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CRA endorsement of osteoporosis guidelines

The Canadian Rheumatology Association endorses the recently published guidelines for the treatment of osteoporosis.¹ We would like to make the readership of *CMAJ* aware that we support these important recommendations.

Janet Pope

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Mandatory pharmacovigilance

A recent *CMAJ* editorial¹ commented on the lack of objective, user-friendly information from Health Canada and the pharmaceutical industry regarding the use and effectiveness of new therapies. However, one cannot help but perceive an element of hypocrisy on the part of *CMAJ*.

Since July 1994, *CMAJ* has provided a means of distribution for Health Canada's *Canadian Adverse Reaction Newsletter* (initially as part of the journal itself and now as an accompanying publication) without any editorial critique of the information presented there. Such critique is warranted for several reasons. In particular, the newsletter publishes information with medicolegal implications for appropriate medical practice.

However, many physicians have serious concerns about Health Canada's continuing reliance on a highly flawed approach to postapproval surveillance

and the department's interpretation of the resulting data. A case in point: the October issue of the newsletter described potentially severe adverse reactions associated with leflunomide,² but when all patients exposed to the drug have been monitored, the rate of adverse events reported for leflunomide has been lower than for methotrexate or other commonly used disease-modifying antirheumatic drugs for rheumatoid arthritis.³ Crude mortality rates were also lower for the patients who received leflunomide. Similar data attesting to the relative safety of leflunomide compared with methotrexate have been presented in another large study monitoring all patients exposed to leflunomide.⁴

In addition to revealing errors of ascertainment, these data highlight the serious limitations in attribution that may occur in surveillance programs that do not monitor exposure to the drug in question. Several countries have recognized and acted on these concerns by implementing surveillance programs that *do* monitor exposure (e.g., the UK National Institute of Clinical Excellence for Surveillance of Biologics). Meanwhile, as *CMAJ*'s editorialists indicated, Health Canada is only hesitantly "grasping the nettle" in addressing this issue. It is therefore all the more essential that the data it presents in its newsletter be subject to the same degree of scrutiny and peer review as any other data submitted to *CMAJ*.

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Competing interests: Dr. Maksymowych has received speaker fees from Merck and educational grants from Aventis.

[The editors of the *Canadian Adverse Reaction Newsletter* respond:]

In responding to Walter Maksymowych's letter about a recent *CMAJ* editorial¹ and an article about leflunomide² in the *Canadian Adverse Reaction Newsletter* (CARN), we would like to emphasize that every drug has benefits and risks. As its name implies, the CARN discusses mainly the risks associated with drugs rather than their benefits. Its purpose is to raise awareness of potential safety issues detected through the review of case reports submitted to Health Canada and to remind health care professionals of ways to minimize the risks. Publication of articles in the CARN is preceded by a comprehensive consultative process with scientific staff within Health Canada, the Regional Adverse Reaction Centres, members of the department's Expert Advisory Committee on Pharmacovigilance and the editor of *CMAJ*.

The leflunomide article² summarized safety information from various sources (e.g., the Arava product monograph, the *Australian Adverse Drug Reaction Bulletin* and documents on leflunomide from the European Medicines Evaluation Agency), rather than drawing conclusions based solely on the adverse reaction data presented in the article. The data in the CARN represent observational results from the Canadian Adverse Drug Reaction Monitoring Program database. Prominent caveats in the newsletter advise readers that adverse reactions to health products are considered suspicions, because a definite causal association is often impossible to determine. Spontaneous reports of adverse reactions cannot be used to estimate the frequency of such events, because adverse reactions remain underreported, and patient exposure is unknown.

Health Canada continues to enhance its postmarketing surveillance and assessment program for health products; the spontaneous adverse reaction report-

ing system represents only one aspect of many activities in this area. Comprehensive risk-benefit evaluations include information from postmarketing surveillance on a global scale, which takes into account exposure to the drug in question and the results of epidemiologic research and clinical trials to determine whether a drug's benefits continue to outweigh its risks. Despite the limitations of spontaneous reporting systems and in the absence of complete evidence, it is well recognized that adverse reaction reports are but one of the factors that may contribute to a signal of potential problems. Drug safety is a shared responsibility, and health care professionals need to be made aware of all drug safety issues to enable informed therapeutic decision-making with their patients.

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Antipsychotic drugs and diabetes

I read with interest Eric Woollorton's article about trials of risperidone involving patients with dementia¹ and would like to clarify an important point. In the article, Woollorton stated that "Risperidone . . . appears to cause diabetes." The cause of diabetes mellitus is in fact unknown. Rather, this condition is a multifactorial phenotype, and it is unlikely that any single factor will be sufficient to explain the illness in most populations. An article of which I was a coauthor² was inappropriately cited as a reference for the suggestion that risperidone causes diabetes mellitus; however, the cited article does not make such a statement.

It is emerging that several of the novel antipsychotics are associated with weight gain. Not only is this effect disquieting for patients, but it may also increase the risk of obesity-related morbidity. Furthermore, some predisposed patients receiving antipsychotic medications may have *de novo* glucose dysregulation, exacerbation of pre-existing diabetes mellitus or the induction of diabetic ketoacidosis. Although the risk associated with each of the commercially available novel antipsychotics is not definitively known, there have been significantly more cases of these problems with clozapine and olanzapine.³⁻⁵ However, that being said, it remains inaccurate to say that either of these drugs "causes" diabetes.

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Competing interests: Dr. McIntyre is a paid consultant to Eli Lilly, Janssen, AstraZeneca, Wyeth, and Organon. He has received speaker fees from Eli Lilly, Janssen Ortho, AstraZeneca, GlaxoSmithKline, Lundbeck, Wyeth, Organon, and ORYX Pharmaceuticals.

Responsibility in advertising

I was very concerned by the pictorial content of an advertisement for Marvelon (desogestrel-ethinyl estradiol) in

a recent issue of *CMAJ*.¹ The ad presents 2 images of the back seat of a car, the second with a child's car seat in place. The car seat appears identical to a model that is designed for rear-facing positioning only. In the ad, the seat is facing forward. This picture evoked a sickening feeling, because of the thought of what might happen to a child in this seat if the car were involved in a collision. I have seen the results of such events, and they can be devastating.

I believe that, given all of the community and manufacturer education that is available about proper installation of car seats, advertisers should also be responsible in their depiction of these restraint devices. The ad itself does not contain many words (and it relates to another subject altogether), but the picture is misleading. I am concerned that a parent might inadvertently, or purposely, install a car seat such as the one depicted in the incorrect manner shown in the ad.

We all know that the proper use and installation of child restraints can reduce the morbidity and mortality associated with motor vehicle collisions.² I urge both advertisers and *CMAJ* to promote and adhere to advertising excellence in a socially responsible manner. As physicians, we owe a duty of care to all who might see ads such as this one while reading *CMAJ*.

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[A representative of Organon responds:]

In response to the letters of Erika Mann and other concerned readers, Organon Canada has already submitted a new version of the "Oh baby!" Marvelon advertisement to Canadian med-