Drug Abuse at the Crossroads Between the Living and the Dead
Biography

Fellow with the American Board of Forensic Toxicology (F-ABFT).

Medical Director of Laboratory services for LabPro Inc. (Harwood Heights, IL).
Interests in toxicology covers a variety of disciplines ranging from environmental/industrial toxins to clinical and forensic toxicology (postmortem, human performance, addiction treatment).

Responsibilities as the director of toxicology included integrating state of the art technologies into the laboratory service while enhancing the clinician/client support; providing interpretive guidance for the medical results and improving the medical care of patients.

He has held senior positions in government, academic, clinical and private laboratories. Each of these institutions has operated under different accrediting guidelines.

Research interests include bio-distribution studies, pharmacogenomics, molecular mechanisms in neurological and metabolic cells/tissues exposed to drugs, metals and other toxins.

Participates in numerous conferences, workshops and as a member of multiple organizations; the following are a representative listing (past/present): AACC (American Association of Clinical Chemistry), SOFT (Society of Forensic Toxicology) and the IATDM (International Association of Therapeutic Drug Monitoring), and AAFS (American Association of Forensic Toxicology).
Learning Objectives - Summarized

• 1  Case didactic review demonstrating Fentanyl therapeutic drug abuse and skills needed to interpret results
• 2  Develop knowledge of synthetic forms of Fentanyl and the risk to overdoses with opiate/heroin addiction
• 3  Identify new challenges first responders face providing care in these types of overdoses
• 4  How to implement the recommended guidelines to investigating opiate overdose deaths
• 5  Identify analytical laboratory services and interpretation recommendations
Fentanyl Abuse or Overdose?

• Case History
  • Gender: M    Race: Caucasian    YOA: 28    Ht: 5’10    Wt: 165
  • Scene: July, 10:43 AM Officer dispatch reference a medical call
    Male found on the floor unconscious;
    Father (caller) attempts CPR – chest compressions.
    Subject lying on the floor (police arrival) unconscious and
    unresponsive Officer attempts AED – negative result.
    Detectives and coroner dispatched to the scene.
  • Scene details: Father explained that at apprx 0330 AM hr noticed son was
    awake listening to music.  0530 AM hr Father notices son is asleep in
    the bed.  Father 10:20 AM finds son laying face up on the bed.  Move
    him to the floor.
Case Hx, Cont’d

• Medical Hx
  • Treated for chronic headaches
  • Prior Hx of heroin use
    • Father not aware of reuse.
• Evidence observed
• Prx Hx:
  • Propranolol
  • Clonazepam
  • Fiorinal
  • Acetaminophen + Diphendramine
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<th>Drug</th>
<th>Subj Name</th>
<th>Pharmacy</th>
<th>Prx no</th>
<th>Dose</th>
<th>Qty prescribed</th>
<th>Number Refills</th>
<th>Qty found</th>
<th>Prx Directions</th>
<th>Date Prx issued</th>
<th>DOD or found</th>
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<td>TMB</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>0</td>
<td>8</td>
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<td>X</td>
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<td>X</td>
<td>X</td>
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<td></td>
<td>X</td>
<td>6</td>
<td>X</td>
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<td></td>
<td>1865840-047xx</td>
<td>X</td>
<td>60</td>
<td></td>
<td>X</td>
<td>40</td>
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<td>441829x-xxxxx</td>
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<td>30</td>
<td>0</td>
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<td>Walmart Ellisville MO</td>
<td>186537-047xx</td>
<td>1 mg</td>
<td>30</td>
<td>3</td>
<td>0</td>
<td>Q.D</td>
<td>6/26/2013</td>
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<tr>
<td>Indomethacin</td>
<td>MGB (father)</td>
<td>Wallgreens Belvidere IL</td>
<td>two 30 dy supplies</td>
<td>50 mg</td>
<td>15</td>
<td>0</td>
<td>5</td>
<td>TID for 5 days</td>
<td>-</td>
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Distance traveled
Autopsy Slides – redacted (three slides)
Autopsy Finding - External

- Ht: 69”  Wt: 181 lbs
- Healed cutaneous scars (hands, legs, knees)
- Eyes brown; 4mm – normal
  - Cornea clear; conjunctivae w/o petechial
- Tongue, buccal mucosa + pharynx normal
- Neck symmetrical w/o abnormalities
- Chest/Back – unremarkable
- Skin – psoriasis-like elbow

- Evidence of Injury - None
- Rigor complete/fixed equal distribution all extremities
Autopsy Internal

• Cardio - Unremarkable
  • 350g LV 15mm RV 4mm Interventricular Septum 19mm
  • No Atherosclerosis, Thrombosis, Calcification
  • Chambers/valves – normal
  • Pulmonary artery – major branches - normal
  • Vena cava – major tributaries/pulmonary veins – free of thrombi

• Liver/Biliary
  • Liver – 2425g smooth/glistening/intact
  • Gallbladder - unremarkable
  • Moderately congestion
  • Extrahepatic biliary - patent
  • No focal lesions
  • Extrahepatic biliary - patent
  • No focal lesions

• Spleen – 310 g
  • Regional lymph nodes – unremarkable; Parenchyma – moderately firm
Autopsy Internal cont’d

• Respiratory
  • R 800g / L 625g fully inflated
  • Intraparenchymal pulmonary arteries – normal, patent, w/o thrombus or embolus
  • Moderate vascular congestion/edema
    • No emphysema, consolidation, granulomata or focal lesions
  • Mild anthracosis

• CNS
  • Brain 1475g –
  • External surface/configuration – normal
  • Dura mater/falx cerebri intact w/o hemorrhage
  • Base including cranial nerves/blood vessels w/o atherosclerosis
  • Coronal section through cerebral hemisphere cortex, white matter + basal nuclei – normal
  • Brain stem + cerebellum – transverse sectional – normal
  • Cervical spinal cord - unremarkable
Reference Ranges - 95% Inclusion

- Brain, 1179-1621 g
- Heart, 233 – 383 g
- Liver, 968-1860 g
- Spleen, 28-226 g
- Right lung, 155-720 g
- Left lung, 112-675 g
- Right kidney, 81-160 g
- Left kidney, 83-176 g
Toxicology

• Comprehensive Testing

• Peripheral Blood
  • 7-Aminoclonazepam 35.3 ng/mL
  • Alprazolam 88.6 ng/mL
  • Fentanyl 10.0 ng/mL

• Urine
  • Alprazolam 957 ng/mL
  • Alpha-OH-Alpraz 1805 ng/mL
  • 7-Aminoclonazepam 1348 ng/mL
  • Fentanyl 12.6 ng/mL
  • Norfentanyl > 100 ng/mL
  • Hydrocodone 217 ng/mL

Therapeutic Range

10 – 40 ng/mL
1 – 3 ng/mL

Additional samples: vitreous
Pathologist Findings

• Few generalized cutaneous scars present
• Chronic dermatitis, elbow, consistent w psoriasis
• Pulmonary vascular congestion and edema, combined weight of lungs 1425 g
• Pulmonary anthracosis, moderate, w/o emphysema
• No evidence of significant natural disease, injury, active infection or congenital anomaly

• Opinion: Death attributed to the adverse effects of fentanyl
Police

• Conclude Fentanyl OD
  • Concentration > 3x’s the therapeutic range
• Medication Diversion
  • Phone records
Fentanyl Prescription Abuse

• Formulations
  • IV – anesthetic, chronic or acute pain
    • Intrathecal, spinal, and epidural
  • Patch – Transdermal 48-72 hr (peak 12-25hr) Gel vs Non-Gel
    • 25, 50, 75 and 100 ug/hr
    • Opiate stable
    • Renal failure
    • Complication w oral formulation (morphine/hydromorphone/oxycodone)
  • Intranasal
    • 50, 100, 200 ug
  • Sublingual
  • Lozenges
    • Actiq – fentanyl citrate on stick
    • Tolerant
    • Cancer pain
    • On set 10-15 min
Drug Abuse Prescription

• Common patterns
  • Diversion
    • Gifting
    • Selling
    • Stealing
    • Recreational
  • Routes of absorption
    • Oral
    • Insufflation
    • Injection
    • Rectal
    • Vaginal
    • Dermal
Fentanyl Abuse

• Gel Patch “Chiclets”
  • Sublingual - placed in the freezer then break open the gel pack and suck on them
  • Transdermal – Heating Pads or Driers

• Non-Gel
  • Extraction – IPA in a double boiler (chop sticks, glass tray scissors)
  • Boil low temp 90-120 min
The INTERSECTION
“Lights Out” reprisal role?

• RI - 2013
  • Real-time Outbreak and Disease Surveillance System - spike in OD fatalities March through May
  • 14 individuals YOA range 19 – 57
    • More not reported – incomplete ER records
    • Cases were clustered in close proximity

• PA
  • 50 deaths

• 13 Other states quickly report similar fatalities

• CDC issues a warning based on the RI cases
  • Recommend large doses of Naloxone should be available for care
Acetyl Fentanyl 2013

• RI Laboratory Clues
  • EIA Drugs Screen – Fentanyl “+”
  • Drug Confirmation - Negative (GC/MS)
    • Unknown peak consistent with ACF

• Drug scenes and Hx
  • Consistent with opiate users and addiction

• DEA
  • Provides a qualitative drug to verify ACF
Chicago - Fast Forward 2016

• 2016 Cook County Medical Examiner - 273 Fentanyl Fatalities
  • Under estimate
  • Dennis A. Wichern, DEA Chicago special agent

• 2015 Cook County Medical Examiner - 102 Fentanyl Fatalities
• 74 heroin OD reported in 72 hours between Tuesday and Friday afternoon (Chicago Tribune – October 3 2015)

• Is new??????
April 2005 – March 2007
Non Pharmaceutical Fentanyl (NPF)

• “Lights Out” – Heroin laced with Fentanyl 1013 NPF related deaths ’05 – ‘07
• The NPF Epidemic in 2006, in Wayne County, Michigan, fentanyl contributed to 195 (32.4%) of 602 deaths resulting from drug use (C. Schmidt, MD, Wayne County Medical Examiner's Office, personal communication, 2007). Although the number of NPF-related deaths identified by the CDC/DEA surveillance system declined substantially in 2007, the relative ease of illicit production and low cost of NPF compared with heroin suggest that future epidemics of NPF overdoses are likely to occur
• DEA began regulating access to N-phenethyl-4-piperidone, a chemical used to make illicit NPF
• One gram of pure fentanyl can be cut into approximately 7,000 doses for street sale
• 81 % male 55/4% Caucasian, 39.8% African American, 4.2 % Hispanic
• An earlier epidemic in the 1980s resulted in at least 110 fatal overdoses caused by 10 different fentanyl analogs (3).
• Chicago, Detroit, and Philadelphia see the greatest report fatalities
• NPF-related deaths were reported in suburban and rural areas of Illinois, Michigan, and Pennsylvania and in Kentucky, Maine, Maryland, Massachusetts, New Hampshire, Ohio, and Virginia during the same period.
US Department of Justice, Drug Enforcement Administration. 21 CFR part 1310. Control of a chemical precursor used in the illicit manufacture of fentanyl as a list 1 chemical. Federal Register 2007;72:20039--47. Available at http://frwebgate.access.gpo.gov/cgi-bin/getpage.cgi?dbname=2007_register&position=all&page=20039
Figure 1 Fentanyl and some Analgesics (5)
CSID = ChemSpider ID; Year = Year Introduced
Reproduced with permission from www.ChemSpider.com
Analysis of Novel Synthetic U-47700, U-50488, Furanyl Fentanyl by LCMSMS PM, JAT Sept 1 2016 BK Logan et al.
Opioids/Analgesic – 65% ID first Quarter CY 2016

Emerging Threat Report CY 2016
The Pill Makers Next Door: How America’s Opioid Crisis Is Spreading
Death Scene Investigation Guidelines - NAME

• A complete autopsy is necessary for optimal interpretation of toxicology results, which must also be considered in the context of the circumstances surrounding death, medical history, and scene findings.

• A complete scene investigation extends to reconciliation of prescription information and pill counts.

• Blood, urine, and vitreous humor, when available, should be retained in all cases. Blood from the femoral vein is preferable to blood from other sites.

• A toxicological panel should be comprehensive and include opioid and benzodiazepine analytes, as well as other potent depressant, stimulant, and antidepressant medications.
NAME, cont’d

• Interpretation of postmortem opioid concentrations requires correlation with medical history, scene investigation, and autopsy findings.

• If death is attributed to any drug or combination of drugs (whether as cause or contributing factor), the certifier should list all the responsible substances by generic name in the autopsy report and on the death certificate.

• The best classification for manner of death in death due to the misuse or abuse of opioids without any apparent intent of self-harm is ‘accident.’ Reserve ‘undetermined’ as the manner for the rare cases in which evidence exists to support more than one possible determination”.

• Recommend additional test as case information needs – consider alternate samples
Forensic Toxicology Guidelines

- Identification of the site of specimen collection. If possible, samples should be collected from peripheral blood vessels.
- Collection and testing of admission (as opposed to autopsy) blood and urine specimens when applicable and available.
- Comprehensive testing for prescription, illicit, and over-the-counter drugs and alcohol.
- Testing of appropriate specimens with an emphasis on urine as a means to effectively detect drugs and drug metabolites.
- The use of an immunoassay screen with a defined level of sensitivity and supplemental immuno-assays for drugs with poor cross-reactivity.
Forensic Toxicology Guidelines

• The determination of free and total drug concentrations in blood specimens, at a minimum, and ideally free and individual glucuronide metabolites.

• Analysis of free and total opiate/opioid concentrations in other tissues as an adjunct to blood concentrations, where appropriate, or where the blood concentrations may be compromised by postmortem artifact.

• Similar standards for cutoff concentrations for confirmatory gas chromatography-mass spectrometry and liquid chromatography-mass spectrometry analysis.

• Use of analytical methods that have been appropriately validated and controlled to provide reliable data.”
Conclusion – Role of Laboratory Medicine

• Inter/Intra Agency Collaboration
  • Real time surveillance
  • Identify action items

• Addiction Services
  • Continue to support

• Scientific Support – Academic + Laboratory Science