

across multiple care jurisdictions can improve information flow and appropriate prescribing and monitoring of medications. Furthermore, many hospital pharmacists and physicians have implemented discharge prescription and communication tools (known variously as prescription/discharge notes form, discharge prescription form, pharmacy discharge letter and pharmacy discharge summary⁵⁻⁷) to enhance transfer of patient information to their primary care colleagues.

We hope that the evidence of the positive impact of hospital pharmacists¹⁻³ will prompt implementation of similar models of interdisciplinary care in the broader health care community to improve patient outcomes and enhance the safety of our system.

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[Two of the authors respond:]

We were not previously aware of the work done by Richard Ogilvie and John Ruedy,^{1,2} and we are grateful to them for bringing this research to our attention. We acknowledge that systematically tracking complications is not a new idea; it dates back at least as far as Ernest Codman's "end results" concept in the early 1900s.^{3,4}

Ogilvie and Ruedy's earlier study has

2 important implications. The first relates to the difference in risk of in-hospital "adverse reactions" between their study and ours: this risk was 24% among medical patients in 1965/66 but only 6% in our study⁵ and approximately 7% in the Canadian Adverse Events Study.⁶ Although this discrepancy could be due to differences in study methods, it might also relate to improvements in health care safety in Canada. This observation challenges the popular notion that health care is in a "crisis."⁷

The second point relates to the method of detecting adverse reactions. The earlier study was based on voluntary reporting by physicians and nurses. Experience at our institution and elsewhere⁸ has shown that incident reporting tools usually capture minor, clinically insignificant events while missing serious outcomes. Therefore, it would be interesting to study and implement the strategies that Ogilvie and Ruedy used in their study to encourage health care workers to report adverse events.

Neil Johnson and Myrella Roy point out the need for integrated pharmacy information systems. We agree that this is an important step toward improving the safety of outpatient prescribing. As recently noted by Tamblyn and colleagues,⁹ patients often have prescrip-

tions from multiple physicians filled at multiple pharmacies. These authors found that a computer intervention that provided prescription information along with some basic decision support significantly decreased inappropriate prescribing.

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Use of Eprex in Canada

We are writing to correct and clarify several points in Barbara Sibbald's article on recombinant human erythropoietin (epoetin alfa [Eprex]).¹ Sibbald erroneously states that Health Canada has advised practitioners "against intravenous injection" of the drug "for patients with chronic renal failure." In fact, Health Canada's advisory of Jan. 13, 2004, recommended that "where intravenous access is available, Eprex HSA-[human serum albumin]

containing formulation should be administered intravenously"; where intravenous access is not available, the HSA-containing formulation may be administered subcutaneously but only after a risk-benefit assessment.² These guidelines for the use of Eprex in Canada are detailed in the text box.

Sibbald correctly communicated the well-documented risk of pure red cell aplasia (PRCA) associated with the use of Eprex but failed to note that the degree of risk differs with the formulation and route of administration. Two formulations are available in Canada, one containing HSA as the stabilizer, the other containing polysorbate-80 (i.e., HSA-free [not "HSA-3," as mentioned in the *CMAJ* article]). The latter has recently been presented in a prefilled syringe intended for subcutaneous administration, whereas the formulation containing HSA is presented in multiuse vials. Most cases of PRCA are associated with HSA-free Eprex administered subcutaneously (this route is associated with increased development of antibodies to an immunogen³). We are not aware of any domestic or foreign reports of PRCA associated with Eprex administered intravenously.

In Europe, Eprex is available only in the HSA-free formulation. Furthermore, contraindications are not absolute in Europe, so use of a "contraindicated" product is not actually prohibited.

Therefore, it was appropriate for the European Medicines Agency to issue an advisory to health care practitioners contraindicating HSA-free Eprex in Europe, given the concern over PRCA with this formulation and the lack of an alternative. In Canada, health care professionals have access to an alternative Eprex formulation (containing HSA and not polysorbate-80), so a "ban" on the product is not appropriate.

Sibbald also stated that Eprex has been banned in Australia. However, a "Dear Healthcare Professional" letter, issued by the sponsor in December 2002, recommends "that Eprex be given by the intravenous route where feasible, as this is thought to reduce the risk of antibody formation."⁴ Therefore, to date, Eprex has not in fact been banned by the Australian Therapeutic Goods Administration.

It should also be noted that PRCA is not always irreversible; only 25% to 50% of patients become transfusion-dependent, and immunosuppressive therapy can be effective in treating the condition.³

An alternative erythropoietin has not been on the Canadian market for long, and therefore the cumulative safety data are less extensive than for older products such as Eprex. In addition, many patients who currently take the newer product have also been exposed to Eprex. The limitation of assessing products that are relatively new to the mar-

Box 1: Guidelines for use of Eprex in Canada²

Eprex HSA-containing formulation, multiuse vials

- Where intravenous access is available (e.g., patients on hemodialysis), HSA-containing formulation of Eprex should be administered intravenously
- Where intravenous access is not available (e.g., patients with renal insufficiency not yet undergoing dialysis or peritoneal dialysis patients), the HSA-containing formulation may be administered subcutaneously, provided a risk-benefit assessment of this route of administration is conducted before initiation of therapy

Eprex polysorbate-80-containing formulation (HSA-free), prefilled syringes

- Polysorbate-80-containing (HSA-free) formulation should be administered by the intravenous route only

Note: HSA = human serum albumin.