G93 Methadone-Related Deaths: A Review of Medical Examiner Cases in a Large Metropolitan Area

Lisa B. Shields, MD, Donna M. Hunsaker, MD, and Tracey S. Corey, MD, Office of the Chief Medical Examiner, Urban Government Center, 810 Barret Avenue, Louisville, KY 40204; John C Hunsaker III, MD, JD, Office of the Associate Chief Medical Examiner, University of Kentucky Department of Pathology and Laboratory Medicine, 100 Sower Boulevard, Suite 202, Frankfort, KY 40601-8272; and Michael K Ward, MS, Kentucky Medical Examiner's Program, Office of Forensic Toxicology, 100 Sower Blvd Suite 202, Frankfort, KY 40601*

The goals of this presentation are to (1) to present a review of methadone-related fatalities encompassing comprehensive medicolegal death investigations conducted at the Office of the Chief Medical Examiner in Kentucky between 2000 and 2004; (2) to offer guidance in the interpretation of toxicological data involving methadone, specifically in the context
(a) of the victim's use of methadone prior to death and (b) of combinations with other drugs, particularly benzodiazepines, antidepressants, and other opiates.

The documented rapid rise in methadone-related deaths in Kentucky and nationally requires a better understanding of its pathophysiology and the ways it contributes to significantly increased morbidity and mortality. A thorough investigation into the practices of procurement and use/abuse of this drug is essential to arrive at the proper designation of the cause of death. The interpretation of blood methadone concentrations alone or in combination with other psychoactive drugs must include inquiry concerning the victim's potential chronic use and tolerance of the drug. Research shows that pharmacogenetics play an equally important role in an individual's metabolism of methadone and other opiates. This presentation will impact the forensic community and/or humanity by demonstrating why further forensic study should focus on the interplay of drug metabolism with potential genetic links in individuals who die from opiate drug intoxication.

Methadone, a synthetic opioid, received approval by the U.S. Food & Drug Administration (FDA) in 1947 for use as an analgesic. By 1950, physicians prescribed it for the treatment of withdrawal symptoms associated with heroin and other opioids. The majority of methadone-associated deaths in this study include at least one other drug, in most cases another opioid or central nervous system depressants such as benzodiazepines. The synergistic effects of methadone in combination with ethanol, benzodiazepines, or other opioids may be lethal. Methadone-associated deaths skyrocketed in the early 2000's: a greater number of these deaths were reported to MedWatch (FDA's Safety Information and Adverse Event Reporting Program) in 2001 alone than in the previous decade; the number doubled once again in 2002. The dramatic increase is likely due to a rise in consumption attributable to either (a) the rise in prescription of oral methadone to outpatients for chronic pain management, or (b) the greater availability of "street" methadone, which may account for overall increases in illicit drug diversion tactics and usage.

This study reviews 176 methadone-related deaths involving postmortem examination with toxicological analyses at the Office of the Chief Medical Examiner in Louisville, Kentucky between 2000 and 2004. Analysis by the Kentucky Office of Forensic Toxicology revealed that more than a ten-fold increase in methadone-related fatalities occurred, varying from 6 cases in 2000 to 68 cases in 2003. Sixty percent were males; all were Caucasian. Individuals ranged between 17 and 60 years (mean age: 38). The average body mass index (BMI) was 26.2. The Coroner's investigation reported methadone use in 95 (54.0%) cases. Of these, 46 (48.4%) involved prescription by private physician, 19 (20.0%) obtained the drug illegally, 9 (9.5%) received it through a methadone treatment clinic, and 21 (22.1%) acquired methadone by unknown means. Of the 46 individuals receiving physician-prescribed methadone, 23 (50.0%) either initiated or refilled their prescriptions < 10 days prior to death. One-third of these had been undergoing pain management, as supported by the Coroner's documented clinical history and, in some cases, in conjunction with a lumbar or other significant surgical scar.

In view of the broad overlap in blood methadone concentrations in cases of toxicity compared to tolerant individuals on maintenance, interpretation of the postmortem blood methadone concentration was uniquely individualized for each subject. Evaluation included consideration of the history of past exposure, including amount, frequency, and duration of consumption, in an effort to determine whether the subject developed tolerance to methadone. With application of this evaluative methodology, a total of
130 (73.9%) individuals had toxic or lethal blood concentrations of methadone. The blood alcohol concentration (BAC) was negative in 152 (86.4%) of cases, while 9.1% had a BAC ? 0.1%; 4.0% had a level between 0.1% - 0.2%; and one victim had a level between 0.2% - 0.3%. The following psychoactive medications were detected in the blood: benzodiazepines (33.0%), antidepressants (39.2%), and other opiates (27.8%). The P450 metabolizers, promethazine and diphenhydramine, were frequently observed in combination with methadone, at 14.2% and in 10.2%, respectively. Urine was collected in 88.1% of cases. In addition to blood concentrations of drugs noted above, the urine screen confirmed cannabinoids in 28.4% and cocaine or its metabolites in 21.9% of all cases.

Methadone, Opiates, Pain

 ** Presenting Author*