1984;59:505-12.
3. Smitz S, Legros JJ, Franchimont P, le Maire M. High molecular weight vasopressin: detection of a large amount in the plasma of a patient. *Clin Endocrinol (Oxf)* 1985;23:379-84.
4. Mizobuchi M, Kunishige M, Kubo K, Komatsu M, Bando H, Saito S. Syndrome of inappropriate secretion of ADH (SIADH) due to small cell lung cancer with extremely high plasma vasopressin level. *Intern Med* 1994;33:501-4.

[Two of the authors respond:]

In our review, we considered the laboratory evaluation of hyponatremic patients.[1] In hospital patients with hyponatremia, the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is commonly implicated, yet it is a diagnosis of exclusion.[2]

SIADH was first described by Schwartz and colleagues in 2 patients with bronchogenic lung carcinoma as early as 1957.[3] The main features of the syndrome consist of hyponatremia and hypotonicity (< 280 mOsm/kg), absence of fluid volume depletion, inappropriate urinary osmolality (> 100 mOsm/kg), increased urinary sodium excretion (> 40 mmol/L) while on normal salt and water intake, and absence of thyroid, adrenal, pituitary or renal dysfunction.[1,2] The assay of serum arginine vasopressin is not mandatory for the diagnosis of this condition.[2-4] An abnormal water load test, inappropriately raised ADH levels relative to plasma osmolality and improvement of serum sodium concentration after fluid restriction are classified as supplemental diagnostic criteria.[2]

As to its pathophysiology, SIADH results from 3 factors:[2-4]

1. Inappropriate stimulation from pulmonary pathology (bacterial pneumonia, tuberculosis, lung abscess or asthma) or drugs (cytotoxics, morphine, barbiturates, nicotine or hypoglycemic agents).
2. Uncontrolled secretion from virtually any central nervous system (CNS) disorder (infections, trauma, vascular disease or neoplasms) or after stress, such as trauma or surgery.
3. Ectopic ADH elaboration by tumours, particularly small cell (oat cell) lung carcinoma (SCLC), duodenum and pancreatic cancers, olfactory neuroblastoma and lymphomas. Indeed, these tissues have been described as increasing ADH secretion in response to osmotic stimulation in vitro.[5]

SIADH is the principal cause of hyponatremia in malignant disease. Early recognition and prompt treatment can prevent serious neurologic sequelae.[6] It has been proposed that measurement of cerebrospinal fluid and plasma concentrations of ADH together with other tumour markers, such as calcitonin, creatine kinase BB, bombesin and neuron-specific enolase, may contribute to the diagnosis of CNS metastases due to SCLC.[7] Most interestingly, the presence of larger forms (high molecular weight) of vasopressin has been demonstrated in patients with SCLC.[8,9] Although SIADH is most commonly due to an increase in paraneoplastic ADH secretion reflecting ineffective therapy, it can also be due to release of ADH from malignant cells in the period of rapid tumour lysis, reflecting effective therapy.[10] However, marker levels, including vasopressin, are not valid in defining the tumour load and cannot be used for clinical decisions on antineoplastic therapy.[7]

Overall, history taking, physical examination and routine laboratory tests suffice for the evaluation of patients presenting with hyponatremia.[1,2,4] SIADH mandates a further diagnostic workup to identify its cause. The physician should consider the possible causes and pursue them with the appropriate diagnostic tests.[2,4] Elaborate tests should be reserved for cases of uncertainty and clinical suspicion.

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References

1. Milionis HJ, Liamis GL, Elisaf MS. The hyponatremic patient: a systematic approach to laboratory diagnosis. *CMAJ* 2002;166(8):1056-62.
2. Kumar S, Berl T. Sodium. *Lancet* 1998;352:220-8.
3. Schwartz WB, Bennett W, Curlop S, Barter FC. Hyponatremia in cases of lung carcinoma. *Am J Med* 1957;23:529-42.
4. Crook MA, Velauthar U, Moran L, Griffiths W. Review of investigation and management of severe hyponatremia in a hospital population. *Ann Clin Biochem* 1999;36:158-62.
5. Kim JK, Summer SN, Wood WM, Schrier RW. Osmotic and non-osmotic regulation of arginine-vasopressin (AVP) release, mRNA and promoter activity in small cell lung carcinoma (SCLC) cells. *Mol Cell Endocrinol* 1996;123:179-86.
6. Keenan AM. Syndrome of inappropriate secretion of antidiuretic hormone in malignancy. *Semin Oncol Nurs* 1999;15:160-7.
7. Hansen M, Pedersen AG. Tumor markers in patients with lung cancer. *Chest* 1986;89(Suppl 4): 219S-224S.
8. Smitz S, Legros JJ, Franchimont P, Le Maire M. High molecular weight vasopressin: detection of a large amount in the plasma of a patient. *Clin Endocrinol* (Oxf) 1985;23:379-84.
9. Mizobuchi M, Kunishige M, Kubo K, Komatsu M, Bando H, Saito S. Syndrome of inappropriate secretion of ADH (SIADH) due to small cell lung cancer with extremely high plasma vasopressin level. *Intern Med* 1994;33:501-4.
10. Vanhees SL, Paridaens R, Vansteenkiste JF. Syndrome of inappropriate antidiuretic hormone associated with chemotherapy-induced tumour lysis in small-cell lung cancer: case report and literature review. *Ann Oncol* 2000;11:1061-5.

Consolidating health care

The article by Steven Lewis[1] proposes some interesting new roles for the federal government in the "bog and fog" of health care. However, these proposals leave me wondering what tinkering with a multilevel governance system would really accomplish in providing better health care to Canadians. I am not a health care economist or a politician, but I keep wondering why none of the multitudes of studies and reports on our medicare system, as if we had one system, did not hint at the possibility of a truly radical reform.

Why do we tolerate multiple levels of bureaucracy at all? If health care is truly a core value of Canadians, why not amend the Constitution to give the federal government complete authority to provide these services? This would eliminate 13 provincial and territorial departments of health, provincial health care associations and regulatory bodies, many federations that collectively represent these bodies at the federal level and the need for transfer payments for health care, among others.

Think about it: no more provincial medical associations or colleges of physicians and surgeons, colleges of nurses, physiotherapy and so forth. No more wrangling about inequalities in

fees or regulations and no more disputes over transfer payments.

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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.

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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.

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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 toxicity and deaths. *CMAJ* 2002;166(7):932.
3. Lessons from cisapride [editorial]. *CMAJ* 2001; 164(9):1269.
4. Sibbald B. Cisapride, before and after: still waiting 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-