fees or regulations and no more disputes over transfer payments.

C.N. Ghent
Liver Diseases and Transplantation
London, Ont.

Reference

1. Lewis S. The bog, the fog, the future: 5 strategies for renewing federalism in health care [commentary]. *CMAJ* 2002;166(11):1421-2.

[The author responds:]

I am delighted C.N. Ghent has pointed out in response to my article[1] the folly of fragmentation that consumes so much energy for so little gain. About a year ago, I drafted an op-ed piece entitled "time to punt." I sent it to a number of newspapers urging the provinces to give up constitutional responsibility for health care and allow Ottawa to create a unitary system. All declined to publish it; perhaps they thought I was kidding and their satire quota had been filled for that month.

If we were just now assigning federal and provincial constitutional powers, would we toss health care into Section 92 (as did the Fathers of Confederation when negotiating the British North America Act) knowing what we know about how big and complicated the sector would grow? I'd suggest no. If we did not have to amend the Constitution to transfer the powers back, perhaps it would be an idea worth pursuing. Unfortunately, there is no chance of amending the Constitution to give Ottawa more power rather than less, even if this would be prudent from the standpoint of the provinces. But if Ghent would like to establish an advocacy group for a truly national and nationally governed health system, I could probably be signed up as a charter member.

Steven Lewis
Centre for Health and Policy Studies
University of Calgary
Calgary, Alta.

Reference

1. Lewis S. The bog, the fog, the future: 5 strategies for renewing federalism in health care [editorial]. *CMAJ* 2002;166(11):1421-2.

Low-dose droperidol

Eric Wooltorton's recent drug alert[1] on droperidol adds little to the scant information initially released by the US Food and Drug Administration (FDA). Droperidol has a long history of safe use, is inexpensive and effectively treats postoperative nausea and vomiting. Millions of patients have received droperidol, suggesting that the rate of cardiac complications is extremely low. The new recommendations for giving droperidol (preoperative electrocardiogram, 2–3 hours of postoperative cardiac monitoring) will effectively kill its use.

Studies of droperidol's effect on cardiac conduction have used doses (0.25 mg/kg) far above those used to control postoperative nausea and vomiting (0.625 mg).[2] The FDA has admitted that it has little data on low-dose droperidol, yet it has published the "black box" warning. The FDA has since announced that it is conducting a "definitive pharmacokinetic/pharmacodynamic study" on low-dose droperidol, as well as a comparison between droperidol and other antiemetics and their respective adverse effects.

Health Canada released a drug safety letter on Feb. 12[3] but did not address it to anesthesiologists. It repeated the December FDA warning without details of the QT prolongation cases that prompted the letter. Perhaps after the cisapride fiasco, Health Canada wished to forestall further criticism rather than actually enlighten physicians. This is not in the public's best interest, especially if they are nauseated postoperative patients.

Greg Allen
Anesthesiologist
Providence St. Peter Hospital
Olympia, Wash.

References

1. Wooltorton E. Droperidol: cardiovascular toxicity and deaths. *CMAJ* 2002;166(7):932.
2. McCormick CG. FDA Alert: Current FDA report on droperidol status and basis for "Black Box" warning. *ASA Newsletter* 2002;66(4):19-20.
3. Health Canada. *Cardiovascular toxicity with injectable droperidol*. Ottawa: Health Canada; 2002 Feb 12. Available: www.hc-sc.gc.ca/hbp- dgps /therapeut/zfiles/english/advisory/tpd/droperidol _e.html (accessed 2002 July 8).

[The author responds:]

Greg Allen highlights certain problems inherent in Canadian "Dear Health Care Professional" letters: one-time maldistribution of information that is missing clinically important content. The original letter[1] signed by Health Canada was addressed to "Hospital Chief of Medical Staff, Otolaryngologists and Pharmacists in Retail Pharmacies." It was overlooked by many who might actually be prescribing the drug, including anesthesiologists, emergency physicians and psychiatrists.[2]

In *CMAJ*'s Health and Drug Alerts, we sought to broaden the awareness of the problem with droperidol and to provide additional clinically relevant information, such as a list of medications that cause QT prolongation. The quality of Health Canada's advisories has been criticized in the past as contributing to preventable medication adverse events,[3,4] and clearly reform is still needed.

Eric Wooltorton
CMAJ

References

1. Health Canada. *Cardiovascular toxicity with injectable droperidol*. Ottawa: Health Canada; 2002 Feb 12. Available: http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/advisory/tpd/droperidol_e.html (accessed 2002 July 8).
2. Wooltorton E. Droperidol: cardiovascular ity and deaths. *CMAJ* 2002;166(7):932.
3. Lessons from cisapride [editorial]. *CMAJ*2 164(9):1269.
4. Sibbald B. Cisapride, before and after: still ing for ADE-reporting reform. *CMAJ* 2001;165 (10):1370.

Latent tuberculosis treatment

Kevin Schwartzman's excellent commentary[1] has highlighted an inconsistency in current Canadian guidelines:[2] he recommends treatment of latent tuberculosis (TB) infection for HIV-infected immigrants from TB-endemic countries, even if that person has a tuberculin skin test (TST) reaction of < 5 mm. This group would be composed of the truly uninfected, who would derive no benefit from this treat-

ment, and those who are infected but anergic. Two studies have found no evidence of significant benefit from treatment of latent tuberculosis infection (LTBI) in the latter.[3,4] Three other studies in high TB prevalence countries, in which results of anergy testing were not reported, also failed to show a benefit of treatment among HIV-infected individuals who had negative tuberculin tests.[5-7]

We do not feel the evidence or other current recommendations[8,9] support routine provision of LTBI treatment to TST-negative, HIV-infected individuals on the basis of geographic origin alone.

Our second concern relates to the statement that the use of the 2-month pyrazinamide and rifampin regimen for latent tuberculosis is "clearly contraindicated for anyone with underlying liver disease or with isoniazid-related hepatatoxicity." We agree that the use of this regimen should be strictly limited to individuals with a particularly high risk of TB reactivation, such as the HIV-infected, and to those in whom completion of a standard 9-month course of isoniazid would be unlikely. However, in many Canadian settings, a high proportion of patients meeting these criteria have some indication of liver disease from hepatitis C infection, excess alcohol use, or both. The reported experience of serious adverse effects from the US[10] appears to have involved self-administration, variable follow-up and insufficient attention to the high liver disease risk of this selected patient group.

For many years, pyrazinamide and rifampin have been used as part of a 4-drug therapy for active tuberculosis, with manageable toxicity in patients with liver disease. We believe that treatment of LTBI with pyrazinamide and rifampin can be administered to carefully selected patients with hepatitis C or a history of excess alcohol use, with an acceptably low risk, if the following criteria are met: directly observed delivery of each dose, immediate assessment of any clinical symptoms of liver disease and measurement of transaminase enzymes at baseline and every 2 weeks during therapy.

Stan Houston
Division of Infectious Diseases
Department of Medicine
University of Alberta
Edmonton, Alta.
Richard Long
Division of Pulmonary Medicine
Department of Medicine
University of Alberta
Edmonton, Alta.
Vernon Hoeppner
Division of Tuberculosis Control
Department of Medicine
University of Saskatchewan
Saskatoon, Sask.

References

1. Schwartzman K. Latent tuberculosis infection: old problem, new priorities [editorial]. *CMAJ* 2002;166(6):759-61.
2. Long RC, editor. *Canadian tuberculosis standards*. 5th ed. Ottawa: Canadian Lung Association, Health Canada; 2000. p. 50, 143.
3. Gordin FM, Matts JP, Miller C, Brown LS, Hafner R, et al. A controlled trial of isoniazid in persons with anergy and human immunodeficieny virus infection who are at high risk for tuberculosis. *N Engl J Med* 1997;337:315-20.
4. Whalen CC, Johnson JL, Okwera A, Horn DL, Huebner R, et al. A trial of three regimens to prevent tuberculosis in Ugandan adults infected with the human immunodeficiency virus. *N Engl J Med* 1997;337:801-8.
5. Mwinga A, Hosp M, Godfrey-Faussett P, Quegley M, Mwaba P, et al. Twice weekly tuberculosis preventive therapy in HIV infection in Zambia. *AIDS* 1998;12:2447-57.
6. Pape JW, Jean SS, Ho JL, Hafner A, Johnson WD. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. *Lancet* 1993;342:268-72.
7. Hawken MP, Meme HK, Elliott LC, Chakaya JM, Morris JS, et al. Isoniazid preventive therapy for tuberculosis in HIV-1-infected adults: results of a randomized controlled trial. *AIDS* 1997;11: 875-82.
8. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 1998;47(RR-20):1-58.
9. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep* 2000;49 (RR-6):1-51.
10. Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations — United States, 2001. American Thoracic Society. *MMWR Morbid Mortal Wkly Rep* 2001;50(34): 733-5.

[The author responds:]

Stan Houston and colleagues correctly point out the discrepancy between current Canadian[1] and US[2] guidelines, with respect to HIV-infected immigrants from high-burden countries. Earlier US guidelines included suggestions that anergic HIV-infected persons be considered potential candidates for treatment of latent TB if they belonged to groups where the expected prevalence of tuberculous infection was 10% or greater.[3] More recent research has cast considerable doubt on the use of anergy testing among HIV-infected people.[4]

My purpose in reproducing the Canadian guidelines was to highlight them, rather than to evaluate them. The treatment of latent tuberculosis infection among anergic HIV-infected persons has not been supported by recent investigations — despite the biologic rationale when the prevalence of undiagnosed latent TB is expected to be high. For example, an estimated incidence of 3.0 cases of active TB per 100-person years was found in a cohort of anergic Italian patients with HIV infection — largely injection-drug users.[5]

Several of the articles cited by Houston and colleagues have limited statistical power. In a US multicentre placebo-controlled clinical trial of isoniazid among HIV-infected people with anergy and TB risk factors, substantially fewer cases of active TB occurred than expected in the placebo arm (6 cases in 257 subjects, or 0.9 per person-year), making a significant treatment effect virtually impossible to detect.[6] This may have reflected concomitant antiretroviral therapy. The Ugandan study cited did not reach target recruitment in the anergic subgroup.[7] Both studies yielded effect estimates compatible with some benefit of isoniazid (though less than for tuberculin-positive cohorts), but very wide confidence intervals.

These findings are consistent with anergic HIV-infected cohorts including people with and without latent TB. The risk of subsequent active TB must reflect the background prevalence of latent infection, the use of antiretroviral therapy, the impact of competing risks, and the risk of *subsequent* tuberculous infection. The prevalence of unidenti-