last year. This work points at a single chemical, normally produced along with cholesterol, as the lynchpin in the development of new muscle problems.

PHI: *So you are saying that when cholesterol is normally formed in the body this chemical is formed with it?*

EB: Yes, and when drugs like Lipitor, Zocor, Crestor, Mevacor (1), among others, are used, they slow the speed of cholesterol formation, and the amount of cholesterol in the blood and muscles decreases. Geranylgeranyl pyrophosphate, the chemical responsible for preventing muscle problems, also decreases, and it does not function as it normally does. This decrease is very likely the cause of muscle-related problems.

PHI: *What happens to the muscle to make it sore from the decreased amount of chemical?*

EB: Apparently there is a gene which becomes active in the muscles of the body if there is a decrease in the normal function of the chemical mentioned above. The gene produces a substance which stops muscles from rebuilding themselves after use so muscles cannot repair normal wear and tear. But remember, this happens to a small minority of patients.

PHI: *How can this new knowledge help polio survivors?*

EB: There are different forms of this gene, so one form may be more damaging than others. Soon we may be able to test for which version of the gene is present. Also, work is now underway to determine exactly what happens to the chemical that is decreased, which results in the activation of the atrophy gene, called atrogen, and so named because it results in muscle atrophy.

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PHI: *Are there any other developments on this subject?*

EB: In 1997, the *New England Journal of Medicine* reported that 60 percent of people who develop muscle problems from statins have a double copy of another gene we can designate as C. So, if you inherited a C gene from your mother and a C gene from your father, you will be CC. If you have neither C but two of an alternative gene, your chance of developing muscle problems is very low.

PHI: *Between the atrogen gene and the C gene how does this change the picture for people experiencing the late effects of polio?*

EB: First of all, muscle problems seem to be controlled by genetic factors, so whether you are a polio survivor may not be likely to have much of an effect on whether you develop increased problems from statins. It seems we may all be in the same boat. Secondly, it is very possible that in the near future we will develop interventions to make the probability of muscle side effects extremely unlikely for everyone even though such effects are already infrequent. When they do occur, they are usually transitory.

PHI: *Are there any other practical issues that we should be aware of to reduce the chance of muscle damage due to statin drugs?*

EB: I think physicians should probably, if they do not already, take into account other medications that a patient is using when prescribing a statin drug.

PHI: *Why is that?*

EB: Because Lipitor, for example, is broken down in the liver by a different chemical than Crestor or some of the

other statins. Other medications are also broken down in the liver by other chemicals. If medications, like the heart drug amiodarone or the hypertension drugs called calcium channel blockers, are taken together with a particular statin like Lipitor, the chemical that breaks down both drugs is the same, so the statin will not be broken down as quickly and will increase in the blood. This may cause muscle soreness.

PHI: *Are there other medications to watch out for?*

EB: Some medication interactions are stronger than others. One particularly powerful interaction is with anti-fungal drugs called azoles. Using them while using statins can increase the amount of statin in the blood significantly and increase the probability of muscle problems.

PHI: *Can you summarize the essence of what you just described?*

EB: Sure, since there are several different statins that use different liver decomposition chemicals, patients should use a statin that is processed by a chemical that is not being used by another medication they are taking.

PHI: *It seems a lot can be done to lessen the likelihood of problems with statins. Is there anything else we should know?*

EB: One principle is that low doses of statins rarely cause problems and that muscle problems increase as the dose of statin increases. So it is prudent to make diet and lifestyle changes and use low doses of statin rather than continue to eat lots of cholesterol-generating fatty foods and rely on a big dose of a statin to reach your cholesterol target. ▲

(1) Lipitor, Zocor, Crestor and Mevacor are the trade names of statin drugs produced by Pfizer, Merck & Co. and AstraZeneca.