claim or the Drug Directorate decides it has pharmacologic activity, it must have a drug identification number (DIN) in order to be marketed legally. However, many products with widely recognized pharmacologic activity are sold in Canada with and without a DIN.

Tanacet, a feverfew-based product highlighted in the article, is correctly identified as the first modern herbal product accorded a DIN for a specific therapeutic application based on orthodox clinical data. However, the article states incorrectly that a DIN was needed "because it exceeds an HPB-specified level of parthenolide, the active ingredient." The DIN is based entirely on the therapeutic claim. As an employee of the Drugs Directorate for 20 years and the official spokesperson on herbal science, I was instrumental in establishing, along with Dr. Stan Heptinstall of the University of Nottingham's Queen's Medical Centre, the criterion of a minimum content of 0.2% parthenolide for feverfew leaf's sesquiterpene lactones in inhibiting in vitro release of serotonin from blood platelets. This theory of the mechanism of migraine is simply the best hypothesis so far and has not been demonstrated to be relevant to the prevention of migraine.

Further, the assertion that "before launching the product, McNeil identified which species of feverfew had the highest level of parthenolide" is false. McNeil was not involved in the DIN application, which was obtained by Herbal Laboratories in the UK. Although 34 species in 2 plant families have been identified as containing parthenolide, so far only feverfew (*Tanacetum parthenium*, dried leaf) has been clinically tested.

Finally, the statement that "Life Brand . . . products are tested to ensure standardization and shelf life of the active ingredients" displays a lack of appreciation of 2 major areas of contention in herbal medicine science today. The active constituents of a herbal medication that are responsible for its pharmacologic effects are rarely known to the degree that dose–response relations can be meaningfully established, making expiry dates a problem. The standardization claimed by many manufacturers often has more bearing on quality control and batch-to-batch consistency than on intensity and reliability of effect and is the subject of intense debate within the industry and certain regulatory agencies.

Dennis V.C. Awang, PhD, FCIC
President
MediPlant Consulting Services
Ottawa, Ont.

[The author responds:]

Clearly, despite considerable efforts to clarify the conditions under which a herbal product requires a DIN, I have not managed to fully grasp the intricacies of the process. Dr. Awang says a product may be classified as a drug requiring a DIN when "the Drug Directorate decides it has pharmacologic activity"; yet he goes on to say that "many products with widely recognized pharmacologic activity are sold in Canada . . . without a DIN." Perhaps I am not alone in failing to understand under what circumstances a product's pharmacologic activity warrants drug classification and thus requires a DIN.

McNeil stressed that Tanacet contains a consistent percentage of parthenolide, the active ingredient, and that the company had chosen to use a type of feverfew known to produce it in high enough levels for its product. I erred in inferring that the company had been active in identifying the species of plant; it was active only insofar as it made use of existing research that identified that plant, some of which must be credited to Awang.

Regarding my statement about the testing of Life Brand products to ensure standardization and shelf life of the active ingredients: I was clearly mistaken to take what I was told at face value. I should have asked for a more specific definition as to whether their standardization and shelf life referred to quality control and batch-to-batch consistency or to reliability of effect, as was implied.

Herbal medicine is indeed fraught with contention, and there are many grey areas surrounding the manufacture, regulation and control of these products that need to be addressed. I apologize for any confusion I may have inadvertently caused, and I hope that Awang's criticisms will help shed light on a complex subject.

Kate Cottrell, BA
Consecon, Ont.

Epidurals and fever: association or cause?

The Research Update item "Epidurals and fever" (*Can Med Assoc J* 1997;156:1262) was certainly newsworthy for *CMAJ* readers; however, the analysis was inaccurate and misleading. The statement that "epidural analgesia during labour *can cause* [our emphasis] fever in mothers

and lead to unnecessary sepsis evaluations and antibiotic treatment in newborns" is incorrect. The conclusion in the original article was that "use of epidural analgesia during labour is *strongly associated* [our emphasis] with the occurrence of maternal intrapartum fever."[1] Changing "strongly associated" to "can cause" is a gross overstatement and only serves to distort well-presented research and mislead readers.

There appears to be a link between epidural analgesia during labour and internal intrapartum fever, and this needs to be further investigated. However, the implication that epidural analgesia causes newborn sepsis is very misleading. In fact, of the 1047 women who had an epidural, 3 (0.29%) of their newborns actually had sepsis, and of the 610 women who did not have an epidural, 1 newborn (0.16%) had sepsis. There are implications for the management and diagnosis of intrapartum fever when a mother has an epidural during labour. However, your opening sentence will add to the misinformation on this very important topic. Taken out of context, your editorial comments may influence less informed individuals to promulgate that untruth and deny women the "gold standard" of safe and effective pain relief during labour.

D. Gray, MD
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Brendan T. Finucane, MB, BCh
Professor and Chair
Department of Anaesthesia
University of Alberta Hospital
Edmonton, Alta.

Reference

1. Lieberman E, Lang JM, Frigoletto F Jr, Richardson DK, Ringer SA, Cohen A, et al. Epidural analgesia, intrapartum fever, and neonatal sepsis evaluation. *Pediatrics* 1997;99:415-9.

[The Research Update editor replies:]

Drs. Gray and Finucane are correct: association is not causation. The words "can cause" were not meant to editorialize or to overstate the outcome of the study by Lieberman and associates.

Furthermore, there was, in the news item, no "implication that epidural analgesia causes newborn sepsis"; on the contrary, I accurately reported Lieberman and associates' conclusion that fever during epidural analgesia can "lead to *unnecessary* [my emphasis] sepsis evaluations and antibiotic treatment in newborns" because the fever may have to do with the epidural analgesia rather than an infection.

What is the nature of the link between epidural analgesia and intrapartum fever? Lieberman and associates studied "1657 nulliparous women with term pregnancies and singleton vertex fetuses who were afebrile at admission. . . . Intrapartum fever > 100.4°F occurred in 14.5% of women receiving an epidural but only 1.0% of women not receiving an epidural (adjusted odds ratio = 14.5, 95% confidence interval 6.3 to 33.2)." *CMAJ* readers may judge for themselves.

Carolyn Joyce Brown
Editor
CMAJ

Facing breast cancer far from radiation therapy centres [correction]

An incorrect telephone number for the national cancer information hotline was published in the response portion of this letter to the editor (*Can Med Assoc J* 1997;157: 253). The correct hotline number is 888 939-3333. — Ed.

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