

Forensic Toxicology

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LEARNING OBJECTIVES:

1. Predict the toxicology results from history and physical findings in a case.
2. Describe the requirements for an acceptable chain of custody.
3. Explain how death can alter the concentration of a drug in blood.
4. Identify the best preservative for cocaine analysis.
5. Determine the specimens that may be collected for toxicologic analysis based on autopsy permit restrictions.
6. Explain why laboratory scientists may be called to testify concerning a laboratory result.

INDEX TERMS: Amphetamines, autopsy, benzodiazepines, chain of custody; cocaine, methadone, opiates, postmortem redistribution.

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Forensic toxicologists investigate suicides, murders, and accidental poisonings and overdoses. In 2009 accidental deaths accounted for over 117,000 deaths in the United States, 4.8% of all the deaths that occurred.¹ Poisonings accounted for 26% of the accidental deaths, second only to deaths from motor vehicle accidents (33%). These “poisonings” are accidental overdoses; this number includes neither intentional, suicidal overdoses nor deaths in which drug intoxication contributed to but did not cause death, which is true for many of the motor vehicle accidents. Medication errors in hospital patients also cause death, both in the United States² and

abroad.³ As Madea et al. point out, physicians may not even recognize that an adverse drug event has occurred, and thus the injury is never detected.³

The few reports cited above are sufficient to show that toxicologic analysis is critical in the medical-legal investigation of deaths. The reports also show that toxicologic analysis can play an important role in the investigation of an unexpected, adverse decline in a patient’s condition in a hospital, even if the decline does not end in death. This article discusses forensic aspects of toxicologic analysis in the medical-legal autopsy setting and then application of those principles in hospital practice.

Forensic Toxicology Practice

Forensic toxicology practice has some similarities to clinical toxicology, but there are also important differences. The analytical methods employed by both fields are often the same; however, clinical toxicology deals primarily with the treatment of patients, while forensic toxicology is concerned with chemical compounds and matters of law. Death investigation is a special form of medical practice, and like all medical practices it depends upon the correlation of history and physical findings to guide the choice of appropriate laboratory tests. History comes in the form of statements from relatives, who may know something of the medical history, circumstances visible at the scene, and physical findings at autopsy. For example, relatives might report that a driver who has run off the road into a tree has a history of brittle diabetes mellitus with previous episodes of loss of consciousness. Such a history would lead to analysis to assess the possibility of diabetic ketoacidosis. The presence of a half dozen open beer cans and an empty bottle of oxycodone on the floorboard of the wrecked car would provide additional history indicating the need to test for ethanol and drugs of abuse in addition to glucose.

Other physical findings that suggest drug abuse are needle track marks or birefringent foreign body material within giant cell macrophages in the lungs, both an

indication of intravenous drug abuse, most commonly heroin, an opiate. Regardless of the findings in an individual case, research has shown that dying in circumstances that bring a body under the jurisdiction of a medical examiner or coroner is sufficient to justify testing for ethanol and drugs of abuse. The prevalence of at least one intoxicating substance in a medical examiner population is 50%.⁴

If the person in the hypothetical case above is injured but alive after the wreck, physicians may request a drug screen, but treatment does not wait upon laboratory results. The unconscious patient will receive naloxone to counteract any opiate that might be present. Intubation and mechanical ventilation will prevent death from respiratory failure due to opiate intoxication. Knowing exactly which opiate was present at what specific concentration does not alter treatment, and so a simple qualitative screening test of urine suffices.

Forensic toxicology practice, however, requires identification and quantification of the specific compound. Forensic toxicologists first perform a screening test. If that screening test is positive for one or more drug classes, such as benzodiazepines and opiates, then the toxicologist proceeds to identify and quantify the specific compounds by additional tests. Gas chromatography/mass spectrometry is commonly used for identification and quantification. Some compounds, such as amphetamines, cannot withstand the temperatures necessary for gas chromatography, and so alternate methods, such as chemical derivatization, high performance liquid chromatography, or liquid chromatography/mass spectrometry may be used for identification and quantification.⁵

Whatever the method used to identify and quantify compounds, forensic practice must satisfy legal requirements so that the results of the studies are admissible in court. This simply means that specimens are transferred to the custody of the toxicology laboratory with a chain of custody, also known as a chain of evidence. Clinical practice requires that each specimen be uniquely linked to the patient from whom the specimen came, typically by name and a unique patient number and, possibly, a bar code. The name of the individual who collected the specimen and everyone who handled it must be included. It is assumed that no

one will tamper with the specimen once it is obtained. Attorneys do not make such assumptions in court, however, and so in addition to proper labeling of the specimen someone must be responsible for the integrity of the specimen from the time it is collected until the specimen is destroyed or the case goes to court. Specimen integrity is maintained by keeping specimens secured in such a way that any attempt at tampering with the specimens would be evident. By following these procedures, attorneys can question anyone who was responsible for the specimen at some time. The attorneys can ask the forensic pathologist, who collected the specimen, if the specimen was properly collected and labeled with the correct name and case number. The attorneys can ask the toxicologist who picked up the specimens from the pathologist what the toxicologist did with the samples. This sort of detailed questioning is rare, but it must always be possible to answer such questions or else the results will be barred from court.

Postmortem toxicology testing differs from hospital testing in the nature of the samples collected. Blood and urine remain the specimens of choice for forensic toxicologists, but urine might not be available. Bile and solid organs such as brain, liver, and vitreous humor are routinely collected as potential matrices for toxicology testing. As time progresses, decomposition begins and leads to the formation of samples never seen in a clinical setting, particularly purge fluid, the noxious liquid that forms as blood and organs decompose beyond recognition. Solid organs and purge fluid must undergo chemical extraction before they can be analyzed.

Even before decomposition becomes apparent, death alters the concentrations of compounds in blood and tissue, a phenomenon known as postmortem redistribution, mainly because blood ceases to circulate. Because of these changes one can no longer assume that substances in the blood are thoroughly mixed as is assumed during life.⁶ For this reason blood is obtained from a peripheral site, preferably the femoral veins, away from contaminating organs like the liver, stomach, and lungs.⁷ Peripheral blood is less likely to show an abnormally high concentration of a substance caused by diffusion from the stomach or by decomposing liver, an important source of drugs after death. Nevertheless, heart blood remains useful, because the heart provides a much greater quantity of blood.

Forensic toxicology testing sometimes requires special or unique approaches. The presence and concentration of cocaine are of great interest in a forensic investigation, but cocaine undergoes spontaneous hydrolysis at an alkaline pH.⁸ Blood normally has a pH of 7.4, so the concentration of cocaine in blood continues to decrease after death. Baselt showed that sodium fluoride inhibits the spontaneous hydrolysis of cocaine,⁸ so sodium fluoride is the anticoagulant used in forensic autopsies. Sodium fluoride is the anticoagulant in gray top tubes used for venipuncture.

Inhalant abuse poses its own problems in toxicologic analysis. Inhalants, such as 1,1,1 trichloroethane, are extremely volatile, so it is important to fill a tube with the matrix, leaving as little head space as possible, and then to keep the tube sealed until time to withdraw a sample for testing.⁹ Clues to inhalant abuse might be obvious, such as a desktop covered by cans of an aerosol product, or more subtle, such as discoloration of a fingertip by spray paint. This is an example of the crime scene investigator or medical examiner providing information to the forensic scientist to guide analyses. Because there are so many drugs of abuse and prescription drugs, if the forensic scientist has access to detailed crime scene reports, laboratory testing can be more efficient and results obtained more rapidly.

Once laboratory tests are completed, the results must be considered along with the circumstances surrounding death in order to accurately determine the cause of death. Interpretation of toxicology results requires the application of clinical judgment to the entire case. Postmortem drug concentrations are notorious for the overlap between concentrations considered lethal in one case and an incidental finding in another case. The difference is the clinical setting in which death occurred. The presence of a blood methadone concentration of 0.1 mg/L in a decedent found dead after reportedly losing consciousness and snoring loudly is a satisfactory explanation for death because the clinical scenario is compatible with decreasing consciousness progressing to respiratory failure. The presence of a blood methadone concentration of 0.42 mg/L would be an incidental finding if reliable witnesses all report that the decedent was conscious and moving when he was shot in an altercation.

Applications to Clinical Practice

Drug intoxication or an adverse drug reaction should be in the differential diagnosis for any patient who has an unexpected decline in health, including death. Circumstances make it impossible to conduct a large study to determine the incidence of illicit drug abuse in hospitalized patients, but anecdotal data make it clear that drug abuse does not stop because a person is a patient in a hospital. The author knows of a death in a hospital patient who did not have a life threatening condition. A friend of the patient injected cocaine into the patient's central line, causing the patient to stop breathing. The friend waited 10 minutes for respirations to resume before reporting to the nurses what she had done. This invaluable medical history made it easy to determine the cause of death. Suppose that the friend had quietly slipped out of the patient's room and left the hospital. In that case, toxicologic analysis for drugs of abuse would not have been done and the cause of death might never have been detected.

Autopsies are uncommon in hospital patients,¹⁰ but an unexpected death generates great interest among physicians and is more likely to lead to an autopsy. Because unsuspected drug use or an adverse drug reaction can cause death, it is important to collect whatever toxicologic samples can be obtained within the limits imposed by the autopsy permit. A chest only autopsy provides access to blood for analysis. An autopsy restricted to the abdomen provides access to blood, liver, bile, and urine, if urine is present. A head only examination allows access to blood (from the dural sinuses), cerebrospinal fluid, and brain. Whatever specimens remain in the laboratory from life should also be retained until the autopsy report is complete. In this way one could show that some substance was in the blood at the time of death but not in blood obtained in a routine draw prior to death. All specimens, whether ante mortem or post mortem, should be refrigerated to retard degradation of both the specimens and any substance that may be in the specimens. Hold the specimens at least until the autopsy report is completed; a pathologist may not realize that toxicologic testing is needed until review of the microscope slides makes clear that no anatomical cause for death is present.

Given the discussion of the importance of chain of custody for court, the reader might question the value of hospital samples for court. However, hospital samples

are invaluable. Whether the sample results are admitted into court or not is a matter that attorneys will argue before a judge according to points of law, but that should not be the primary concern of the medical team. The role of the medical team is diagnosing and treating disease, and an autopsy is a medical examination that calls for medical approaches to achieve proper diagnoses. This does not mean that the medical team should ignore the law, but neither should the requirements of court inhibit thorough and sound medical practice. Unexpected outcomes such as a cerebral hemorrhage or death are especially likely to lead to a lawsuit. Finding unsuspected and unprescribed substances in the blood of a patient who has had such an unexpected outcome will explain the patient's clinical course and help exonerate the medical team and hospital from any charge of malpractice.

In the past, laboratory personnel have rarely had to go to court as a consequence of their job, but a 2009 ruling by the United States Supreme Court has greatly increased the likelihood of being called to court to testify. In the case of *Melendez-Diaz v. Massachusetts*, the Supreme Court upheld the 6th Amendment of the Constitution, which guarantees individuals on trial in court the right to confront their accusers and challenge the statements of the accusers.¹¹ If a trial concerns whether an individual was driving while intoxicated, then a laboratory report that indicates a blood ethanol concentration in excess of the legal limit is obviously important. The Supreme Court's ruling means that if the defendant's attorney demands that the laboratory scientist who performed the test come to court to testify regarding the laboratory results, then the laboratory scientist must testify in court. The report cannot stand alone if challenged by the attorneys.

Testifying in court is daunting, especially if one is new to the experience. Written resources are available to help prepare for court,¹²⁻¹³ and one could always consult with a forensic toxicologist or pathologist for advice, but the best preparation should come from an attorney involved in the case. In responding to the subpoena to appear in court, let an attorney representing each side know that you will be happy to discuss the case and that you in turn wish to learn how to present your evidence most effectively. Consider whatever advice the attorneys give and decide whether the advice is good or bad. Then, when testifying, present the evidence as clearly as

possible.

Despite the unfamiliarity of being in court, testifying is somewhat similar to presenting before a group of medical personnel. The presenter must be prepared, present the material clearly, and then answer questions about the material presented, clarifying points that are confusing or addressing points that were not covered. And so it is for an expert witness testifying in court. Expert witnesses can be confident in their knowledge of their field, but an expert witness should never be smug or arrogant, in part because such arrogance is inappropriate and in part because sometimes the attorneys in the courtroom are knowledgeable about the expert's field, too. The secret to success in court is nothing more than to always tell the truth and to tell it politely.

SUMMARY

Toxicologic analysis is an integral part of death investigation, and the use or abuse of an unsuspected substance belongs in the differential diagnosis of patients who have a sudden, unexpected change in their condition. History and physical findings may alter suspicion that intoxication played a role in a patient's decline or death, but suspicions cannot be confirmed unless toxicologic analysis is performed, and no toxicologic analysis is possible unless someone collects the proper specimens necessary for analysis.

In a hospital autopsy the only specimens that can rightfully be collected are those within the restrictions stated in the autopsy permit. Autopsies performed by the medical examiner do not have these restrictions. Sometimes the importance of toxicologic testing in a case is not evident until days or weeks after the change in the patient's status, thus retaining the appropriate specimens until investigation of that case has ended is important. Proper interpretation of toxicologic findings requires integrating the clinical setting and findings with the toxicologic results in a way that makes medical sense. If called upon to testify concerning findings, answer the questions truthfully, politely, and in a way that is understandable to someone who has no special training in toxicology.

REFERENCES

1. Kochanek KD, Xu JQ, Murphy SL, et al. Deaths: Preliminary data for 2009. National vital statistics reports; vol 59 no 4. [Internet] Hyattsville, MD: National Center for Health

- Statistics; 2011 [cited 2011 Dec 19]. Available from http://www.cdc.gov/nchs/data/nvsr/nvsr59/nvsr59_04.pdf. Accessed 2011 Nov 22.
2. Kohn LT, Corrigan JM, Donaldson MS, editors. *To err is human: building a safer health system*. Washington, DC: National Academy Press, 2000.
 3. Madea B, Musshoff F, Preuss J. Medical negligence in drug associated deaths. *Forensic Sci Int*. 2009;190:67-73.
 4. 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;28:103-6.
 5. Drummer OH. Requirements for bioanalytical procedures in postmortem toxicology. *Anal Bioanal Chem*. 2007;388:1495-503.
 6. Ferner RE. Post-mortem clinical pharmacology. *Br J Clin Pharmacol*. 2008;66:430-43.
 7. Prouty RW, Anderson WH. The forensic science implications of site and temporal influences on postmortem blood-drug concentrations. *J Forensic Sci*. 1990;35:243-70.
 8. Baselt RC. Stability of cocaine in biological fluids. *J Chromatogr*. 1983;268:502-5.
 9. Wille SM, Lambert WE. Volatile substance abuse – post-mortem diagnosis. *Forensic Sci Int*. 2004;142:135-56.
 10. Burton EC, Collins KA. Autopsy rate and physician attitudes toward autopsy. [Internet] eMedicine from Medscape. [updated 8 April 2010; cited 2011 Dec 19]. Available at: <http://emedicine.medscape.com/article/1705948-overview#a1>.
 11. *Melendez-Diaz v. Massachusetts*, 557 U.S.; Docket No. 07-591 (2009).
 12. Davis GG. The art of attorney interaction and courtroom testimony. *Arch Pathol Lab Med*. 2006;130:1305-8.
 13. Davis GG. *Pathology and Law: A Practical Guide for the Pathologist*. New York: Springer; 2004.

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