The Norwegian–Lithuanian study[3] was the first controlled study to examine the association between rear-end collisions and the development of chronic neck pain and headaches. Following the sudden occurrence in Norway of a devastating "epidemic" in which 70 000 people, from a population of 4.5 million, claimed to have been disabled by whiplash, Harald Schrader and his Norwegian colleagues wanted to learn more about the course of whiplash uncomplicated by the availability of insurance and fashionable beliefs that whiplash causes disabling symptoms. They chose Lithuania, a country in which there was no personal injury insurance and where few people had heard of whiplash.

They matched each of 202 Lithuanian drivers whose cars had been rear-ended in the previous 3 years with a control subject from the same city as the collision victim. Without revealing the purpose of the study, the investigators sent health questionnaires to all study subjects. Thirty-three percent of the collision group reported neck pains, but so did 33% of the controls. Fifty-three percent of the accident group had headaches, but so did 50% of the controls.[3] When told the results, the Lithuanians were amazed that anyone would attribute persistent headache and neck pains to a minor car collision. In contrast, in much of the developed world, where whiplash is believed to cause chronic symptoms, collision victims, particularly those already in psychosocial distress, "capture" persistent whiplash symptoms.[1]

The publication of the Norwegian–Lithuanian study in the *Lancet*[3] caused a furor among professionals who make a living from whiplash. The Norwegian researchers repeated their study, incorporating refinements designed to answer legitimate criticisms of the first study, but the results remained substantially unchanged.[4]

A case–control study, such as those of Schrader and his colleagues, is the only acceptable way to exclude a causal link between collisions and the development of chronic whiplash symptoms. As to obtaining a sufficient number of subjects to reach significance, this problem now appears to have been solved[5] by combining the results of the 2 studies.[3,4]

To reach significance in a study of whiplash, a large number of subjects is needed because the prevalence of neck pains and headache in the community is high, and any possible addition caused by whiplash injury is small. This means that for any individual whiplash claimant, the chances of persistent symptoms being due to the collision rather than to the ordinary exigencies of life are much below the 50% probability required by civil law for the perpetrator of the accident to be held financially liable. If lawyers and medical expert witnesses refrained from bringing to court "junk" whiplash science, judges would seldom award compensation for whiplash complaints. Given that the high cost of auto insurance premiums reflects the excessive cost of whiplash claims, premiums could thereby be reduced to more manageable levels.

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References

1. Malleson A. *Whiplash and other useful illnesses*. Montreal and Kingston: McGill-Queen's University Press; 2002.
2. Rø M, Borchgrevink G, Daehli B, Finset A, Lilleås F, Laake K, et al. *SMM Report 5/2000: Whiplash injury — diagnosis and evaluatio*n [English summary online]. Oslo: Senter for Medisinsk metodevurdering [Norwegian Centre for Health Technology Assessment]; 2000. Available: www.oslo.sintef.no/smm/Publications/Engsmdrag/FramesetPublications.htm (accessed 2003 Sep 2).
3. Schrader H, Obelieniene D, Bovim G, Surkiene D, Mickeviciene D, Miseviciene I, et al. Natural evolution of late whiplash syndrome outside the medicolegal context. *Lancet* 1996;347:1207-11.
4. Obelieniene D, Schrader H, Bovim G, Miseviciene I, Sand T. Pain after whiplash: a prospective controlled inception cohort study. *J Neurol Neurosurg Psychiatry* 1999;66:279-83.
5. Ferrari R, Schrader H. The late whiplash syndrome: a biopsychosocial approach. *J Neurol Neurosurg Psychiatry* 2001;70:722-6.

[Harald Schrader, Gunnar Bovim and Trond Sand respond:]

Harold Merskey, in attacking Walter Rosser's review[1] of Andrew Malleson's book,[2] makes the misleading allegation that one of our studies was "denied validity" by the Norwegian Centre for Health Technology Assessment. In fact, the Centre's report,[3] after praising our study design in terms of selection of material and use of control groups, concluded (as did we) that it seems impossible to document a causal relation between whiplash trauma and the development of chronic symptoms.

However, it was emphasized that for the demonstration of small differences in symptoms between collision victims and controls, a greater number of subjects would be required than we used in our study. The final statement of the report[3] concluded that whiplash should be managed as "an acute self-limiting process." Incidentally, Magne Rø, the leader of the investigative group for the assessment, has praised Malleson's book in a published review.[4]

Studies from Western countries indicate that 15% to 58% of people with a whiplash injury experience the late whiplash syndrome.[5-9] Our 2 controlled studies[10,11] were conducted in Lithuania, a country where whiplash injury provides little opportunity for "secondary gain" and where there is little awareness that whiplash injury is a reputed cause of chronic pain and disability. Altogether, we evaluated 412 people who had been involved in rear-end collisions, which gave an estimated minimum of 180 subjects with acute whiplash injury (i.e., acute symptoms).[12] According to previous reports this number should have yielded between 27 and 104 people with late whiplash syndrome. Yet we identified no subjects with chronic symptoms related to the collision. If the late whiplash syndrome does exist, it seems to occur very infrequently in Lithuania.

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References
1. Rosser WW. Dubious diagnoses. *CMAJ* 2002; 167(8):902.
2. Malleson A. *Whiplash and other useful illnesses*. Montreal and Kingston: McGill-Queen's University Press; 2002.
3. Rø M, Borchgrevink G, Daehli B, Finset A, Lilleås F, Laake K, et al. *SMM Report 5/2000: Whiplash injury — diagnosis and evaluation*. Oslo: Senter for Medisinsk metodevurdering [Norwegian Centre for Health Technology Assessment]; 2000.
4. Rø M. Nakkesleng som tidsfenomen. *Tidsskr Nor Laegeforen* 2002;122:1858.
5. Mcnab I. Acceleration injuries to the cervical spine. *J Bone Joint Surg* 1964;8:1797-9.
6. Norris SH, Wart I. The prognosis of neck injuries resulting from rear-end vehicle collision. *J Bone Joint Surg Br* 1983;65:608-11.
7. Deans GT, Magalliard JN, Kerr M, Rutherford WH. Neck sprain — a major cause of disability following car accidents. *Injury* 1987;18:10-2.
8. Pearce JMS. Whiplash injury. A reappraisal. *J Neurol Neurosurg Psychiatry* 1989;52:1329-31.
9. Borchgrevink GE, Lereim I, Røyneland L, Bjorndal A, Haraldseth O. National health insurance consumption and chronic symptoms following mild neck sprain injuries in car collisions. *Scand J Soc Med* 1996;24:264-71.
10. Schrader H, Obelieniene D, Bovim G, Surkiene D, Mickeviciene D, Miseviciene I, et al. Natural evolution of late whiplash syndrome outside the medicolegal context. *Lancet* 1996;347:1207-11.
11. Obelieniene D, Schrader H, Bovim G, Miseviciene I, Sand T. Pain after whiplash: a prospective controlled inception cohort study. *J Neurol Neurosurg Psychiatry* 1999;66:279-83.
12. Ferrari R, Schrader H. The late whiplash syndrome: a biopsychosocial approach. *J Neurol Neurosurg Psychiatry* 2001;70:722-6.

Editor's note: In the course of preparing a response to Harold Merskey's letter, Andrew Malleson contacted Harald Schrader, the lead author of a study of Lithuanian drivers involved in rear-end collisions, and shared Dr. Merskey's letter with him. Dr. Schrader and his colleagues prepared their own response to the initial letter, and we have included that letter here, along with Dr. Malleson's.

Acute hepatitis associated with levofloxacin in a patient with renal insufficiency

Jon-David Schwalm and Christine Lee[1] reported a case of acute hepatitis in a hemodialysis patient taking oral levofloxacin. We observed profuse epistaxis and an acute rise in hepatic enzyme levels, particularly alkaline phosphatase, with levofloxacin therapy in a 63-year-old patient with mitral valve disease, coronary artery disease and chronic renal insufficiency, which resolved with discontinuation of the drug. The hepatic enzyme levels rose again when another drug in the same class, ciprofloxacin, was initiated. A full description of this case is available as an eletter on *eCMAJ* (www.cmaj.ca/cgi/eletters/168/7/847).

Coagulopathy associated with use of a fluoroquinolone and warfarin, as observed in this patient, is relatively well established.[2] An increase in hepatic enzymes is less well established, although it has been observed with other drugs in the same class.[3] Delayed hepatotoxicity can occur with accumulation of amiodarone (used to manage atrial fibrillation in this patient) but is usually heralded by a rise in alanine aminotransferase months after initiation of therapy, unless the reaction is idiosyncratic and occurs within the first 4 weeks.[4] The initial rise in hepatic enzymes in this patient occurred within days of initiation of levofloxacin and of the rechallenge with the second fluoroquinolone (ciprofloxacin). This patient had acute-on-chronic renal failure, as did the patient described by Schwalm and Lee.[1] The creatinine level was 212 mol/L on initiation of levofloxacin, peaking at 407 mol/L at the time of presentation with epistaxis and decreasing to 177 mol/L 4 days after discontinuation of levofloxacin. Nephrotoxicity and allergic nephritis have been linked to levofloxacin.[5] Renal dysfunction might have been the underlying problem, with altered renal clearance increasing the potential for hepatoxicity. The creatinine level did not increase with the ciprofloxacin rechallenge.

Physicians should be alert to the possibility of fluoroquinolone-associated hepatotoxicity. Comorbidities such as renal failure may increase the potential for such toxic effects.

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References
1. Schwalm J, Lee C. Acute hepatitis associated with oral levofloxacin therapy in a hemodialysis patient. *CMAJ* 2003;168(7):847-8.
2. Jones CB, Fugate SE. Levofloxacin and warfarin interaction. *Ann Pharmacother* 2002;36(10):1554-7.
3. Cunha BA. Antibiotic side effects. *Med Clin North Am* 2001;85:149-85.
4. Pollak PT, You YD. Monitoring of hepatic function during amiodarone therapy. *Am J Cardiol* 2003;91(5):613-6.
5. Famularo G, De Simone C. Nephrotoxicity and purpura associated with levofloxacin. *Ann Pharmacother* 2002;36(9):1380-2.

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Violence in Liberia

Contrary to the caption below the photo of a Liberian child with an intravenous drip in his scalp,[1] children who die of cholera in Monrovia are indeed "felled by violence."

Civil wars kill more civilians than soldiers. Most of these deaths are not sustained at the front lines, but they are still a direct result of the violence. Wars ruin all the structures of civil society, immunization and health care often being among the first to go. While I was volunteering for Doctors Without Borders/Médecins Sans Frontières (MSF) in southern Sudan, many children under our care died violent deaths, mostly from malnutrition, pneumonia and dehydration. Watching a baby rigid with tetanic spasms, I was struck by the thought that this seemed a particularly violent way to die.

As physicians, a privileged and educated elite, we have a duty to be informed about how war affects health and to advocate always for peace.

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Reference
1. Not all victims of Liberia's brutal war were felled by violence [photo caption]. *CMAJ* 2003; 169(4):328.

Correction

A death notice for Dr. James E. Dimmick of Parksville, BC, who assures us that he is alive and well, was wrongly submitted to *CMAJ* and appeared in a recent edition.[1] We apologize for its publication.

Reference
1. Deaths. *CMAJ* 2003;169(6):639.