

Toxicology News

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Alternative Drug-Delivery Systems are Subject to Abuse

By Jeffrey M. Jentzen

From the diversion of methadone from treatment programs to the abuse of Benzedrine inhalers to the alteration of automated drug-delivery systems to the use of designer drugs, individuals have constantly attempted to bypass controls on medication administration to attain enhanced drug effects. Since the development of alternative drug therapies, there have been regular attempts to abuse them (1, 2).

Automated drug-delivery systems

Programmable, portable automated drug-delivery systems were first developed in the 1970s to dispense regularly scheduled pain medications based on the individual patient's needs. These systems have evolved into implantable subcutaneous drug-delivery pumps. Health-care professionals responsible for the maintenance of these systems can be especially prone to abusing them. The following case report represents the abuse potential of automated drug-delivery systems.

Case report: A 36-year-old male was found unresponsive at home. He had a history of back pain for which he had received subcutaneous intrathecal morphine because of his previous addiction to oral morphine. The unit had been replaced four days before due to crimping of the catheter. The pump was loaded to its full capacity of 18 mL at that time. A puncture wound was located over the pump site. Drug concentrations were 0.460 mg/L unconjugated morphine and 0.624 mg/L total morphine in the subclavian blood; 0.095 mg/L total morphine (by gas chromatography/mass spectrometry) and 0.099 mg/L unconjugated morphine (by radioimmunoassay) in the cerebrospinal fluid; and 0.080 mg/L morphine in the vitreous humor.

The pump contained only 8 mL instead of the

expected 17 mL, or 230 mg morphine instead of the expected 488 mg. The high blood morphine level did not correlate with the intrathecal infusion dose. The pump was found to be fully functional. The death was caused by overdose due to self-intoxication from medication withdrawn from the pump (3).

Transdermal drug-delivery systems

Transdermal drug-delivery systems were developed in the late 1980s. They were initially for cardiac medications and have evolved to include pain control systems. The pain medication fentanyl (Sublimaze) has been widely abused. When transdermal fentanyl patches became available under the trade name of Duragesic, reports of their abuse began to circulate almost immediately. The transdermal patches contain from 2.5 to 10 mg of fentanyl and provide continuous dosages of 25, 50, 75, or 100 µg/hr for 72 hours (4). They deliver a specific dose at a constant rate. Patients are instructed to change the patch every three days.

Even after the prescribed application time has elapsed, enough fentanyl remains within a patch to provide a potentially lethal dose. The patches can be manipulated for abuse by many methods, including oral ingestion, smoking, extraction of drug, or application of multiple continuous patches.

Patients intending to abuse the drug can easily cut open the plastic Duragesic patches and chew them. The patches are called "Chiclets" by users because their square shape suggests this chewing gum.

Case report: A 51-year-old male, who was known to abuse cocaine, heroin, and fentanyl patches, was found dead at home. The autopsy found marked pulmonary congestion and left ventricular

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Case Studies Show Principles Of Pediatric TDM: Part 1

By Holly D. Maples and Henry C. Farrar

The goal of therapeutic drug monitoring (TDM) is to optimize the effectiveness of treatment while minimizing the risks of toxicity. Typically, a TDM service evaluates the drug concentrations, correlates these concentrations with patient-care issues, and makes recommendations for dosing adjustments and subsequent monitoring of therapy.

Optimal patient care can be achieved only if therapeutic decisions are based on accurate information about the patient, the drug, and the determined drug concentration. Considering only the drug concentration, without regard to patient-care issues, will result in "treatment" of the drug concentration rather than the patient.

This review uses hypothetical cases based on actual patient situations to demonstrate important concepts in the clinical use and evaluation of drug concentrations in patient care, including appropriate sample collection and appropriate target concentrations for specific treatment.

Case 1: Sample collection site

An adolescent with cystic fibrosis and worsening pulmonary status was admitted for antibiotic therapy and respiratory care. The antibiotic regimen included intravenous tobramycin, intravenous ticarcillin/clavulanate, and inhaled tobramycin. The peak and trough tobramycin concentrations were 10 mg/L and 4 mg/L, respectively. (Usual peak and trough therapeutic values are 6–10 mg/L and 1–2 mg/L, respectively.) Thus, the trough concentration was elevated, although the peak concentration was within the therapeutic range.

A review of the case found that the tobramycin dose was appropriate for age and weight and that the test samples had been obtained at the appropriate time. However, the patient's nurse disclosed that the trough blood sample had been obtained by a fingerstick shortly after the patient had received inhaled tobramycin. During these treatments, patients hold an aerosol device over their faces while the drug is being nebulized for approximately 15 minutes. Thus, there was concern that the blood sample obtained by fingerstick had been contaminated by the aerosolized tobramycin. A repeat trough concentration obtained by venous sampling was within the therapeutic range.

In this case, a significantly elevated trough in the presence of a therapeutic peak concentration

might raise concern that the patient was not eliminating the drug appropriately or that the dosing interval was inappropriate. The natural inclination would be to extend the dosing interval. However, the important caveat is that clinicians should question a drug concentration that does not seem reasonable given the clinical setting. In this case, the child appeared to have normal renal function, as assessed by urine output, blood urea nitrogen, serum creatinine, and urine analysis, and was receiving tobramycin at an appropriate dosing interval.

This case demonstrates the importance of documenting the sampling site, which enabled the TDM service to conclude that the fingerstick sample had been contaminated. This finding avoided multiple attempts to adjust the dosing based on an incorrect drug concentration.

Another consideration in evaluating samples collected by fingerstick methods is that this blood contains a mixture of arterial blood, venous blood, and lymph fluid. This mixture can lead to variations in drug concentrations compared with venous sampling, especially at low drug concentrations or with highly tissue-bound drugs.

Case 2: Clearing the line

A child with leukemia was admitted for fever and neutropenia. Because of a history of staphylococcal central line infections, vancomycin was included in the antibiotic regimen. Peak and trough vancomycin concentrations were 50 mg/L and 8 mg/L, respectively. (Usual therapeutic peak and trough values are 20–40 mg/L and 5–10 mg/L, respectively.) The dose was appropriate for age, weight, and normal renal function, and the samples were collected at the appropriate times.

A review of the case revealed that the vancomycin had been infused and the blood sample obtained through the same central line. Based on the patient's normal renal function and estimated volume of distribution, the peak concentration was estimated using the trough concentration and was determined to be within the therapeutic range. Thus, no dosing adjustments were made.

This case is an example of a common problem in medicine, balancing the need for accurate information with the need for patient comfort and safety. Oncology patients are more susceptible to complications of frequent blood draws because of their immunosuppression and thrombocytopenia. Also, because of the frequency of blood sampling, the caregivers of pediatric oncology patients are reluctant to obtain additional peripheral blood samples. Central lines, including peripherally inserted central catheters

(PICC lines), are frequently placed in pediatric patients to limit the number of venous blood samples that must be obtained and to ease drug administration. Therefore, while it is generally accepted that a sample should not be obtained from the same line through which the drug is administered, caregivers may resist obtaining a blood sample from a peripheral site when a central line is available.

Two important aspects of clearing a line prior to blood sampling include assuring that the drug is completely infused and withdrawing enough blood back through the line to further assure that the sample is uncontaminated. In those situations in which a sample is collected through the same line that is used for infusion, sufficient fluid needs to be used to completely clear the line of the infused drug. Approximately five to seven times the volume of the line is generally required. Most standard intravenous tubing has a volume of 15 mL between the reservoir where the drug is placed and the actual intravenous site, so the volume of flush that should be infused after the drug is administered is 75 to 100 mL. Although this volume may seem insignificant in an adult patient, it could represent 40 mL/kg of additional fluid per day in a one-year-old child, which is quite substantial. Thus the volume of flush to be used to clear a line will be influenced by the age of the child, with increased flush volumes being more appropriate in older children and adults.

There are other options that can reduce the volume of flush needed to clear a line. First, the drug could be administered through a port near the intravenous insertion site, using smaller bore tubing with a syringe pump. Second, the drug could be administered in a retrograde manner, by infusing the drug in a proximal port while clamping the line between the site and the patient, allowing the drug to fill the line toward the reservoir. While these two options limit the volume of flush needed to clear the line, they can increase the risk of a line infection because of multiple entry points into the line rather than a single entry point at the reservoir.

Another option is to follow only trough concentrations, as was done in this case. If the patient appears to have a normal volume of distribution and normal renal function, this is the most desirable option because the peak concentration can be estimated with reasonable accuracy for most clinical situations. Because the peak immediately follows drug administration, it is the sample most likely to be contaminated by incomplete clearing of the intravenous line. Thus, in these situations, the trough drug concentration is the one most likely to be accurate.

This case, again, demonstrates that when evaluating a drug concentration it is important to know the

site from which a blood sample was obtained. In developing TDM policies and protocols for sample collection, it is important that clinicians balance ideal sampling methods with minimal patient discomforts and risks. It is also important to evaluate the techniques used to obtain samples.

Part 2

In the next issue, the second part of this article will include cases showing the importance of reporting times, defining the therapeutic range, the timing of sample collection, and choosing the correct drug concentration to measure.

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NACB Publishes Emergency Toxicology Lab Guidelines

By Dave Armbruster

The National Academy of Clinical Biochemistry (NACB) recently published practice guidelines for toxicology tests used to assess poisoned patients presenting in the emergency room (1).

The guidelines were created by an expert committee of emergency department physicians and clinical toxicologists. The committee's recommendations were presented at forums for discussion at several professional society meetings in the United States, Australia, and Canada in 2001. General forensic toxicology applications, including workplace and medical examiner testing, athletic drug testing, and testing for various compliance programs, were purposely excluded from the guidelines.

Degrees of consensus

The committee did not reach unanimous agreement on all the recommendations for toxicology tests that should be available for assessment of the poisoned patient, so the recommendations include qualitative ratings for the degree of consensus. An "A" indicates general approval by most participants, and a "B" indicates either no consensus or that a recommendation was not applicable to all situations. The lack of unanimity is certainly due in part to the difficulty in striking a balance between the need for

quick decision-making in the emergency room and the time required to obtain toxicology results on which to base those decisions.

Wide-spectrum, comprehensive toxicology screening may have little clinical utility because of the time such testing requires and because the screening may include compounds for which even positive results are inconsequential. Hence, the guidelines walk a fine line between the essential minimal testing and the “shotgun” approach, weighing the need to make rapid patient management decisions against the ready availability of toxicology tests. The guidelines are meant to be the starting point for educated decision-making about the best toxicology laboratory support for a given institution or situation, not a “one size fits all” edict.

The drugs considered by the expert panel were selected from the Drug Abuse Warning Network data, which is drawn from emergency department visits. Other toxic agents, such as organophosphate compounds, rodenticides, heavy metals, carbon monoxide, and toluene, were also considered, based on poison control center data.

Part I, Tier I

Part I of the guidelines lays out a two-tiered approach to classify the assays. Tier I consists of those quantitative tests for serum or plasma specimens that may have an immediate impact on patient management (see Table 1). This list is nearly identical to that proposed by the United Kingdom’s National Poisons Information Service and the Association of Clinical Biochemists (2).

The recommended turnaround time for Tier I assays is one hour or less. While the majority of participants supported this recommendation, they debated exactly how to calculate turnaround time. The question is whether the clock should start when the

specimen is received by the lab for testing or when the test is ordered in the emergency room. A lab’s ability to meet the one-hour turnaround time depends on its resources, the structure and operation of the facility (e.g., independent stat lab or central lab, whether specimens are collected by lab staff or emergency room staff, the nature of the laboratory and hospital information and reporting system, etc.), and the definition of turnaround time chosen. Concern was expressed that labs may not be able to meet the one-hour deadline, but it must be emphasized that this is an ideal goal, not a standard of care.

Part I, Tier II

The Tier II tests are more time-consuming and/or involve longer term medical problems due to toxicity than the Tier I tests. They consist of qualitative urine screening assays (see Table 2). This list elicited serious debate. Some physicians questioned the need for urine drug screening because of inaccurate results and the potential lack of impact on patient management. Positive urine screening results may be purely coincidental as opposed to causative findings, and are unnecessary if the patient is asymptomatic. However, it was recognized that facilities that already use urine screening are unlikely to stop the practice in response to these guidelines.

The committee decided to publish the Tier II tests in part to urge manufacturers to improve the performance of urine screening tests, including improving specificity, performing cross-reactivity studies, establishing appropriate cutoff levels, and establishing a clearer definition of positive and negative results.

The screening assays for tricyclic antidepressants (TCAs) provide an example of some of these problems (3). A low TCA cutoff of 300 µg/L is appropriate for therapeutic purposes, but a 1000 µg/L cutoff is more appropriate for detecting toxicity in the emergency room. TCA assays generally exhibit poor specificity, so a 300 µg/L cutoff can result in false-positive results that might be avoided with the 1000 µg/L cutoff. But the marketing of a separate TCA test with a cutoff for emergency toxicology is unlikely.

Table 1. Tier I toxicology tests

Acetaminophen
Carbamazepine
Co-oximetry for oxygen saturation, carboxyhemoglobin, and methemoglobin
Digoxin
Ethanol
Ethylene glycol
Iron
Lithium
Methanol
Phenobarbital
Salicylates
Theophylline
Transferrin
Valproic acid

Table 2. Tier II toxicology tests

Amphetamine
Barbiturates
Cocaine
Opiates
Phencyclidine (PCP)
Propoxyphene
Tricyclic antidepressants

The committee did not recommend a turnaround time for the Tier II tests because they apply to patients requiring long-term management or substance abuse counseling.

The two-tiered approach is designed to meet the needs of most facilities to deal with the majority of emergency room patients. Each facility needs to take into account its unique requirements and laboratory methodologies. The committee concluded that a particular test should not be provided solely because an automated or inexpensive assay is commercially available. Hence, testing was not recommended for cannabinoids, LSD, methaqualone, ibuprofen, and cotinine. Either the prevalence of these drugs is low (although that can be location-dependent) or they are unlikely to cause major acute clinical problems.

There was broad consensus that chain-of-custody documentation is not necessary for emergency toxicology testing and should be discouraged. Although the chain of custody is essential for forensic toxicology purposes, it doesn't contribute to patient care and may even delay treatment. However, it should be available if emergency toxicology testing is likely to have medico-legal implications, as in the case of ethanol testing of a driver suspected of being under the influence.

Part II: Immunoassays

In Part II, the guidelines recognize the serious limitations of immunoassays, which are routinely used for toxicological analyses because they are fast and available in automated format. Many emergency room physicians do not understand the weaknesses of immunoassays, especially in terms of sensitivity and specificity. The committee recommends that the emergency medicine department and the laboratory jointly provide continuing education to emergency room physicians to explain the proper interpretation of immunoassay results.

Laboratory reports should make it clear that immunoassays are "screening tests" and that positive results are "presumptive" unless confirmed by a more specific method.

In particular, laboratories should provide cross-reactivity profiles for the immunoassays they offer. These reports should clearly state that a negative urine drug screen is not definitive proof of the absence of drugs of abuse. Conversely, reports should indicate that a positive urine drug screen can result from the presence of cross-reacting drugs. Manufacturers should provide clear cross-reactivity information and should test both the therapeutic range and toxic concentrations of interfering compounds. Ideally, cross-reactivity data should be expressed as the percentage of interference caused by the compound

tested (4). The committee calls for a standardized approach for conducting cross-reactivity studies and presenting the data.

Another issue with immunoassays is the cutoff concentrations. The designated cutoffs for some immunoassays are set to meet the needs of workplace drug testing, not clinical toxicology. A pertinent example is the cutoff for opiate assays. In 1998, the Substance Abuse and Mental Health Services Administration raised the federally mandated cutoff for opiates (that is, morphine and codeine) from 300 ng/mL to 2,000 ng/mL (5). The previous 300-ng/mL cutoff is better suited for determining the presence of opiate compounds in emergency room patients. The new 2,000-ng/mL cutoff has effectively reduced the number of false-positive screening results in workplace testing programs caused by test subjects ingesting poppy seeds or taking prescription pain medications. Unfortunately, the presence of opiates well below the 2,000-ng/mL level may be useful information for the diagnosis and treatment of emergency room patients.

Benzodiazepine-class assays provide a prime example of the immunoassay specificity problem. Whether one of these assays will detect the presence of a benzodiazepine compound depends on the specific benzodiazepine used to calibrate the assay and the specific benzodiazepine and metabolites present in the patient's specimen. Many benzodiazepine assays are relatively insensitive to some of the newer benzodiazepine compounds that appeared after the assays were developed.

Guideline recommendations include that manufacturers should reformulate benzodiazepine assays to improve their detection ability or that laboratories should treat specimens with beta-glucuronidase prior to testing (6). The committee recognizes that reformulation of assays by manufacturers is unlikely to occur quickly. Pretreatment of specimens is effective, but at a time when the technical capabilities of many labs are decreasing, or at least being seriously challenged, increased sophistication of benzodiazepine testing may be unlikely.

The guidelines also address issues with opioid immunoassays and amphetamine-class immunoassays.

Part III: Ethanol

Part III covers recommendations for ethanol and other toxic alcohols. Ethanol testing is traditional in emergency toxicology. Law enforcement has been using portable and benchtop ethanol analyzers for years. Breathalyzers are used in many emergency rooms because they are accurate, precise, and inexpensive. However, the American Association for

Clinical Chemistry's Task Force on Therapeutic Drug Monitoring and Clinical Toxicology does not necessarily recommend replacing serum or plasma ethanol tests with breathalyzers because stringent quality control is needed and is perhaps best provided by laboratory oversight (7).

Some laboratories report ethanol results in g/L or g/dL in whole blood, while others report in mg/dL in serum or plasma. There can be a sizable disparity in ethanol measured in whole blood versus serum or plasma because of the difference in water content (8). A single conversion factor for blood to serum or plasma, or vice versa, cannot be used due to the differences in inter-individual hematocrits. The guidelines recommend that ethanol be reported in units clearly defined by the laboratory, and that the matrix tested (whole blood, serum, plasma, urine, or breath) and the methodology used be stated. The guidelines also discuss the analysis of methanol, ethylene glycol, isopropyl alcohol, propylene glycol, and acetoacetic acid, and the use of osmolality for the differentiation of poisoning due to various types of alcohols.

Part IV: Assays for specific compounds

Part IV of the guidelines is devoted to recommendations for assays for specific compounds found in poisoned patients. Because acetaminophen is so commonly used and readily accessible, the availability of universal quantitative screening for it is recommended. A single determination of serum or plasma acetaminophen can confirm its ingestion and, in the case of overdose, the Rumack-Matthew nomogram can allow proper therapy to be initiated (9).

Routine screening was not recommended for another very common drug, salicylate. If a patient's symptoms point to the need for salicylate screening, a qualitative test is sufficient for clinical utility.

Cyanide and hydrogen sulfide are toxic gases that can cause lethal asphyxia. Emergency department physicians rely on patient history and physical presentation to decide on treatment with a cyanide antidote. Treatment must be initiated immediately, with the decision made before toxicology test results will be available. The committee recommends that a specimen be collected in cases of suspected cyanide or hydrogen sulfide poisoning so later analysis can prove exposure.

Patients who have ingested toxic concentrations of anticoagulants, such as rodenticides, should be monitored by tests of coagulation status, such as the prothrombin time assay. The identity and concentration of the specific anticoagulant is not necessary for treatment.

Acute lead poisoning is another situation that

does not require stat testing. Although a specimen for lead testing should be drawn in the emergency room under conditions that preclude contamination by environmental lead, availability of the results within 24 hours is acceptable.

In contrast, the committee recommended that laboratories should provide the capability for stat analysis of iron in serum or plasma. The symptoms of iron toxicity are nonspecific. If the patient history and clinical presentation suggest iron overdose, a serum or plasma iron test is very useful to confirm the diagnosis. An iron assay is readily available in most clinical laboratories.

Poisoning by the heavy metals arsenic and mercury result in serious chronic conditions, but poisoning by these metals rarely results in acute toxicity. The preferred specimens are 12- or 24-hour urine collections, so arsenic and mercury assays are not stat procedures, and it is adequate to provide results within 48 hours of specimen collection. The guidelines do not recommend broad spectrum screening for the trace elements unless occupational or environmental exposure to them is suspected.

Pesticides containing carbamates and organophosphates inhibit cholinesterase and are potentially lethal. The definitive test for exposure to cholinergic agents is the red blood cell cholinesterase assay. The recommendation is that laboratories provide access to this assay for screening purposes, for example, though a reference laboratory, with an expected turnaround time of 24–48 hours.

Inhalants, such as those containing toluene, are popular substances for abuse, especially among children and adolescents. Unfortunately, emergency room physicians must rely on the signs and symptoms of inhalant abuse for the diagnosis. Stat tests for these toxicants are not currently available. Testing is typically only available at specialty laboratories and the turnaround time does not allow for the support of emergency situations.

Drugs and chemicals that are oxidizing agents include nitrates, chlorates, quinones, sulfonamides, procaine, benzocaine, and lidocaine. They can convert the regular forms of hemoglobin to methemoglobin, which doesn't bind oxygen (10). Toxic levels of methemoglobinemia can result in tissues becoming oxygen-starved. The guidelines recommend that, when methemoglobinemia is suspected, co-oximetry be used to measure oxygen saturation. Co-oximetry distinguishes the four major forms of hemoglobin: oxyhemoglobin, deoxyhemoglobin, carboxyhemoglobin, and methemoglobin. Pulse-oximetry is not recommended as it does not measure methemoglobin and overestimates oxygen saturation. Clinical labs are not necessarily familiar with these techniques.

Conclusion

The final recommendation of the committee acknowledges that most clinical laboratories cannot adopt the guidelines in their entirety. A typical laboratory lacks the spectrum of sophisticated methodology, knowledge, and experience to adhere to these guidelines in toto 24 hours a day, 365 days a year. Thus it is recommended that specialized regional toxicology centers be established to meet as many of the guidelines as feasible for a large geographical area. A reasonable turnaround time for a regional toxicology reference laboratory is around four hours.

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Drug-Delivery System Abuse

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hypertrophy. A 1.0-cm by 0.9-cm piece of clear plastic imprinted with blue devil faces was recovered from the pharynx. Toxicological analysis revealed 7.0 µg/L fentanyl, 12.0 µg/L norfentanyl, 106 µg/L cocaine, and 1080 µg/L benzoylecognine in the subclavian blood. The cause of death was certified as mixed drug toxicity.

Fentanyl patch abuse

Fentanyl patch smoking has also been recently reported. The fentanyl can be obtained by cutting the patch open and heating it, after which the residue can be easily scraped off and smoked.

Case report: A 37-year-old female with a history of drug abuse was found unresponsive and apneic after smoking a “pipe with fentanyl.” She reportedly had refrained from opioid abuse during the previous six months. In the emergency department her urine tested positive for benzoylecgonine and negative for opiates. After two doses of 2 mg of naloxone (Narcan) she regained consciousness and remained alert, requiring no further therapy. She described her preparation of the drug by cutting the edges of a 75- or 100-µg fentanyl patch and peeling apart the plastic. She placed the gel portion in a 500° oven and baked it for approximately 10 minutes until it became brown and bubbled. She then scraped off the residue and smoked it in a pipe (5).

Deaths from intravenous injection of fentanyl extracted from transdermal patches have also been reported.

Case report: A 43-year-old male was found dead in a locked bathroom of a residential halfway house. He held a syringe in his hand. A fentanyl transdermal patch with opened manufacturer’s packaging was present at the scene. The autopsy revealed an acute injection site in the antecubital vein. Analysis of the syringe revealed the presence of fentanyl. Iliac blood and serum concentrations of fentanyl were 15.0 ng/mL and 16.5 ng/mL, respectively. In addition, iliac serum concentrations of fentanyl and norfentanyl performed at a reference laboratory were reported at 14.0 ng/mL and 1.9 ng/mL, respectively.

In a recent report by the North Carolina Office of the Medical Examiner of four deaths due to in-

travenous abuse of transdermal fentanyl patches, aortic blood fentanyl concentrations ranged from 5.0 to 27.0 ng/mL (6).

OxyContin

OxyContin (Purdue Pharma) is a biphasic drug-delivery system that uses a non-dissolvable matrix infiltrated with oxycodone to provide long-term sustained release of the drug and an outer coating that provides immediate relief. Crushing the pill matrix, which liberates a high concentration of the drug, is a common method of abuse with this delivery system (7). The crushed pills are then administered by insufflation or parenteral injection. Special plastic crushing devices are occasionally recovered from the scene of fatal cases.

Case report: A 39-year-old female with a history of intravenous drug abuse was found dead in her residence. She had a tourniquet around her ankle, where there were recent injection sites. A blood-tinged syringe and a chunky-white substance recovered at the scene both tested positive for oxycodone. Toxicology examination of subclavian blood revealed an oxycodone level of 2006 µg/L, codeine of 10 µg/L, diazepam of 0.43 mg/L, and desmethyldiazepam of 0.71 mg/L. The death was certified as an acute oxycodone overdose.

The demonstration of the abuse potential of newer drug-delivery systems is intended to alert medical professionals, death investigators, and toxicologists to the reality of abuse for these devices. In-

vestigators and toxicologists should be aware of these unique methods of abuse.

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