

## Letters

### ***Drug Crime Is a Source of Abused Pain Medications in the United States***

To the Editor:

The International Narcotics Control Board consistently reports that, despite an extremely large number of transactions, little or no narcotic drugs are diverted from licit international trade into illicit channels.<sup>1</sup> Most diversion occurs within countries, where governments attempt to prevent diversion during the manufacture and distribution of controlled substances to the retail level (e.g., pharmacies and hospitals). In the United States, diversion occurs despite a closed distribution system of licensing, security, and record keeping.

Public dialogue about prescription drug abuse in the United States focuses largely on inappropriate physician prescribing and patient misuse.<sup>2,3</sup> National media reports and high-profile charges against physicians enhance the perception that physician prescribing for pain is the main cause of increases in opioid analgesic abuse.

An important but mostly overlooked diversion source involves thefts, including armed robberies, night break-ins, and employee and customer pilferage. The Controlled Substances Act makes thefts of controlled substances from Drug Enforcement Administration (DEA) registrants a federal crime, and requires pharmacists, manufacturers, and distributors to report significant thefts and losses.

The authors submitted a Freedom of Information Act request to the DEA to obtain data from Form 106 "Report of Theft or Loss of Controlled Substances." An electronic database was provided with annual data for 2000–2003. Each incident of theft/loss

included the number of dosage units, as well as the generic name, trade name, dosage strength, and formulation of the controlled substance. We evaluated six opioid medications used for moderate to severe pain that we have studied previously:<sup>4</sup> fentanyl, hydromorphone, meperidine, methadone, morphine, and oxycodone.

The database contained analyzable data from registrants in only 22 Eastern states, representing 53% of the U.S. population. A total of 12,894 theft/loss incidents were reported in these states between 2000 and 2003. Theft/losses were primarily from pharmacies (89.3%), with smaller portions from medical practitioners, manufacturers, distributors, and some addiction treatment programs that reported theft/losses of methadone.

Over the 4-year period, almost 28 million dosage units of all controlled substances were diverted. The total number of dosage units for the six opioids is as follows:

- 4,434,731 for oxycodone
- 1,026,184 for morphine
- 454,503 for methadone
- 325,921 for hydromorphone
- 132,950 for meperidine
- 81,371 for fentanyl

The number of dosage units diverted varied considerably from year to year and from drug to drug (see [Table 1](#)). The greatest increase in theft/loss between 2000 and 2003 was for fentanyl (161.3%); however, fentanyl comprised the smallest amount compared to other opioids. The second largest increase (147.2%) was for hydromorphone, but represented only 2.45% of all dosage units lost in 2003. Morphine was the only opioid showing a decrease (–57.4%). There was an 18.5% increase in losses of oxycodone; however, the proportion of oxycodone losses, compared to losses all

*Table 1*  
**Number of Dosage Units for Selected Opioid Analgesics Listed in the U.S. DEA's Theft/Loss Database<sup>a</sup>**

Year and Total Annual Dosage Units Lost or Stolen	Fentanyl	Hydromorphone	Meperidine	Methadone	Morphine	Oxycodone
2000, <i>n</i> = 6,404,965	17,644 (0.28)	75,965 (1.19)	32,447 (0.51)	99,073 (1.55)	491,356 (7.67)	1,052,305 (16.43)
2001, <i>n</i> = 8,640,891	5,759 (0.07)	28,400 (0.33)	36,966 (0.43)	82,521 (0.96)	172,387 (2.00)	979,683 (11.34)
2002, <i>n</i> = 5,157,442	11,867 (0.23)	33,739 (0.65)	25,850 (0.50)	166,288 (3.22)	153,222 (2.97)	1,155,471 (22.40)
2003, <i>n</i> = 7,652,099	46,101 (0.60)	187,817 (2.45)	37,687 (0.49)	106,621 (1.39)	209,219 (2.73)	1,247,272 (16.30)
Percentage change, 2000–2003	161.3	147.2	16.2	7.6	–57.4	18.5

<sup>a</sup>Values are expressed as number (percentage) of dosage units lost or stolen.

controlled substances was slightly lower in 2003 than in 2000, as was the case for meperidine and methadone.

#### *Comment*

This exploratory study suggests that theft is an important source of prescription opioids diverted into the illicit market. In 2003 alone, a total of 7,652,099 dosage units of controlled substances were stolen/lost, of which 1,834,717 (24.0%) dosage units were the six opioid analgesics. As a comparison, hydrocodone, an opioid analgesic frequently prescribed but not indicated for moderate to severe pain, accounted for 3,995,402 dosage units (52.2%) lost or stolen in 2003—more than twice the amount of the six study drugs combined.

We conclude that pain medications, regardless of schedule, are being stolen from the drug distribution chain prior to being prescribed, contributing to their illicit availability, abuse, and associated morbidity and mortality. National discussion about pain medication abuse and diversion should be better informed by reliable information about whether abused drugs are coming from those registered to handle controlled substances lawfully or from those who engage in criminal activities.<sup>5</sup>

If we accept uncritically that drug diversion stems only from prescriptions, we risk distorting our view of the medical profession and patients through a lens of substance abuse, which

further weakens physicians' desire to treat pain and worsens patient access to pain care. We must eliminate the impact of illegal actions on law-abiding physicians and patients.

The unchecked flow of pain medications diverted from nonmedical sources will not be addressed if diversion control focuses only on prescribers and patients. Instead, this may provoke greater scrutiny of the medical system rather than street level pharmacy crime. To achieve a positive regulatory environment for pain management and palliative care, diversion control efforts must target the correct sources and not subject law-abiding prescribers and patients to unwarranted scrutiny. Once identified, diversion sources should be addressed in a public health context, and in ways that are appropriate and proportional; vulnerabilities in the distribution system may require improved security, while responses to individual practitioners should be based on standards of professional conduct, reserving criminal prosecution for intentional diversion.

Better use must be made of existing national drug abuse databases<sup>6</sup> to put an evidence-based face on how abused prescription pain medications are obtained. A balanced response to diversion must be the goal, in which the collective resources of education, prescription monitoring, professional discipline, and law enforcement are correctly targeted without interfering with legitimate medical practice and patient care.

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## References

1. International Narcotics Control Board. Report of the International Narcotics Control Board for 2004. New York: United Nations, 2005.
2. Cicero TJ, Inciardi JA. Diversion and abuse of methadone prescribed for pain management [letter]. *JAMA* 2005;293(3):297–298.
3. Drug Enforcement Administration—Office of Diversion Control. The diversion of drugs and chemicals—A descriptive report of the programs and activities of DEA's Office of Diversion Control. Washington, DC: Drug Enforcement Administration, 1999. Available from: <http://www.dea/diversion.usdoj.gov/pubs/program/activities/index.html>. Accessed October 6, 2005.
4. Gilson AM, Ryan KM, Joranson DE, Dahl JL. A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997–2002. *J Pain Symptom Manage* 2004; 28(2):176–188.
5. Brushwood DB, Kimberlin CA. Media coverage of controlled substance diversion through theft or loss. *J Am Pharm Assoc (Wash DC)* 2004;44(4):439–444.
6. The Council of State Governments. Trends alert: Drug abuse in America—Prescription drug diversion. The Council of State Governments, Lexington, KY, 2004.

## *Intravenous Infusion of Midazolam and Flunitrazepam for Insomnia on Japanese Palliative Care Units*

To the Editor:

Insomnia is a common and highly distressing symptom in cancer patients.<sup>1–3</sup> Although a large proportion of terminal cancer patients receive hypnotic drugs,<sup>4,5</sup> many cannot use these drugs due to dysphagia or intestinal obstruction. There have been few reports describing treatment approaches when oral administration of a hypnotic agent becomes difficult in terminally ill cancer patients.

Midazolam is a short-acting, frequently used sedative for patients with refractory symptom in Japan. Midazolam, with rapid onset and short duration of action, is most frequently used as a sedative for patients with refractory symptoms.<sup>6,7</sup> Recently, some clinical reports have suggested that longer use of midazolam can lead to tolerance, and other long-acting benzodiazepines, such as flunitrazepam, have been recommended.<sup>8</sup> When patients have no oral or rectal routes available, benzodiazepines, such as midazolam and flunitrazepam, are empirically administered via intravenous infusion on Japanese palliative care units.

Before the intervention trials, we performed a national survey to clarify physician-reported practices in the use of intravenous midazolam and flunitrazepam for insomnia on Japanese palliative care units. A questionnaire was mailed to 140 representative physicians at all certified palliative care units in November, 2004.

A total of 112 physicians returned the questionnaires (response rate, 80%). Intravenous midazolam for insomnia was used in 89 institutions (79%) and intravenous flunitrazepam for insomnia in 59 institutions (53%); a combination was used in 13 institutions (12%). In nine institutions (8%), these sedatives were not used. Other drugs used with the benzodiazepines were haloperidol ( $n = 25$ ), chlorpromazine ( $n = 4$ ), diazepam ( $n = 2$ ), hydroxyzine ( $n = 2$ ), ketamine ( $n = 1$ ), propofol ( $n = 1$ ), secobarbital sodium ( $n = 1$ ), phenobarbital ( $n = 1$ ), and an oral hypnotic ( $n = 2$ ).

The administration protocol varied widely among institutions. For midazolam, continuous intravenous infusion from night till morning was the most common method (78%), and infusion until the patient fell asleep was second (12%). For flunitrazepam, infusion until the patient fell asleep was the most frequent method (42%), and infusion for a scheduled duration, such as 30 or 60 minutes at night, was second (31%).

This study revealed that, when oral use of a hypnotic became difficult, intravenous infusion of midazolam and flunitrazepam was frequently performed on palliative care units in Japan, but the administration protocol varied among institutions. A prospective study to evaluate the efficacy of these benzodiazepines for primary insomnia is strongly needed.