The Negative Autopsy

Jennie V. Duval, M.D.
Chief Medical Examiner
New Hampshire
THINK Positive
Learning Objectives

- Recognize the importance of integrating medical history, scene investigation, autopsy findings and additional studies in order to accurately determine cause of death
“A pathologist who searches for recent pathological alterations to explain every death is doomed to failure”

Spitz and Fisher 2006
Classification of Autopsy Findings

- **Class I**
  - COD identified by pathologic findings with certainty
  - 5% of natural deaths

- **Class II**
  - Disease or circumstances capable of causing death
  - Most natural deaths

- **Class III**
  - Marginal pathology

- **Class IV**
  - Lethal lesion not structurally demonstrable

- **Class V**
  - Undetermined COD
  - Up to 5%

*Spitz and Fisher 2006*
Undetermined COD in N.H.

- SUID: 12 (50%)
- Sudden cardiac death: 8 (33%)
- Unexplained drowning: 1 (4%)
- Decomp: 3 (13%)

24 (2%) cases 7/1/2015 – 6/30/2017
The Negative Autopsy

- No or inadequate anatomic cause of death
  - Excluding decomposed/incomplete remains
- Functional cause of death
  - Electrical excitation or depression of the heart/CNS
- COD based on scene and circumstances and additional testing
- COD may be a diagnosis of exclusion
- COD may not be identifiable
Negative/Minimal/Nonspecific Findings

Natural
- Nonstructural heart disease
  - Channelopathies
- Noncardiac disease
  - SUID/SIDS/SUDC
  - SUDEP
  - Metabolic disorders
  - Anaphylaxis
  - Sepsis
  - Excited delirium syndrome

Non-natural
- Excited delirium syndrome
- Toxicologic
- Asphyxias
- Drowning
- Hyperthermia
- Hypothermia
- Low voltage electrocution
- Commotio cordis
- Fatal concussion
- Air embolism
Negative Autopsy Case Studies
Case 1 History

- 24 yo female found dead in bedroom in AM
- H/o schizoaffective disorder with recent voluntary hospitalization
- Prescribed olanzapine, haloperidol, lorazepam
Autopsy

- Negative
## Toxicology

### Positive Findings:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
<th>Units</th>
<th>Matrix Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotinine</td>
<td>Positive</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>&lt;5.0</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>180</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Delta-9 Carboxy THC</td>
<td>&lt;5.0</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Delta-9 THC</td>
<td>1.0</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
</tbody>
</table>

The following side effects have been reported following use of this compound; disturbances of body temperature, cardiovascular complications, altered mental status and tardive dyskinesia (uncontrolled movements of extremities). In 3 reported fatalities involving acute overdoses of the drug, postmortem blood concentrations ranged from 1000 - 4900 ng/mL.
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Additional Information

- LKA at 01:45 previous day returning home after spending evening with friends at bar
- Medications appear underused
- Three weeks earlier brought to ER after found on lawn incoherent and “flapping her arms contorting her body”
  - “like a wrestlers bridge, on the back of her head and heels”
- Symptoms resolved with olanzapine and diphenhydramine
- Admitted she did not take medications that day because “they smelled funny”
Death Certification

- **Cause of death?**
  - Positional asphyxia due to tardive dystonia due to olanzapine therapy for schizoaffective disorder

- **Manner of death**
  - Accident
Tardive Dyskinesia

- Chronic blockade of dopamine receptors leads to upregulation and supersensitivity?
- Tardive dystonia classic features are retrocollis, opisthotonic trunk posturing and arm extension
Positional Asphyxia

- Position of body or kinking of neck interferes with respiration
- Frequently inverted
  - Weight of abdominal organs impedes diaphragm
  - Impaired venous return
- Inability to change position
- Autopsy negative
Case 2 History

- 34 yo male inmate observed striking head repeatedly on edge of sink in cell
- Ultimately subdued after multiple CEW discharges and prone restraint
- Secured to stretcher in prone position with handcuffs and leg shackles
- Turned blue and stopped breathing
Autopsy

- Multiple scalp lacerations
- CEW wounds
- Scattered abrasions and contusions
- Cardiac hypertrophy (400 g)
- Arteriolonephrosclerosis
## Toxicology

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</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>47</td>
<td>ng/mL</td>
<td>004 - Femoral Blood</td>
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<tr>
<td>Caffeine</td>
<td>Positive</td>
<td>mcg/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Bupropion</td>
<td>130</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Hydroxybupropion</td>
<td>140</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>110</td>
<td>ng/mL</td>
<td>002 - Heart Blood</td>
</tr>
</tbody>
</table>
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Past Medical History

- Paranoid schizophrenia
  - Prescribed olanzapine and gabapentin
  - Prior agitation and self injury after stopping medications
  - Refused meds and witnessed pacing with clenched fists previous day
- Remote history of IVDA
Surveillance videos show breathing/movement after secured to stretcher
Witnessed to turn blue and stop breathing 5–6 minutes later
AED no shock advised
Initial rhythm asystole
Core temp 36.8°F (4.5 hrs after death)
Death Certification

- Cause of death?
  - Excited Delirium Syndrome due to paranoid schizophrenia
  - Prolonged exertion during physical restraint
- Manner of death?
  - Accident
## EDS Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Frequency, % (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance to pain</td>
<td>100 (83–100)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>100 (83–100)</td>
</tr>
<tr>
<td>Sweating</td>
<td>95 (75–100)</td>
</tr>
<tr>
<td>Agitation</td>
<td>95 (75–100)</td>
</tr>
<tr>
<td>Hyperthermia to touch</td>
<td>95 (75–100)</td>
</tr>
<tr>
<td>Noncompliance to police commands</td>
<td>90 (68–99)</td>
</tr>
<tr>
<td>Lack of tiring</td>
<td>90 (68–90)</td>
</tr>
<tr>
<td>Unusual strength</td>
<td>90 (68–90)</td>
</tr>
<tr>
<td>Dressed inappropriately for environment</td>
<td>70 (45–88)</td>
</tr>
<tr>
<td>Attraction to mirrors or glass</td>
<td>10 (not reported)</td>
</tr>
</tbody>
</table>

Gerold 2015
Excited Delirium Syndrome

- Life-threatening condition with many causes
  - Stimulant drug use
  - Psychiatric illness
- Death preceded by sudden cessation of struggling against restraints
  - Peak catecholamines and low potassium
- Autopsy fails to detect disease or injury that explains death
Case 3 History

- 46 yo male found dead seated at kitchen counter
- h/o epilepsy, drug abuse, smoker, ETOH
- LKA passed out and snoring previous night
Autopsy

- Negative
# Toxicology

**Positive Findings:**

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<tr>
<th>Compound</th>
<th>Result</th>
<th>Units</th>
<th>Matrix Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>66</td>
<td>ng/mL</td>
<td>002 - Femoral Blood</td>
</tr>
<tr>
<td>Oxycodone - Free</td>
<td>110</td>
<td>ng/mL</td>
<td>002 - Femoral Blood</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>8.0</td>
<td>mcg/mL</td>
<td>002 - Femoral Blood</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>29</td>
<td>ng/mL</td>
<td>002 - Femoral Blood</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Positive</td>
<td>mcg/mL</td>
<td>001 - Heart Blood</td>
</tr>
<tr>
<td>Cotinine</td>
<td>Positive</td>
<td>ng/mL</td>
<td>001 - Heart Blood</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Presump Pos</td>
<td>ng/mL</td>
<td>003 - Urine</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>Presump Pos</td>
<td>ng/mL</td>
<td>003 - Urine</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Presump Pos</td>
<td>ng/mL</td>
<td>003 - Urine</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Presump Pos</td>
<td>ng/mL</td>
<td>003 - Urine</td>
</tr>
</tbody>
</table>
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Additional Information

- Drinking with neighbor and working on replacing electrical outlets
- While using screwdriver there was spark
- Neighbor told him to stop for night and sober up
- LKA snoring with head resting on folded arms on counter
“the outlet in question was in proper working order and it did not appear that electricity contributed to the death”
Operation

**WARNING: Risk of Electrocution.** High-voltage circuits, both AC and DC, are very dangerous and should be measured with great care.

**WARNING: Risk of Electrocution.** Before using to check for voltage in a socket, always test the detector on a known live circuit to verify that the detector is working properly.

**WARNING: Risk of Electrocution.** Keep hands and fingers on the body of the detector and away from the test leads.

- Insert the red (A) and black (B) test leads into an outlet socket, electrical contacts, or the conductor to be tested. If voltage is present, the 110V (C) and 220V (D) indicator lights glow at the approximate voltage level indicated.
- To determine which socket is hot on either two-wire or three-wire ground, insert the red test lead (A) into alternating sides of the receptacle. If the screw or outlet is properly grounded, the indicator lights (C and D) will glow on the hot side.
Death Certification

- Cause of death?
  - Low voltage electrocution
- Manner of death?
  - Accident
Low Voltage Electrocution

- < 600 – 1000 Volts
- Small burns in 50%
  - Typical crater with central charring
  - Abrasion-like
  - Thermal burn
- Mechanism of death is ventricular fibrillation
  - Lag time
Case 4 History

- 53 yo male found dead in bed in boarding house
- Previous night heard yelling ("help" or "hello") and repeating "I’ll talk to you tomorrow"
- Depressed with financial problems
- No known drug use
- Regular exercise (running)
Autopsy

- Negative
Histology

- Negative
Toxicology

- Negative
Questions

- Now what?
# Vitreous Chemistry

<table>
<thead>
<tr>
<th>TEST-NAME</th>
<th>AB</th>
<th>RESULT</th>
<th>NRML-RANGE</th>
<th>UNITS</th>
<th>VERIFIED</th>
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<tbody>
<tr>
<td><strong>Screening/Monitoring</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specimen YEL Collected 04/11/17 12:00 Received 04/11/17 16:47</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetone</td>
<td></td>
<td>Pos 1-32</td>
<td>Negative</td>
<td></td>
<td>04/11/17 16:49</td>
</tr>
<tr>
<td><strong>CSF/Fluid Testing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Specimen PLC Collected 04/11/17 12:00 Received 04/11/17 15:11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fluid type: Vitreous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, Fluid</td>
<td></td>
<td>190</td>
<td>mmol/L</td>
<td>04/11/17 16:47</td>
<td></td>
</tr>
<tr>
<td>Potassium, Fluid</td>
<td></td>
<td>14.9</td>
<td>mmol/L</td>
<td>04/11/17 16:47</td>
<td></td>
</tr>
<tr>
<td>Chloride, Fluid</td>
<td></td>
<td>156</td>
<td>mmol/L</td>
<td>04/11/17 16:47</td>
<td></td>
</tr>
<tr>
<td>Glucose, Fluid</td>
<td></td>
<td>777</td>
<td>mg/dL</td>
<td>04/11/17 16:47</td>
<td></td>
</tr>
<tr>
<td>BUN, Fluid</td>
<td></td>
<td>112</td>
<td>mg/dL</td>
<td>04/11/17 16:47</td>
<td></td>
</tr>
<tr>
<td>Enz. Creatinine, Fluid</td>
<td></td>
<td>2.6</td>
<td>mg/dL</td>
<td>04/11/17 16:47</td>
<td></td>
</tr>
</tbody>
</table>

Reference range not applicable.
Death Certification

- Cause of death?
  - Diabetic ketoacidosis
- Manner
  - Natural
Diabetic Ketoacidosis

- Hyperglycemia
- Ketoacidosis
- Ketonuria
Signs and Symptoms of DKA

Central
- Headache
- Sleepiness
- Confusion
- Loss of consciousness
- Coma

Respiratory
- Shortness of breath
- Coughing

Muscular
- Seizures
- Weakness

Intestinal
- Diarrhea

Heart
- Arrhythmia
- Increased heart rate

Gastric
- Nausea
- Vomiting
Postmortem Diagnosis of DKA

- Biochemical tests
  - Vitreous (or CSF) glucose > ± 200 mg/dL
  - Blood (or vitreous) BHB > 250 mg/L
  - Blood hemoglobin A1c > 4%

- Variable and nonspecific autopsy findings
  - Dehydration
  - Armanni Ebstein lesion
  - Fatty liver

*Milroy 2012*
Case 5 History

- 59 yo female found dead in bed
- LKA previous evening sleeping on couch
- h/o epilepsy (topiramate, levetiracetam, lacosamide)
Autopsy

- Negative
# Toxicology

**Positive Findings:**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
<th>Units</th>
<th>Matrix Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>270</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Desmethylsertraline</td>
<td>930</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Topiramate</td>
<td>14000</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>58</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>120</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>160</td>
<td>ng/mL</td>
<td>001 - Femoral Blood</td>
</tr>
<tr>
<td>Lacosamide</td>
<td>2.0</td>
<td>mcg/mL</td>
<td>001 - Femoral Blood</td>
</tr>
</tbody>
</table>
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Additional Information

- Suffered several seizures day before
- Found prone in bed with face in pillow
Death Certification

- Cause of death?
  - Sudden unexpected death in epilepsy (SUDEP)

- Manner
  - Natural
SUDEP

- Seizures
  - Provoked (acute symptomatic)
    - Fever, drug intoxication or withdrawal, electrolyte imbalance
  - Unprovoked
    - Genetic, developmental, acquired (e.g. trauma) or unknown cause

- Epilepsy
  - Two or more unprovoked seizures

- SUDEP
  - Sudden, unexpected, witnessed or unwitnessed, nontraumatic and nondrowning death, occurring in benign circumstances, in an individual with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a cause of death
SUDEP Pathophysiology

Devinsky 2016

Figure 2: Model of sudden unexpected death in epilepsy pathophysiology
Suppression of brainstem function, arousal, and respiration seem to be crucial mechanisms, along with many other factors that can contribute to risk of sudden unexpected death in epilepsy.
Epilepsy and Sudden Death

- Mortality rates 11-fold higher
  - Natural causes
  - Nonnatural causes
- Sudden death 24 to 27-fold higher
  - Bradyarrhythmias/asystole vs SCD
- Risk factors
  - Poor GTC seizure control
  - Prone position
SUDEP

- Autopsy “findings”
  - Tongue trauma (17–50%)
  - Urinary incontinence
  - Pulmonary edema
  - Neuropathology (46–71%)
  - Toxicology

- Alcohol
  - Acute symptomatic seizure
  - Risk factor for epilepsy

- AED
  - Subtherapeutic/absent (57–92%)
  - Postmortem alterations
Neuropathology Report

FINAL DIAGNOSES

I. History of epilepsy (by report).
   a. Neuronomegaly and oligodendroglial satellitosis, left frontal cortex.
   b. Mineralization and gliosis of stratum lacunosum-moleculare, right hippocampus.
Case 6 History

- 19 yo male found dead on couch
- h/o drug abuse (snorting crushed oxycodone)
Autopsy

- Negative
## Toxicology Results

### Positive Findings:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
<th>Units</th>
<th>Matrix Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta-9 THC</td>
<td>1.9</td>
<td>ng/mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Delta-9 Carboxy THC</td>
<td>9.3</td>
<td>ng/mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Cotinine</td>
<td>Positive</td>
<td>ng/mL</td>
<td>Heart Blood</td>
</tr>
</tbody>
</table>
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Additional Information

- No drug paraphernalia found
- LKA at 6:00 am sleeping on couch when aunt left for work
- Found dead at 4:30 pm when aunt came home from work
Supplemental Toxicology Results

Positive Findings:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
<th>Units</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Delta-9 THC</td>
<td>1.9</td>
<td>ng/mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Delta-9 Carboxy THC</td>
<td>9.3</td>
<td>ng/mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Cotinine</td>
<td>Positive</td>
<td>ng/mL</td>
<td>Heart Blood</td>
</tr>
<tr>
<td>Delta-9 Carboxy THC</td>
<td>29</td>
<td>ng/mL</td>
<td>Urine</td>
</tr>
<tr>
<td>Codeine - Total</td>
<td>230</td>
<td>ng/mL</td>
<td>Urine</td>
</tr>
<tr>
<td>Morphine - Total</td>
<td>&gt;5000</td>
<td>ng/mL</td>
<td>Urine</td>
</tr>
<tr>
<td>6-Monoacetylmorphine - Free</td>
<td>220</td>
<td>ng/mL</td>
<td>Urine</td>
</tr>
</tbody>
</table>

See Detailed Findings section for additional information
Death Certification

- Cause of death?
  - Acute heroin intoxication
- Manner
  - Accident
Case 7 History

- 61 yo female found dead partially seated on toilet 2 days after LKA
- 3 months earlier diagnosed with seizure disorder due to electrolyte imbalance and chronic alcoholism
- Prescribed levetiracetam
- No alcohol use since then
- No complaints at PCP visit 3 days PTD
Autopsy

- Negative
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Additional Information

- 61 yo husband found deceased on bed in loft bedroom
- h/o CAD, Afib, HTN, obesity, ?ETOH abuse
- Two dogs and cat all “very lively”
- All windows closed
- No detectable carbon monoxide
# Toxicology Results

## Positive Findings:

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<th>Compound</th>
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<th>Matrix Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboxyhemoglobin</td>
<td>43</td>
<td>%</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Ethanol</td>
<td>22</td>
<td>mg/dL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Blood Alcohol Concentration (BAC)</td>
<td>0.022</td>
<td>g/100 mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>3.4</td>
<td>mcg/mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Sertraline</td>
<td>660</td>
<td>ng/mL</td>
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<td>Desmethylsertraline</td>
<td>1300</td>
<td>ng/mL</td>
<td>Femoral Blood</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Positive</td>
<td>mcg/mL</td>
<td>Heart Blood</td>
</tr>
</tbody>
</table>
Fire Marshal Investigation

- Traced CO leak to malfunctioning wall mounted propane oven
  - Ambient CO max 485 ppm during preheat
- Further questioning of first responders indicated that pets appeared lethargic and had to be carried out of residence.
Death Certification

- Cause of death?
  - Carbon monoxide poisoning
- Manner
  - Accident
Case 8 History

- 43 yo female brought to ED by husband with abdominal pain
- h/o anxiety, HTN, obesity s/p gastric bypass
- Trazodone, venlafaxine, alprazolam, amlodipine
- Diagnosed with ARF and anion gap acidosis
- Suspicions of DV and ethylene glycol poisoning
- Expired on HD #3
Autopsy

- Negative
Histology

- Acute bronchopneumonia
- Shock liver
- No crystals in kidney
# Toxicology

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</tr>
</thead>
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<td>Caffeine</td>
<td>Positive</td>
<td>mcg/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>61</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>120</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>O-Desmethy/venlafaxine</td>
<td>1300</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>53</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
</tbody>
</table>

See Detailed Findings section for additional information.

## Testing Requested:

<table>
<thead>
<tr>
<th>Analysis Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>90025B</td>
<td>Postmortem, Expanded, Blood (Forensic) (CSA)</td>
</tr>
<tr>
<td>2062B</td>
<td>Ethylene Glycol, Blood</td>
</tr>
</tbody>
</table>
Questions

- What questions do you have for the medicolegal death investigator?
- What is cause of death?
- What is manner of death?
Police Investigation

- Celebrated his birthday day before with “few drinks of vodka”
- Next morning she was shaking, throwing up and stumbling
- He found empty prescription bottle
- No prior suicidality but some time ago saw hose and duct tape in car
- Brought her to ED
H&P

- Admitted drinking xs alcohol and ingesting meds previous night in suicide attempt
  - Empty new and old prescriptions (alprazolam, amlodipine, venlafaxine)
- Hypotensive and tachycardic on admission
Hospital Lab Tests

- Alcohol not detected
- Urine tox positive for benzos
- Severe metabolic acidosis
- Elevated lactate
- Rare calcium oxalate crystals in urine
Ethylene Glycol Poisoning

- Odorless, colorless, bittersweet in antifreeze, de-icing
- 100 mL fatal dose
- Severe anion gap acidosis, ARF, seizures, arrhythmias
- Delayed toxicity due to metabolites (glycolic acid, oxalic acid)
- Calcium oxalate crystals in kidneys, urine, etc
- May also be seen with ingestion or increased absorption of dietary oxalates
Hospital Course

- PEA arrest on HD #2 with resuscitation complicated by multiorgan failure
- Transitioned to CMO and expired on HD #3
Supplemental Toxicology Report

Positive Findings:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
<th>Units</th>
<th>Matrix Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine</td>
<td>Positive</td>
<td>mcg/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>61</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>120</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>O-Desmethylvenlafaxine</td>
<td>1300</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>53</td>
<td>ng/mL</td>
<td>001 - Antemortem Blood</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>160</td>
<td>ng/mL</td>
<td>002 - Antemortem Serum or Plasma</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Positive</td>
<td>mcg/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>470</td>
<td>mcg/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>150</td>
<td>ng/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>230</td>
<td>ng/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>Alpha-Hydroxyalprazolam</td>
<td>290</td>
<td>ng/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>27000</td>
<td>ng/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>O-Desmethylvenlafaxine</td>
<td>98000</td>
<td>ng/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>2500</td>
<td>ng/mL</td>
<td>004 - Antemortem Urine</td>
</tr>
</tbody>
</table>

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<td>Ethylene Glycol, Urine</td>
</tr>
<tr>
<td>0420B</td>
<td>Betahydroxybutyric Acid, Blood</td>
</tr>
<tr>
<td>0315SP</td>
<td>Amlodipine, Serum/Plasma</td>
</tr>
<tr>
<td>2062B</td>
<td>Ethylene Glycol, Blood</td>
</tr>
<tr>
<td>8052U</td>
<td>Postmortem, Expanded, Urine (Forensic)</td>
</tr>
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</table>
Death Certification

- Cause of death?
  - Complications of acute amlodipine intoxication
- Manner
  - Suicide
Amlodipine Overdose

- Calcium channel blocker (antihypertensive drug)
- 48% of fatal cardiovascular drug overdoses from CCBs
- Profound refractory hypotension, bradycardia and pulmonary edema
- Acute kidney injury and severe anion gap metabolic acidosis
Investigating Toxicologic Deaths

- Testing should be directed by history, scene and autopsy
- Results must be interpreted in conjunction with history, scene and autopsy
Interpreting Toxicology Results

- High drug level considerations
  - Intoxication death
  - Tolerance
  - Postmortem redistribution

- Low drug level considerations
  - Drug not detected by routine testing
  - Drug metabolism
  - Cumulative effect of co-ingested drugs
  - Adverse effect (e.g., QT prolongation, anaphylaxis)
The Positive Autopsy

"Gee... Nothing says 'I'm dead' like a severed head."
Case 9 History

- 56 yo male h/o AD found dead in bed with empty bottle of Southern Comfort next to him and several nips in trash
- PMH remote alcoholism
- Wife spoke to him previous day and he was without complaint
Case Disposition

- Certified without autopsy
  - COD = Acute and chronic alcoholism
  - MOD = Natural

- Autopsy subsequently performed at MBH
Autopsy Findings

FINAL PATHOLOGIC DIAGNOSIS
ATHEROSCLEROTIC CORONARY ARTERY DISEASE AND ISCHEMIC HEART DISEASE.
  Cardiomegaly with biatrial dilatation.
  REMOTE MYOCARDIAL INFARCTION (2.5 cm) posterior left ventricle.
  Atherosclerosis of epicardial arteries with maximal stenoses as follows:
    Left anterior descending: 50%.
    Left circumflex: 50%.
    Right coronary artery: 90%.

Patchy pneumonia, consistent with aspiration.
  Patchy pulmonary parenchymal hemorrhage.

Centrilobular hepatic congestion.

Diverticulosis of the sigmoid colon.

Nephrosclerosis, mild.
Autopsy Findings Continued

FINAL NEUROPATHOLOGIC DIAGNOSIS

Brain (1500 g) with:

Alzheimer Disease Neuropathologic Change:
  - Thal stage 5 for amyloid deposition
  - Braak and Braak tangle stage V/VI
  - CERAD age related plaque score: 3
  - NIA-Alzheimer Association score: A3B3C3
    - High probability of dementia due to Alzheimer Disease

CEREBROVASCULAR DISEASE:
  - Cerebral amyloid angiopathy (CAA), moderate, diffuse, cortical and
    leptomeningeal (Vonsattel grade 1 of 4).
  - Arteriolosclerosis, moderate
Autopsy Conclusion

Comment:
The examination of this case was hindered by extensive post-mortem autolysis associated with post-mortem bacterial overgrowth. The heart was enlarged with biatrial dilatation. There was moderate to focally severe atherosclerosis of the coronary arteries with no acute or recent plaque changes. There was an old (remote) 2.5 cm myocardial infarction in the posterior left ventricle. The remaining myocardium showed mild interstitial/replacement fibrosis. A Congo red stain of ventricular myocardium was negative for amyloid. The lungs showed patchy pneumonia consistent with aspiration, and patchy parenchymal hemorrhage. The liver showed centrlobular congestion. There was scarring in the pancreas, consistent with chronic pancreatitis. There was mild renal nephrosclerosis and colonic diverticulosis.
Follow Up

- Wife wants COD changed
- “she has a copy of autopsy report and death was ruled a heart attack”
- Insists he was not an alcoholic anymore and only recently began drinking again
  - Protective custody one week earlier (BRaC = .36)
## Toxicology

<table>
<thead>
<tr>
<th>ALCOHOL/VOLATILES (GC/FID)</th>
<th>RESULTS</th>
<th>EXPANDED UNCERTAINTY*</th>
<th>LIMIT OF QUANTITATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>Negative</td>
<td></td>
<td>0.01 g/100ml</td>
</tr>
<tr>
<td>Ethanol</td>
<td>0.35 g/100ml</td>
<td>0.351 +/- 0.021 g/100ml</td>
<td>0.01 g/100ml</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>Negative</td>
<td></td>
<td>0.01 g/100ml</td>
</tr>
<tr>
<td>Methanol</td>
<td>Negative</td>
<td></td>
<td>0.01 g/100ml</td>
</tr>
</tbody>
</table>
Final Disposition

› Cause of death
  • Part I = Coronary artery atherosclerosis
  • Part II = Acute ethanol intoxication with aspiration pneumonia

› Manner of death
  • Accident (consumed alcoholic beverages)
“Pathologists will make fewer medicolegal blunders if they do not attempt to use the autopsy as a substitute for a case investigation”

*Spitz and Fisher 2006*