Science Online

forensic toxicology

The founding father of forensic toxicology was a physician named Orfila, who developed the art of chemical analysis and applied it to the investigation of criminal poisoning. It was the testimony by Professor Orfila in the 1840 homicide-by-arsenic trial of Madame Lafarge that is often credited with bringing the science of forensic toxicology into the criminal courts, and thus planting the seeds of modern toxicology.

Early in the development of the field, forensic toxicologists were considered to be coroners' chemists, who were limited to the application of routine laboratory benchwork. During the last few decades, this view has changed. The forensic toxicologist must determine what and how much poisonous substance is present in human tissue samples and interpret these results through an understanding of the episode of intoxication. Academic programs in forensic toxicology were once few but are now found in several universities in the United States.

Forensic toxicologists are very much like scientific detectives. Since poisons continue to be named as causes of death and disease, forensic toxicologists must continue to carry out their job as seekers of the truth. As technology advances, toxicologists continue to adopt highly sensitive, modern analytical methods to investigate the role of chemicals in causing illness and death.

Types of Investigations

Forensics is the application of many different fields of science to the legal system. This may involve criminal activity or civil actions. Forensic toxicology is a field of forensics that applies the principles of toxicology to legal purposes. It includes three major categories: postmortem toxicology, human performance toxicology, and forensic drug testing. Early forensic toxicology dealt with only postmortem investigations, but today forensic toxicologists are involved in a variety of cases. All work or opinions of the toxicologist must withstand the scrutiny of a court of law. Reports and findings may be introduced as evidence and the toxicologist is often asked to testify. A forensic toxicologist must consider all aspects of an investigation, such as any possible symptoms, evidence found at a crime scene, or any relevant information related to the history of a case. Armed with this information and samples for analysis, the forensic toxicologist determines what toxic substances may be related to the case and at what concentrations they are present. He or she must then interpret the probable role that a drug or poison played in the case.

Toxic Agents

Many toxic substances do not produce any overt lesions, so in the absence of other suspect causes of death or injury, a toxic reaction may be suspected. Since all things are potentially toxic, these agents can exist in several forms: gases, liquids, or solids that can be of animal (e.g., biological toxins), mineral (e.g., metals), or vegetable origins. They can be therapeutic or abused drugs, venoms, household and industrial chemicals, environmental pollutants, or naturally occurring substances, to name but a few. The routes of exposure include inhalation, ingestion, injection, and absorption through the skin. They can enter the body in a single, large dose or in smaller doses over time. The concentrations found in the body can range from trace (almost not detectable) amounts to larger quantities.

Some toxins may be detected intact, but the body quickly transforms others into new compounds called metabolites. This means that a toxicologist must test for metabolites of a toxin, perhaps in addition to the toxin itself. For example, heroin is almost immediately metabolized into morphine and other metabolites, which can be readily detected, while the heroin content is rapidly reduced and more difficult to detect.

Causes of Death

Certainly, the role the forensic toxicologist plays is quite daunting. The number of deaths and injuries related to drugs, alcohol, and poisons is highly significant.

- About 3 in every 10 Americans will be involved in an alcohol-related traffic accident at some time in their lives. Motor vehicle crashes are the leading cause of death for people 33 years old or younger.

- There were an estimated 5,800 pedestrian deaths and 90,000 injuries in the year 2000. Bicycling resulted in about 800 deaths due to collisions with motor vehicles in which alcohol and drugs played a significant role.
- The four leading fatal events are poisonings, falls, fires and burns, and suffocation by an ingested object.
- The leading cause of death in the home, poisoning, took the lives of 11,500 people in 2001. This number includes deaths from drugs, medicines, other solid and liquid substances, and gases and vapors. The 25 to 44 age group had the highest death rate.
- Falls took the lives of 9,000 people, 4 out of 5 of them over the age of 65 in the year 2000.
- Smoke inhalation (carbon monoxide and cyanide poisoning) accounts for the preponderance of deaths in home fires, and alcohol is detected in a large majority of victims in such cases.
- Recreational boating resulted in 701 deaths in 2000. Alcohol was reported to be involved in 31% of these deaths.
- Each year, use of NSAIDs (nonsteroidal anti-inflammatory drugs) accounts for an estimated 7,600 deaths and 76,000 hospitalizations in the United States. NSAIDs include aspirin, ibuprofen, and naproxen.
- Illicit drug use is associated with suicide, homicide, car accidents, HIV infection, pneumonia, violence, mental illness, and hepatitis. It is estimated that more than 3 million individuals in the United States have serious drug problems.
  source: Mokdad, A.H., J.S. Marks, D.F. Stroup, and J.L. Gerberding. "Actual Causes of Death in the United States." Journal of the American Medical Association *291, no. 10 (March 10, 2004): 1238–1245.*

Due to the lack of proper reporting, the exact number of poisonings in the United States is not known. The leading cause of fatal injury across all age groups and for both sexes is motor vehicle crashes and as many as 50% of these are alcohol- and drug-related. The number one cause of nonfatal injuries is falls and, again, alcohol is a significant contributor. Violence-related deaths also rank high among the leading causes of death, and drugs are known to contribute greatly to violent deaths. Females are much more likely than males to attempt suicide, with higher nonfatal self-harm injury rates; however, males are more likely to commit suicide. For females, suicide by poisoning is among the 10 leading causes of death.

About 2 million poisoning cases are officially documented each year. In the United States, fatalities from poisoning usually number in the tens of thousands each year. Of all poisonings reported, young children (under age 6) account for the largest percentage. However, adults account for the majority of fatal poisonings, with the greatest number of these being intentional (suicide) or accidental drug overdoses.

The Toxicological Investigation

In a perfect world, we could categorize all substances as either toxic or nontoxic. However, as Paracelsus said, "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy." So, it is not really proper to say a substance is never toxic. However, we can still figure out the level of risk of exposure to a chemical based upon how toxic it is compared to other chemicals. People differ widely in their responses to many substances. Nonetheless, the forensic toxicologist is charged with detecting and keeping track of a large number of chemical agents in biological samples. The significance of the results must often be explained to a jury. The pharmacology, toxicology, local patterns of drug abuse, and postmortem changes can all affect the results. In any case, a good toxicologist must be prepared to answer the following questions:

1. What drug was taken, when, and how?
2. Was the drug or drugs sufficient to kill or to affect behavior?
3. Was a substance taken for therapeutic purposes, was it abused recreationally, was it used for suicidal purposes, or was it administered homicidally?
4. Was the person intoxicated at the time of the incident?
5. What are the effects on behavior or performance?
6. How would a person show intoxication with this substance?
7. Is there an alternative explanation for the findings?
8. What additional tests might shed light on these questions?

The Modern Forensic Toxicology Laboratory

For an investigation, a forensic toxicologist receives samples of body fluids, tissues, and organs that are removed at autopsy.

There will also be access to the case history, which may contain helpful information regarding possible symptoms of poisoning as well as other relevant pre- and postmortem information. In order to accurately interpret these findings, the toxicologist needs a thorough knowledge of how drugs and chemicals enter the body, what happens to them once they enter (i.e., how the body chemically transforms them), and how they are excreted.

The drugs must be separated and isolated from the tissues and potentially interfering substances must be removed. Most drugs are acidic or basic and they are separated from biological samples by acidic or basic extraction. Acidic drugs are extracted with an organic solvent at a pH solution of less than 7; basic drugs are extracted with a solution that has a pH greater than 7. Neutral drugs can be extracted at any pH. For example, cocaine is a basic drug that would be soluble in organic solvent at a basic pH, while barbiturates would be soluble at an acidic pH due to their acidic groups.

Following various sample preparation and separation techniques, forensic toxicological analysis consists of two major steps: preliminary screening tests and confirmational analysis. Confirmation is the use of methods that give structurally specific information about a compound in order to eliminate the potential for false positive results. Screening tests allow the toxicologist to rapidly test for a variety of drugs and toxins. Screening tests give preliminary results, and then a positive result must be verified with a confirmatory test.

Testing for Poisons

Screening methods provide information regarding the presence of drugs or poisons. This may be relatively specific to a particular drug or poison or to a particular class of drugs. No single technique can detect everything, but a screening protocol should detect or eliminate as many substances as possible. Screening tests include immunoassays, chromatography, and color tests. Certain drugs and chemicals are more commonly encountered by the toxicologist (alcohol, cocaine, opiates, amphetamines, and sedatives), therefore specific screening tests will look for these substances. If a more exotic agent is suspected in a case, then additional tests may be requested. Often the nature of the poison is unidentified and termed a general unknown. In cases of this type, a full toxicology screen of all available specimens by several different techniques is required.

When a presumptive positive result is obtained for a substance, it must then be confirmed and quantified. Confirmation means obtaining analytic data from which it may be concluded with reasonable scientific certainty that a particular substance is present. This is necessary since presumptive positive findings may often be false positives due to interference in the test sample from contamination, improper handling, or the presence of other drugs. Confirmation tests look for structurally specific information about a compound in order to eliminate the potential for false positive results.

The most common technique used for confirmational analysis is gas chromatography/mass spectrometry (GC/MS). GC/MS combines gas-liquid chromatography for separation of the components and mass spectrometry to identify different substances within the test sample. In addition to drug detection, it is used for a variety of forensic applications, including seized drug analysis, arson and explosives investigations, and airport security to screen baggage for illicit substances. GC/MS is considered the best method for forensic substance identification and confirmational analysis.

In the GC/MS, the gas chromatograph separates the chemical components based on differences in their chemical properties.

*****IMAGE*****

The result is that the molecules pass through the GC column at different rates, thus separating them based upon their individual retention times on the column. As the substances leave the gas chromatograph, they enter the mass spectrometer to be identified. The most common mass spectrometer uses a high-energy electron beam to break up the molecules and ionizes the sample material into fragments. Each molecule has an identifiable spectrum that can be compared by a computer to a library of thousands of spectra for a match.

*****IMAGE*****

By using GC/MS, a very accurate identification is possible. The likelihood that two different samples could have the same retention time and the same spectra is near impossible. When a specific mass spectrum appears at a retention time for a particular compound, it is considered to be proof, with a very high degree of scientific certainty, that the particular molecule in the sample has been positively identified. Another widely used technique is liquid chromatography/mass spectrometry (LC/MS), in which the separation phase uses a liquid rather than a gas. Here the LC portion of the technique is used for preliminary separation of the components.

Qualitative analysis itself can only tell us what drug or poison was present. Information as to the possible role it played in a death or accident, or the person's level of intoxication, requires quantitative analysis. The samples used for this purpose are typically from blood, or the liver or other organs. Stomach contents may also be analyzed for total amount of drug present. Typically, quantities are determined by chromatography, either GC/MS or LC/MS.

Toxicology in the Courtroom

The results of a toxicological investigation may be included in court testimony. Either the forensic pathologist or a qualified toxicologist may be asked to give an opinion as to whether a drug or toxin contributed to a death or accident or played a role in a violent crime. Often, the defense will call its own experts to dispute the opinions given by the plaintiff or prosecutor's medical experts. Cases involving drugs and toxins often become a battle of the experts and such proceedings can become quite intense, with the jury left to decide which expert opinion seems most likely to be true.

The following is a sampling of the types of questions that the forensic toxicologist might be asked by medical, legal, or law enforcement professionals:

- Was the driver intoxicated at the time of a car crash?
- Was a defendant under the influence of PCP (angel dust) when he shot and killed two acquaintances?
- Was cocaine-induced psychosis a likely explanation for a person's bizarre and violent behavior?
- Was alcohol involved when a person fell down a flight of stairs?
- (In the case of a death in a fire) Was the victim burned? Is the death consistent with smoke inhalation? Was the victim dead before the fire started?
- Were drugs used to incapacitate a girl during an alleged date rape?
- Was a drug used to commit suicide?
- Was a person murdered with a poison?

The forensic toxicologist must be able to provide accurate and concise answers to these questions using language that is easily understood by juries, judges, and lawyers. Furthermore, the opinions expressed by the toxicologist must always be impartial and based only on the scientific facts involved.