Forensic Toxicology: Role in the Overdose Epidemic

Trista Wright, Ph.D.

Disclosures

- Work as a forensic toxicologist for the Virginia Department of Forensic Science (DFS)
- The scientific methods are specific to DFS and protocols maybe different at other agencies
- Fatal overdose trends discussed in this presentation were published in the “VDH Fatal Drug Overdose Quarterly Report-2nd Quarter 2019” in Oct 2019
- Graphic pictures from death scenes are included in this presentation
Objectives

- Describe the role of forensic toxicology in the Commonwealth of Virginia.
- Explain the methods used to detect drugs and their metabolites in biological specimens.
- Evaluate the role of forensic toxicology to address cause of death in suspected overdose deaths.

TRIAD IN TOXICOLOGIC INVESTIGATIONS

Autopsy

History (Investigation)  Toxicology (Laboratory)
Specimens Collection

- Blood
- Urine
- Vitreous
- Gastric
- Bile
- Liver
- Other tissues like spleen or lung

Not all blood is created equal

Best
- Subdural
- Femoral
- Iliac
- Brachial
- Subclavian
- Heart
- Chest

Worse
Postmortem Redistribution

- A phenomenon whereby increased concentrations of some drugs are observed in postmortem samples and/or site dependent differences in drug concentrations may be observed.
- Typically central blood samples are more prone to postmortem changes (will have greater drug concentrations than peripheral blood samples).

Urine

- Many drugs and metabolites are present in higher concentrations.
- Drugs remain in urine for days or longer after use.
- Helpful in delayed death cases.
Vitreous

- Good stability
- Resides in an anatomically isolated area
- Location, location, location
  - More resistant to putrefactive changes than other specimens
- Helpful for the interpretation of postmortem blood ethanol concentration

Gastric

- Helpful in overdose situations
- Tablets in stomach contents can provide easy identification of ingested substance in still intact
- Large contents of drug can also be detected in stomach content if pills are dissolved
- Examples:
  - Limited blood samples (~2 mL)
  - Empty pill capsules were identified as venlafaxine
  - The extended release capsules were still intact, but drug had already absorbed
  - Lab was able to specifically quantitate venlafaxine
  - Lethal concentration of venlafaxine was present in blood
**Bile**

- Can be used in the absence of urine
- Certain drugs such as narcotics and benzodiazepines can be concentrated

**Liver**

- Parent drugs and their metabolites can be higher in concentration
- Can make detection easier
- Many drugs like tricyclic antidepressants are sequestered in the liver
- Disadvantage: drugs must be isolated from difficult matrix
Other Tissues

- Lung: collected in cases involving inhalation of a volatiles substances
- Spleen (rich in red blood cells): can be used for carbon monoxide analysis if blood is not available or unsuitable.
Forensic Toxicology

- The application of toxicology for the purpose of the law
  - Postmortem forensic toxicology
  - Human performance toxicology
  - Forensic drug testing

Forensic Toxicology: How Can We Help?

- The use of multiple scientific disciplines to \textit{AID} medical or legal investigation of death, poisoning, or drug use.

- Identify and quantify drugs and alcohol in biological specimens to \textit{HELP} determine whether they caused or contributed to death.

- Offer expert witness testimony regarding the effects of drugs and alcohol on human performance and \textit{INTERPRET} toxicological findings.
Types of Testing Performed at DFS Toxicology

- Alcohols: Ethanol, inhalants, other small volatile compounds

- Drug screens for common classes of drugs
  - 18 drugs and/or drug classes comprise initial screening
  - Expanded testing includes additional prescription drugs and over the counter medications

- Drug identity confirmation and quantification in a case sample is done using a more sensitive and accurate analytical method.

Blood Alcohol Content

- Positive samples are analyzed twice, on separate days
- If available another specimen type (i.e., vitreous or urine) will be used to confirm previously ran specimen
- Two results are averaged and reported to 3 decimal places
Case History
20-year-old male was found in a crashed vehicle in wooded area by hikers.
Girlfriend stated that couple had a fight and had not spoken or seen each other in 3 days.
Toxicology results:
- Chest cavity blood ethanol concentration: 0.095% weight by volume
- Vitreous humor: none detected

What may explain the difference in ethanol concentrations between specimens??
- Deceased was drinking shots at a bar prior to accident. There was extensive trauma to the chest from crash which compromised the stomach and GI tract.
- Chest cavity blood was likely falsely elevated by unabsorbed alcohol and postmortem alcohol production.
- Vitreous humor was not contaminated due to its peripheral location and uncompromised vesicle.

Why are testing multiple specimens important?

ELISA Drug Screen

Cocaine
Opiates
Oxycodone
Methamphetamine/MDMA
PCP (Angel Dust)
Barbiturates
Benzodiazepines
Carisoprodol (Soma)
Buprenorphine

Fentanyl
Methadone
Marijuana (THC)
Zolpidem (Ambien)
Diphenhydramine (Benadryl)
Dextromethorphan
Tramadol
Tricyclic Antidepressants
Amphetamine/Phentermine

Presumptive positive results sent to confirmation/quantitation.
Presumptive Drug Screens

**Advantages**

- Able to look for the most commonly abused/used drugs and/or drug classes
- Minimizes analyst time and amount of sample used

**Disadvantages**

- Requires additional testing to confirm identity and determine the concentration of the drug
- Not an exhaustive screen

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**Confirmation Testing - Extraction Steps**

- **GOAL:** Isolate the drug(s) of interest from the evidence (biological matrix).
- **PROCESS:** Manipulation of biochemical principles to remove proteins, cells, and other unwanted material from a sample.
- **END RESULT:** Unknown drugs of interest in a solution amenable to testing.
Other instrumentation

- Gas Chromatograph-Mass Spectrometer (GC-MS)
- Gas Chromatograph-Nitrogen Phosphate Detector (GC-NPD)
- Manuals are published on Virginia DFS website

Carbon Monoxide
- Normal COHb saturation: 0-3
- Smokers: 3-8
- Dizziness, nausea, vomiting: 30-40
- Coma/Death: >50

Inhalants
- Gasoline, glue, paint, etc...
- Difluoroethane: found in “dust off”
- Short acting, intense high

Can cause both impairment and death
Case Example

- **History**
  - Forty-three-year old male found dead in motel room

- **Autopsy**
  - No evidence of trauma or injury
  - Pulmonary edema
  - Needle tracks

Case Example

- **Toxicology--Urine:**
  - morphine
  - 6-monoacetylmorphine
  - cocaine and metabolites

- **Toxicology--Blood:**
  - morphine: 0.65 mg/L (fatal approx 0.40)
  - cocaine: none detected
Case Example

- Cause of Death: Narcotic Intoxication
- Manner of Death: Accidental

Trends in Overdose Death Investigations

- Virginia Department of Health- Office of Chief Medical Examiner’s Office publishes Quarterly Fatal Overdose Report
- The full report can be found at: http://www.vdh.virginia.gov/medical-examiner/forensic-epidemiology/
 Fatal Drug Overdose Categories

- Benzodiazepines
- Cocaine
- Fentanyl
- Heroin
- Prescription Opioids (excluding Fentanyl)
Benzodiazepines

Total Number of Fatal Benzodiazepine Overdoses by Quarter and Year of Death, 2007-2019*
(Data for 2019 is a Predicted Total for the Entire Year)

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<th>Year</th>
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Benzodiazepines

Total Number of Fatal Benzodiazepine Overdoses by Drug Name and Year of Death, 2007-2019*
(Data for 2019 is a Predicted Total for the Entire Year)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Number of Fatalities</th>
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<td>Desipramine</td>
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*Data for 2019 is a Predicted Total for the Entire Year

†Paroxetine, lorazepam, milontam, oxazepam, cipralex, temazepam and trazaporan were excluded from this analysis because of low annual case counts (>2 deaths per year)

‡Each benzodiazepine is listed by each time it caused or contributed to death (analyzed from either toxicoLOGY or the cause of death statement) and therefore the total number of benzodiazepines will be greater than the actual number of fatalities.
Cocaine

Total Number of Fatal Cocaine Overdoses by Quarter and Year of Death, 2007-2019*
(Data for 2019 is a Predicted Total for the Entire Year)

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Fentanyl

Total Number of Fatal Fentanyl Overdoses by Quarter and Year of Death, 2007-2019*
(Data for 2019 is a Predicted Total for the Entire Year)

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Fatal Fentanyl Origin

Total Number of Fatal Fentanyl Overdoses by Fentanyl Origin and Month of Death, 2016-2019*
(Data for 2019 is a Predicted Total for the Entire Year)

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Total Number of Fatal Fentanyl Analog Overdoses by Quarter and Year of Death, 2014-2019*

1. Methadone
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134. Methan affordable

*Each fentanyl analog is listed by time and cause of death (as noted on the cause of death statement). Therefore, the total number of analogs does not add up to the actual number of deaths.
Heroin

Methamphetamine
Prescription Opioid

Fatal drug overdose has been the leading method of unnatural death in Virginia since 2013
Opioids have been the driving force behind the large increases in fatal overdoses since 2013
In 2015 statewide, the number of illicit opioids deaths surpassed prescription opioid deaths. This trend continued at a greater magnitude in 2016, 2017, and 2018.
There has not been a significant increase or decrease in fatal prescription opioid overdoses over the 12-year time span (2007-2018)
Fentanyl (prescription, illicit, and/or analogs) caused or contributed to death in nearly 55% of all fatal overdoses in 2018
For the first time since 2012, the number of fatal overdoses in 2018 actually decreased from the previous year
Fatal non-opioid illicit drug overdoses are on the rise. In 218 compared to 2017, fatal cocaine overdose increased 11.5% and fatal methamphetamine overdoses increased 44.3%

All information regarding fatal overdose trends were published in the VDH Quarterly report Oct 2019
7202 Brook Road – Trailer # 15
THIS FIRE WAS SO HOT, THAT IT BURNED AND DAMAGED THE TRAILER ADJACENT TO IT.
Wife advised that when she left the trailer, husband was lying on the couch watching television.
The victim was located less than 2 feet from the hallway door

Fire Fighters advised us that upon their arrival, all the doors to the trailer were locked, and they had to force entry.
It was later determined that one of the Fire Fighters stepped on the victim causing this injury while he was trying to locate survivors and extinguish the fire.
It was determined by Investigator that the fire originated in the living room in the area of the couch.
Was this arson?

- Investigator determined the area of origin of the fire
- Investigator thoroughly considered each of the potential causes of the fire
- Investigator ruled out every potential cause except arson, including:
  - Electrical
  - Portable heating units
  - Oil furnace
  - Cooking
  - Gas stove

- Also considered during the investigation were:
  - Hot water heater
  - Dish washer
  - Washer/Dryer: Operational, only external damage, and not in the area of origin

- It was also checked, and there were no lightning strikes in the area.
Investigator concluded that the fire was most likely “incendiary in nature” or intentionally set.
Computer Crimes Investigator executed search warrants on the computers that were found in the trailer. We learned that wife had been e-mailing her ex-husband, and stated that she would kill her current husband, “that son-of-a-bitch” if she ever caught him cheating. It was also determined that someone had accessed the husband’s life insurance information from this computer.

Couple had two vehicles. Both were taken as possible evidence. It was determined that husband primarily drove the red Mitsubishi Mirage and wife drove the black Nissan Pathfinder. Search Warrants were executed on both of the vehicles. No evidence of value was recovered from the Mitsubishi Mirage.
However, the search of the Nissan Pathfinder proved to be substantially more interesting.
Victim’s Toxicology Results

- **Blood**
  - Diphenhydramine 0.1 mg/L (Benadryl)
  - Venlafaxine 3.3 mg/L (Effexor)
  - Carbon Monoxide > 60% saturation

- **Liver**
  - Diphenhydramine 3 mg/kg
  - Venlafaxine 24 mg/kg

- **Gastric Contents**
  - Diphenhydramine 9 mg/L
  - Venlafaxine 420 mg/L
Venlafaxine

- Antidepressant
- Daily dose 25-200 mg
- Toxic Side Effects: sedation, drowsiness, confusion, hallucinations, disorientation, fatigue, nausea, vomiting, seizures, coma and death
- Formulations
  - Regular immediate release tablets
  - Time release capsules (XR-extended release)
Evidence for Tampering with Effexor XR Time Release Mechanism

- Venlafaxine levels in blood and liver nearly 10X greater than metabolite (acute, recent, ingestion)

- 420 mg/L venlafaxine in gastric contents (acute, recent ingestion)

- Venlafaxine levels clearly toxic, potentially lethal

- Levels of venlafaxine/metabolite suggest acute ingestion of 25-35 pills yet gastric contents did not contain 25-35 pill containing "spheroids"
Conclusions

- Victim died from smoke inhalation
- Venlafaxine levels were substantial and would have significantly affected his state of mind, consciousness and ability to get out of the fire
- Time release mechanism of Venlafaxine XR was altered
  - Acute (not absorbed over 24 hrs, little metabolism)
  - High levels of venlafaxine in gastric yet very few “spheroids” from venlafaxine XR
Autopsy Results

PATHOLOGICAL DIAGNOSES:
Carbon monoxide poisoning due to soot and smoke inhalation due to house fire:
Soot in trachea, bronchi, and esophagus.
First degree burns of face and torso (less than 10% of total body surface area).
Incised wound (non-lethal) of right forearm.
No injuries to major blood vessels.
Atherosclerosis, moderate to marked, coronary arteries.

Postmortem Toxicology:
- Blood – carbon monoxide greater than 60% saturation,
  diphenhydramine 0.1 mg/L,
  venlafaxine 3.3 mg/L,
  paroxetine less than 0.1 mg/L.
- Alcohol, benzo diazepines, and other alkali-extractable drugs not detected.
- Vitreous – alcohol not detected.
- Liver – diphenhydramine 3 mg/Kg.
- venlafaxine 24 mg/Kg.
- paroxetine 0.8 mg/Kg.
- Gastric Contents – diphenhydramine 9 mg/L,
  venlafaxine 420 mg/L.

Cause of Death: Carbon monoxide poisoning due to soot and smoke inhalation.

Provisional Report: 05/22/03
Final Report: 09/30/03

Investigation and Prosecution
Wife made statements to the family before and after the fire:

- “I hope he dies, because I get $150,000”
- “If I have to, I’d kill him myself to get the money so we could go on vacation”
- “How can I kill somebody without getting caught?”

Witness #1 (a friend of the wife) testified that in the past, she had seen wife break up medicine and place them in husband’s drink.

Witness #2 testified that she observed wife put pills in husband’s drink. She said the pills dissolved and when husband drank the drink, he went to sleep.

Witness #3 (wife’s son-in-law) testified that wife asked him to get rid of a mortar and pestle the weekend before the fire.

On May 19th, 2003, the night before the fire, Witness #4 observed wife trying to get husband to eat a bowl of food even though it appeared that he didn’t want to.

When Witness #4 asked if he could have some of the food, wife said that he didn’t want any of it.
Wife received 2 life sentences for the commission of the crime of murder and burning an occupied dwelling.
Thank You!
Questions?

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