The Opioid Epidemic: What labs have to do with it?

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Overview

- Overdose trends
- Opioids and their effects
- Analytical testing approaches
- Toxicology laboratories
Opioid overdose crisis

Overdose Deaths Involving Opioids, United States, 2000-2016

Opioid overdose crisis

Drug overdose deaths per 100,000 population by state, US 2016.

Opiates and Opioids

• Opiates vs. Opioids
• Opiates:
  Naturally occurring, derived from the poppy plant
• Opioids:
  “Opiate-like” drugs in effects, not chemical structure
  Includes opiates
• Narcotic analgesics
• CNS depressants
• DEA Schedule I or II controlled substances
• Additive effect with other CNS depressant drugs
Efficacy of Opioids

- How do opioids work?
- Bind with opioid receptors
- Brain, spinal cord, GI tract, and throughout the body
- Pain, emotion, breathing, movement, and digestion
Effects of Opioids

Physiological
- Pain relief
- Cough suppression
- GI motility
- Respiratory depression
- Pupillary constriction
- Itching
- Constipation
- Dependence

Psychological
- Drowsiness/ sedation
- Mental confusion
- Loss of memory
- Lethargy/ apathy
- Euphoria/ tranquility
- Mood swings
- Depression
- Withdrawal
- Dependence
Opiates

• Naturally occurring alkaloids

Opium

• Latex from the opium poppy plant

Codeine:

• Mild to moderate pain
• Antitussive

Morphine:

• Severe pain
• Metabolite of codeine and heroin
Opiates

Semi-synthetic Opiates:
- Synthesized from a natural opiate

Heroin:
- Schedule I narcotic

Hydrocodone (Vicodin):
- Mild to moderate pain
- Metabolizes to hydromorphone (Dilaudid)

Oxycodone (Oxycontin/Percocet):
- Moderate to severe pain
- Metabolizes to oxymorphone (Opana)
Opioids

All drugs with “Opiate-like” effects
- Psychological and physical
- Includes natural opiates
- Synthetic: different chemical structures

Methadone:
- Moderate to severe pain
- Treats narcotic addiction
- Syrup or pills

Meperidine (Demerol)

Tramadol (Ultram):
- Moderate to severe pain
Synthetic opioids

- **Fentanyl** (Duragesic, Sublimaze):
  - Powerful, fast acting narcotic analgesic
  - 80-100 times more potent than morphine
  - 50 times more potent than heroin

- **Rx:**
  - to treat severe pain or as a surgical anesthetic
  - IV, pills, patches, lozenges, lollipops

- **Illicit:**
  - powder shipped from China or Mexico
  - counterfeit pills
  - frequently sold as heroin
  - snorted, smoked, or injected
Novel or “designer” opioids

- Synthetic drugs of abuse
- Minor change to the original chemical structure (more than 1400 compounds described in literature)
- Analog of a pharmaceutical or research drug
- Mimic effects of the original drug
- Circumvent existing legal restrictions/ DEA scheduling
- Illicitly produced/ Not clinically tested or FDA approved
- “Not for human consumption”
- “Research chemical”
- Pills, powders, counterfeit tablets
Designer Opioids

- **Fentanyl analogs:**
  - Acetyl-
  - Acryl-
  - Butyryl-
  - Furanyl-
  - Carfentanil
  - 4-ANPP

- **Designer Opioids:**
  - AH-7921
  - MT-45
  - U-47700 (Pink/Pinky)
Fentanyl Analogs

- **Acetyl Fentanyl:**
  - tablets or powder
  - ~10 times more potent than morphine
  - less potent than fentanyl
  - Rhode Island: 2013
  - 15 deaths

- **Furanyl Fentanyl:**
  - pills or powder
  - More potent than morphine
  - Less potent than fentanyl
  - Both cross-react with fentanyl ELISA assay
  - Both DEA Schedule I
Fentanyl Analogs

- **Carfentanil:**
  - tranquilizing agent for large mammals
  - DEA Schedule II drug
  - small amount is fatal
  - absorbed through skin
  - 10,000 times the potency of morphine
  - 100 times more potent than fentanyl
  - white powder or pills
  - mixed in heroin
  - No cross-reactivity with fentanyl ELISA screening assay
Opioids Potency
Drug toxicology testing

**Preliminary** screening
- Presumptive result
- Classes of drugs

**Confirmatory** testing:
- Specific/directed testing
- Mass spectrometry methodology preferred
Preliminary Tests

**Immunoassay**
- Presumptive Screens
- Qualitative assays
- Designed to narrow down the classes of drugs

**Disadvantages**
- Limited scope of testing
- False negatives and positives are possible
- Not forensically defensible without confirmation

Newer technologies increasingly in use: e.g. HR MS (TOF)
ELISA Tecan System
ELISA screening at RISHL

- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabinoids
- Carisoprodol
- Cocaines
- Methamphetamines
- Tricyclic Antidepressants
- Zolpidem

- Opioids:
  - Fentanyl
  - Methadone
- Opiates:
  - Oxycodone
  - Buprenorphine
Confirmatory Testing

• Second phase of forensic (but not necessarily clinical) drug testing

• Positive screening tests can be confirmed utilizing a more specific and sensitive chemical principle.

• Qualitative or quantitative analysis

• Gas or liquid chromatography
• Mass spectrophotometer detector
• GC/MS, LC/MS, LC/MS/MS
Confirmatory Testing

Advantage:
• Detect and identify specific drugs present
• Broad scope of analytes, including metabolites
• Detect minute amounts
• Forensically defensible
• Widely accepted methodology
• Extensive scientific literature and information

Disadvantage:
• Requires separation of the drug from the sample matrix
• Labor intensive
• Expensive instrumentation
GC/MA and LC/MS/MS
The universe of toxicology laboratories

- Clinical toxicology
  (therapeutic drug monitoring, overdoses or poisonings, diagnosis, pain management clinics)

- Employment drug testing, addiction treatment centers, athletic performance-enhancing checks (sports doping)

- Forensic toxicology
  (cause of death investigations, including fatal overdoses)
Laboratories and overdose surveillance

- Commercial Laboratories
- Government Forensic Laboratories
- Public Health Laboratories
- Potential opioid surveillance data
- Hospital Laboratories
Opioid Surveillance

Death certificates

Drug use surveys

Opioid surveillance data

Hospital ED data

Prescribing data

2018 ANNUAL SURVEILLANCE REPORT OF DRUG-RELATED RISKS AND OUTCOMES

UNITED STATES
Current issues in toxicology testing

• Scope of testing (list of analytes) not standardized
• Different methodologies
• No clear reference laboratory system
• Inadequate capacity (specially in the forensic area)
• Inadequate capability to test for novel analogs—“designer opioids”
Barriers to a standardized approach

- Expensive instrumentation
- Expensive calibration/IS/QC standards for isotope dilution LC/MS/MS
- Differing accreditation requirements for clinical vs. forensic laboratories
- Regulatory oversight
- Lack of standardization of methodology or defined list of target analytes
New public health initiatives

- Funding for the states:
  - CDC ESOOS Enhanced State Opioid Overdose Surveillance
  - Opioid Crisis Cooperative Agreement: “SURGE”
- New requirement for “biosurveillance” for non-fatal overdoses
- New testing programs for public health laboratories
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