Heroin Use by Motorists in Sweden Confirmed by Analysis of 6-Acetylmorphine in Urine

To the Editor:

Because of its very short elimination half-life of 3–6 min (1,2), heroin is never detected in blood samples from drug-impaired drivers in Sweden. Moreover, heroin's specific metabolite 6-acetylmorphine (6-AM) also has a relatively short half-life in blood and is rarely identified above the limit of quantitation (LOQ) by current gas chromatographic–mass spectrometric (GC–MS) methods (2,3). The median time interval from arrest to obtaining body fluids for toxicological analysis is about 60 min, so the time from last intake of a drug to obtaining body fluids is probably much longer. The combined influences of time delay, LOQ of the method, and the pharmacokinetic properties of the drug make it very difficult to obtain conclusive proof of heroin use from the analysis of a blood sample. Fortunately, the Swedish police strive to obtain urine samples from individuals suspected for driving under the influence of drugs (DUID). The longer elimination half-lives and higher concentrations of drugs and their metabolites in urine considerably expand the window of detection. Moreover, depending on the frequency of urination, the specimen submitted for analysis might reflect the blood concentration of drugs and metabolites several hours earlier because of a pooling effect. Unequivocal proof of heroin use is obtained by measuring its specific metabolite 6-AM in urine (4,5).

Interpreting toxicological results from analysis of opiates in body fluids is not always easy because of their metabolic conversion to morphine (3–7). The analgesic effect of codeine is generally attributed to the action of morphine, which is produced by O-demethylation (5,6). The identification of codeine together with morphine in blood or urine from DUID suspects might reflect taking a prescription drug containing codeine (5,6). If morphine sulfate, which contains about 0.04% codeine, is administered for chronic pain, one can expect extremely small concentrations of codeine in blood but definitely no 6-AM (4–6). Antitussive medication containing ethyl morphine as an active ingredient also gives morphine as a metabolite, according to analysis of blood and urine by GC–MS (7,8). Eating pastries containing poppy seeds leads to positive findings of morphine and codeine in urine, which is a well-known problem in connection with workplace drug-testing programs (9).

Since the introduction of a zero-tolerance law for driving under the influence of scheduled narcotic drugs in Sweden (1st July 1999), the number of cases submitted by the police for toxicological analysis has increased about fivefold. Blood and urine specimens are sent by the police to our laboratory, and after an initial screening analysis for five classes of abused drugs (opiates, cannabinoids, amphetamine analogues, cocaine metabolites, and benzodiazepines) by immunoassay techniques such as EMIT and CEDIA with the Hitachi 717, positive results are verified by more specific methods. For opiates this entails making a solid-phase extraction followed by GC–MS analysis with deuterium-labeled internal standards. The opiates in blood are converted to their PFPA derivatives prior to GC, and opiates in urine are converted to trimethylsilyl esters after treatment with BSTFA. The concentrations of opiates in blood and urine (morphine, codeine, ethyl morphine, and 6-AM) are quantitatively determined in a single GC–MS run and calibration plots are linear with a concentration of 1000 ng/mL used as an upper limit.

When prosecuting DUID offenders it is important to know whether toxicological findings of morphine and codeine in body fluids stem from the use of heroin or a prescription medication containing codeine. Fifty cases representative of all opiate DUID cases submitted for toxicological analysis were selected for detailed examination provided that both blood and urine specimens

| Table I. Unconjugated Concentrations of Morphine, Codeine, and 6-AM in Whole Blood and Urine Verified by GC–MS in 50 Cases of DUID in Sweden* |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Opiate present in blood and urine** | **LOQ** | **Cases verified positive** | **Median drug concentration** | **Concentration range** |
| **B-morphine** | 5 ng/g | 46 | 30 ng/g | 5 to 290 ng/g |
| **B-codeine** | 5 ng/g | 25 | 10 ng/g | 5 to 90 ng/g |
| **B-6AM** | 5 ng/g | 1 | 7 ng/g | – |
| **U-morphine** | 20 ng/mL | 50 | > 1000 ng/mL | 40 to > 1000 ng/mL |
| **U-codeine** | 20 ng/mL | 50 | 900 ng/mL | 20 to > 1000 ng/mL |
| **U-6AM** | 20 ng/mL | 41 | 700 ng/mL | 40 to > 1000 ng/mL |

* Note that 1000 ng/mL was the highest point on the calibration curve for assay of opiates in urine.

1 Limit of quantitation by GC–MS.
were available and that opiates had been verified as present. The mean age of the DUID offenders was 30 years (range 21–52 years), and 10% of them were women. Besides opiates, many other drugs of abuse were confirmed positive in body fluids including ethanol, scheduled drugs (cannabis and amphetamine), and therapeutic agents (mainly sedative-hypnotics like benzodiazepines).

Table I shows free-drug concentrations of morphine, codeine, and 6-AM determined in blood and urine by GC–MS. Of the 50 cases, only 1 contained 6-AM above LOQ in blood (5 ng/g), which suggests fairly recent use of heroin. By contrast, 41 individuals (82%) were actually verified as having taken heroin, probably within 24 h of sampling, as shown by a positive finding of 6-AM in urine (4,10).

This high prevalence of heroin use by DUID suspects would have gone unreported if urine had not been available for toxicological analysis (11). When 6-AM was identified in urine, the concentration of morphine in blood was normally 4–12 times higher than that of codeine. In 20 instances, morphine was present in blood but codeine was below the LOQ, although morphine, codeine, and 6-AM were detected in urine in high concentrations. In the 9 DUID cases without 6-AM present in urine, the morphine-to-codeine concentration ratio in blood was normally very close to or less than unity. This suggests that a reference interval of morphine-to-codeine concentration ratios in blood could be used to indicate whether a person had taken heroin as opposed to a prescription drug containing codeine. Furthermore, if proof of heroin use is a critical element in the case, then the analytical method might be modified to lower the LOQ for 6-AM in blood. Otherwise, finding 6-AM in blood above the limit of detection (LOD) but below the LOQ by GC–MS might be reported as presumptive evidence of heroin use without specifying the actual concentration of 6-AM present.

In parts of the U.S. and countries that only receive blood specimens for toxicological analysis, the finding of high morphine-to-codeine concentration ratios in blood from DUID suspects strongly suggests use of heroin. It is widely known that the source of codeine in blood and urine from heroin users reflects the presence of acetylcodeine as an impurity in the illicit heroin preparation (12,13). If opiates were administered as analgesics (e.g., for emergency treatment of victims of traffic accidents), the medical record should contain this information.

Amphetamine and cannabis are the most popular drugs of abuse in Sweden and the ones most frequently encountered among DUID suspects. However, morphine and codeine are high on the list of substances identified in body fluids from apprehended drivers, and it now seems certain that these opiates are derived from use of heroin. Finding a high ratio of morphine-to-codeine concentrations in blood should flag for presumptive use of heroin and not medication with codeine. Even if 6-AM is below the LOQ in blood samples, this proximate metabolite of heroin is invariably identified in urine samples (82% of cases) in the present set of opiate-positive DUID suspects. Another clue for use of heroin might be the occurrence of various nonopiate drugs of abuse in blood along with morphine and codeine. Polydrug use is common among DUID suspects in Sweden and elsewhere.

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References


