An Underestimation of Heroin Deaths Due to the Use of “Acute Opiate Intoxication” on Death Certificates

James R. Gill, Gregory A. Vincent, Allison Toriello, Lewis S. Nelson

ABSTRACT

Introduction: Deaths due to drug intoxications in the United States have increased. Public health agencies track the specific intoxicants using death certificate data in order to develop and focus prevention strategies. Criteria used to decide what deaths need toxicological investigation and how these deaths are certified will affect this data.

Methods: We retrospectively reviewed the investigative, autopsy, and toxicology reports of 118 fatal intoxications that were certified as “acute opiate intoxication.”

Results: Of the 113 decedents in whom morphine was detected, 84 were determined to involve heroin. For 61 of 84 heroin deaths, the heroin diagnosis was based upon the detection of diacetylmorphine, 6-acetylmorphine, and/or a lower blood codeine to morphine concentration. For 23 of 84 deaths, the determination was based upon morphine detection and illicit substances and/or paraphernalia at the scene. Of the 61 of 84 heroin deaths diagnosed by direct toxicology results, 33 of the 61 (54%) did not have illicit substances or paraphernalia at the scene. Toxicology identified 33 of 84 (39%) heroin fatalities that would not have been distinguished from morphine intoxication by the scene investigation.

Conclusions: The majority of deaths due to opioids can be further classified based upon the toxicological analysis and scene investigation. As heroin deaths may have no illicit substances/paraphernalia at the scene, investigators should not solely base their decision to perform an autopsy/toxicology on the scene absence of illicit drugs/paraphernalia. In our study sample, if toxicology testing were to be only performed when illicit substances/paraphernalia were found at the scene, a high portion of heroin deaths (39%) would have been missed. *Acad Forensic Pathol.* 2016 6(1): 114-121

AUTHORS

James R. Gill MD, Connecticut Office of the Chief Medical Examiner

Roles: Project conception and/or design, data acquisition, analysis and/or interpretation, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, principal investigator of the current study, general supervision, general administrative support, writing assistance and/or technical editing.

Gregory A. Vincent MD, Connecticut Office of the Chief Medical Examiner

Roles: Data acquisition, analysis and/or interpretation, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, writing assistance and/or technical editing.

Allison Toriello MA, Office of Chief Medical Examiner of the City of New York

Roles: Data acquisition, analysis and/or interpretation, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, general administrative support.

Lewis S. Nelson MD, New York University School of Medicine - Emergency Medicine

Roles: Project conception and/or design, data acquisition, analysis and/or interpretation, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, writing assistance and/or technical editing.

CORRESPONDENCE

James R. Gill MD, 11 Shuttle Rd, Farmington CT 06032, jgill@ocme.org

ETHICAL APPROVAL

As per Journal Policies, ethical approval was not required for this manuscript

STATEMENT OF HUMAN AND ANIMAL RIGHTS

This article does not contain any studies conducted with animals or on living human subjects

STATEMENT OF INFORMED CONSENT

No identifiable personal data were presented in this manuscript

DISCLOSURES & DECLARATION OF CONFLICTS OF INTEREST

The authors, reviewers, editors, and publication staff do not report any relevant conflicts of interest

FINANCIAL DISCLOSURE

The authors have indicated that they do not have financial relationships to disclose that are relevant to this manuscript

KEYWORDS

Forensic pathology, Forensic toxicology, Opiate, Opioids, Heroin, Fatality

INFORMATION

ACADEMIC FORENSIC PATHOLOGY: THE OFFICIAL PUBLICATION OF THE NATIONAL ASSOCIATION OF MEDICAL EXAMINERS

©2017 Academic Forensic Pathology International • (ISSN: 1925-3621) • <https://doi.org/10.23907/2016.012>

Submitted for consideration on 5 Jan 2016. Accepted for publication on 12 Feb 2016

INTRODUCTION

Fatalities due to opioids in the United States have increased substantially in the past decade (1). Heroin and prescription opioid pharmaceuticals make up a large portion of these deaths (2, 3). Public health officials track these deaths and are interested in the specific opioids involved in order to develop and focus prevention strategies (3). Criteria used to decide what deaths need toxicological investigation and how these deaths are reported/certified will affect this public health data (4, 5). Medical examiners/coroners (ME/C) who investigate and certify these deaths use investigative criteria and terminology that varies among individual practitioners and jurisdictions (5-8). For example, some may use nonspecific terms such as “multidrug intoxication” or “polypharmacy.” But even more specific terminology such as “acute opiate intoxication” may not be sufficiently accurate. The National Association of Medical Examiners (NAME) and the American College of Medical Toxicology (ACMT) published a position paper that recommended that this all-inclusive practice be abandoned and that the specific names of the substances implicated in the cause of death be included on the death certificate (5, 6).

We examined 118 deaths certified as “acute opiate intoxication” with the goal of elucidating the specific opioid that caused the death. In addition, we examined how useful the scene investigation and circumstances are for the determination of the causes of these deaths.

METHODS

We reviewed 3125 medical examiner death certificates in which the death was certified between January 1, 2006 and December 31, 2010 to identify all deaths that had been certified as “acute opiate intoxication.” The New York City Office of Chief Medical Examiner (NYC OCME) investigates all unexpected, violent, and suspicious deaths in New York City. By statute, these deaths must be reported to the OCME.

The extracted death certificate data were analyzed in an electronic spreadsheet with categories that included cause and manner of death, contributing con-

ditions, location of injury, place of death, how injury occurred, age, gender, and toxicology results. The toxicology results were extracted for each death from the toxicology reports by two of the authors (JRG, AT). These results included blood concentrations for morphine, codeine, 6-acetylmorphine (6-AM), oxycodone, oxymorphone, hydrocodone, hydromorphone, propoxyphene, methadone, buprenorphine, fentanyl, meperidine, tramadol, and “opiates (screen).” In addition, qualitative results for 6-acetylmorphine and diacetylmorphine in urine and quantitative results for 6-acetylmorphine in the vitreous were extracted. Medicolegal investigative reports were reviewed for the circumstances.

Per protocol, postmortem blood was collected, preserved with sodium fluoride, and stored at 4°C. Toxicological analysis was performed on all decedents by the Forensic Toxicology Laboratory at the Office of Chief Medical Examiner. Ethanol concentrations were determined in blood using head space gas chromatography. Specimens of all decedents were routinely screened for opioids, barbiturates, amphetamines, benzoylecgonine (BE), and benzodiazepines by enzyme immunoassay or radioimmunoassay. Confirmation and quantitation of morphine, codeine, and benzoylecgonine were performed using gas chromatography/mass spectrometry (GC/MS). Urine (if present) or blood of all decedents also was analyzed by gas chromatography for basic drugs, including cocaine, phencyclidine (PCP), and methadone, with confirmation by GC/MS. In addition, morphine, codeine, 6-acetylmorphine (blood and vitreous), oxycodone, oxymorphone, hydrocodone, hydromorphone, propoxyphene, methadone, buprenorphine, fentanyl, meperidine, tramadol are included in the toxicological analysis.

For forensic pathologists, the conclusion that death was caused by acute intoxication requires that the toxicology results are within the range typically encountered in such fatalities, that the history and circumstances are consistent with a fatal intoxication, and that the autopsy fails to disclose a disease or physical injury that has an extent or severity inconsistent with continued life. In some instances, a determination of

an acute intoxication was made without an autopsy. The majority of these instances include deaths with family objections to autopsy with compelling clinical evidence of intoxication and/or instances of delayed intoxication deaths following hospital admission with medical evaluation.

Scene investigations were performed by OCME medicolegal investigators, the majority of whom are full-time OCME staff and trained physician assistants. They investigate the scene of death and document (with digital images and written reports) specific findings. Drug paraphernalia includes glass or metal pipes, syringes, tourniquets, cookers, and drug packets. "Cooks" are items (e.g., spoon, bottle cap) used to dissolve the heroin in water by the application of heat (e.g., cigarette lighter, candle). Prior to the arrival of police or the medicolegal investigator, scenes may be altered by friends or family who may dispose of the drugs or drug paraphernalia.

According to the policies of the New York City Office of Chief Medical Examiner and New York University School of Medicine, this research did not require institutional review board (IRB) approval, however, it was submitted to and approved by the OCME legal office to ensure that it complies with OCME policies and did not require IRB approval.

RESULTS

We identified 118 decedents whose death was certified as "acute opiate intoxication" (i.e., those in which a spe-

cific opioid or other drug was not included in the cause of death). Medical examiners certified all 118 deaths and 100 of the 118 underwent autopsy. The ages ranged from 18 to 66 years (mean = 44 years) and the racial/ethnic breakdown included 41 White, 46 Hispanic/Other, and 31 Black. There were 97 men and 21 women.

Toxicological results for all decedents are in **Table 1**. Of the 118 decedents whose death was certified as acute opiate intoxication, there were five decedents without morphine detected in blood and/or urine: codeine (two), oxycodone (two), and hydrocodone (one). Of the 113 decedents in which morphine was detected, 84 were determined to be due to heroin. For 61 of the 84 heroin deaths, this diagnosis was based upon the detection of diacetylmorphine in urine, 6-acetylmorphine in urine, blood, and/or vitreous, and/or a lower blood concentration of codeine compared to morphine (**Table 2**). For 23 out of 84 deaths, the determination was based upon the detection of morphine in the blood and illicit substances (drug packets) and/or paraphernalia (e.g., syringes, cookers) at the scene.

There were 24 out of 113 decedents in whom pharmaceutical morphine use could not be reasonably distinguished from heroin use because of the lack of distinct heroin metabolites or congeners and/or scene findings for heroin abuse (see discussion). Of these 24, however, 20 had a known history of substance abuse. One decedent had a morphine concentration of <0.05 mg/L and a codeine concentration of 0.62 mg/L. This intoxication death involved a former intravenous drug abuser who was receiving methadone and acetamino-

Table 1: Toxicology Results of 118 Deaths Certified as "Acute Opiate Intoxication"

	N	Morphine Detected	Codeine Detected	Diacetylmorphine Detected	6- acetylmorphine Detected**
Morphine	113	113	30*	18	38
Codeine without morphine	2	0	2	0	0
Oxycodone	2	0	0	0	0
Hydrocodone	1	0	0	0	0
Total	118	113	32	18	38

* One decedent had a lower morphine concentration (<0.05 mg/L) than codeine (0.62 mg/L) consistent with codeine, not heroin use.

** Blood or vitreous

phen with codeine in a nursing home. There were five of 113 decedents in whom only morphine was detected and prescription morphine was found at the scene. One of these decedents had a history of heroin abuse and another had a history of morphine abuse.

For heroin deaths, the morphine concentration ranged from <0.05 to 1.4 mg/L with an average of 0.31 mg/L for all instances with a concentration of 0.05 mg/L or greater (results below levels of quantitation were seen in delayed hospital deaths and decomposed remains). Of the 61 of 84 heroin deaths diagnosed by the toxicological results, 28 of the 61 (46%) also had illicit substances (drug packets) or paraphernalia (syringes, cookers, etc.) at the scene (**Table 2**). Therefore, toxicology analysis identified 33 of 84 (39%) heroin fatalities that were without diagnostic scene findings.

Diacetylmorphine was detected in the urine of 18 of 84 of the heroin deaths. 6-AM was detected in the blood of 16 of the 84 (<0.05 to 1.0 mg/L) and in the vitreous of 34 of the 84 (<0.05 - 0.12 mg/L) heroin deaths. Overall, 38 decedents had 6-acetylmorphine detected in the blood and/or vitreous.

In eight of the 113 deaths with morphine detected, additional opioids also detected were: methadone (six), tramadol (two), hydrocodone (one), and fentanyl (one). Among the 84 heroin deaths, tramadol was detected in one and methadone in three. The remaining were sole heroin intoxications.

Codeine was detected in 29 of the 84 heroin deaths and all had codeine concentrations <0.1 mg/L. Of these 29 heroin deaths with both morphine and codeine, 26

also had illicit drugs/paraphernalia at the scene (15/29) and/or heroin/6-AM (21/29) detected in the toxicological analysis. There were 83 fatalities in which morphine but no codeine was detected in the blood. Of these, 52 of 83 (63%) had illicit drugs/paraphernalia at the scene (26/52), heroin/6-AM detected (12/52), or both heroin/6-AM and illicit drugs/paraphernalia at the scene (14/52). An additional 20 of the remaining 31 of 83 had a history of substance abuse. Five of the 83 had pharmaceutical morphine at the scene including one decedent with 6-AM detected in the urine.

During this time period, there were 3125 accidental drug intoxication deaths. The majority involved multiple intoxicants. Of these 3125, there were 712 deaths in which "opiate" was included on the death certificate including 118 as "acute opiate intoxication" and four with "heroin" also listed. There were 475 deaths in which "heroin" was included in the cause of death statement including 110 deaths certified as "acute heroin intoxication." There were 798 deaths with "methadone" on the death certificate including 47 certified as "acute methadone intoxication." There were 294 deaths with oxycodone, 88 with fentanyl, and 1340 with cocaine in which these intoxicants caused or contributed to death wither alone or in combination with other substances.

DISCUSSION

In 1966, Milton Helpert published a study of heroin deaths (intravenous narcotism) in which the autopsy (*sans* toxicology) and scene findings were heavily relied upon to diagnose the intoxication death (9). In 1972, he stated that:

Table 2: Diagnoses of 84 Heroin Deaths Based on Toxicology and Circumstances

	N	Morphine	Diacetylmorphine (urine)	6-acetylmorphine*	Morphine > Codeine	Circumstances**
Heroin diagnosis by toxicological analysis	61	61	18	38	23	28
Heroin diagnosis by circumstances	23	23	0	0	0	23

* 6-acetylmorphine (6-AM) was detected in 22 instances in vitreous specimens, 12 blood and vitreous, 6 urine, and 4 blood. 6-AM only was detected in 6 decedents in urine. Diacetylmorphine also was detected in conjunction with 6-AM in 11 decedents.

** Instances with illicit substances (drug packets) and/or paraphernalia (syringes, cookers, etc.) at the scene.

A diagnosis of an acute death from narcotic addiction is more reliably arrived at from the investigation of the circumstances under which the body is found and the findings of the complete postmortem examination than from the toxicologic analysis which has proven revealing in less than half the cases (10).

The analytical abilities available in 1972 were not as sophisticated as current techniques. Despite these improved techniques, there are still limits to toxicological analysis and scene investigation. Gruszecki et al. retrospectively reviewed the history and scene investigation of 1180 deaths for indications of alcohol or drugs of abuse. They predicted that alcohol or drugs were likely to be detected in 369 cases yet toxicology testing revealed an intoxicating substance in 589 of the deaths (11). With regard to heroin, analytical limitations are related to the rapid metabolism of diacetylmorphine (heroin) and 6-acetylmorphine. The current concentrations needed for quantitation and reporting of these compounds have improved but some acute heroin intoxication deaths still do not reach the detection thresholds.

Morphine, which has a longer half-life than heroin or 6-acetylmorphine, is usually detected in heroin deaths while heroin or 6-acetylmorphine may not. This raises the dilemma as to whether the death is due to heroin or pharmaceutical morphine. Given the social stigma attached to heroin and the importance of proper diagnosis for public health statistics, some ME/C are reluctant to certify a death as “heroin” unless heroin (diacetylmorphine) or 6-acetylmorphine (a unique metabolite of heroin) is detected. This need for certainty may delay the death certification as additional samples will need to be sequentially tested for 6-AM since it may be detected in urine or vitreous when it is not detected in blood (12). This testing adds an additional cost either through increased labor and materials or through commercial laboratory costs. The use of prescription drug monitoring programs may provide further information about the intoxicant and the issue of use versus abuse (13, 14).

Studies have demonstrated that the detection of morphine associated with a trace amount of codeine is

consistent with heroin use (15, 16). Although codeine may be metabolized to morphine, morphine is not metabolized to codeine (17, 18) and the trace amount of codeine found in heroin deaths is believed to result from impurities of naturally occurring codeine in the opium from which the heroin is synthesized (15, 16). This contamination is less likely in pharmaceutical quality morphine but it has been reported (19). West et al. studied urine toxicological analysis of 535 pain patients prescribed various pharmaceutical morphine preparations. They observed 24 samples that contained codeine >20 ng/mL, of which nine samples were >50 ng/mL, including seven with high concentrations indicating codeine use. Of these, one was from a patient who had a prescription for codeine and one was positive for 6-acetylmorphine (19). Surreptitious use of heroin explains at least one of these results. The reverse observation (concentration of codeine > morphine) is consistent with codeine use.

Our data support the use of this morphine-codeine detection ratio to diagnose heroin use as 26 of the 29 morphine > codeine deaths also had illicit drugs/paraphernalia at the scene and/or heroin/6-AM detected. The inability to “confirm” three of the 29 deaths may be explained by limitations of the toxicology testing, scene investigation issues (see below), or the rare but possible pharmaceutical morphine contamination. In addition, there were two deaths due to codeine intoxication in which morphine was not detected and one codeine/morphine death in which the codeine concentration was greater than the morphine concentration. None of these three decedents had heroin/6-AM detected or drug packets/paraphernalia at the scene. These likely were pure codeine intoxications in which any codeine biotransformed to morphine was below the level of detection in two of the three.

Positive scene findings may be useful in these deaths. For example, a 19-year-old man was found in an abandoned building with a syringe in his arm with glassine envelopes stamped “horse” and a cooker (spoon) with rolled up cotton balls in it. He had a known intravenous drug abuse history and had linear scars of his arms in a vascular distribution. His toxicological analysis detected only morphine, but this is probably a

death due to heroin. From a public health perspective, it is imperative that these deaths be properly certified.

During this study period, there were 475 deaths in which “heroin” was included on the death certificate and 708 in which “opiate” was included without a mention of heroin. Of these 708 “opiate” deaths, a subset of 118 was certified as “acute opiate intoxication.” A detailed review of this subset, diagnosed 84 of the 118 (71%) heroin deaths which increases the total number of reported heroin deaths by 17%. If the remaining 590 opiate deaths included a similar composition of heroin deaths (i.e., 71%), the total number of heroin deaths would double those reported on the death certificate. As public health officials can only rely upon information on the death certificate, these heroin deaths were underestimated. In addition, at least ten of these 118 “acute opiate intoxication” deaths were due to pharmaceutical opioids. Therefore, one should not assume that all “acute opiate intoxication” deaths are due to heroin.

All of these deaths were certified by the same medical examiner office where the convention for decades was to certify morphine/codeine deaths as “acute opiate intoxications.” This may have been reasonable when 6-AM was not routinely detected and/or reported. But even when 6-AM could be routinely detected and reported, some continued to use the “acute opiate intoxication” terminology by tradition. The toxicology reports typically included a screening result for “opiates” along with specific results of confirmed opioids.

Since vital statistic bureaus rely exclusively on death certificate data, more specific data on the death certificate is preferred. This was one reason for the Centers for Disease Control and Prevention grant for NAME and ACMT to publish a joint position paper on the proper investigation and certification of these deaths. The position paper recommended listing the specific drugs on the death certificate and not using terms such as multidrug intoxication given their limited granularity (6). Neither the scene investigation nor the toxicology results alone are capable of correctly diagnosing all heroin deaths. For example, family or friends may “clean up” the scene (dispose of drugs and parapher-

nal) prior to arrival of the police. To rely solely on the scene findings without toxicology testing may miss up to 39% of heroin deaths in our study sample, while relying solely on the toxicology results without considering the scene, may misdiagnose up to 27% of heroin deaths. It is the role of the ME/C to consider the scene, autopsy, and toxicology findings when determining the cause of death.

Additional opioids were detected (methadone, hydrocodone, fentanyl, and tramadol) in eight of the 113 morphine deaths that were certified as acute opiate intoxications. Instead of including all of these under the general term of opiates or opioids, it is preferred to list each separately (5, 6). This is important because public health and law enforcement agents rely on this information to determine if, for example, fentanyl has come on to the illicit market. The use of “opiate or opioid” masks these deaths.

The use of a modifier is another option in morphine-only deaths. Some have recommended using “probable heroin” to acknowledge some doubt about the diagnosis (16). Since the degree of certainty for death certification is a probability (that is, more likely than not, >50%), the addition of the word “probable” seems redundant. In fact, for vital statistic purposes, these “probable” certifications would be coded as heroin deaths (16). Some forensic pathologists will state “acute opioid intoxication” for the cause of death and list the specific substances in the “how injury occurred” section (“injected heroin” or “ingested morphine”) to indicate the specific opioid; this additional injury data is on the death certificate and so it is available to vital statistic bureaus. There are instances in which deaths due to heroin cannot be definitively distinguished from deaths due to pharmaceutical morphine based upon current testing and investigative methods. In these instances, one may state the detected substance: “acute morphine intoxication.”

Harruff et al. recommend an alternative/modified death certification method for opioid deaths (16). They proposed terminology for the cause of death statement based on the toxicology and scene findings. For example, if 6-AM was detected, the death is certified as

“acute opiate (heroin) intoxication.” If morphine with a relatively lower codeine concentrations and scene findings supportive of intravenous drug abuse, the death would be certified as “acute opiate (probable heroin) intoxication.” A key point of this system is that the forensic pathologist should not be obligated to detect 6-AM to include heroin on the death certificate.

Decisions regarding routine toxicological testing typically are made on a practical basis designed to meet the basic statutory obligations of the office in the most cost efficient and time conscious manner. Ultimately, pathologists are required to choose how much or how little toxicology can be performed for a given death while still meeting statutory mandates (7). As Cina noted:

There is no consistency with respect to the degree of toxicological analysis performed on forensic cases across international jurisdictions as well as in the United States. Medical examiners and coroners apparently value the role of adjunctive studies to the autopsy to a variable degree. Between states, and even adjacent counties, offices will differ in their access to toxicological analysis and the budgets granted to them to perform necessary testing (7).

Forensic pathology is a medical specialty and as such it is appropriate to use objective data and clinical findings to make diagnoses and provide medical opinions. The cause of death is, in fact, a medical opinion. The degree of certainty required for an accidental intoxication death is a probability. The forensic pathologist should base the diagnosis of heroin intoxication on all available toxicological and investigative findings and not require the detection of 6-AM or diacetylmorphine in order to make the diagnosis. The scene of death may be helpful in making the diagnosis but the absence of drugs/paraphernalia does not exclude a drug intoxication death. Given the public health importance of understanding trends and details of opioid deaths (e.g., if heroin is increasing, or if oxycodone is decreasing), it is imperative that death certificates specifically state these substances and that ME/C diligently investigate these suspected deaths.

REFERENCES

- 1) Warner M, Chen LH, Makuc DM, et al. Drug poisoning deaths in the United States, 1980-2008. *NCHS Data Brief*. 2011 Dec; (81):1-8. PMID: 22617462.
- 2) Sgarlato A, deRoux SJ. Prescription opioid related deaths in New York City: a 2 year retrospective analysis prior to the introduction of the New York State I-STOP law. *Forensic Sci Med Pathol*. 2015 Sep; 11(3):388-94. PMID: 26233936. <http://dx.doi.org/10.1007/s12024-015-9699-z>.
- 3) Cicero TJ, Ellis MS, Harney J. Shifting patterns of prescription opioid and heroin abuse in the United States. *N Engl J Med*. 2015 Oct 29; 373(18):1789-90. PMID: 26510045. <http://dx.doi.org/10.1056/nejmc1505541>.
- 4) Paulozzi LJ, Ibrahimova A, Rudd RA, et al. A comparison of Florida Medical Examiners' reports and death certificates for specific drug related overdose deaths. *Acad Forensic Pathol*. 2012 Jun; 2(2):190-7.
- 5) Davis GG, National Association of Medical Examiners and American College of Medical Toxicology Expert Panel on Evaluating and Reporting Opioid Deaths. Recommendations for the investigation, diagnosis, and certification of deaths related to opioid drugs. *Acad Forensic Pathol*. 2013 Mar; 3(1):62-76.
- 6) Davis GG, National Association of Medical Examiners and American College of Medical Toxicology Expert Panel on Evaluating and Reporting Opioid Deaths. National Association of Medical Examiners position paper: Recommendations for the investigation, diagnosis, and certification of deaths related to opioid drugs. *Acad Forensic Pathol*. 2013 Mar; 3(1):77-83.
- 7) Cina SJ, Collins KA, Goldberger BA. Toxicology: what is routine for medicolegal death investigative purposes. *Acad Forensic Pathol*. 2011 Jul; 1(1):28-31.
- 8) Warner M, Paulozzi LJ, Nolte KB, et al. State Variation in certifying manner of death and drugs involved in drug intoxication deaths. *Acad Forensic Pathol*. 2013 Jun; 3(2):231-7.
- 9) Helpert M, Rho YM. Deaths from narcotism in New York City. Incidence, circumstances, and postmortem findings. *N Y State J Med*. 1966 Sep 15; 66(18):2391-408. PMID: 5222195.
- 10) Helpert M. Fatalities from narcotic addiction in New York City. Incidence, circumstances, and pathologic findings. *Hum Pathol*. 1972 Mar; 3(1):13-21. PMID: 4551317. [http://dx.doi.org/10.1016/s0046-8177\(72\)80050-9](http://dx.doi.org/10.1016/s0046-8177(72)80050-9).
- 11) Gruszecki AC, Booth J, Davis GG. The predictive value of history and scene investigation for toxicology results in a medical examiner population. *Am J Forensic Med Pathol*. 2007 Jun; 28(2):103-6. PMID: 17525557. <http://dx.doi.org/10.1097/paf.0b013e318061956d>.
- 12) Wyman J, Bultman S. Postmortem distribution of heroin metabolites in femoral blood, liver, cerebrospinal fluid, and vitreous humor. *J Anal Toxicol*. 2004 May-Jun; 28(4):260-3. PMID: 15189677. <http://dx.doi.org/10.1093/jat/28.4.260>.
- 13) Cordy C, Kelly P. Patterns of prescribing - the Rhode Island prescription monitoring program. *R I Med J (2013)*. 2013 Nov 1; 96(11):36-7. PMID: 24187677.
- 14) Greenwood-Ericksen MB, Poon SJ, Nelson LS, et al. Best practices for prescription drug monitoring programs in the emergency department setting: results of an expert panel. *Ann Emerg Med*. 2015 Nov 24. pii: S0196-0644(15)01415-8 [Epub ahead of print]. PMID: 26619757. <http://dx.doi.org/10.1016/j.annemergmed.2015.10.019>.
- 15) Ceder G, Jones AW. Concentrations of unconjugated morphine, codeine and 6-acetylmorphine in urine specimens from suspected drugged drivers. *J Forensic Sci*. 2002 Mar; 47(2):366-8. PMID: 11908609.

- 16) Harruff RC, Couper FJ, Banta-Green CJ. Tracking the opioid drug overdose epidemic in King County, Washington using an improved methodology for certifying heroin related deaths. *Acad Forensic Pathol*. 2015 Sep; 5(3):499-506.
- 17) Boerner U. The metabolism of morphine and heroin in man. *Drug Metab Rev*. 1975; 4(1):39-73. PMID: 1204496. <http://dx.doi.org/10.3109/03602537508993748>.
- 18) Adler TK, Fujimoto JM, Way EL, Baker EM. The metabolic fate of codeine in man. *J Pharmacol Exp Ther*. 1955 Jul; 114(3):251-62. PMID: 13243236.
- 19) West R, Crews B, Mikel C, et al. Anomalous observations of codeine in patients on morphine. *Ther Drug Monit*. 2009 Dec; 31(6):776-8. PMID: 19935365. <http://dx.doi.org/10.1097/FTD.0b013e3181c1082a>.