Frequently Asked Questions (FAQ) about Statin Adverse Effects

Table of Contents

Frequently Asked Questions about Statin Adverse Effects ................................................ 3
Introduction......................................................................................................................... 3
What are the names of the Statin drugs?......................................................................... 4
What is the “Statin Study”?............................................................................................ 4
Where can I look to find information on research studies of statin drugs? ............... 5
Why does my physician have such a difficult time believing that my physical problems might be an adverse effect of Lipitor or one of the other statins? .................. 5
OK, I understand the doctor’s need to read clinical study results, but where can I find out what other people are experiencing in plain language, and maybe share my experiences? ....................................................................................................... 7
Are there any books on the topic?................................................................................... 7
What are the Lipitor warnings and side-effects listed by the manufacturer on the physicians’ information?................................................................. 8
What are the Lipitor Adverse Events in Placebo-Controlled Studies listed by Pfizer in the Physician’s information? ................................................................. 8
What are the Lipitor Averse Events reported in patients treated with Lipitor in clinical trials listed by Pfizer in the Physician’s information? .................................. 8
What are the Lipitor Averse events associated with Lipitor therapy reported since market introduction, that are not listed above, listed by Pfizer in the Physician’s information? ................................................................................................... 9
REPORTING ADVERSE EFFECTS FROM STATINS ................................................... 9
Where should I report adverse effects from statins?.................................................... 9
Report to the FDA....................................................................................................... 9
Report to the Statin Study........................................................................................... 9
OK, what should I take to my doctor?.......................................................................... 10
NERVE DAMAGE & STATINS..................................................................................... 10
Frequently Asked Question: What medical research studies have been done on Statins and Nerve Damage that I can bring to my doctor’s attention? ...................... 10
MEMORY LOSS & STATINS ........................................................................................ 15
Frequently Asked Question: What medical research studies have been done on Statins and Memory Loss, or other mental problems that I can bring to my doctor’s attention? ........................................................................................................... 15
AMNESIA & STATINS................................................................................................... 20
Frequently Asked Question: Amnesia is one of the Lipitor side effects reported by Pfizer on the Physician’s Information, where can I find out more about people who have had amnesia episodes while taking the drug? ................................................. 20
Lipitor, Thief of Memory, by Duane Graveline M.D. .................................................... 20
Australian Adverse Drug Reactions Bulletin............................................................ 20
CHEST PAIN & STATINS .............................................................................................. 21
Frequently Asked Question: Chest pain, that my cardiologist cannot explain via angiogram, stress test, EEG or EKG, is one of the side-effects I see is reported by many people. Is there any information on chest pain associated with statins? ........................................ 21

STATINS & MITOCHONDRIAL CYTOPATHY ................................................................. 23

COENZYME Q10 (UBIQUINONE) DEFICIENCY CAUSED BY STATINS ........... 23

Do statins cause a CoQ10 deficiency? ................................................................ 23

Merck Patent application stating that statins interfere with CoQ10 and that deficiency causes problems .................................................................................................................. 24

Introduction to the Citizen's petition to the FDA .................................................. 24

CARNITINE DEFICIENCY CAUSED BY STATINS ...................................................... 29

Can statins cause carnitine deficiency? ................................................................. 29

JOINT PAIN AND STATINS ...................................................................................... 29

Frequently Asked Question: Can statins have something to do with my joint pain? ... 29

QUITTING STATINS .................................................................................................. 30

Frequently Asked Question: Can it be dangerous to just stop taking statins? ........ 30

STATIN BIRTH DEFECTS .......................................................................................... 30

Frequently Asked Question: Is statin intake during pregnancy dangerous for unborn children? .................................................. 30

VIOLENCE AND LOW CHOLESTEROL ................................................................. 30

Frequently Asked Questions: Can it be the statins making me so irritable and prone to angry outbursts? ................................................................. 30

IMMUNE SYSTEM AND STATINS ........................................................................... 31

Frequently Asked Question: Can statins depress my immune system? ............. 31

Could a depressed immune system lead to infection? ........................................... 32

STATINS AND CANCER ............................................................................................ 33

Frequently Asked Question: What are the cancer rates for people on statins? ....... 33

Women and statins ................................................................................................ 34

ERECTILE DYSFUNCTION (ED) AND STATINS ....................................................... 36

Frequently Asked Question: Can statins interfere with my sex life? ................. 36

LUPUS-LIKE SYMPTOMS AND STATINS ............................................................... 38

Frequently Asked Question: Can statins cause Lupus symptoms? ...................... 38

MYOPATHY AND STATINS ....................................................................................... 40

Frequently Asked Question: Do statins cause muscle damage, muscle pain, myopathy, myositis, and muscle cell death (apoptosis) with or without elevated CK? .................... 40

Rhabdomyolysis AND STATINS ............................................................................. 64

Frequently Asked Question: Which statins cause deadly Rhabdomyolysis? ...... 64

STATINS AND LIVER OR KIDNEY DAMAGE .......................................................... 78

Frequently Asked Question: Do statins damage liver or kidneys? ..................... 78

ELDERLY AND STATINS .......................................................................................... 80

Frequently Asked Question: Should people over 70 take statins? ...................... 80

IS THERE AN INDUSTRY BIAS IN STATIN PUBLICATIONS? ......................... 82

Why are most studies so positive about statins, and why are there relatively so few published that show problems? Do Medical Journals agree that there is bias in drug-industry funded medical studies? .......................................................... 82
Updated 13 March 2005:

**Frequently Asked Questions about Statin Adverse Effects**

**Introduction**

Statin adverse effects include muscle damage, nerve damage, cognitive damage, memory loss, amnesia, chronic pain, chronic fatigue, and many other problems. Some, like rhabdomyolysis, kidney and liver damage, can be fatal. Others can cause serious disability. Statin users and their families should be aware of the possible adverse effects, so that they can detect them early and discuss them with their doctors.

This FAQ includes references to studies published in medical journals that may help the physician better understand statin adverse effects.

If adverse effects are detected, the patient should request that the doctor report them to the FDA and the NIH-funded Statin Study. This request to the doctor can be made in writing, similar to the example below:

To my physician,

I believe that my symptoms may be due to the adverse effects associated with cholesterol-lowering statin drugs. I need your help to understand the cause of my symptoms, treatment options, and the prognosis for my recovery.

Please review the references below, published medical studies that show similar problems associated with statin drugs. These are made available via the National Institutes of Health (NIH, [http://www.ncbi.nlm.nih.gov/Entrez/](http://www.ncbi.nlm.nih.gov/Entrez/)) library of biomedical journal citations and other major repositories of medical research.

Also, I am respectfully requesting that you file an adverse effects report with the FDA ([http://www.fda.gov/medwatch/how.htm](http://www.fda.gov/medwatch/how.htm)), and that you please send a copy of the report to the to the NIH-funded Statin Study, attention: Dr. Beatrice Golomb, Principal Investigator.

Statin Study website: [http://medicine.ucsd.edu/statin/](http://medicine.ucsd.edu/statin/)
Statin Study contact info: [http://medicine.ucsd.edu/statin/contactinfo.html](http://medicine.ucsd.edu/statin/contactinfo.html)

UCSD STATIN STUDY E-MAIL ADDRESS: statinstudy@ucsd.edu
MAILING ADDRESS: UCSD Statin Study 9500 Gilman Dr. La Jolla, CA 92093-0995
PHONE NUMBER: (858) 558-4950
What are the names of the Statin drugs?

The Cholesterol-lowering Statin Drug Names: Lipitor, Crestor, Mevacor, Pravachol, Zocor, Lescol, and Baycol, aka atorvastatin, rosuvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, and simvastatin; This class of drugs is also known as HMG-CoA Reductase Inhibitors, short for 3-Hydroxy-3-Methyl-Glutaryl Coenzyme A Reductase.

What is the “Statin Study”?

Dr. Beatrice Golomb is doing research for the National Institutes of Health (NIH) into “non-cardiac endpoints” of the statin drugs. In other words, what do statins do besides reducing serum cholesterol? The UCSD Statin Study is conducted at the University of California, San Diego, and it accepts NO INDUSTRY FUNDING. You can, and should, contact the Statin Study with information on any adverse effects. It is to everyone’s benefit that the UCSD Statin Study has the most complete set of information on statin adverse effects in the world. You can email, write, or call:
statinstudy@ucsd.edu
UCSD Statin Study
9500 Gilman Dr.
La Jolla, CA 92093-0995

(858) 558-4950

More information at the website: http://medicine.ucsd.edu/statin/index.htm
Where can I look to find information on research studies of statin drugs?

The National Institutes of Health has a website, http://www.ncbi.nlm.nih.gov/Entrez/ that offers a search engine that is useful in finding the latest studies that have been published in medical journals (over 11,000,000 biomedical journal citations) and other major repositories of medical research. Each study usually comes with an Abstract, or summary of the findings. In most cases, should you want to see the full text of the study, the full article can be purchased online for approximately $25 to $40, depending on the journal, which is much cheaper than a subscription.

Note that journals publish new studies every month, so revisit the site often. Also, if you find a study that is pertinent to what you are looking for, check the links to the right that will take you to similar studies on the same topic. Finally, if you don’t get a ‘hit’ on what you are looking for, try medical terminology synonyms. Search results are different when using different search terms. So, for example: “statin” or “atorvastatin” or “lipitor” or “reductase inhibitor” or “HMG-CoA”. Similarly, “cholesterol” will return different results from “Dyslipidemia.”

Why does my physician have such a difficult time believing that my physical problems might be an adverse effect of Lipitor or one of the other statins?

Statins are now the most widely prescribed of all prescription drugs, making them very big business. The Wall Street Journal Online, in a June 13, 2003 article, “As Drug Sales Teams Multiply, Doctors Start to Tune them Out; 'Arms Race' by Pfizer and Rivals Boosts Pill Prices, Ire, but No One Dares Retreat”, reported that Pfizer’s sales of Lipitor alone were $8 BILLION for the year 2002. That is just for Lipitor alone, one of FIVE statins on the market today. The article states that in 2002 the drug companies spent over $12 Billion on their sales forces. According to the article, “Last year, a few Pfizer reps brought along a guest speaker who was both a doctor and lawyer to a lunch meeting with doctors at Clinical Associates, a group practice in suburban Baltimore. He said they risked being sued if their patients didn't reach their cholesterol goals”. Doctors are the ones who are primarily targeted by the advertising blitz to make the expectations of increased sales come true. In addition, consumers are marketed with slick commercials and ads. Doctors are very busy, and they are inundated with positive statin spin. They may think that, since everyone is taking it, if there were problems they would have heard about it. They may not take the time to dig out negative information, and there are no major sponsors to fund equal time for negative reports.
Only last year, in 2002, did the Journal of the American Medical Association begin annotating publications with the author’s ties to the company studied, citing potential conflict of interest.

The British Journal of Medicine in their May 31, 2003 issue on the theme “Time to untangle doctors from drug companies”, ran no less than 6 articles saying that too many of the published drug studies are no more than industry-sponsored infomercials, and cited the selective reporting bias whereby only pro-industry studies are published. These articles were entitled: “Research sponsored by drug companies is biased”; ” Drug representatives may increase unnecessary GP prescribing”; ”Reporting of clinical trials of drugs shows bias”; “Characteristics of General Practitioners who Frequently see Drug Industry Representatives: National Cross-Sectional Study ”; “No more free lunches; Patients will benefit from doctors and drug companies disentangling”; “Information from drug companies and opinion leaders; Double standards in information for medical journals and practitioners should go” http://bmj.com/content/vol326/issue7400/

The Canadian CBC News ran a series of consumer articles on March 25, 2003, on the prevalent problem of medical ghostwriting. In this scheme, drug companies write a study favorable to their product and then “reward” a doctor who prescribes the drug by listing his name as the “author” in the publication. http://www.cbc.ca/consumers/market/files/health/ghostwriting/links.html

Your physician should look into your physical adverse effects, regardless of suspected cause. Do not permit your physician to put you off when you express a concern. Too many people are reporting long-term, perhaps permanent, damage when statin therapy is continued despite the appearance of adverse effects. With rhabdomyolysis, death can result. With other side effects, disability can result.

Oddly, people consistently report doctors who are dubious of reported problems being due to statins, even when the problem is listed by the manufacturer on the Physicians’ Information page for the drug. It may help, if you identify your problems with the findings of a published study, to print out a copy and bring it with you to the doctor’s appointment. In some cases, the doctor may simply be terrified of a malpractice charge.

That is one of the purposes for this FAQ – to give people an additional tool to help them to communicate with their doctors.

Note: These articles documenting or speculating on adverse effects of statins are in the vast minority. Hundreds, even thousands, of articles and research have praised statins. Certainly the people with side effects are in the minority, and the benefits are fantastic. Still, the doctors who do attempt to publish about problems associated with statins are often very bitter: they feel they are up against a tremendous political bias and going against an incredibly powerful industry. Med Journal editors tend to insist that all negative findings be couched in terms of how, overall, the statins are doing tremendous good, and the major studies finding problems with statins have been the subject of a pro- statin editorial in the same journal. Further, the popular press is extremely reluctant to
cover negative research findings for the companies who are among their heaviest advertisers.

**OK, I understand the doctor’s need to read clinical study results, but where can I find out what other people are experiencing in plain language, and maybe share my experiences?**

Yahoo Groups has a “Stopped_Our_Statins” group:
http://health.groups.yahoo.com/group/Stopped_Our_Statins/messages

The International Network of Cholesterol Skeptics is a doctors’ discussion group that is open for viewing at:
http://www.thincs.org/

The Dispace statin boards were an excellent source, but were damaged by internet vandalism, and may or may not return. The URLs were:

AARP ran an article on statin drugs and asked for responses, these posts start at:
http://community.aarp.org/n/mb/message.asp?webtag=rp-health&msg=743.1
(At the bottom of the page, you can click to the next post)

Another board:
http://www.rxlist.com/rxboard/lipitor.pl
http://www.rxlist.com/rxboard/lescol.pl
http://www.rxlist.com/rxboard/mevacor.pl
http://www.rxlist.com/rxboard/pravachol.pl
http://www.rxlist.com/rxboard/zocor.pl

WebMD has a roundtable on Cholesterol:
http://boards.webmd.com/roundtable_topic/1121

Also, there is a newsgroup (access via your email program):
sci.med.cardiology

**Are there any books on the topic?**

Dr. Graveline, retired family MD, USAF Flight Surgeon, researcher in space medicine and US Astronaut, who suffered adverse effects from Lipitor, maintains several websites
and has written an excellent book about statin-related memory loss and amnesia, “Lipitor, Thief of Memory”, available through Amazon.com and elsewhere, with more info available at:
www.spacedoc.net (you can start here and read about his life and his books)
http://www.spacedoc.net/lipitor_thief_of_memory.html
http://www.spacedoc.net/lipitor.htm
http://www.spacedoc.net/statin_dialogues.htm

See:
http://www.spacedoc.net/statin_side_effects.html

What are the Lipitor warnings and side-effects listed by the manufacturer on the physicians’ information?

For a full introduction to the list, view http://www.lipitor.com/pi/default.asp. Summary of some of the items on the website includes Warnings of liver dysfunction, and skeletal muscle rhabdomyolysis for the physicians information updated as of July 2004.

What are the Lipitor Adverse Events in Placebo-Controlled Studies listed by Pfizer in the Physician’s information?

For a full introduction to the list, view http://www.lipitor.com/pi/default.asp, the information below is from the version updated as of April 2002:
Body as a whole: Infection, Headache, Accidental Injury, Flu Syndrome, Abdominal Pain, Back Pain, Allergic Reaction, Asthenia;
Digestive system: Constipation, Diarrhea, Dyspepsia, Flatulence;
Respiratory system: Sinusitis, Pharyngitis;
Skin and Appendages: Rash;
Musculoskeletal system: Arthralgia, Myalgia.

What are the Lipitor Averse Events reported in patients treated with Lipitor in clinical trials listed by Pfizer in the Physician’s information?

For a full introduction to the list, view http://www.lipitor.com/pi/default.asp, the information below is from the version updated as of April 2002:
Body as a Whole: Chest pain, face edema, fever, neck rigidity, malaise, photosensitivity reaction, generalized edema.
Digestive System: Nausea, gastroenteritis, liver function tests abnormal, colitis, vomiting, gastritis, dry mouth, rectal hemorrhage, esophagitis, eructation, glossitis, mouth ulceration, anorexia, increased appetite, stomatitis, biliary pain, cheilitis, duodenal ulcer,
dysphagia, enteritis, melena, gum hemorrhage, stomach ulcer, tenesmus, ulcerative stomatitis, hepatitis, pancreatitis, cholestatic jaundice.

Respiratory System: Bronchitis, rhinitis, pneumonia, dyspnea, asthma, epistaxis.

Nervous System: Insomnia, dizziness, paresthesia, somnolence, amnesia, abnormal dreams, libido decreased, emotional lability, incoordination, peripheral neuropathy, torticollis, facial paralysis, hyperkinesia, depression, hypesthesia, hypertonia.

Musculoskeletal System: Arthritis, leg cramps, bursitis, tenosynovitis, myasthenia, tendinous contracture, myositis.

Skin and Appendages: Pruritus, contact dermatitis, alopecia, dry skin, sweating, acne, urticaria, eczema, seborrhea, skin ulcer.

Urogenital System: Urinary tract infection, urinary frequency, cystitis, hematuria, impotence, dysuria, kidney calculus, nocturia, epididymitis, fibrocystic breast, vaginal hemorrhage, albuminuria, breast enlargement, metrorrhagia, nephritis, urinary incontinence, urinary retention, urinary urgency, abnormal ejaculation, uterine hemorrhage.

Special Senses: Amblyopia, tinnitus, dry eyes, refraction disorder, eye hemorrhage, deafness, glaucoma, parosmia, taste loss, taste perversion.

Cardiovascular System: Palpitation, vasodilatation, syncope, migraine, postural hypotension, phlebitis, arrhythmia, angina pectoris, hypertension.

Metabolic and Nutritional Disorders: Peripheral edema, hyperglycemia, creatine phosphokinase increased, gout, weight gain, hypoglycemia.

Hemic and Lymphatic System: Ecchymosis, anemia, lymphadenopathy, thrombocytopenia, petechia.

What are the Lipitor Adverse events associated with Lipitor therapy reported since market introduction, that are not listed above, listed by Pfizer in the Physician’s information?

For a full introduction to the list, view http://www.lipitor.com/pi/default.asp It includes the following: anaphylaxis, angioneurotic edema, bullous rashes (including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), and rhabdomyolysis.

REPORTING ADVERSE EFFECTS FROM STATINS

Where should I report adverse effects from statins?

Report to the FDA
http://www.fda.gov/medwatch/how.htm

Report to the Statin Study
Also, it is important to report side-effects to the Statin Study, funded by the National Institutes of Health and conducted at the University of California, San Diego.
OK, what should I take to my doctor?

The citations below are grouped by different categories of damage. You can take the entire list, but it may be better to select those areas that describe the adverse effects you are concerned with. You would do well, however, to look at all of them, as people frequently have other concerns they thought were unrelated until viewing the list of adverse effects.

NERVE DAMAGE & STATINS

Frequently Asked Question: What medical research studies have been done on Statins and Nerve Damage that I can bring to my doctor’s attention?

Golomb BA, Yang E, Denenberg J, Criqui M (2003), Statin-associated adverse events. P95. Presented at the 43rd Annual Conference on Cardiovascular Disease Epidemiology and Prevention. Miami; March 5-8.


“Based on epidemiologic studies as well as case reports, a risk of peripheral neuropathy associated with statin use may exist; however, the risk appears to be minimal. On the other hand, the benefits of statins are firmly established. These findings should alert prescribers to a potential risk of peripheral neuropathy in patients receiving any of the statins; that is, statins should be considered the cause of peripheral neuropathy when other etiologies have been excluded.”

Rajabally YA, Varakantam V, Abbott RJ.
Disorder resembling Guillain-Barre syndrome on initiation of statin therapy.
PMID: 15389662 [PubMed - indexed for MEDLINE]
“We report a disorder resembling Guillain-Barre syndrome, occurring on initiation of simvastatin, in a 58-year-old man, who had experienced a similar but milder episode after starting pravastatin 6 months earlier. This case suggests that acute polyradiculoneuropathy may represent a rare but serious side-effect of statin treatment. It also raises the issue of the pathophysiology of acute neuropathy on statin exposure, with a hypersensitivity reaction resulting in an immune-mediated process being possible instead of the hypothesized mitochondrial dysfunction in chronic cases.”

Scola RH, Trentin AP, Germiniani FM, Piovesan EJ, Werneck LC.
Simvastatin-induced mononeuropathy multiplex: case report.
PMID: 15273860 [PubMed - in process]
“The association between the use of statins and neuromuscular disease is currently being intensely discussed. We relate a 63 years old man with possible case of statin-induced neuropathy in a patient with dislipidemia in use of simvastatin at high doses. The electrophysiologic studies disclosed findings compatible with mononeuropathy multiplex, suggested by clinical prescutation of asymmetrical numbness and weakness. More common causes of mononeuropathy multiplex were excluded and the patient improved after the discontinuation of the drug.”

Statins and risk of polyneuropathy, A case-control study
D. Gaist, MD, PhD; U. Jeppesen, MD, PhD; M. Andersen, MD, PhD; L.A. García Rodríguez, MD, MSc; J. Hallas, MD, PhD; and S.H. Sindrup, MD, PhD
http://213.4.18.135/135/87.pdf full text
From the abstract: “The authors verified a diagnosis of idiopathic polyneuropathy in 166 cases. The cases were classified as definite (35), probable (54), or possible (77). The odds ratio linking idiopathic polyneuropathy with statin use was 3.7 (95% CI 1.8 to 7.6) for all cases and 14.2 (5.3 to 38.0) for definite cases. The corresponding odds ratios in current users were 4.6 (2.1 to 10.0) for all cases and 16.1 (5.7 to 45.4) for definite cases. For patients treated with statins for 2 or more years the odds ratio of definite idiopathic polyneuropathy was 26.4 (7.8 to 45.4). CONCLUSIONS: Long-term exposure to statins may substantially increase the risk of polyneuropathy.”

Are users of lipid-lowering drugs at increased risk of peripheral neuropathy?
David Gaist, Luis Alberto García Rodríguez • Consuelo Huerta • Jesper Hallas • Søren H. Sindrup
http://213.4.18.135/135/75.pdf full text
Pharmacodynamics: Statins and peripheral neuropathy
U. Jeppesen (2), D. Gaist (1)(2), T. Smith (1), S. H. Sindrup (1)(2)
(1) Department of Neurology, Odense University Hospital, DK-5000 Odense C, Denmark
Tel.: +45-6541-2474, Fax: +45-6541-3389
(2) Department of Clinical Pharmacology Odense University, Odense, Denmark
Received: 6 July 1998 / Accepted in revised form: 1 October 1998
http://link.springer-ny.com/link/service/journals/00228/bibs/9054011/90540835.htm

Association of HMG-CoA reductase inhibitors with neuropathy.
Backes JM, Howard PA.
Department of Pharmacy Practice and Lipid, Atherosclerosis, Metabolic and LDL-Apheresis Clinic, University of Kansas Medical Center, Kansas City, KS 66160-7231, USA. jbackes@kumc.edu
“Epidemiologic studies and case reports suggest an increased risk of peripheral neuropathy with statin drugs… The majority of cases were at least partially reversible with drug cessation.” (emphasis added)

Moosmann B, Behl C.
Selenoprotein synthesis and side-effects of statins.
PMID: 15031036 [PubMed - indexed for MEDLINE]
“We noted that the pattern of side-effects associated with statins resembles the pathology of selenium deficiency, and postulated that the mechanism lay in a well established, but often overlooked, biochemical pathway—the isopentenylation of selenocysteine-tRNA([Ser]Sec). A negative effect of statins on selenoprotein synthesis does seem to explain many of the enigmatic effects and side-effects of statins, in particular, statin-induced myopathy.”

Statin therapy and small fibre neuropathy: a serial electrophysiological study.
Lo YL, Leoh TH, Loh LM, Tan CE.
Department of Neurology, Singapore General Hospital, Outram Road, Singapore.
gnryl@sgh.com.sg
Describes 3 patients who developed neuropathy after ONE MONTH of statin therapy. “One patient redeveloped small and large fibre neuropathy when the similar drug was readministered.”

Peripheral Neuropathy and Lipid-Lowering Therapy
Paul E. Ziajka, MD, PhD, and Tammy Wehmeier, RN, Orlando, Fla.
Abstract: We report a case of peripheral neuropathy induced and exacerbated by several commonly used HMG-CoA reductase inhibitors including lovastatin, simvastatin, pravastatin, and atorvastatin, and the vitamin niacin. A review of the literature shows similar cases with individual lipid-lowering drugs, but this case shows the cross-reactivity of the neuropathic process to different HMG-CoA reductase inhibitors, and is the first reported case of a peripheral neuropathy exacerbated by the use of niacin.

Phan T, McLeod JG, Pollard JD, Peiris O, Rohan A, Halpern JP.
Peripheral neuropathy associated with simvastatin.
PMID: 7745415 [PubMed - indexed for MEDLINE]

Ahmad S.
Lovastatin and peripheral neuropathy.
PMID: 7484806 [PubMed - indexed for MEDLINE]

Jacobs MB.
HMG-CoA reductase inhibitor therapy and peripheral neuropathy.
PMID: 8172444 [PubMed - indexed for MEDLINE]

Medication-induced peripheral neuropathy.
Weimer LH.
Neurological Institute of New York, 710 West 168th Street, Unit 55, New York, NY 10032, USA. Lhw1@columbia.edu
PMID: 12507417 [PubMed - indexed for MEDLINE]
“Although most cases demonstrate acute or subacute onset after exposure, recent experiences with statin drugs raise the possibility of occult toxic causes of chronic idiopathic neuropathy.”

Of interest:


General background medical Info from

Neuromuscular Disease Center
Washington University School of Medicine, St. Louis, MO

Under Disorders & Syndromes:
Select:
Myopathy: http://www.neuro.wustl.edu/neuromuscular/maltbrain.html
Neuropathy: http://www.neuro.wustl.edu/neuromuscular/naltbrain.html
Neuromuscular: http://www.neuro.wustl.edu/neuromuscular/syaltbrain.html
CNS (Central Nervous System):
http://www.neuro.wustl.edu/neuromuscular/syaltbrain.html#cns

Specifics,
MYOGLOBINURIA – Rhabdomyolysis
http://www.neuro.wustl.edu/neuromuscular/msys/myoglob.html
Then see Lipid Lowering Agent Myopathies
http://www.neuro.wustl.edu/neuromuscular/msys/myoglob.html#lipid
Note that this connects to CARDIAC + MYOPATHY
http://www.neuro.wustl.edu/neuromuscular/msys/cardiac.html
And to TOXIC NEUROPATHIES:
http://www.neuro.wustl.edu/neuromuscular/nother/toxic.htm#statin
OR Locally supplied Search on “Statin” leads to:
TOXIC MYOPATHIES
http://www.neuro.wustl.edu/neuromuscular/mother/myotox.htm

Note also that under Mitochondrial Disorders, the list of problems associated with Coenzyme Q10 Deficiency
http://www.neuro.wustl.edu/neuromuscular/msys/myoglob.html#coq10

MITOCHONDRIAL MYOPATHIES
Facts About Mitochondrial Myopathies from the Muscular Dystrophy Association
MEMORY LOSS & STATINS

Frequently Asked Question: What medical research studies have been done on Statins and Memory Loss, or other mental problems that I can bring to my doctor’s attention?

(Statins: Lipitor, Mevacor, Pravachol, Zocor, Lescol, and Baycol, aka atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, and simvastatin; Nerve Damage: Neuropathy, peripheral neuropathy, polyneuropathy; See separate FAQ for memory loss, cognitive damage, amnesia and aphasia, i.e., central nervous system (CNS) damage)

**Randomized trial of the effects of simvastatin on cognitive functioning in hypercholesterolemic adults.**
Muldoon MF, Ryan CM, Sereika SM, Flory JD, Manuck SB.
Center for Clinical Pharmacology, University of Pittsburgh, Pennsylvania 15260, USA. mfm10@pitt.edu
“This study provides partial support for minor decrements in cognitive functioning with statins. Whether such effects have any long-term sequelae or occur with other cholesterol-lowering interventions is not known.” This is the second of two studies by Muldoon, both showing measurable cognitive decline in statin groups after only 6 months, using Neuropsych testing. Further, the cognitive deficits appear consistently in specific areas.


Golomb BA, Yang E, Denenberg J, Criqui M (2003),
**Statin-associated adverse events.** P95. Presented at the 43rd Annual Conference on Cardiovascular Disease Epidemiology and Prevention. Miami; March 5-8.

Muldoon MF, Ryan CM, Flory JD, Manuck SB (2002),
**Effects of simvastatin on cognitive functioning.**
Presented at the American Heart Association Scientific Sessions. Chicago; Nov. 17-20.

Muldoon MF, Barger SD, Ryan CM, Flory JD, Lehoczky JP, Matthews KA, Manuck SB.
**Effects of lovastatin on cognitive function and psychological well-being.**
After 6 months, 100% of the patients on placebos showed a measurable increase in cognitive function, and 100% of the statin patients showed a measurable decrease in cognitive function.
Cognitive impairment associated with atorvastatin and simvastatin.
King DS, Wilburn AJ, Wofford MR, Harrell TK, Lindley BJ, Jones DW.
Department of Medicine, University of Mississippi Medical Center, Jackson, Mississippi 39216, USA. dking@pharmacy.umsmed.edu
“we report two women who experienced significant cognitive impairment temporally related to statin therapy. One woman took atorvastatin, and the other first took atorvastatin, then was rechallenged with simvastatin. Clinicians should be aware of cognitive impairment and dementia as potential adverse effects associated with statin therapy.”  PMID: 14695047

Cognitive impairment associated with atorvastatin.
King DS, Jones DW, Wofford MR et al. (2001), Presented at the American College of Clinical Pharmacy Spring Practice and Research Forum. Salt Lake City; April 22-25.

Australian Adverse Drug Reactions Bulletin (Australia’s equivalent to the FDA)
Volume 17, Number 3, August 1998, section 3, page 3
Simvastatin is listed under “DRUGS THAT MAKE YOU FORGET” Recognizing the 14 reports of Amnesia under that drug, .8% of the total adverse effects for that drug.

Statin-associated memory loss: analysis of 60 case reports and review of the literature.
Wagstaff LR, Mitton MW, Arvik BM, Doraiswamy PM.

This study searched the MedWatch drug surveillance system of the Food and Drug Administration (FDA) from November 1997-February 2002 for reports of statin-associated memory loss. They also reviewed the published literature. References from the study are good for follow-up research.
Abstract:

Full Study Text free on Medscape:
The Role of Lipid-Lowering Drugs in Cognitive Function: A Meta-Analysis of Observational Studies
from Pharmacotherapy
Posted 06/30/2003
Mahyar Etminan, Pharm.D., Sudeep Gill, M.D., FRCPC, Ali Samii, M.D., FRCPC

Although this study does bring the cognitive issues to light, it is a very poor study. The authors left out the pivotal study by Dr. Muldoon, that showed nearly 100% of statin users had a measurable loss of cognitive ability after 6 months, while 100% of the placebo group improved their scores.

Abstract:
Full Study Text free on Medscape:

Simvastatin-Associated Memory Loss
Amanda Orsi, Pharm.D., Olga Sherman, Pharm.D., and Zegga Woldeselassie, Pharm.D.,

Abstract: The statins are widely used to treat dyslipidemias. They are generally associated with mild adverse effects, but rarely, more serious reactions may occur. A 51-year-old man experienced delayed-onset, progressive memory loss while receiving simvastatin for hypercholesterolemia. His therapy was switched to pravastatin, and memory loss resolved gradually over the next month, with no recurrence of the adverse effect.

from Pharmacotherapy
Posted 06/01/2001
Page 1 of 3:
CajAh5clptzOAHJSZuNBobSwWmi9veWjdJ2A3%7C-
1468812056489609316/184161392/6/7001/7001/7002/7002/7001/-1


ADR of the Month
September 2001 Vol. 6 No. 9
EDITORS
Michelle W. McCarthy, Pharm.D.
Anne E. Hendrick, Pharm.D.

University of Virginia Health System
Department of Pharmacy Services
Drug Information Center
The Tablet, a general member benefit published by the British Columbia Pharmacy Association, September 2001, Volume 10 no 8.

Excerpt:

**Do HMG-CoA reductase inhibitors impair memory?** After taking simvastatin for a year, a 51-year-old patient developed short term memory loss, to the extent of being unable to complete his sentences because he would forget what he was going to say. The drug was discontinued, replaced by pravastatin, and within one month his memory returned.14 In a separate case, a 67-year-old woman developed impaired short-term memory, altered mood, social impairment, cognitive impairment and dementia after one year of atorvastatin therapy. When atorvastatin was discontinued, her memory, mood and cognition improved completely.15 Memory impairment in a patient receiving atorvastatin has been reported to the BC Regional ADR Centre.

REFERENCES:


See page 11 of 16:

See also:

**Statins and risk of polyneuropathy, A case-control study**
D. Gaist, MD, PhD; U. Jeppesen, MD, PhD; M. Andersen, MD, PhD; L.A. Garcia Rodriguez, MD, MSc;
J. Hallas, MD, PhD; and S.H. Sindrup, MD, PhD
http://213.4.18.135/87.pdf full text

**Preclinical safety evaluation of cerivastatin, a novel HMG-CoA reductase inhibitor.**
von Keutz E, Schluter G.
Institute of Toxicology, PH-Product Development, Bayer AG, Wuppertal, Germany
Am J Cardiol. 1998 Aug 27;82(4B):11J-17J.
PMID: 9737641
“In dogs, the species most sensitive to statins, cerivastatin caused erosions and hemorrhages in the gastrointestinal tract, bleeding in the brain stem with fibroid degeneration of vessel walls in the choroid plexus, and lens opacity.”
Subchronic toxicity of atorvastatin, a hydroxymethylglutaryl-coenzyme A reductase inhibitor, in beagle dogs.


Walsh KM, Albassam MA, Clarke DE.
Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, Michigan 48105, USA.

“The toxicity of atorvastatin (AT), an inhibitor of hydroxymethylglutaryl-coenzyme A reductase (HMG), was evaluated in beagle dogs… hemorrhage in gallbladder and brain, demyelination of optic nerve, and skeletal muscle necrosis”

Finally, on memory loss and statins: Sworn testimony from the Baycol trial in Corpus Christi, Texas. From the transcript of the AM Session on 03-05-03, in the case Hollis Haltom Vs. Bayer Corporation. Testifying under oath, in response to the plaintiff’s attorney’s question, “What is your current position at Bayer?”, LAWRENCE POSNER, M.D of BAYER stated: “I'm the -- currently I'm the head of worldwide regulatory affairs for our prescription drug business, which means I have responsibility in somewhere between 60 and 100 countries where we sell products for registrations, compliance, things of that nature.” Excerpts from the trial transcript follow, with the Q indicating counsel’s Question, and the A indicating Dr. Posner’s Answer:

Q. So there are some concerns addressed here back in 1995 about testing up to .8. And do you know what the nature of the concern was?
A. Yes. It was related to a side effect that occurred in the brain.
Q. Of what kind of animal?
A. It occurred in the brain of dogs.
Q. Okay. So there was a side effect that occurred in dogs, and then there was a concern about whether you wanted to go forward and test at this higher dose level in human beings, given what you had learned about the dogs, right?
A. That's correct.
Q. Okay. Now, did you just say, well, let's forget about these concerns and we'll go ahead and put .8 on the market anyway, or did you do some further analysis that was not mentioned the other day?
A. Yes. The authors of this had -- they had two concerns. One concern was the toxicity that they found in the brain of dogs. But the other was that they had no way to identify this and who might be at risk before it happened. So there was no way to detect that someone was at risk for this side effect.

[skip some testimony on other topics]

Q. Do you remember in one kind of animal there had been some studies done that there could be a particular kind of problem with one kind of animal?
A. Oh, yeah. Yes, from the -- that's correct, from the toxicology studies.
Q. Okay. And were you able to demonstrate to your own satisfaction, to SmithKline's satisfaction, to the FDA's satisfaction, that that particular problem that showed up with that kind of animal is not something that happens in human beings?
A. Yes. We did it -- we did it by explaining the toxicology data. We also explained it on the basis of kinetic data. That actually at the higher levels of drug, what happens is a
certain amount of drug is bound to proteins in the body that circulate; and therefore, is not -- cannot cause side effects. And actually, a much smaller proportion of the drug is free. And that what you corrected for that, you actually found out that the margins of safety were in fact greater than you would predict just from the animal data.

Q. And as you move forward then and got approval and sold Baycol from 1997 through 2001, did that problem that had shown up with that one kind of animal ever become a problem with human beings?

A. It was actually shown with other statins as well. It wasn't unique to cerivastatin. It was a problem -- it was identified early on with lovastatin and some of the others. In fact, for none of the statins did it ever predict for any clinical problem or toxicity.

Q. So these animals would have that same problem regardless of which statin -- or at least with other statins?

A. Certainly with lovastatin it was true.

Q. But when it came time to human beings, that just wasn't something that happened to human beings?

A. And I think today no one pays much attention to it.

---

**AMNESIA & STATINS**

**Frequently Asked Question:** Amnesia is one of the Lipitor side effects reported by Pfizer on the Physician’s Information, where can I find out more about people who have had amnesia episodes while taking the drug?

**Lipitor, Thief of Memory, by Duane Graveline M.D.**

Dr. Graveline, retired family MD, USAF Flight Surgeon, researcher in space medicine and US Astronaut, who suffered adverse effects from Lipitor, maintains several websites and is working on a second book about statin adverse effects, including statin-related memory loss and amnesia at:

www.spacedoc.net (you can start here and read about his life and his books)

http://www.spacedoc.net/lipitor_thief_of_memory.html

http://www.spacedoc.net/lipitor.htm

http://www.spacedoc.net/statin_dialogues.htm

**Australian Adverse Drug Reactions Bulletin** (Australia’s equivalent to the FDA)

Volume 17, Number 3, August 1998, section 3, page 3

Simvastatin is listed under “DRUGS THAT MAKE YOU FORGET”

Recognizing the 14 reports of Amnesia under that drug, .8% of the total adverse effects for that drug.

CHEST PAIN & STATINS

Frequently Asked Question: Chest pain, that my cardiologist cannot explain via angiogram, stress test, EEG or EKG, is one of the side-effects I see is reported by many people. Is there any information on chest pain associated with statins?

Naturally, chest pain should be first evaluated by a cardiologist. If the usual explanations for chest pain do not apply to you, and you believe that statin adverse-effect may be the cause, here are some articles that may give you some background, or may be useful to give to your doctor. Some are specific to statins and cardiomyopathy, some are background on how statins affect CoQ10 production and how a CoQ10 deficiency affects the cells.

Most of these research articles have been found via a search of the National Institutes of Health website http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=&DB=PubMed, a repository for hundreds of medical journals. In most cases, only the abstract is available and the full article must be purchased. Many of the others can be found via a Google or other net search, or were discovered via posts on the Lipitor message boards.

See:
http://www.lipitor.com/pi/default.asp Pfizer's Physician's Info for prescribing Lipitor, includes documented known adverse effects. Note "Body as a Whole: Chest pain," the italics indicate that the incidence was > 2% in original trials.

Phillips PS, Phillips CT, Sullivan MJ, Naviaux RK, Haas RH.
Statin myotoxicity is associated with changes in the cardiopulmonary function.
PMID: 15488882 [PubMed - in process]
Scripps Mercy Clinical Research Center, Scripps Mercy Hospital, Cardiology (Mer 74), Catheterization Laboratories, Scripps Mercy Hospital, 4077 Fifth Avenue, San Diego, CA 92103, USA. phillips.paul@scrippshealth.org
"The mechanism of the muscle toxicity associated with lipid-lowering therapy remains obscure. Pathological and biochemical findings in patients with statin myotoxicity suggest impaired fatty acid oxidation. Exhaled gas analysis can be used to assess substrate utilization including fatty acid oxidation. In order to determine if muscle toxicity due to lipid-lowering therapy might be related to abnormalities in lipid oxidation, exhaled gas analysis was performed in the fasted state on 11 patients subsequent to statin-associated myositis reactions. Results were compared to those of 16 normal controls who were measured both on and off statin therapy. Post-myositis patients showed a depressed anaerobic threshold (AT) (P=0.009) compared to controls while age-adjusted maximal oxygen consumption (VO2max) and ventilatory efficiency (VE/VCO2) were not significantly different. The fasting respiratory exchange ratio (RER) of post-myositis
patients off statins was abnormally increased (P=0.00001) as was their S1-slope (P=0.023). Controls demonstrated a significant increase in their RER while taking statins consistent with decreased lipid oxidation (P <0.00001). These findings suggest that abnormal lipid oxidation in certain patients may predispose them to the myotoxicity caused by lipid-lowering therapies.”

1: Silver MA, Langsjoen PH, Szabo S, Patil H, Zelinger A. 
**Effect of atorvastatin on left ventricular diastolic function and ability of coenzyme Q10 to reverse that dysfunction.**
PMID: 15541254 [PubMed - indexed for MEDLINE]
“This study evaluated left ventricular diastolic function with Doppler echocardiography before and after statin therapy. Statin therapy worsened diastolic parameters in most patients; coenzyme Q(10) supplementation in patients with worsening diastolic function with statin therapy improved parameters of diastolic function.”

2: Silver MA, Langsjoen PH, Szabo S, Patil H, Zelinger A. 
**Statin cardiomyopathy? A potential role for Co-Enzyme Q10 therapy for statin-induced changes in diastolic LV performance: description of a clinical protocol.**
PMID: 14695927 [PubMed - indexed for MEDLINE]
“Lipid-lowering statins are thought to have a favorable safety profile. Statins inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting step of mevalonate synthesis. Mevalonate is the substrate for further synthesis of cholesterol and Co Enzyme Q10 (CoQ10). CoQ10 plays an important role during oxidative phosphorylation in the myocardial cell. Since myocardial diastolic function is a highly ATP dependent, we reasoned that early changes of diastolic function may be an early marker of ventricular dysfunction. METHODS: Patients who are to commence on statin therapy will be enrolled in the trial. Baseline measurements of plasma CoQ10, total cholesterol, LDL, HDL, CoQ10/LDL ratio, peak E, peak A velocities, E/A ratio, deceleration time, isovolumetric relaxation time, color M-mode propagation velocity will be performed and patients will then begin to take Oral atorvastatin (Lipitor, Parke-Davis) 20 mg daily for three to six months. All baseline measurement will be repeated after 3 to 6 months of statin therapy. Those patients demonstrating > 1 measurement of diastolic LV function that worsened during the 3 to 6 months of statin therapy will be supplemented with CoQ10 300 mg. daily for 3 months. A followup echocardiogram and blood CoQ10 level will be measured in patients who received CoQ10 supplementation. RESULTS: Statistical analysis will be performed using the paired t test to compare coenzyme levels and echocardiographic indices at baseline and after treatment and after supplementation.”

3: Langsjoen PH, Langsjoen AM. 
**The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications.**
PMID: 14695925 [PubMed - indexed for MEDLINE]
“The depletion of the essential nutrient CoQ10 by the increasingly popular cholesterol lowering drugs, HMG CoA reductase inhibitors (statins), has grown from a level of concern to one of alarm. With ever higher statin potencies and dosages, and with a steadily shrinking target LDL cholesterol, the prevalence and severity of CoQ10 deficiency is increasing noticeably. An estimated 36 million Americans are now candidates for statin drug therapy. Statin-induced CoQ10 depletion is well documented in animal and human studies with detrimental cardiac consequences in both animal models and human trials. This drug-induced nutrient deficiency is dose related and more notable in settings of pre-existing CoQ10 deficiency such as in the elderly and in heart failure. Statin-induced CoQ10 deficiency is completely preventable with supplemental CoQ10 with no adverse impact on the cholesterol lowering or anti-inflammatory properties of the statin drugs. We are currently in the midst of a congestive heart failure epidemic in the United States, the cause or causes of which are unclear. As physicians, it is our duty to be absolutely certain that we are not inadvertently doing harm to our patients by creating a wide-spread deficiency of a nutrient critically important for normal heart function.”

STATINS & MITOCHONDRIAL CYTOPATHY,
COENZYME Q10 (UBIQUINONE) DEFICIENCY CAUSED BY STATINS

Do statins cause a CoQ10 deficiency?

Study report: http://www.annals.org/issues/v137n7/nts/200210010-00004.html
Dr. Phillips study mentioned in a Wall Street Journal article (This is smooth muscle, not cardiac muscle.) Conclusion "statin therapy may be associated with increased oxidation injury…mild adverse effects of statins that are difficult to assess might be much more prevalent than widely considered"
http://www.impostertrial.com Is Myopathy Part Of Statin Therapy? Dr. Phillips study website, with info for Patient and Physician

Cohen & Gold, Mitochondrial Cytopathy in Adults: What we know so far
http://www.ccjm.org/pdffiles/COHEN701.PDF
(See "Heart" in table page 4, and section on page 7) CoQ10 If statins cause CoQ10 deficiency, and CoQ10 deficiency causes mitochondrial disease, what are the symptoms of mitochondrial disease? Heart pain is one of them.
Oxidation Injury in Patients Receiving HMG-CoA Reductase Inhibitors: Occurrence in Patients without Enzyme Elevation or Myopathy.
see also subsequent related patents: Do a search by patent number at:
http://patft.uspto.gov/netahtml/srchnum.htm

Merck Patent application stating that statins interfere with CoQ10 and that deficiency causes problems. They documented that they knew this about statins in 1989, 10 years before the 100+ deaths by Rhabdomyolysis!

http://sites.huji.ac.il/malaria/maps/ubiquinonemetpath.html

Malaria Parasite Metabolic Pathways Ubiquinone Metabolism
another version:

DEFINITION Ubiquinone biosynthesis - Reference pathway. Diagram of the Ubiquinone (aka CoQ10) metabolic pathway, highlighting exactly where the Statins interrupt it. All of the 17 or so steps have to happen correctly for the body to produce CoQ10, but statins interrupt (or retard) this in step #2.

Introduction to the Citizen’s petition to the FDA:
http://www.vaccinationnews.com/DailyNews/July2002/StatinInduced8.htm by Dr. Peter Langsjoen This is the introduction to the petition. (It is aimed at getting attention, and the wording may be more alarming than necessary.)

To the FDA: "Citizen Petition To Change The Labeling For All Statin Drugs (Mevacor, Lescol, Pravachol, Zocor, Lipitor, And Advicor) Recommending Use Of 100-200mg Per Day Of Supplemental Co-Enzyme Q10 To Reduce The Risk Of Statin-Induced Myopathies (Including Cardiomyopathy And Congestive Heart Failure)," by Dr. Julian Whitaker, MD: http://www.fda.gov/ohrms/dockets/dailys/02/May02/052902/02p-0244-cp00001-01-vol1.pdf or as html: http://216.239.33.100/search?q=cache:4qAiX-YbZLYC:www.fda.gov/ohrms/dockets/dailys/02/May02/052902/02p-0244-cp00001-01-vol1.pdf+Statin-Induced+Cardiomyopathy+Introduction+To+The+Citizen%27s+Petition+On+Statins&hl=en&ie=UTF-8

Statin Depletion of CoQ10 is linked to heart problems.
Exhibit A of FDA Petition: "The clinical use of HMG CoA-reductase inhibitors (statins) and the associated depletion of the essential co-factor coenzyme Q10; a review of pertinent human and animal data." by Dr. Peter Langsjoen MD:
http://www.fda.gov/ohrms/dockets/dailys/02/May02/052902/02p-0244-cp00001-02-Exhibit_A-vol1.pdf
Effect of atorvastatin on left ventricular diastolic function and ability of coenzyme Q10 to reverse that dysfunction.
Silver MA, Langsjoen PH, Szabo S, Patil H, Zelinger A.
Heart Failure Institute, Department of Medicine, Advocate Christ Medical Center, University of Illinois/Christ Cardiovascular Disease Fellowship Program, Oak Lawn, Illinois 60453, USA. marc.silver@advocatehealth.com

"This study evaluated left ventricular diastolic function with Doppler echocardiography before and after statin therapy. Statin therapy worsened diastolic parameters in most patients; coenzyme Q(10) supplementation in patients with worsening diastolic function with statin therapy improved parameters of diastolic function.”

Examples of the heart and other problems associated with statin depletion of CoQ10.

1: Silver MA, Langsjoen PH, Szabo S, Patil H, Zelinger A.
   Effect of atorvastatin on left ventricular diastolic function and ability of coenzyme Q10 to reverse that dysfunction.
   PMID: 15541254 [PubMed - indexed for MEDLINE]

2: Rundek T, Naini A, Sacco R, Coates K, DiMauro S.
   Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke.
   PMID: 15210526 [PubMed - indexed for MEDLINE]

3: Ornato JP.
   Questions & answers. I take a statin to lower my LDL (bad) cholesterol level, but I’ve heard statins inhibit the production of coenzyme Q10 (CoQ10). Should I take a CoQ10 supplement?
   PMID: 15088591 [PubMed - indexed for MEDLINE]

4: Silver MA, Langsjoen PH, Szabo S, Patil H, Zelinger A.
   PMID: 14695927 [PubMed - indexed for MEDLINE]

5: Passi S, Stancato A, Aleo E, Dmitrieva A, Littarru GP.
   Statins lower plasma and lymphocyte ubiquinol/ubiquinone without affecting other antioxidants and PUFA.
6: Langsjoen PH, Langsjoen AM.  
**The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications.**  
PMID: 14695925 [PubMed - indexed for MEDLINE]

7: Pettit FH, Harper RF, Vilaythong J, Chu T, Shive W.  
**Reversal of statin toxicity to human lymphocytes in tissue culture.**  
PMID: 14682607 [PubMed - indexed for MEDLINE]

8: Wolters M, Hahn A.  
**Plasma ubiquinone status and response to six-month supplementation combined with multivitamins in healthy elderly women--results of a randomized, double-blind, placebo-controlled study.**  
PMID: 12847998 [PubMed - indexed for MEDLINE]

9: Hargreaves IP.  
**Ubiquinone: cholesterol's reclusive cousin.**  
PMID: 12803831 [PubMed - indexed for MEDLINE]

10: [No authors listed]  
**Extra co-enzyme Q10 for statin-users?**  
PMID: 11570288 [PubMed - indexed for MEDLINE]

11: Fosslien E.  
**Mitochondrial medicine--molecular pathology of defective oxidative phosphorylation.**  
PMID: 11314862 [PubMed - indexed for MEDLINE]

12: Kaikkonen J, Nyysonen K, Tomasi A, Iannone A, Tuomainen TP, Porkkala-Sarataho E, Salonen JT.  
**Antioxidative efficacy of parallel and combined supplementation with coenzyme Q10 and d-alpha-tocopherol in mildly hypercholesterolemic subjects: a randomized placebo-controlled clinical study.**  
PMID: 10993487 [PubMed - indexed for MEDLINE]

13: Levin WM.
**Statin drugs: a double-edged sword?**
PMID: 9275961 [PubMed - indexed for MEDLINE]

**Lipid-lowering drugs and mitochondrial function: effects of HMG-CoA reductase inhibitors on serum ubiquinone and blood lactate/pyruvate ratio.**
PMID: 8877024 [PubMed - indexed for MEDLINE]

15: Fjelstrup A.
**Statin therapy and heart failure. There is a difference between statins**
PMID: 8079255 [PubMed - indexed for MEDLINE]

16: Carlsen SM, Fougner KJ.
**Statin therapy, Q10 and heart failure. Is there any difference between statins?**
PMID: 8079217 [PubMed - indexed for MEDLINE]

17: Hyams DE, Roylance PJ, Kruger K, Bodd E.
**Do we kill our cardiac patients with statin therapy? Coenzyme Q10, what do we know?**
PMID: 7748252 [PubMed - indexed for MEDLINE]


**Lovastatin decreases coenzyme Q levels in humans.**


http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/C/CellularRespiration.html

**Primer on how cells breathe normally (Note the role of CoQ10, called "Ubiquinone" in "The Respiratory Chain" section.**
Lipid-lowering drugs and risk of myopathy: a population-based follow-up study. Dr. Gaist is in Denmark and studies populations of entire countries for epidemiology information.

Others:


**Statin-associated myopathy.**
Thompson PD, Clarkson P, Karas RH. Preventive Cardiology and Cardiovascular Research, Division of Cardiology, Hartford Hospital, Hartford, Conn 06102, USA. pthomps@harthosp.org
“recent evidence suggests that statins reduce the production of small regulatory proteins that are important for myocyte maintenance”

**Statins and myotoxicity.**
PMID: 12573193 Farmer JA.
Baylor College of Medicine, One Baylor Plaza, Room 525D, Houston, TX 77030, USA. jfarmer@bcm.tmc.edu

**CARNITINE DEFICIENCY CAUSED BY STATINS**

**Can statins cause carnitine deficiency?**

**JOINT PAIN AND STATINS**

**Frequently Asked Question: Can statins have something to do with my joint pain?**

QUITTING STATINS

Frequently Asked Question: Can it be dangerous to just stop taking statins?

One study indicated that there are more coronary events when people stop taking statins (Definitely talk with your doctor on this):
http://www.lipidsonline.org/commentaries/al_abstract.cfm?abs_id=Abs030

STATIN BIRTH DEFECTS

Frequently Asked Question: Is statin intake during pregnancy dangerous for unborn children?

Edison RJ, Muenke M.
Central nervous system and limb anomalies in case reports of first-trimester statin exposure.
PMID: 15071140 [PubMed - indexed for MEDLINE]

VIOLENCE AND LOW CHOLESTEROL

Frequently Asked Questions: Can it be the statins making me so irritable and prone to angry outbursts?

It may be that the angry outbursts are caused by the Low Cholesterol, the result of taking Lipitor or other statins.
Dr. Beatrice Golomb, who is now conducting the NIH funded Statin Study, published 2 articles/studies on the connection between violence and low cholesterol levels.
See:

Golomb BA, Kane T, Dimsdale JA (2004), Severe irritability associated with statin cholesterol-lowering drugs. QJM 97(4):229-235.
**Low cholesterol and violent crime.** Golomb BA, Stattin H, Mednick S. Department of Medicine, University of California, Los Angeles, CA 92093-0995, USA. J Psychiatr Res 2000 Jul-Oct;34(4-5):301-9

and


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**IMMUNE SYSTEM AND STATINS**

*Frequently Asked Question: Can statins depress my immune system?*

It is a tribute to the imaginations of the drug marketers to see how successfully they have put positive “spin” on a very alarming proposition, that statins depress the immune system (or is it just arrogance?). If the known side effect of statins is to depress your immune system, and it is so beneficial to transplant recipients and others with autoimmune disease, what about people with pre-statins 'normal' immune systems? I'm not the only one astonished and disgusted with this, check out Dr. Mercola's comment (scroll down for his response to the article) on http://www.mercola.com/2000/dec/24/statins.htm

Excerpts: "This is an amazing example of positive "spin" put on a very negative result. People with high cholesterol certainly don't need their immune systems suppressed...If suppressing the helper T cells is considered such great benefit then there is a disease going around that does this quite well - AIDS...if the mechanism of action of the drug is not understood, how can the manufacturer or the FDA claim that it is safe"

It sounds like he is talking about this article http://pub.ucsf.edu/today/print.php?news_id=200211062, but actually he is describing the last time the drug companies tried to feed us a myth about how great it is that statins depress immune systems: (available for online purchase from Nature Medicine: http://www.nature.com/dynasearch/app/dynasearch.taf?sp-w=Exact&_action=search&search_fulltext=&sp-p=All&search_volume=&search_startpage=&search_title=&search_author=&search_abstract=statins+as+immunosuppressors&issue_start_month=12&issue_start_year=2000&issue_end_month=01&issue_end_year=2001&pickerCount=You+have+selected+1+journal+to+search.&rolloverMessage=&sp_k=NM

**Atorvastatin suppresses interferon-gamma -induced neopterin formation and tryptophan degradation in human peripheral blood mononuclear cells and in monocytic cell lines.**

Summary: Recent findings indicate that statins also have anti-inflammatory properties and can modulate the immune response...statins inhibit T cell activation within the cellular immune response...atorvastatin directly inhibits IFN-gamma-mediated pathways in monocyctic cells, suggesting that both immunoreactivity of T cells and of monocyte-derived macrophages are down-regulated by this statin.


A novel anti-inflammatory role for simvastatin in inflammatory arthritis.
Leung BP, Sattar N, Crilly A, Prach M, McCarey DW, Payne H, Madhok R, Campbell C, Gracie JA, Liew FY, McInnes IB.
PMID: 12538717 [PubMed - in process]

Immunomodulation: a new role for statins?
Wulf Palinski
SUMMARY: Statins reduce the expression of the class II major histocompatibility complex (MHCII) by arterial cells, leading to a decreased T-cell response. This indicates that statins...

HMG-CoA reductase inhibitors as immunomodulators: potential use in transplant rejection.
Raggatt LJ, Partridge NC.
These findings suggest that statins have the potential to regulate an immune response in vivo and that more investigation is essential in order to explain the opposing clinical data.
PMID: 12381218 [PubMed - in process]

Statins as a newly recognized type of immunomodulator
Brenda Kwak, Flore Mulhaupt, Samir Myit, François Mach
SUMMARY: Inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, or statins, are effective lipid-lowering agents, extensively used in medical practice. Statins have never been shown to...

Could a depressed immune system lead to infection? See:

Statin-induced fibrotic nonspecific interstitial pneumonia.
STATINS AND CANCER

Frequently Asked Question: What are the cancer rates for people on statins?

This new study breakthrough explains one mechanism that would explain why statins are associated with increased incidence of cancer.

Cholesterol is essential for cellular signaling - when the amount of cholesterol within the lipid domains gets too low, ERK becomes overactive. Overactive ERK is associated with multiple cancers:

http://www8.utsouthwestern.edu/utsw/cda/dept37389/files/210108.html

DALLAS - March 3, 2005 - Cholesterol, often stigmatized for its role in heart disease, has long been known to be essential for the health of the fat-laden membranes that surround individual cells. New findings by researchers at UT Southwestern Medical Center highlight a novel role for cholesterol inside the cell itself - anchoring a signaling pathway linked to cell division and cancer.

These findings appear in the March 4 issue of Science and are available online.

"Cell signals have to be tightly controlled," said Dr. Richard G.W. Anderson, chairman of cell biology and senior author of the study. "If the signaling machines do not work, which can happen when the cell doesn't have enough cholesterol, the cell gets the wrong information, and disease results." Researchers discover a good side to cholesterol in controlling cell signals

The cell membrane, which is fluid in nature, contains cholesterol. Dr. Anderson's research focuses on regions of the membrane where cholesterol is enriched. These regions, called lipid domains, are more rigid than the rest of the cell membrane because of cholesterol and play a critical role in organizing signaling machinery at the cell surface. The correct arrangement of signaling modules in these domains is vital for communication inside the cell and is dependent on proper levels of cholesterol.

While studying how cholesterol moves to the membrane to get to lipid domains, Dr. Anderson, who holds the Cecil
H. Green Distinguished Chair in Cellular and Molecular Biology, and colleagues found that cholesterol can work outside the membrane to regulate a key signaling pathway that occurs inside the cell. Through an interaction with a protein called the oxysterol binding protein (OSBP), cholesterol holds together a group of enzymes that deactivates extracellular signal-related kinase (ERK). Overactive ERK is associated with multiple cancers.

When the amount of cholesterol in lipid domains is normal, the OSBP-cholesterol complex keeps the amount of active ERK under control. When cholesterol in the domains gets too low, however, the complex falls apart, leading to abnormally high levels of active ERK.

Dr. Anderson and colleagues noticed that OSBP has binding sites for both cholesterol and the other proteins in the complex. They believe that when cholesterol binds OSBP it changes shape to bind the key enzymes in a way that allows them to work together to control deactivation of ERK. When lipid domain cholesterol gets low, OSBP loses its cholesterol and no longer is able to bind the enzymes that deactivate ERK, keeping it active.

"OSBP appears to work like a cholesterol-regulated scaffolding protein that controls a key signaling pathway," Dr. Anderson said "This work shows a new way that lipids can regulate key signaling pathways and raises the possibility that other lipid regulated signaling scaffolds can malfunction in other diseases."

Other UT Southwestern contributors to the study were Dr. Jian Weng, assistant professor of cell biology, and Dr. Ping-Yuan Wang, postdoctoral researcher in cell biology and lead author.

This work was supported by the National Institutes of Health and the Perot Foundation.

[Photo caption: Dr. Richard G.W. Anderson, chairman of cell biology at UT Southwestern (center), Dr. Ping-Yuan Wang, postdoctoral fellow (left), and Dr. Jian Weng, assistant professor of cell biology, have discovered that cholesterol anchors a signaling pathway linked to cell division and cancer.

**Women and statins** "in women from the age of 50 onward only, low cholesterol was significantly associated with all-cause mortality, showing significant associations with death through cancer, liver diseases, and mental diseases."

Why Eve is not Adam: prospective follow-up in 149650 women and men of cholesterol and other risk factors related to cardiovascular and all-cause mortality.
Ulmer H, Kelleher C, Diem G, Concin H.
Institute of Biostatistics and Documentation, Leopold Franzens University of Innsbruck, Innsbruck, Austria. Hanno.Ulmer@uibk.ac.at

PURPOSE: To assess the impact of sex-specific patterns in cholesterol levels on all-cause and cardiovascular mortality in the Vorarlberg Health Monitoring and Promotion Programme (VHM&PP). METHODS: In this study, 67413 men and 82237 women (aged 20-95 years) underwent 454448 standardized examinations, which included measures of blood pressure, height, weight, and fasting samples for cholesterol, triglycerides, gamma-glutamyl transferase (GGT), and glucose in the 15-year period 1985-1999. Relations between these variables and risk of death were analyzed using two approaches of multivariate analyses (Cox proportional hazard and GEE models). RESULTS: Patterns of cholesterol levels showed marked differences between men and women in relation to age and cause of death. The role of high cholesterol in predicting death from coronary heart disease could be confirmed in men of all ages and in women under the age of 50. In men, across the entire age range, although of borderline significance under the age of 50, and in women from the age of 50 onward only, low cholesterol was significantly associated with all-cause mortality, showing significant associations with death through cancer, liver diseases, and mental diseases. Triglycerides > 200 mg/dl had an effect in women 65 years and older but not in men. CONCLUSIONS: This large-scale population-based study clearly demonstrates the contrasting patterns of cholesterol level in relation to risk, particularly among those less well studied previously, that is, women of all ages and younger people of both sexes. For the first time, we demonstrate that the low cholesterol effect occurs even among younger respondents, contradicting the previous assessments among cohorts of older people that this is a proxy or marker for frailty occurring with age.

PMID: 15006277 [PubMed - indexed for MEDLINE]

Despite the infomercial-type hype in recent press releases under titles like, “Does Lipitor prevent cancer?” (note it is a question, not an assertion), the numbers from recent studies tell the opposite story:

Statin use and the risk of breast cancer.
Beck P, Wysowski DK, Downey W, Butler-Jones D.
The PROSPER Study (PROspective study of pravastatin in the elderly at risk)
[Article in French]
Kulbertus H, Scheen AJ.
Service de Diabetologie, Nutrition et Maladies metaboliques et deMedecine Interne
Generale, CHU Liege.
“New cancers were more frequent amongst pravastatin-treated individuals (+25%;
p = 0.020).”

Major Outcomes in Moderately Hypercholesterolemic, Hypertensive Patients
Randomized to Pravastatin vs Usual Care
The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
(ALLHAT-LLT)
ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group.
The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial.

Deaths by cancer during the ALLHAT study: Pravastatin= 163; Usual Care= 148
6-year rate per 100 Participants: Pravastatin= 4.1; Usual Care= 3.7

ERECTILE DYSFUNCTION (ED) AND STATINS

Frequently Asked Question: Can statins interfere with my sex life?

Do lipid-lowering drugs cause erectile dysfunction? A systematic review.

Rizvi K, Hampson JP, Harvey JN.
University of Wales College of Medicine, Wrexham Academic Unit, Wrexham, UK.

BACKGROUND: Erectile dysfunction (ED) is common although under-reported by patients. Along with the better known causes of ED, drug-induced impotence needs to be considered as a cause of this symptom. Lipid-lowering drugs have been prescribed increasingly. Their relationship to ED is controversial. OBJECTIVES: Our aim was to clarify the relationship between lipid-lowering therapy and ED. A secondary aim was to assess the value of the systematic review procedure in the area of adverse drug reactions. METHODS: A systematic review was carried out using computerized biomedical
databases and Internet sources. Terms denoting ED were linked with terms referring to lipid-lowering drugs. Information was also sought from regulatory agencies. RESULTS: A significant literature was identified, much from obscure sources, which included case reports, review articles, and information from clinical trials and from regulatory agencies. Information from all of these sources identified fibrates as a source of ED. A substantial number of cases of ED associated with statin usage have been reported to regulatory agencies. Case reports and clinical trial evidence supported the suggestion that statins can also cause ED. Some information on possible mechanisms was obtained, but the mechanism remains uncertain. CONCLUSIONS: The systematic review procedure was applied successfully to collect evidence suggesting that both statins and fibrates may cause ED. More numerous reports to regulatory agencies complemented more detailed information from case reports to provide a new perspective on a common area of prescribing.


ERECTILE DYSFUNCTION AND STATIN THERAPY: INTERACTION WITH CARDIOVASCULAR RISK FACTORS AND DRUG THERAPIES
H. Solomon1, J. Man1, Y.P. Samarasinghe2, M.D. Feher2, A.S. Wierzbicki3, G. Jackson1
1Department of Cardiology, St. Thomas' Hospital, 2Beta Cell Diabetes Centre, Chelsea & Westminster Hospital, 3Department of Chemical Pathology, St. Thomas' Hospital, London UK
Erectile dysfunction has been associated with atherosclerotic risk factors and drugs used in their treatment. This study investigated the relationship of erectile function with cardiovascular risk factors and specific drug therapies. International Index of Erectile Function (IIEF) scores measured in 100 men attending cardiovascular risk clinics. Cardiovascular risk factors and drug therapies were assessed prior to initiation and after 6 months of statin therapy. Before statin therapy no correlation was observed between IIEF score and any individual cardiovascular risk factor though better scores were observed in patients on warfarin or angiotensin-II receptor blocker therapy (r=0.42; p <0.001). After 6 months of statin therapy, significant correlations were observed between lower IIEF scores (r=0.62; P<0.001) and age, smoking, diabetes and usage of warfarin or angiotensin-2 type 1 receptor blocker (ARB) therapy. Differences in dose, relative efficacy or relative lipophilicity of statin prescribed showed no correlation with change in IIEF score. This study suggests impotence following statin therapy is likelier in patients with more severe endothelial dysfunction due to established cardiovascular risk factors including age, and smoking and diabetes. This is complicated by adverse interactions between statin therapy and concomitant treatment with warfarin or angiotensin-II type I receptor blockers.
http://www.kenes.com/73eas/program/abstracts/126.doc

Drug Information Center: Information on Statin Drugs
“On March 7, 2002, Colorado HealthSite interviewed Beatrice A. Golomb, MD, PhD, principal investigator of a study on Statin Drugs by the National Institutes of Health. Dr. Golomb noted that the most common problems reported about statin drugs pertain to muscle pain or weakness, fatigue, memory and cognitive problems, sleep problems, and neuropathy. Erectile dysfunction, problems with temperature regulation (feeling hot or cold, or having sweats) are among the other problems reported. “
http://www.coloradohealthsite.org/pharmacology/statins.html

“Question: What are the common complaints of patients who take statins?
Dr. Golomb: The most common problems we hear reported pertain to muscle pain or weakness, fatigue, memory and cognitive problems, sleep problems, and neuropathy. Erectile dysfunction, problems with temperature regulation (feeling hot or cold, or having sweats), are among the other problems reported. ”
http://www.coloradohealthsite.org/topics/interviews/golomb.html

BBC News: Wednesday, 15 March, 2000, 19:02 GMT
**Heart drug impotence warning**
"Statins prevent heart attacks by reducing the levels of dangerous cholesterol in the bloodstream.
However, a small number of men prescribed the life-saving drug have complained that they are unable to achieve an erection."

"Dr John Harvey, from the Wrexham Maelor Hospital in Wales, identified 220 men who appeared to have lost their "virility" after starting to take statins. "
http://news.bbc.co.uk/1/hi/health/678811.stm

Bailey DG, Dresser GK.  
**Interactions between grapefruit juice and cardiovascular drugs.**  
PMID: 15449971 [PubMed - indexed for MEDLINE]

Blumentals WA, Brown RR, Gomez-Caminero A.  
**Antihypertensive treatment and erectile dysfunction in a cohort of type II diabetes patients.**  
PMID: 14562130 [PubMed - indexed for MEDLINE]

**LUPUS-LIKE SYMPTOMS AND STATINS**

**Frequently Asked Question: Can statins cause Lupus symptoms?**
Drug-induced lupus-like syndrome associated with severe autoimmune hepatitis.
Graziadei IW, Obermoser GE, Sepp NT, Erhart KH, Vogel W.
PMID: 12765306 [PubMed - in process]
“Atorvastatin and other members of the statin family are widely used for the treatment of hypercholesterolaemia in order to reduce the risk of atherosclerosis and cardiovascular disease. Atorvastatin-induced adverse events are mostly mild and only a few cases of lupus-like syndrome or severe acute hepatitis have been documented. In this case report we describe a patient who developed an atorvastatin-induced severe autoimmune hepatitis. In addition, this patient presented with a concomitant systemic lupus-like syndrome which has been already described for statins but not in association with severe liver disease. Although the drug was immediately withdrawn the disease persisted and even deteriorated to a fulminant disease with evidence of acute hepatic failure. The patient failed to respond to conventional immunosuppression with corticosteroids and azathioprine. Only the introduction of intense immunosuppressive therapy, as used in solid organ transplantation, led to a complete and sustained recovery of the patient. Interestingly, the patient was HLA DR3- and HLA DR4-positive, which are well-known genetic factors associated with autoimmune diseases. This case is the first report of a drug-induced lupus-like syndrome concomitant with a severe autoimmune hepatitis in a genetically predisposed patient.”

Noel B, Panizzon RG.
Lupus-like syndrome associated with statin therapy.
PMID: 15118389 [PubMed - indexed for MEDLINE]
“Statins are among the most widely prescribed drugs. An increasing number of lupus-like syndrome has recently been reported with these lipid-lowering agents. We describe a new case associated with simvastatin therapy. The presence of anti-dsDNA antibodies in the serum is for the first time reported confirming that statins may also induce a systemic autoimmune reaction. Statin-induced lupus-like syndrome is characterized by the long delay between the beginning of therapy and the skin eruption. Antinuclear antibodies may persist for many months after drug discontinuation. The causal relationship may be therefore difficult to establish, and probably many cases are unrecognized. Early diagnosis may avoid unnecessary immunosuppressive therapy. Copyright 2004 S. Karger AG, Basel”

Lantuejoul S, Brambilla E, Brambilla C, Devouassoux G.
Statin-induced fibrotic nonspecific interstitial pneumonia.
PMID: 11936540 [PubMed - indexed for MEDLINE]
“Statins inhibit the 3-hydroxy-3-methylglutaryl coenzyme A reductase, reduce the serum level of low-density lipoprotein cholesterol, and are extensively prescribed to prevent cardiovascular mortality and morbidity. Few systemic adverse effects, such as pseudopolymyositis, lupus-like syndromes, and anecdotal hypersensitivity pneumonitis,
have been reported. A simvastatin-induced diffuse interstitial pneumonia associated with a nonspecific interstitial pneumonia pattern at histological analysis is reported here. Ultrastructural analysis showed a diffuse cytoplasmic accumulation of intralysosomal lamellar inclusions in type II pneumonocytes, histiocytes and endothelial cells, suggesting a shared pathogenesis with amphiphilic drug-induced toxic lung injury. Because statins are increasingly prescribed, statin-induced interstitial lung disorders may be more frequently observed and early recognition will be required.”

Chazerain P, Hayem G, Hamza S, Best C, Ziza JM. 
**Four cases of tendinopathy in patients on statin therapy.** 
PMID: 11707010 [PubMed - indexed for MEDLINE]  
“During the last decade, statins have been widely prescribed as lipid-lowering drugs. Their overall safety profile is good. The main musculoskeletal side effects have consisted of muscle pain and weakness, peripheral neuropathy, and a few cases of drug-induced lupus. We report the first four cases of tendinopathy in patients receiving statin therapy. There were three men and one woman. The diagnoses were extensor tenosynovitis at the hands (case 1), tenosynovitis of the tibialis anterior tendon (case 2), and Achilles tendinopathy (cases 3 and 4). Two patients were on simvastatin and two on torvastatin. The tendinopathy developed 1 to 2 months after treatment initiation. The outcome was consistently favorable within 1 to 2 months after discontinuation of the drug. Similar cases have been reported to French pharmacovigilance centers. This report of four cases of tendinopathy draws attention to a possible and heretofore unrecognized side effect of a drug class that is becoming increasingly popular. Statins are effective in lowering high cholesterol levels in patients with type IIa or IIb hypercholesterolemia. They have been widely used for the last decade, particularly in the secondary and primary prevention of major coronary events. Statins act by inhibiting the enzyme hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase. Although most patients tolerate statins extremely well, a few experience side effects requiring treatment discontinuation. Reported musculoskeletal side effects include myalgia and a few cases of rhabdomyolysis and polymyositis. Induced lupus and peripheral neuropathy are exceedingly rare.”

**MYOPATHY AND STATINS**

_Frequently Asked Question: Do statins cause muscle damage, muscle pain, myopathy, myositis, and muscle cell death (apoptosis) with or without elevated CK?_

1: Phillips PS. 
**Ezetimibe and statin-associated myopathy.** 
PMID: 15492351 [PubMed - indexed for MEDLINE]
2: Phillips PS, Phillips CT, Sullivan MJ, Naviaux RK, Haas RH.
**Statin myotoxicity is associated with changes in the cardiopulmonary function.**
PMID: 15488882 [PubMed - in process]

**Statin-associated myopathy with normal creatine kinase levels.**
PMID: 12353945 [PubMed - indexed for MEDLINE]

And more:

Search terms “**STATIN + MYOPATHY**”:
1: Koller H, Neuhaus O, Schroeter M, Hartung HP.
[Myopathies under therapy with lipid-lowering agents.]
PMID: 15609055 [PubMed - as supplied by publisher]

2: [No authors listed]
**A warning about one statin at a high dose.**
PMID: 15580669 [PubMed - indexed for MEDLINE]

3: Graham DJ, Staffa JA, Shatin D, Andrade SE, Schech SD, La Grenade L, Gurwitz JH, Chan KA, Goodman MJ, Platt R.
**Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs.**
PMID: 15572716 [PubMed - indexed for MEDLINE]

4: [No authors listed]
**Safety of aggressive statin therapy.**
PMID: 15557874 [PubMed - indexed for MEDLINE]

5: Anfossi G, Massucco P, Bonomo K, Trovati M.
**Prescription of statins to dyslipidemic patients affected by liver diseases: a subtle balance between risks and benefits.**
PMID: 15553600 [PubMed - in process]

6: Hexeberg S, Retterstol K.
**[Hypertriglyceridemia--diagnostics, risk and treatment]**
7: Cheng JW.
Rosuvastatin in the management of hyperlipidemia.
PMID: 15531000 [PubMed - in process]

8: Sniderman AD.
Is there value in liver function test and creatine phosphokinase monitoring with statin use?
Am J Cardiol. 2004 Nov 4;94(9A):30F-34F. Review.
PMID: 15519289 [PubMed - indexed for MEDLINE]

9: Johnson TE, Zhang X, Bleicher KB, Dysart G, Loughlin AF, Schaefer WH, Umbenhauer DR.
Statins induce apoptosis in rat and human myotube cultures by inhibiting protein geranylgeranylation but not ubiquinone.
PMID: 15504460 [PubMed - indexed for MEDLINE]

10: Davidson MH.
Rosuvastatin safety: lessons from the FDA review and post-approval surveillance.
PMID: 15500414 [PubMed - in process]

11: Phillips PS.
Ezetimibe and statin-associated myopathy.
PMID: 15492351 [PubMed - indexed for MEDLINE]

12: Alsheikh-Ali AA, Kuvin JT, Karas RH.
Risk of adverse events with fibrates.
Am J Cardiol. 2004 Oct 1;94(7):935-8.
PMID: 15464682 [PubMed - indexed for MEDLINE]

13: Baker SK, Goodwin S, Sur M, Tarnopolsky MA.
Cytoskeletal myotoxicity from simvastatin and colchicine.
PMID: 15389652 [PubMed - in process]

Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial.
15: Krivosic-Horber R, Depret T, Wagner JM, Maurage CA.  
**Malignant hyperthermia susceptibility revealed by increased serum creatine kinase concentrations during statin treatment.**  
PMID: 15318472 [PubMed - indexed for MEDLINE]

16: Livingstone C, Al Riyami S, Wilkins P, Ferns GA.  
**McArdle's disease diagnosed following statin-induced myositis.**  
PMID: 15298748 [PubMed - in process]

17: Chang JT, Staffa JA, Parks M, Green L.  
**Rhabdomyolysis with HMG-CoA reductase inhibitors and gemfibrozil combination therapy.**  
PMID: 15269925 [PubMed - indexed for MEDLINE]

18: Carvalho AA, Lima UW, Valiente RA.  
**Statin and fibrate associated myopathy: study of eight patients.**  
PMID: 15235728 [PubMed - in process]

**The cerivastatin withdrawal crisis: a "post-mortem" analysis.**  
PMID: 15212862 [PubMed - indexed for MEDLINE]

**[Worsening for using statin in carnitine palmityol transferase deficiency myopathy]**  
PMID: 15202093 [PubMed - indexed for MEDLINE]

21: Takagi A, Shiio Y.  
**[Pravastatin-associated polymyositis, a case report]**  
PMID: 15199734 [PubMed - indexed for MEDLINE]

22: Jamal SM, Eisenberg MJ, Christopoulos S.  
**Rhabdomyolysis associated with hydroxymethylglutaryl-coenzyme A reductase inhibitors.**  
23: Bellosta S, Paoletti R, Corsini A.  
**Safety of statins: focus on clinical pharmacokinetics and drug interactions.**  
PMID: 15198967 [PubMed - indexed for MEDLINE]

*[Statin-induced rhabdomyolysis and renal failure: also with fluvastatine]*  
PMID: 15176926 [PubMed - indexed for MEDLINE]

25: Guyton JR.  
**Extended-release niacin for modifying the lipoprotein profile.**  
PMID: 15163282 [PubMed - indexed for MEDLINE]

26: Takagi S.  
*[Neurological complication due to the drug and the maneuver for the treatment and prevention of cerebrovascular diseases: iatrogenic neurology]*  
PMID: 15152491 [PubMed - indexed for MEDLINE]

27: Shepherd J.  
**A prospective study of pravastatin in the elderly at risk: new hope for older persons.**  
PMID: 15133425 [PubMed - indexed for MEDLINE]

28: Rando LP, Cording SA, Newnham HH.  
**Successful reintroduction of statin therapy after myositis: was there another cause?**  
PMID: 15115429 [PubMed - indexed for MEDLINE]

29: Fux R, Morike K, Gundel UF, Hartmann R, Gleiter CH.  
**Ezetimibe and statin-associated myopathy.**  
PMID: 15096354 [PubMed - indexed for MEDLINE]

30: Roten L, Schoenenberger RA, Krahenbuhl S, Schlienger RG.  
**Rhabdomyolysis in association with simvastatin and amiodarone.**  
PMID: 15069169 [PubMed - indexed for MEDLINE]


39: Jamil S, Iqbal P.
Rhabdomyolysis induced by a single dose of a statin.
PMID: 14676266 [PubMed - indexed for MEDLINE]

40: Riesco-Eizaguirre G, Arpa-Gutierrez FJ, Gutierrez M, Toribio E.
Severe polymyositis with simvastatin use
PMID: 14634922 [PubMed - indexed for MEDLINE]

41: Zeman M, Zak A, Vecka M, Romaniv S.
Long-term hypolipidemic treatment of mixed hyperlipidemia with a combination
of statins and fibrates
PMID: 14626567 [PubMed - indexed for MEDLINE]

42: Wang TD, Chen WJ, Lin JW, Cheng CC, Chen MF, Lee YT.
Efficacy of fenofibrate and simvastatin on endothelial function and
inflammatory markers in patients with combined hyperlipidemia: relations with
baseline lipid profiles.
PMID: 14612213 [PubMed - indexed for MEDLINE]

43: Foody JM, Krumholz HM.
Are statins indicated for the primary prevention of CAD in octogenarians?
antagonist viewpoint.
PMID: 14610384 [PubMed - indexed for MEDLINE]

44: Shammas NW, Kapalis MJ, Deckert J, Harris M, Dippel EJ, Labroo A, McKinney
D.
Effectiveness of statin-gemfibrozil combination therapy in patients with mixed
hyperlipidemia: experience of a community lipid clinic and safety review from
the literature.
Prev Cardiol. 2003 Fall;6(4):189-94.
PMID: 14605512 [PubMed - indexed for MEDLINE]

45: Pasternak R.
Ask the doctor. I am a 64-year-old woman with high cholesterol caused by bad
genes (familial hypercholesterolemia). Without medication, my cholesterol is
above 450 mg/dL. So I am taking high-dose Lipitor (80 mg/day), WelChol, and
Zetia to lower my cholesterol. I sometimes have pain and stiffness in my knees,
and my shoulder, elbow, and wrist joints, plus the muscles in between, are stiff
in the morning and hurt during the day. Two years ago I was diagnosed with
bursitis in my hips. Could these problems be from the Lipitor? If so, is there
another statin I could take that wouldn't do this?
46: Corsini A.  
**The safety of HMG-CoA reductase inhibitors in special populations at high cardiovascular risk.**  
PMID: 14574085 [PubMed - indexed for MEDLINE]

47: Johi RR, Mills R, Halsall PJ, Hopkins PM.  
**Anaesthetic management of coronary artery bypass grafting in a patient with central core disease and susceptibility to malignant hyperthermia on statin therapy.**  
PMID: 14570802 [PubMed - indexed for MEDLINE]

48: Newman CB, Palmer G, Silbershatz H, Szarek M.  
**Safety of atorvastatin derived from analysis of 44 completed trials in 9,416 patients.**  
PMID: 12972104 [PubMed - indexed for MEDLINE]

49: Wolszakiewicz J, Bilinska M, Wolkanin-Bartnik J, Piotrowicz R.  
**[Skeletal myopathy associated with concomitant use of statin and cyclosporin in a heart transplant patient - case report]**  
PMID: 12961006 [PubMed - in process]

50: Luh JY, Karnath BM.  
**Issues in statin-associated myopathy.**  
PMID: 12928463 [PubMed - indexed for MEDLINE]

51: Hyman MH.  
**Issues in statin-associated myopathy.**  
PMID: 12928462 [PubMed - indexed for MEDLINE]

52: Kiortsis DN, Nikas S, Hatzidimou K, Tsianos E, Elisaf MS.  
**Lipid-lowering drugs and serum liver enzymes: the effects of body weight and baseline enzyme levels.**  
PMID: 12914553 [PubMed - indexed for MEDLINE]

53: [No authors listed]  
**Statins: new data in secondary prevention and diabetes. Pravastatin and**
simvastatin are the best-assessed statins.
PMID: 12908497 [PubMed - indexed for MEDLINE]

54: Muller T.
PMID: 12904874 [PubMed - indexed for MEDLINE]

55: Bannwarth B.
Drug-induced myopathies.
PMID: 12904161 [PubMed - indexed for MEDLINE]

56: Davidson MH.
Controversy surrounding the safety of cerivastatin.
PMID: 12904136 [PubMed - indexed for MEDLINE]

57: Jacobson TA.
Combination lipid-lowering therapy with statins: safety issues in the postcerivastatin era.
PMID: 12904106 [PubMed - indexed for MEDLINE]

58: Ito MK.
Advances in the understanding and management of dyslipidemia: using niacin-based therapies.
PMID: 12901026 [PubMed - indexed for MEDLINE]

59: Clotet B, Negredo E.
HIV protease inhibitors and dyslipidemia.
PMID: 12875104 [PubMed - indexed for MEDLINE]

60: Arenas J, Martin MA.
[Metabolic intolerance to exercise]
PMID: 12838448 [PubMed - indexed for MEDLINE]

61: Andrejak M, Gras V, Massy ZA, Caron J.
[Adverse effects of statins]
62: Liem AH, Jukema JW, van Veldhuisen DJ.
Secondary prevention in coronary heart disease patients with low HDL: which options do we have?
PMID: 12821213 [PubMed - indexed for MEDLINE]

63: Teichholz LE.
Statin-associated myopathy with normal creatine kinase levels.
PMID: 12809468 [PubMed - indexed for MEDLINE]

64: Torgovnick J, Arsura E.
Statin-associated myopathy with normal creatine kinase levels.
PMID: 12809467 [PubMed - indexed for MEDLINE]

65: Hyman MH.
Statin-associated myopathy with normal creatine kinase levels.
PMID: 12809466 [PubMed - indexed for MEDLINE]

66: Toma E, Loignon M.
Statin-associated myopathy with normal creatine kinase levels.
PMID: 12809465 [PubMed - indexed for MEDLINE]

67: Ornato JP.
Should you worry about the side effects of statins? Statin dose, health, and other drugs affect side-effect risk.
PMID: 12793395 [PubMed - indexed for MEDLINE]

68: Davidson MH.
Combination lipid-lowering therapy in diabetes.
PMID: 12762976 [PubMed - indexed for MEDLINE]

69: Schmitz G, Drobnik W.
Pharmacogenomics and pharmacogenetics of cholesterol-lowering therapy.
70: Worz CR, Bottorff M.
Treating dyslipidemic patients with lipid-modifying and combination therapies.
PMID: 12741437 [PubMed - indexed for MEDLINE]

71: Bays H, Dujovne C.
Colesevelam HCl: a non-systemic lipid-altering drug.
PMID: 12740000 [PubMed - indexed for MEDLINE]

72: Paragh G, Balogh Z, Romics L.
Antilipemic therapy and rhabdomyolysis
PMID: 12731338 [PubMed - indexed for MEDLINE]

73: Gotto AM Jr.
Risks and benefits of continued aggressive statin therapy.
PMID: 12708633 [PubMed - indexed for MEDLINE]

74: Thompson PD, Clarkson P, Karas RH.
Statin-associated myopathy.
PMID: 12672737 [PubMed - indexed for MEDLINE]

75: Braun RN, Halhuber MJ, Hitzenberger G.
Information regarding adverse drug effects and treatment indications ("package inserts") exemplified by cervistatin (Lipobay)
PMID: 12658968 [PubMed - indexed for MEDLINE]

76: Lee TH.
Ask the doctor. At age 62 I'm a bit overweight and have diabetes. I take a statin, and my LDL cholesterol is good (84 mg/dL). But my HDL is low (30 mg/dL) and my triglycerides are above 300 mg/dL. Are high triglycerides a problem?
PMID: 12654588 [PubMed - indexed for MEDLINE]

77: [No authors listed]
How a statin might destroy a drug company.
PMID: 12642039 [PubMed - indexed for MEDLINE]

78: Smith CC, Bernstein LI, Davis RB, Rind DM, Shmerling RH.
Screening for statin-related toxicity: the yield of transaminase and creatine kinase measurements in a primary care setting.
PMID: 12639201 [PubMed - indexed for MEDLINE]

79: Gotto AM Jr.
Safety and statin therapy: reconsidering the risks and benefits.
PMID: 12639194 [PubMed - indexed for MEDLINE]

Risk for myopathy with statin therapy in high-risk patients.
PMID: 12622602 [PubMed - indexed for MEDLINE]

81: Bennett WE, Drake AJ 3rd, Shakir KM.
Reversible myopathy after statin therapy in patients with normal creatine kinase levels.
PMID: 12614104 [PubMed - indexed for MEDLINE]

82: Farmer JA.
Statins and myotoxicity.
PMID: 12573193 [PubMed - indexed for MEDLINE]

83: Glueck CJ, Streicher P.
Cardiovascular and medical ramifications of treatment of subclinical hypothyroidism.
PMID: 12562546 [PubMed - indexed for MEDLINE]

84: Sinzinger H.
Statin-induced myositis migrans.
PMID: 12528328 [PubMed - indexed for MEDLINE]

85: Yim BT, Chong PH.
Niacin-ER and lovastatin treatment of hypercholesterolemia and mixed dyslipidemia.
PMID: 12503944 [PubMed - indexed for MEDLINE]

Neuromuscular toxicity in nephrotic patients treated with fluvastatin.
PMID: 12495286 [PubMed - indexed for MEDLINE]

87: Black C, Jick H.
Etiology and frequency of rhabdomyolysis.
PMID: 12495162 [PubMed - indexed for MEDLINE]

88: Xydakis AM, Ballantyne CM.
Combination therapy for combined dyslipidemia.
PMID: 12467937 [PubMed - indexed for MEDLINE]

Myopathy due to statin/fibrate use in the Netherlands.
PMID: 12452761 [PubMed - indexed for MEDLINE]

Safety considerations for statins.
PMID: 12441888 [PubMed - indexed for MEDLINE]

91: Prasad GV, Wong T, Meliton G, Bhaloo S.
Rhabdomyolysis due to red yeast rice (Monascus purpureus) in a renal transplant recipient.
PMID: 12438974 [PubMed - indexed for MEDLINE]

92: Kind AH, Zakowski LJ, McBride PE.
Rhabdomyolysis from the combination of a statin and gemfibrozil: an uncommon but serious adverse reaction.
PMID: 12426921 [PubMed - indexed for MEDLINE]

93: Schuff-Werner P, Kohlschein P.
[Current therapy of hypercholesterolemia. How much statin does your patient need?]
PMID: 12422725 [PubMed - indexed for MEDLINE]

94: Hare CB, Vu MP, Grunfeld C, Lampiris HW.
Simvastatin-nelfinavir interaction implicated in rhabdomyolysis and death.


103: Bae J, Jarcho JA, Denton MD, Magee CC.
**Statin specific toxicity in organ transplant recipients: case report and review of the literature.**
PMID: 12113605 [PubMed - indexed for MEDLINE]

104: de Sauvage Nolting PR, Buirma RJ, Hutten BA, Kastelein JJ; Dutch ExPRESS Investigator Group.
**Two-year efficacy and safety of simvastatin 80 mg in familial hypercholesterolemia (the Examination of Probands and Relatives in Statin Studies With Familial Hypercholesterolemia [ExPRESS FH]).**
PMID: 12106856 [PubMed - indexed for MEDLINE]

**Combined treatment with fibrates and small doses of atorvastatin in patients with mixed hyperlipidemia.**
PMID: 12094821 [PubMed - indexed for MEDLINE]

106: Williams D, Feely J.
**Pharmacokinetic-pharmacodynamic drug interactions with HMG-CoA reductase inhibitors.**
PMID: 12036392 [PubMed - indexed for MEDLINE]

107: Sinzinger H.
**Flu-like response on statins.**
PMID: 12011782 [PubMed - indexed for MEDLINE]

108: [No authors listed]
**Statin stories.**
PMID: 11993442 [PubMed - indexed for MEDLINE]

109: Maxa JL, Melton LB, Ogu CC, Sills MN, Limanni A.
**Rhabdomyolysis after concomitant use of cyclosporine, simvastatin, gemfibrozil, and itraconazole.**
PMID: 11978159 [PubMed - indexed for MEDLINE]
110: Foxton J.  
**Statin safety.**  
PMID: 11977679 [PubMed - indexed for MEDLINE]

111: Gensini GF, Conti AA, Conti A, Panti A.  
*[From prevention to cardiovascular rehabilitation: statins and evidence-based medicine]*  
PMID: 11899580 [PubMed - indexed for MEDLINE]

112: Sica DA, Gehr TW.  
**3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors and rhabdomyolysis: considerations in the renal failure patient.**  
PMID: 11856903 [PubMed - indexed for MEDLINE]

113: Omar MA, Wilson JP.  
**FDA adverse event reports on statin-associated rhabdomyolysis.**  
PMID: 11847951 [PubMed - indexed for MEDLINE]

114: Prieto JC.  
*[Safety profile of statins]*  
PMID: 11836874 [PubMed - indexed for MEDLINE]

115: Sica DA, Gehr TW.  
**Rhabdomyolysis and statin therapy: relevance to the elderly.**  
PMID: 11773716 [PubMed - indexed for MEDLINE]

116: Banga JD.  
*[Myotoxicity and rhabdomyolysis due to statins]*  
PMID: 11770264 [PubMed - indexed for MEDLINE]

117: Hamilton-Craig I.  
**Statin-associated myopathy.**  
PMID: 11758079 [PubMed - indexed for MEDLINE]

118: Bernini F, Poli A, Paoletti R.  
**Safety of HMG-CoA reductase inhibitors: focus on atorvastatin.**  
PMID: 11713888 [PubMed - indexed for MEDLINE]
**Four cases of tendinopathy in patients on statin therapy.**  
PMID: 11707010 [PubMed - indexed for MEDLINE]

120: Federman DG, Hussain F, Walters AB.  
**Fatal rhabdomyolysis caused by lipid-lowering therapy.**  
PMID: 11702815 [PubMed - indexed for MEDLINE]

121: Baker SK, Tarnopolsky MA.  
**Statin myopathies: pathophysiologic and clinical perspectives.**  
PMID: 11603510 [PubMed - indexed for MEDLINE]

122: Igel M, Sudhop T, von Bergmann K.  
**Metabolism and drug interactions of 3-hydroxy-3-methylglutaryl coenzyme A-reductase inhibitors (statins).**  
PMID: 11599653 [PubMed - indexed for MEDLINE]

123: Tomlinson B, Chan P, Lan W.  
**How well tolerated are lipid-lowering drugs?**  
PMID: 11599634 [PubMed - indexed for MEDLINE]

124: Bangratz S.  
**[Complications in heart transplantation: diagnosis and treatment]**  
PMID: 11577591 [PubMed - indexed for MEDLINE]

125: Omar MA, Wilson JP, Cox TS.  
**Rhabdomyolysis and HMG-CoA reductase inhibitors.**  
PMID: 11573861 [PubMed - indexed for MEDLINE]

126: Boger RH.  
**Drug interactions of the statins and consequences for drug selection.**  
PMID: 11563683 [PubMed - indexed for MEDLINE]

127: Comarow A.  
**Rest easy, statin users. Benefits dwarf risks for these cholesterol drugs.**  
128: Shek A, Ferrill MJ.
**Statin-fibrate combination therapy.**
PMID: 11485144 [PubMed - indexed for MEDLINE]

129: Lupattelli G, Palumbo B, Sinzinger H.
**Statin induced myopathy does not show up in MIBI scintigraphy.**
PMID: 11388581 [PubMed - indexed for MEDLINE]

130: Fosslien E.
**Mitochondrial medicine--molecular pathology of defective oxidative phosphorylation.**
PMID: 11314862 [PubMed - indexed for MEDLINE]

131: Moghadasian MH, Mancini GB, Frohlich JJ.
**Pharmacotherapy of hypercholesterolaemia: statins in clinical practice.**
PMID: 11249510 [PubMed - indexed for MEDLINE]

**Rhabdomyolysis and acute renal failure after changing statin-fibrate combinations.**
PMID: 11173785 [PubMed - indexed for MEDLINE]

133: Sinzinger H, Lupattelli G, Chehne F.
**Increased lipid peroxidation in a patient with CK-elevation and muscle pain during statin therapy.**
PMID: 11058722 [PubMed - indexed for MEDLINE]

134: Guyton JR.
**Combination drug therapy for combined hyperlipidemia.**
PMID: 10980849 [PubMed - indexed for MEDLINE]

135: Ozdemir O, Boran M, Gokce V, Uzun Y, Kocak B, Korkmaz S.
**A case with severe rhabdomyolysis and renal failure associated with cerivastatin-gemfibrozil combination therapy--a case report.**
PMID: 10959522 [PubMed - indexed for MEDLINE]
136: Gavish D, Leibovitz E, Shapira I, Rubinstein A. 
**Bezafibrate and simvastatin combination therapy for diabetic dyslipidaemia: efficacy and safety.**  
PMID: 10809995 [PubMed - indexed for MEDLINE]

137: Liebhaber MI, Wright RS, Gelberg HJ, Dyer Z, Kupperman JL.  
**Polymyalgia, hypersensitivity pneumonitis and other reactions in patients receiving HMG-CoA reductase inhibitors: a report of ten cases.**  
PMID: 10084510 [PubMed - indexed for MEDLINE]

138: Guyton JR, Capuzzi DM.  
**Treatment of hyperlipidemia with combined niacin-statin regimens.**  
PMID: 9915667 [PubMed - indexed for MEDLINE]

139: Athyros VG, Papageorgiou AA, Hatzikonstandinou HA, Didangelos TP, Carina MV, Kranitsas DF, Kontopoulos AG.  
**Safety and efficacy of long-term statin-fibrate combinations in patients with refractory familial combined hyperlipidemia.**  
PMID: 9294990 [PubMed - indexed for MEDLINE]

140: Tikkanen MJ.  
**Statins: within-group comparisons, statin escape and combination therapy.**  
PMID: 9117143 [PubMed - indexed for MEDLINE]

**Lipid-lowering drugs and mitochondrial function: effects of HMG-CoA reductase inhibitors on serum ubiquinone and blood lactate/pyruvate ratio.**  
PMID: 8877024 [PubMed - indexed for MEDLINE]

142: Reijneveld JC, Koot RW, Bredman JJ, Joles JA, Bar PR.  
**Differential effects of 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors on the development of myopathy in young rats.**  
PMID: 8725265 [PubMed - indexed for MEDLINE]

143: Peters TK.  
**Safety profile of fluvastatin.**  
PMID: 8729586 [PubMed - indexed for MEDLINE]
144: Laaksonen R, Jokelainen K, Sahi T, Tikkanen MJ, Himberg JJ.
Decreases in serum ubiquinone concentrations do not result in reduced levels in muscle tissue during short-term simvastatin treatment in humans.
PMID: 7828383 [PubMed - indexed for MEDLINE]

145: Leitersdorf E, Muratti EN, Eliav O, Meiner V, Eisenberg S, Dann EJ, Sehayek E, Peters TK, Stein Y.
Efficacy and safety of a combination fluvastatin-bezafibrate treatment for familial hypercholesterolemia: comparative analysis with a fluvastatin-cholestyramine combination.
PMID: 8192170 [PubMed - indexed for MEDLINE]

146: Dromer C, Vedrenne C, Billey T, Pages M, Fournie B, Fournie A.
[Rhabdomyolysis due to simvastin. Apropos of a case with review of the literature]
PMID: 1496277 [PubMed - indexed for MEDLINE]

Search terms: STATIN + MYOSITIS

1: [No authors listed]
Safety of aggressive statin therapy.
PMID: 15557874 [PubMed - indexed for MEDLINE]

2: Sniderman AD.
Is there value in liver function test and creatine phosphokinase monitoring with statin use?
Am J Cardiol. 2004 Nov 4;94(9A):30F-34F. Review.
PMID: 15519289 [PubMed - indexed for MEDLINE]

Statin myotoxicity is associated with changes in the cardiopulmonary function.
PMID: 15488882 [PubMed - in process]


4: Livingstone C, Al Riyami S, Wilkins P, Ferns GA.
McArdle's disease diagnosed following statin-induced myositis.
5: Takagi A, Shiio Y.  
**[Pravastatin-associated polymyositis, a case report]**  
PMID: 15199734 [PubMed - indexed for MEDLINE]

6: Bellosta S, Paoletti R, Corsini A.  
**Safety of statins: focus on clinical pharmacokinetics and drug interactions.**  
PMID: 15198967 [PubMed - indexed for MEDLINE]

7: Rando LP, Cording SA, Newnham HH.  
**Successful reintroduction of statin therapy after myositis: was there another cause?**  
PMID: 15115429 [PubMed - indexed for MEDLINE]

**[Polymyositis induced or associated with lipid-lowering drugs: five cases]**  
PMID: 15050796 [PubMed - indexed for MEDLINE]

9: Riesco-Eizaguirre G, Arpa-Gutierrez FJ, Gutierrez M, Toribio E.  
**[Severe polymyositis with simvastatin use]**  
PMID: 14634922 [PubMed - indexed for MEDLINE]

10: Foody JM, Krumholz HM.  
**Are statins indicated for the primary prevention of CAD in octogenarians? antagonist viewpoint.**  
PMID: 14610384 [PubMed - indexed for MEDLINE]

11: Shammas NW, Kapalis MJ, Deckert J, Harris M, Dippel EJ, Labroo A, McKinney D.  
**Effectiveness of statin-gemfibrozil combination therapy in patients with mixed hyperlipidemia: experience of a community lipid clinic and safety review from the literature.**  
Prev Cardiol. 2003 Fall;6(4):189-94.  
PMID: 14605512 [PubMed - indexed for MEDLINE]

12: Badawy O, Wierzbicki AS, Hilton R.  
**Combination fibrate-statin therapy for the treatment of severe**
hypertriglyceridaemia in renal disease.
PMID: 12723736 [PubMed - indexed for MEDLINE]

13: Thompson PD, Clarkson P, Karas RH.
Statin-associated myopathy.
PMID: 12672737 [PubMed - indexed for MEDLINE]

14: Sinzinger H.
Statin-induced myositis migrans.
PMID: 12528328 [PubMed - indexed for MEDLINE]

15: Black C, Jick H.
Etiology and frequency of rhabdomyolysis.
PMID: 12495162 [PubMed - indexed for MEDLINE]

16: Lawrence JM, Reckless JP.
Fluvastatin.
PMID: 12437496 [PubMed - indexed for MEDLINE]

17: Mehra MR, Uber PA, Vivekananathan K, Solis S, Scott RL, Park MH, Milani RV, Lavie CJ.
Comparative beneficial effects of simvastatin and pravastatin on cardiac allograft rejection and survival.
PMID: 12427413 [PubMed - indexed for MEDLINE]

18: Evans M, Rees A.
Effects of HMG-CoA reductase inhibitors on skeletal muscle: are all statins the same?
PMID: 12137559 [PubMed - indexed for MEDLINE]

19: Aronow WS.
Pharmacologic therapy of lipid disorders in the elderly.
PMID: 12091773 [PubMed - indexed for MEDLINE]

20: Patel DN, Pagani FD, Koelling TM, Dyke DB, Baliga RR, Cody RJ, Lake KD, Aaronson KD.
Safety and efficacy of atorvastatin in heart transplant recipients.
PMID: 11834348 [PubMed - indexed for MEDLINE]

Search terms: **STATIN + MYALGIA**

1: Koller H, Neuhaus O, Schroeter M, Hartung HP.  
[Myopathies under therapy with lipid-lowering agents.]  
PMID: 15609055 [PubMed - as supplied by publisher]

2: Rundek T, Naini A, Sacco R, Coates K, DiMauro S.  
**Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke.**  
PMID: 15210526 [PubMed - indexed for MEDLINE]

3: Takagi A, Shiio Y.  
[Pravastatin-associated polymyositis, a case report]  
PMID: 15199734 [PubMed - indexed for MEDLINE]

4: Scott LJ, Curran MP, Figgitt DP.  
**Rosuvastatin: a review of its use in the management of dyslipidemia.**  
PMID: 15049723 [PubMed - indexed for MEDLINE]

5: Newman CB, Palmer G, Silbershatz H, Szarek M.  
**Safety of atorvastatin derived from analysis of 44 completed trials in 9,416 patients.**  
PMID: 12972104 [PubMed - indexed for MEDLINE]

6: Andrejak M, Gras V, Massy ZA, Caron J.  
[Adverse effects of statins]  
PMID: 12822204 [PubMed - indexed for MEDLINE]

7: Thompson PD, Clarkson P, Karas RH.  
**Statin-associated myopathy.**  
PMID: 12672737 [PubMed - indexed for MEDLINE]

8: Athyros VG, Papageorgiou AA, Athyrou VV, Demitriadis DS, Pehlivandiis AN, Kontopoulos AG.  
**Atorvastatin versus four statin-fibrate combinations in patients with familial combined hyperlipidaemia.**  
PMID: 11984215 [PubMed - indexed for MEDLINE]
Tolerability of statin-fibrate and statin-niacin combination therapy in dyslipidemic patients at high risk for cardiovascular events. 
PMID: 11835917 [PubMed - indexed for MEDLINE]

Four cases of tendinopathy in patients on statin therapy. 
PMID: 11707010 [PubMed - indexed for MEDLINE]

11: Penzak SR, Chuck SK, Stajich GV. 
Safety and efficacy of HMG-CoA reductase inhibitors for treatment of hyperlipidemia in patients with HIV infection. 
PMID: 10999499 [PubMed - indexed for MEDLINE]

12: Speiker LE, Noll G, Hannak M, Luscher TF. 
Efficacy and tolerability of fluvastatin and bezafibrate in patients with hyperlipidemia and persistently high triglyceride levels. 
PMID: 10710119 [PubMed - indexed for MEDLINE]

13: Papadakis JA, Ganotakis ES, Jagroop IA, Winder AF, Mikhailidis DP. 
Statin + fibrate combination therapy fluvastatin with bezafibrate or ciprofibrate in high risk patients with vascular disease. 
Int J Cardiol. 1999 Jun 1;69(3):237-44. 
PMID: 10402106 [PubMed - indexed for MEDLINE]

14: Peters TK. 
Safety profile of fluvastatin. 
PMID: 8729586 [PubMed - indexed for MEDLINE]

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PMID: 11707010 [PubMed - indexed for MEDLINE]

PMID: 15613049 [PubMed - in process]

RHABDOMYOLYSIS AND STATINS

Frequently Asked Question: Which statins cause deadly Rhabdomyolysis?

All of them. See:
FDA adverse event reports on statin-associated rhabdomyolysis.
PMID: 11847951
Of 871 reports detailing 601 cases in a 29 month time frame, the list of statin, number of cases, and percentage of the whole follows:
simvastatin, 215 (35.8%);
cerivastatin, 192 (31.9%);
atorvastatin, 73 (12.2%);
pravastatin, 71 (11.8%);
lovastatin, 40 (6.7%);
fluvastatin, 10 (1.7%)

As of August, 2001, there were at least 81 rhabdomyolysis deaths associated with Non-Baycol statins. http://www.essentialdrugs.org/edrug/archive/200108/msg00064.php

The Public Citizen petition to the FDA, August 20,2001:
At that time the count of deaths by statin-induced rhabdomyolysis:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of Cases</th>
<th>Percent of Total Deaths</th>
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<tr>
<td>Deaths</td>
<td></td>
<td></td>
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<tr>
<td>Atorvastatin</td>
<td>13</td>
<td>18.1%</td>
</tr>
<tr>
<td>Cerivastatin</td>
<td>20</td>
<td>27.8%</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>1</td>
<td>1.4%</td>
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<tr>
<td>Lovastatin</td>
<td>5</td>
<td>6.9%</td>
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<tr>
<td>Pravastatin</td>
<td>9</td>
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<tr>
<td>Simvastatin</td>
<td>24</td>
<td>33.3%</td>
</tr>
</tbody>
</table>


6: Graham DJ, Staffa JA, Shatin D, Andrade SE, Schech SD, La Grenade L, Gurwitz
JH, Chan KA, Goodman MJ, Platt R.  
Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs.  
PMID: 15572716 [PubMed - indexed for MEDLINE]

7: [No authors listed]  
Safety of aggressive statin therapy.  
PMID: 15557874 [PubMed - indexed for MEDLINE]

8: [No authors listed]  
PMID: 15532136 [PubMed - indexed for MEDLINE]

9: Sniderman AD.  
Is there value in liver function test and creatine phosphokinase monitoring with statin use?  
Am J Cardiol. 2004 Nov 4;94(9A):30F-34F. Review.  
PMID: 15519289 [PubMed - indexed for MEDLINE]

10: Johnson TE, Zhang X, Bleicher KB, Dysart G, Loughlin AF, Schaefer WH, Umbenhauer DR.  
Statins induce apoptosis in rat and human myotube cultures by inhibiting protein geranylgeranylation but not ubiquinone.  
PMID: 15504460 [PubMed - indexed for MEDLINE]

11: Davidson MH.  
Rosuvastatin safety: lessons from the FDA review and post-approval surveillance.  
PMID: 15500414 [PubMed - in process]

12: Alsheikh-Ali AA, Kuvin JT, Karas RH.  
Risk of adverse events with fibrates.  
Am J Cardiol. 2004 Oct 1;94(7):935-8.  
PMID: 15464682 [PubMed - indexed for MEDLINE]

13: Baker SK, Goodwin S, Sur M, Tarnopolsky MA.  
Cytoskeletal myotoxicity from simvastatin and colchicine.  
PMID: 15389652 [PubMed - in process]
14: Chang JT, Staffa JA, Parks M, Green L.  
**Rhabdomyolysis with HMG-CoA reductase inhibitors and gemfibrozil combination therapy.**  
PMID: 15269925 [PubMed - indexed for MEDLINE]

**The cerivastatin withdrawal crisis: a "post-mortem" analysis.**  
PMID: 15212862 [PubMed - indexed for MEDLINE]

16: Rundek T, Naini A, Sacco R, Coates K, DiMauro S.  
**Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke.**  
PMID: 15210526 [PubMed - indexed for MEDLINE]

17: Jamal SM, Eisenberg MJ, Christopoulos S.  
**Rhabdomyolysis associated with hydroxymethylglutaryl-coenzyme A reductase inhibitors.**  
PMID: 15199341 [PubMed - indexed for MEDLINE]

18: Bellosta S, Paoletti R, Corsini A.  
**Safety of statins: focus on clinical pharmacokinetics and drug interactions.**  
PMID: 15198967 [PubMed - indexed for MEDLINE]

**[Statin-induced rhabdomyolysis and renal failure: also with fluvastatine]**  
PMID: 15176926 [PubMed - indexed for MEDLINE]

20: Takagi S.  
**[Neurological complication due to the drug and the maneuver for the treatment and prevention of cerebrovascular diseases: iatrogenic neurology]**  
PMID: 15152491 [PubMed - indexed for MEDLINE]

21: Roten L, Schoenenberger RA, Krahenbuhl S, Schlienger RG.  
**Rhabdomyolysis in association with simvastatin and amiodarone.**  
PMID: 15069169 [PubMed - indexed for MEDLINE]
**Polymyositis induced or associated with lipid-lowering drugs: five cases**
PMID: 15050796 [PubMed - indexed for MEDLINE]

23: Moosmann B, Behl C.  
**Selenoprotein synthesis and side-effects of statins.**
PMID: 15031036 [PubMed - indexed for MEDLINE]

24: Manhas A, Farmer JA.  
**Hypolipidemic therapy and cholesterol absorption.**
PMID: 15023291 [PubMed - indexed for MEDLINE]

25: Koumis T, Nathan JP, Rosenberg JM, Cicero LA.  
**Strategies for the prevention and treatment of statin-induced myopathy: is there a role for ubiquinone supplementation?**
PMID: 15018231 [PubMed - indexed for MEDLINE]

26: Dreier JP, Endres M.  
**Statin-associated rhabdomyolysis triggered by grapefruit consumption.**
PMID: 14981197 [PubMed - in process]

27: Schaefer WH, Lawrence JW, Loughlin AF, Stoffregen DA, Mixson LA, Dean DC, Raab CE, Yu NX, Lankas GR, Frederick CB.  
**Evaluation of ubiquinone concentration and mitochondrial function relative to cerivastatin-induced skeletal myopathy in rats.**
PMID: 14728975 [PubMed - indexed for MEDLINE]

28: Andreou ER, Ledger S.  
**Potential drug interaction between simvastatin and danazol causing rhabdomyolysis.**
PMID: 14712320 [PubMed - indexed for MEDLINE]

29: Ehrhardt M, Lindenmaier H, Burhenne J, Haefeli WE, Weiss J.  
**Influence of lipid lowering fibrates on P-glycoprotein activity in vitro.**
PMID: 14698041 [PubMed - indexed for MEDLINE]

30: Jamil S, Iqbal P.
Rhabdomyolysis induced by a single dose of a statin.
PMID: 14676266 [PubMed - indexed for MEDLINE]

31: Zeman M, Zak A, Vecka M, Romaniv S.
[Long-term hypolipidemic treatment of mixed hyperlipidemia with a combination
of statins and fibrates]
PMID: 14626567 [PubMed - indexed for MEDLINE]

32: Foody JM, Krumholz HM.
Are statins indicated for the primary prevention of CAD in octogenarians?
antagonist viewpoint.
PMID: 14610384 [PubMed - indexed for MEDLINE]

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D.
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hyperlipidemia: experience of a community lipid clinic and safety review from
the literature.
Prev Cardiol. 2003 Fall;6(4):189-94.
PMID: 14605512 [PubMed - indexed for MEDLINE]

34: Corsini A.
The safety of HMG-CoA reductase inhibitors in special populations at high
cardiovascular risk.
PMID: 14574085 [PubMed - indexed for MEDLINE]

35: Klotz U.
Pharmacological comparison of the statins.
PMID: 14558433 [PubMed - indexed for MEDLINE]

36: Newman CB, Palmer G, Silbershatz H, Szarek M.
Safety of atorvastatin derived from analysis of 44 completed trials in 9,416
patients.
PMID: 12972104 [PubMed - indexed for MEDLINE]

37: Kajinami K, Takekoshi N, Saito Y.
Pitavastatin: efficacy and safety profiles of a novel synthetic HMG-CoA
reductase inhibitor.
PMID: 12931254 [PubMed - indexed for MEDLINE]
38: Luh JY, Karnath BM.  
**Issues in statin-associated myopathy.**  
PMID: 12928463 [PubMed - indexed for MEDLINE]

39: [No authors listed]  
**Statins: new data in secondary prevention and diabetes. Pravastatin and simvastatin are the best-assessed statins.**  
PMID: 12908497 [PubMed - indexed for MEDLINE]

40: Muller T.  
PMID: 12904874 [PubMed - indexed for MEDLINE]

41: Chuck SK, Penzak SR.  
**Risk-benefit of HMG-CoA reductase inhibitors in the treatment of HIV protease inhibitor-related hyperlipidaemia.**  
PMID: 12904155 [PubMed - indexed for MEDLINE]

42: Davidson MH.  
**Controversy surrounding the safety of cerivastatin.**  
PMID: 12904136 [PubMed - indexed for MEDLINE]

43: Jacobson TA.  
**Combination lipid-lowering therapy with statins: safety issues in the postcerivastatin era.**  
PMID: 12904106 [PubMed - indexed for MEDLINE]

44: Ito MK.  
**Advances in the understanding and management of dyslipidemia: using niacin-based therapies.**  
PMID: 12901026 [PubMed - indexed for MEDLINE]

45: Parker RA, Huang Q, Tesfamariam B.  
**Influence of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitors on endothelial nitric oxide synthase and the formation of oxidants in the vasculature.**
PMID: 12860247 [PubMed - indexed for MEDLINE]

46: Andrejak M, Gras V, Massy ZA, Caron J.  
[Adverse effects of statins]  
PMID: 12822204 [PubMed - indexed for MEDLINE]

Statin-fibrate combination: therapy for hyperlipidemia: a review.  
PMID: 12814127 [PubMed - indexed for MEDLINE]

48: Schmitz G, Drobnik W.  
Pharmacogenomics and pharmacogenetics of cholesterol-lowering therapy.  
PMID: 12747606 [PubMed - indexed for MEDLINE]

49: Bays H, Dujovne C.  
Colestevlam HCl: a non-systemic lipid-altering drug.  
PMID: 12740000 [PubMed - indexed for MEDLINE]

50: Paragh G, Balogh Z, Romics L.  
[Antilipemic therapy and rhabdomyolysis]  
PMID: 12731338 [PubMed - indexed for MEDLINE]

51: Gotto AM Jr.  
Risks and benefits of continued aggressive statin therapy.  
PMID: 12708633 [PubMed - indexed for MEDLINE]

52: Thompson PD, Clarkson P, Karas RH.  
Statin-associated myopathy.  
PMID: 12672737 [PubMed - indexed for MEDLINE]

53: Clark LT.  
Treating dyslipidemia with statins: the risk-benefit profile.  
PMID: 12660659 [PubMed - indexed for MEDLINE]

54: Braun RN, Halhuber MJ, Hitzenberger G.  
[Information regarding adverse drug effects and treatment indications ("package
55: [No authors listed]

How a statin might destroy a drug company.
PMID: 12642039 [PubMed - indexed for MEDLINE]

56: Gotto AM Jr.

Safety and statin therapy: reconsidering the risks and benefits.
PMID: 12639194 [PubMed - indexed for MEDLINE]


Risk for myopathy with statin therapy in high-risk patients.
PMID: 12622602 [PubMed - indexed for MEDLINE]

58: Farmer JA.

Statins and myotoxicity.
PMID: 12573193 [PubMed - indexed for MEDLINE]

59: Black C, Jick H.

Etiology and frequency of rhabdomyolysis.
PMID: 12495162 [PubMed - indexed for MEDLINE]

60: Bolego C, Baetta R, Bellosta S, Corsini A, Paoletti R.

Safety considerations for statins.
PMID: 12441888 [PubMed - indexed for MEDLINE]

61: Prasad GV, Wong T, Meliton G, Bhaloo S.

Rhabdomyolysis due to red yeast rice (Monascus purpureus) in a renal transplant recipient.
PMID: 12438974 [PubMed - indexed for MEDLINE]

62: Lawrence JM, Reckless JP.

Fluvastatin.
PMID: 12437496 [PubMed - indexed for MEDLINE]
Comparative beneficial effects of simvastatin and pravastatin on cardiac allograft rejection and survival.
PMID: 12427413 [PubMed - indexed for MEDLINE]

64: Kind AH, Zakowski LJ, McBride PE.
Rhabdomyolysis from the combination of a statin and gemfibrozil: an uncommon but serious adverse reaction.
PMID: 12426921 [PubMed - indexed for MEDLINE]

65: Schuff-Werner P, Kohlschein P.
[Current therapy of hypercholesterolemia. How much statin does your patient need?]
PMID: 12422725 [PubMed - indexed for MEDLINE]

66: Hare CB, Vu MP, Grunfeld C, Lampiris HW.
Simvastatin-nelfinavir interaction implicated in rhabdomyolysis and death.
PMID: 12410494 [PubMed - indexed for MEDLINE]

Optimizing bexarotene therapy for cutaneous T-cell lymphoma.
PMID: 12399758 [PubMed - indexed for MEDLINE]

Comparison in patients with type 2 diabetes of fibric acid versus hepatic hydroxymethyl glutaryl-coenzyme a reductase inhibitor treatment of combined dyslipidemia.
PMID: 12370858 [PubMed - indexed for MEDLINE]

69: Lewin JJ 3rd, Nappi JM, Taylor MH.
Rhabdomyolysis with concurrent atorvastatin and diltiazem.
PMID: 12243603 [PubMed - indexed for MEDLINE]

70: Sinzinger H, Chehne F, Lupattelli G.
Oxidation injury in patients receiving HMG-CoA reductase inhibitors: occurrence in patients without enzyme elevation or myopathy.
PMID: 12241128 [PubMed - indexed for MEDLINE]
71: Aboulafia DM, Johnston R.
Simvastatin-induced rhabdomyolysis in an HIV-infected patient with coronary artery disease.
PMID: 12240878 [PubMed - indexed for MEDLINE]

72: Evans M, Rees A.
The myotoxicity of statins.
PMID: 12151857 [PubMed - indexed for MEDLINE]

73: Evans M, Rees A.
Effects of HMG-CoA reductase inhibitors on skeletal muscle: are all statins the same?
PMID: 12137559 [PubMed - indexed for MEDLINE]

74: Bae J, Jarcho JA, Denton MD, Magee CC.
Statin specific toxicity in organ transplant recipients: case report and review of the literature.
PMID: 12113605 [PubMed - indexed for MEDLINE]

75: Williams D, Feely J.
Pharmacokinetic-pharmacodynamic drug interactions with HMG-CoA reductase inhibitors.
PMID: 12036392 [PubMed - indexed for MEDLINE]

76: [No authors listed]
Statin stories.
PMID: 11993442 [PubMed - indexed for MEDLINE]

77: Martinez-Castelao A, Ramos R, Gonzalez MT, Castineiras MJ.
[Dyslipidemia and cardiovascular risk in type 2 diabetes mellitus patients with associated diabetic nephropathy]
PMID: 11987671 [PubMed - indexed for MEDLINE]

78: Maxa JL, Melton LB, Ogu CC, Sills MN, Limanni A.
Rhabdomyolysis after concomitant use of cyclosporine, simvastatin, gemfibrozil, and itraconazole.
PMID: 11978159 [PubMed - indexed for MEDLINE]
79: Foxton J.  
**Statin safety.**  
PMID: 11977679 [PubMed - indexed for MEDLINE]  

80: Ambrosi P, Gayet JL, Andrejak M.  
**[The best of 2001. Clinical pharmacology]**  
PMID: 11901897 [PubMed - indexed for MEDLINE]  

81: Gensini GF, Conti AA, Conti A, Panti A.  
**[From prevention to cardiovascular rehabilitation: statins and evidence-based medicine]**  
PMID: 11899580 [PubMed - indexed for MEDLINE]  

82: Sica DA, Gehr TW.  
**3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors and rhabdomyolysis: considerations in the renal failure patient.**  
PMID: 11856903 [PubMed - indexed for MEDLINE]  

83: Omar MA, Wilson JP.  
**FDA adverse event reports on statin-associated rhabdomyolysis.**  
PMID: 11847951 [PubMed - indexed for MEDLINE]  

84: Prieto JC.  
**[Safety profile of statins]**  
PMID: 11836874 [PubMed - indexed for MEDLINE]  

85: Patel DN, Pagani FD, Koelling TM, Dyke DB, Baliga RR, Cody RJ, Lake KD, Aaronson KD.  
**Safety and efficacy of atorvastatin in heart transplant recipients.**  
PMID: 11834348 [PubMed - indexed for MEDLINE]  

86: Sica DA, Gehr TW.  
**Rhabdomyolysis and statin therapy: relevance to the elderly.**  
PMID: 11773716 [PubMed - indexed for MEDLINE]  

87: Banga JD.  
**[Myotoxicity and rhabdomyolysis due to statins]**
88: Hamilton-Craig I.  
**Statin-associated myopathy.**  
PMID: 11758079 [PubMed - indexed for MEDLINE]

89: Bernini F, Poli A, Paoletti R.  
**Safety of HMG-CoA reductase inhibitors: focus on atorvastatin.**  
PMID: 11713888 [PubMed - indexed for MEDLINE]

90: Chazerain P, Hayem G, Hamza S, Best C, Ziza JM.  
**Four cases of tendinopathy in patients on statin therapy.**  
PMID: 11707010 [PubMed - indexed for MEDLINE]

**Effect of fluvastatin on acute renal allograft rejection: a randomized multicenter trial.**  
PMID: 11703619 [PubMed - indexed for MEDLINE]

92: Federman DG, Hussain F, Walters AB.  
**Fatal rhabdomyolysis caused by lipid-lowering therapy.**  
PMID: 11702815 [PubMed - indexed for MEDLINE]

93: Igel M, Sudhop T, von Bergmann K.  
**Metabolism and drug interactions of 3-hydroxy-3-methylglutaryl coenzyme A-reductase inhibitors (statins).**  
PMID: 11599653 [PubMed - indexed for MEDLINE]

94: Bangratz S.  
**[Complications in heart transplantation: diagnosis and treatment]**  
PMID: 11577591 [PubMed - indexed for MEDLINE]

95: Omar MA, Wilson JP, Cox TS.  
**Rhabdomyolysis and HMG-CoA reductase inhibitors.**  
PMID: 11573861 [PubMed - indexed for MEDLINE]

96: Boger RH.  
**Drug interactions of the statins and consequences for drug selection.**  
PMID: 11563683 [PubMed - indexed for MEDLINE]

97: Comarow A.  
**Rest easy, statin users. Benefits dwarf risks for these cholesterol drugs.**  
PMID: 11550394 [PubMed - indexed for MEDLINE]

98: Shek A, Ferrill MJ.  
**Statin-fibrate combination therapy.**  
PMID: 11485144 [PubMed - indexed for MEDLINE]

99: Moghadasian MH, Mancini GB, Frohlich JJ.  
**Pharmacotherapy of hypercholesterolaemia: statins in clinical practice.**  
PMID: 11249510 [PubMed - indexed for MEDLINE]

**Rhabdomyolysis and acute renal failure after changing statin-fibrate combinations.**  
PMID: 11173785 [PubMed - indexed for MEDLINE]

101: Guyton JR.  
**Combination drug therapy for combined hyperlipidemia.**  
PMID: 10980849 [PubMed - indexed for MEDLINE]

102: Ozdemir O, Boran M, Gokce V, Uzun Y, Kocak B, Korkmaz S.  
**A case with severe rhabdomyolysis and renal failure associated with cerivastatin-gemfibrozil combination therapy--a case report.**  
PMID: 10959522 [PubMed - indexed for MEDLINE]

**Efficacy and safety of pravastatin vs simvastatin after cardiac transplantation.**  
PMID: 10867332 [PubMed - indexed for MEDLINE]
104: Scheen AJ.  
[Treatment of combined hyperlipidemia: fibrate and/or statin?]  
PMID: 10495679 [PubMed - indexed for MEDLINE]

105: Guyton JR, Capuzzi DM.  
Treatment of hyperlipidemia with combined niacin-statin regimens.  
PMID: 9915667 [PubMed - indexed for MEDLINE]

106: Athyros VG, Papageorgiou AA, Hatzikonstandinou HA, Didangelos TP, Carina MV, Kranitsas DF, Kontopoulos AG.  
Safety and efficacy of long-term statin-fibrate combinations in patients with refractory familial combined hyperlipidemia.  
PMID: 9294990 [PubMed - indexed for MEDLINE]

The effect of simvastatin treatment on natural antioxidants in low-density lipoproteins and high-energy phosphates and ubiquinone in skeletal muscle.  
PMID: 8623738 [PubMed - indexed for MEDLINE]

108: Shviro I, Leitersdorf E.  
The patient at risk: who should we be treating?  
PMID: 8729587 [PubMed - indexed for MEDLINE]

109: Peters TK.  
Safety profile of fluvastatin.  
PMID: 8729586 [PubMed - indexed for MEDLINE]

[Rhabdomyolysis due to simvastin. Apropos of a case with review of the literature]  
PMID: 1496277 [PubMed - indexed for MEDLINE]

STATINS AND LIVER OR KIDNEY DAMAGE

Frequently Asked Question: Do statins damage liver or kidneys?

Kaplowitz N.
**Statin-induced hepatotoxicity.**  
PMID: 15481021 [PubMed - indexed for MEDLINE]

Kubota T, Fujisaki K, Itoh Y, Yano T, Sendo T, Oishi R.  
**Apoptotic injury in cultured human hepatocytes induced by HMG-CoA reductase inhibitors.**  
PMID: 15163549 [PubMed - indexed for MEDLINE]

de Denus S, Spinler SA, Miller K, Peterson AM.  
**Statins and liver toxicity: a meta-analysis.**  
PMID: 15162892 [PubMed - indexed for MEDLINE]

**[Statin-induced rhabdomyolysis and renal failure: also with fluvastatine]**  
PMID: 15176926 [PubMed - indexed for MEDLINE]

Jacobson TA.  
**Combination lipid-lowering therapy with statins: safety issues in the postcerivastatin era.**  
PMID: 12904106 [PubMed - indexed for MEDLINE]

Braun RN, Halhuber MJ, Hitzenberger G.  
**[Information regarding adverse drug effects and treatment indications ("package inserts") exemplified by cervistatin (Lipobay)]**  
PMID: 12658968 [PubMed - indexed for MEDLINE]

Lewin JJ 3rd, Nappi JM, Taylor MH.  
**Rhabdomyolysis with concurrent atorvastatin and diltiazem.**  
PMID: 12243603 [PubMed - indexed for MEDLINE]

Bae J, Jarcho JA, Denton MD, Magee CC.  
**Statin specific toxicity in organ transplant recipients: case report and review of the literature.**  
PMID: 12113605 [PubMed - indexed for MEDLINE]

Omar MA, Wilson JP, Cox TS.  
**Rhabdomyolysis and HMG-CoA reductase inhibitors.**
**Rhabdomyolysis and acute renal failure after changing statin-fibrate combinations.**  
PMID: 11173785 [PubMed - indexed for MEDLINE]

Ozdemir O, Boran M, Gokce V, Uzun Y, Kocak B, Korkmaz S.  
**A case with severe rhabdomyolysis and renal failure associated with cerivastatin-gemfibrozil combination therapy--a case report.**  
PMID: 10959522 [PubMed - indexed for MEDLINE]

**ELDERLY AND STATINS**

**Frequently Asked Question: Should people over 70 take statins?**

Lack of association between cholesterol and coronary heart disease mortality and morbidity and all-cause mortality in persons older than 70 years.  
Krumholz HM, Seeman TE, Merrill SS, Mendes de Leon CF, Vaccarino V, Silverman DI, Tsukahara R, Ostfeld AM, Berkman LF.  
Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520-8017.

"CONCLUSIONS--Our findings do not support the hypothesis that hypercholesterolemia or low HDL-C are important risk factors for all-cause mortality, coronary heart disease mortality, or hospitalization for myocardial infarction or unstable angina in this cohort of persons older than 70 years."

Another study showing people over 65 do not benefit from cholesterol reduction:

Long-Term Prognostic Importance of Total Cholesterol in Elderly Survivors of an Acute Myocardial Infarction: The Cooperative Cardiovascular Pilot Project.  
Foody JM, Wang Y, Kiefe CI, Ellerbeck EF, Gold J, Radford MJ, Krumholz HM.  
Section of Cardiovascular Medicine, Department of Medicine, and Section of Chronic Disease Epidemiology, Department of Epidemiology and Public Health, Yale School of Medicine, New Haven, Connecticut; Qualidigm, Middletown, Connecticut; Yale-New Haven Hospital Center for Outcomes Research and
"PARTICIPANTS: Four thousand nine hundred twenty-three Medicare beneficiaries from four states aged 65 and older"

"CONCLUSION: Among elderly survivors of AMI, elevated total serum cholesterol measured postinfarction is not associated with an increased risk of all-cause mortality in the 6 years after discharge. Furthermore, this study found no evidence of an increased risk of all-cause mortality in patients with low total cholesterol. Further studies are needed to determine the relationship of postinfarction lipid subfractions and mortality in older patients with coronary artery disease (CAD)."

**High-density vs low-density lipoprotein cholesterol as the risk factor for coronary artery disease and stroke in old age.**
Weverling-Rijnsburger AW, Jonkers IJ, van Exel E, Gussekloo J, Westendorp RG.
Section of Gerontology and Geriatrics, Department of General Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands. a.w.e.weverling-rijnsburger@lumc.edu


“In contrast to high LDL cholesterol level, low HDL cholesterol level is a risk factor for mortality from coronary artery disease and stroke in old age.”

**Total cholesterol and risk of mortality in the oldest old.**
Department of General Internal Medicine, Leiden University Medical Center, The Netherlands.

“In people older than 85 years, high total cholesterol concentrations are associated with longevity owing to lower mortality from cancer and infection. The effects of cholesterol-lowering therapy have yet to be assessed.”

Golomb BA, Criqui MH, White HL, Dimsdale JE.
**The UCSD Statin Study: a randomized controlled trial assessing the impact of statins on selected noncardiac outcomes.**
IS THERE AN INDUSTRY BIAS IN STATIN PUBLICATIONS?

Why are most studies so positive about statins, and why are there relatively so few published that show problems? Do Medical Journals agree that there is bias in drug-industry funded medical studies?

Yes, as does an observational study.

Association of Funding and Conclusions in Randomized Drug Trials
A Reflection of Treatment Effect or Adverse Events?
http://jama.ama-assn.org/cgi/content/abstract/290/7/921
Bodil Als-Nielsen, MD; Wendong Chen, MD; Christian Gluud, MD, DMSc; Lise L. Kjaergard, MD
JAMA. 2003;290:921-928 Vol 290 No 7, August 20, 2003

"The experimental drug was recommended as treatment of choice in 16% of trials funded by nonprofit organizations, 30% of trials not reporting funding, 35% of trials funded by both nonprofit and for-profit organizations, and 51% of trials funded by for-profit organizations (P<.001; 2 test). Logistic regression analyses indicated that funding, treatment effect, and double blinding were the only significant predictors of conclusions. Adjusted analyses showed that trials funded by for-profit organizations were significantly more likely to recommend the experimental drug as treatment of choice (odds ratio, 5.3; 95% confidence interval, 2.0-14.4) compared with trials funded by nonprofit organizations. This association did not appear to reflect treatment effect or adverse events."

"Conclusions Conclusions in trials funded by for-profit organizations may be more positive due to biased interpretation of trial results. Readers should carefully evaluate whether conclusions in randomized trials are supported by data." 

"Author Affiliations: The Copenhagen Trial Unit, Center for Clinical Intervention Research, Copenhagen University Hospital, Copenhagen, Denmark."
Clearly JAMA came to the conclusion that funding biases the findings in 2002, when they quite publicly changed their editorial policy to require funding information for studies they publish.

Further, you are invited to view the British Journal of Medicine, May 31, 2003 (Volume 326, Issue 7400), which has focused attention on bias and spin in industry-sponsored studies. They carried the following articles at http://bmj.com/content/vol326/issue7400/#TWIB:

**Research sponsored by drug companies is biased**
http://bmj.com/content/vol326/issue7400/0

**No more free lunches**
Kamran Abbasi and Richard Smith
http://bmj.com/cgi/content/full/326/1155 text
http://bmj.com/cgi/reprint/326/1155 pdf

**Drug company sponsorship of education could be replaced at a fraction of its cost**
http://bmj.com/cgi/content/full/326/1163 text
http://bmj.com/cgi/reprint/326/1163 pdf

**Drug companies advised to publish unfavourable trial results**
http://bmj.com/cgi/content/full/326/1163-a text
http://bmj.com/cgi/reprint/326/1163-a pdf

**World body reviews doctors' links to drug industry**
http://bmj.com/cgi/content/abridged/326/1165-a abridged text
http://bmj.com/cgi/reprint_abr/326/1165-a abridged pdf
http://bmj.com/cgi/content/full/326/1165-a full text

**Pharmaceutical industry sponsorship and research outcome and quality: systematic review**
Joel Lexchin, Lisa A Bero, Benjamin Djulbegovic, and Otavio Clark
http://bmj.com/cgi/content/full/326/1167 full text
http://bmj.com/cgi/reprint/326/1167 pdf

**Evidence b(i)ased medicine—selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications**
Hans Melander, Jane Ahlqvist-Rastad, Gertie Metjier, and Björn Beermann
http://bmj.com/cgi/content/full/326/1171 full text
http://bmj.com/cgi/reprint/326/1171 pdf
Characteristics of general practitioners who frequently see drug industry representatives: national cross sectional study
Chris Watkins, Laurence Moore, Ian Harvey, Patricia Carthy, Elizabeth Robinson, and Richard Brawn
http://bmj.com/cgi/content/full/326/7400/1178 full text
http://bmj.com/cgi/reprint/326/7400/1178 pdf

Who pays for the pizza? Redefining the relationships between doctors and drug companies. 1: Entanglement
Ray Moynihan
http://bmj.com/cgi/content/full/326/7400/1189 full text
http://bmj.com/cgi/reprint/326/7400/1189 pdf

Who pays for the pizza? Redefining the relationships between doctors and drug companies. 2: Disentanglement
Ray Moynihan
http://bmj.com/cgi/content/full/326/7400/1193 full text
http://bmj.com/cgi/reprint/326/7400/1193 pdf

How to dance with porcupines: rules and guidelines on doctors' relations with drug companies
Elizabeth Wager
http://bmj.com/cgi/content/full/326/7400/1196 full text
http://bmj.com/cgi/reprint/326/7400/1196 pdf

How can research ethics committees protect patients better?
Silvio Garattini, Vittorio Bertele, and Luca Li Bassi
http://bmj.com/cgi/content/full/326/7400/1199 full text
http://bmj.com/cgi/reprint/326/7400/1199 pdf

Medical journals and pharmaceutical companies: uneasy bedfellows
Richard Smith
BMJ 2003; 326: 1202-1205.
http://bmj.com/cgi/content/full/326/7400/1202 text
http://bmj.com/cgi/reprint/326/7400/1202 pdf

Unhealthy spin
Bob Burton and Andy Rowell
http://bmj.com/cgi/content/full/326/7400/1205 text
http://bmj.com/cgi/reprint/326/7400/1205 pdf
Relationships between the pharmaceutical industry and patients' organisations
Andrew Herxheimer
http://bmj.com/cgi/content/full/326/7400/1208 text
http://bmj.com/cgi/reprint/326/7400/1208 pdf

Journals should select drug advertisements more carefully
James J Oliver and Simon R Maxwell
BMJ 2003; 326: 1211. http://bmj.com/cgi/content/full/326/7400/1211

Charities and patient groups should declare interests
Jenny Hirst
http://bmj.com/cgi/content/full/326/7400/1211-a

Bioethics are difficult to balance
Asad J Raja
BMJ 2003; 326: 1215.
http://bmj.com/cgi/content/full/326/7400/1215-c

Then check out the astonishing articles on medical ghostwriting, starting at

It may inspire you to earn extra income, because it points out that a Medical Ghostwriter
can make $100,000 per year writing favorable drug reports! YMMV

Difficult to question if there is bias in drug-industry studies after reading the above.

Two recent examples of bias in the presentation of pivotal findings are:

1) Dr. Gaist’s study that proves statins cause polyneuropathy http://213.4.18.135/87.pdf.
   If you read the entire research article, you will note the vast difference between his
   findings and the tone of the descriptive abstract, which tends to water down the findings.
   Further, the journal ran an editorial that provided further pro-statin spin as damage
   control.

2) The ALLHAT study, published in JAMA, was the largest to date. It ran for years and
   encompassed 10,000 people. Their study website http://allhat.sph.uth.tmc.edu/default.htm
   These folks were funded by NIH, and they have published what the drug companies do
   not want to hear: that statins do not prevent deaths. Again, there was a pro-statin damage
   control editorial in the same issue, and the news carriers did not highlight the findings. In
   fact, CNN buried it inside an article on the other finding: that diuretics worked better than
   other blood-pressure medications, where no reader looking for cholesterol drug results
   would find it.
Glossary of some search terms & equivalents:

Lipitor = atorvastatin
Coenzyme Q10 = CoQ10 = Ubiquinone = Ubidecarenone
Statins = hydroxymethylglutaryl coenzyme A reductase inhibitors = HMG-CoA Reductase Inhibitors
Lipitor, Mevacor, Pravachol, Zocor, Lescol, and Baycol = atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, and simvastatin

More to come: FAQs with published medical research on other aspects of statin adverse effects.