The Opioid Epidemic: The Medical Examiner Perspective

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Agenda

- Define opioids
- National stats on drug use and drug deaths
- New Hampshire drug death stats
- Heroin and fentanyl
- Toxicology testing
- Investigating drug deaths
- Case examples

What is an Opioid?

- Any agent that binds to opioid receptors
  - Endogenous opioid (i.e. endorphins)
  - Natural opiates (e.g. morphine, codeine)
  - Semi-synthetic opioids (e.g. heroin, hydrocodone, oxycodone, buprenorphine)
  - Fully synthetic opioids (e.g. methadone, fentanyl)

Opioid Receptors

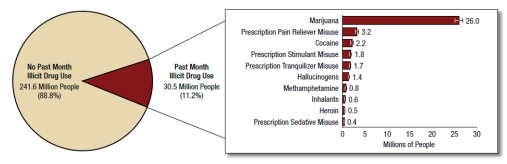
Opioid Receptor Class	Effects
Mu_1	Euphoria, supraspinal analgesia, confusion, dizziness, nausea, low addiction potential
Mu_2	Respiratory depression, cardiovascular and gastrointestinal effects, meiosis, urinary retention
Delta	Spinal analgesia, cardiovascular depression, decreased brain and myocardial oxygen demand
Kappa	Spinal analgesia, dysphoria, psychomimetic effects, feedback inhibition of endorphin system

http://www.pharmacytimes.com/publications/issue/2011/june2011/an-overview-of-opioids

Drug Use in the U.S.

Illicit Drug Use in the U.S.

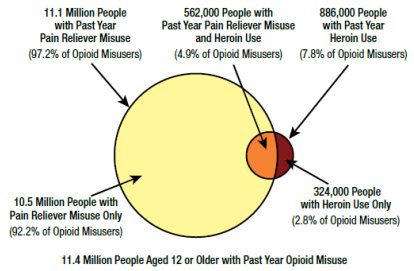
Figure 11. Numbers of Past Month Illicit Drug Users among People Aged 12 or Older: 2017



Note: Estimated numbers of people refer to people aged 12 or older in the civilian, noninstitutionalized population in the United States. The numbers do not sum to the total population of the United States because the population for NSDUH does not include people aged 11 years or younger, people with no fixed household address (e.g., homeless or transient people not in shelters), active-duty military personnel, and residents of institutional group quarters, such as correctional facilities, nursing homes, mental institutions, and long-term care hospitals.
Note: The estimated numbers of current users of different illicit drugs are not mutually exclusive because people could have used or misused more than one type of illicit drug in the past month.

https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf

Opioid Misuse in Past Year

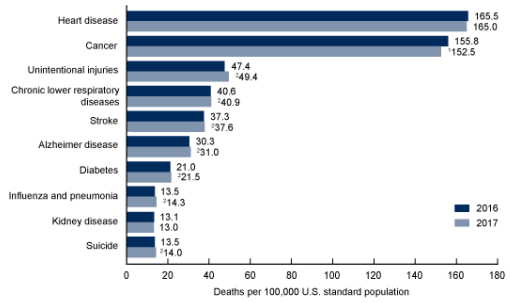


11.4 Million People Aged 12 or Older with Past Year Opioid Misuse

https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf

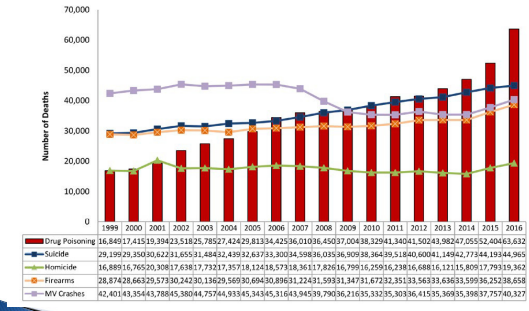
Drug Deaths in the U.S.

Leading COD in U.S.



https://www.cdc.gov/nchs/products/databriefs/db328.htm

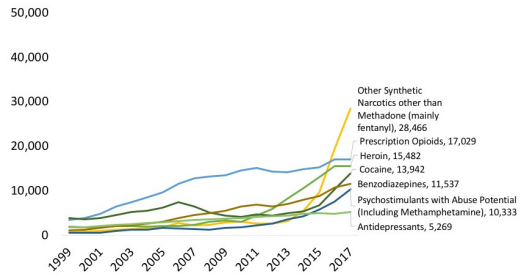
Injury Deaths in the U.S.



	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Drug Poisoning	16,849	17,415	19,394	23,518	25,785	27,424	29,813	34,425	36,010	36,450	37,004	38,329	41,340	41,502	43,982	47,055	52,404	63,632
Suicide	29,199	29,350	30,622	31,655	31,484	32,439	32,637	33,300	34,598	36,035	36,909	38,364	39,518	40,600	41,149	42,773	44,193	44,965
Homicide	16,889	16,765	20,308	17,638	17,732	17,357	18,124	18,573	18,361	17,826	16,799	16,259	16,238	16,688	16,121	15,809	17,793	19,362
Firearms	28,874	28,663	29,573	30,242	30,136	29,569	30,694	30,896	31,224	31,593	31,347	31,672	32,351	33,563	33,636	33,599	36,252	38,658
MV Crashes	42,401	43,354	43,788	45,380	44,757	44,933	45,343	45,316	43,945	39,790	36,216	35,332	35,303	36,415	35,369	35,398	37,757	40,327

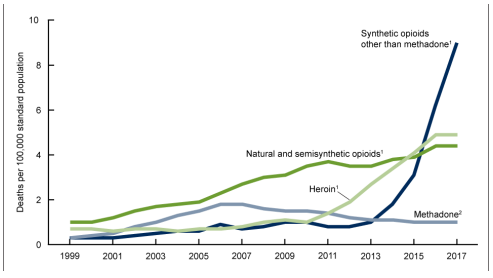
https://www.[illegible]/sites/default/files/2018-11/DIR-032-18%202018%20NDTA%20%5Bfinal%5D%20low%20resolution11-20.pdf

U.S. Drug Deaths



https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

Opioid Deaths in US



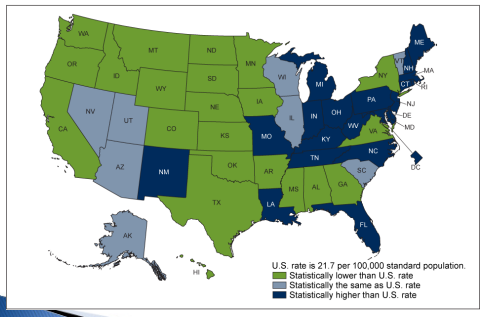
https://www.cdc.gov/nchs/products/databriefs/db329.htm

Synthetic Opioids

- Methadone
- Meperidine
- Tramadol
- Fentanyl
- Fentanyl analogs

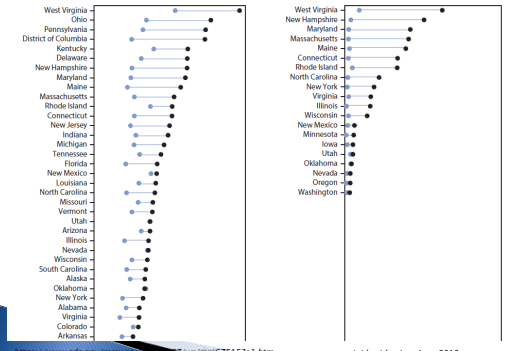
Drug Deaths by State

Figure 3. Age-adjusted drug overdose death rates, by state: United States, 2017



https://www.cdc.gov/nchs/products/databriefs/db329.htm

U.S. Overdose Deaths 2013–2017



https://www.cdc.gov/mmwr/volumes/...mm6751e2_htm

Drug Deaths in New Hampshire

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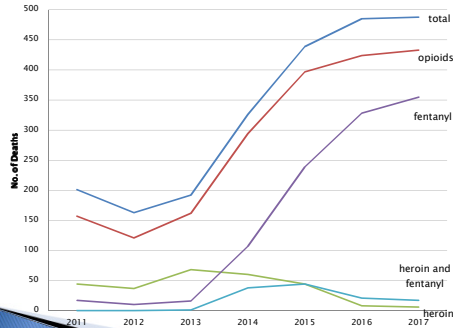


Heroin

Heroin History

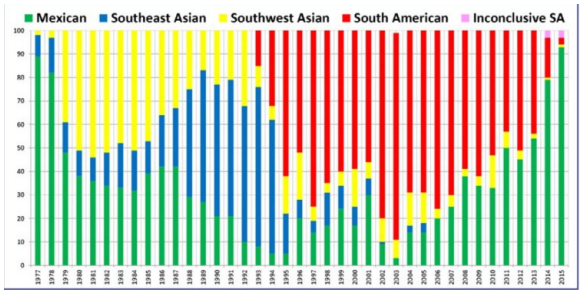
- Antiquity – medicinal and recreational use of opium from poppy plant
- 1803 – morphine isolated from opium
- 1800s – miracle drugs
- 1853 – syringe introduced
- 1874 – diacetylmorphine synthesized
- 1898 – medicinal use of heroin by Bayer
- 1900s – regulatory laws
- 1956 – heroin illegal

Top Opium Producing Countries

Rank	Country	Land Area Devoted To Cultivating Illicit Opium Poppies
1	Afghanistan	225,000 hectares
2	Myanmar	58,000 hectares
3	Mexico	15,000 hectares
4	India	12,250 hectares
5	Laos	6,200 hectares
6	Pakistan	2,300 hectares
7	Colombia	298 hectares
8	Iran	100 hectares

https://www.worldatlas.com/articles/top-opium-poppy-producing-countries.html

Origin of Heroin Seizures

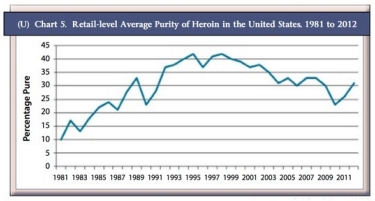


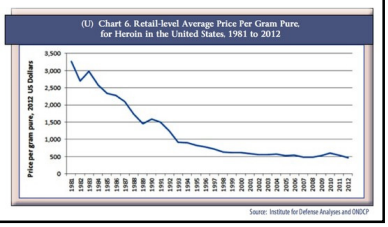
https://www.businessinsider.com/sinaloa-cartel-sending-mexican-herion-to-the-us-2017-11

New England Heroin Trafficking

http://www.masslive.com/news/index.ssf/2015/06/opioid_crisis_highway_to_hell.html

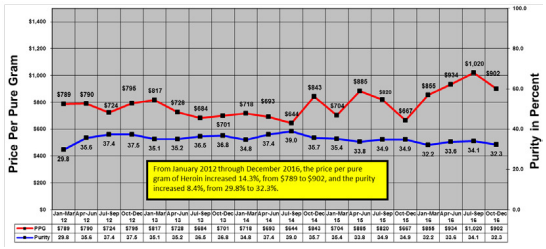
Heroin Cost vs. Purity





http://www.dailykos.com/story/2016/8/14/1554978/-Circling-the-drain-of-the-opioid-addiction-epidemic

Heroin Cost vs. Purity

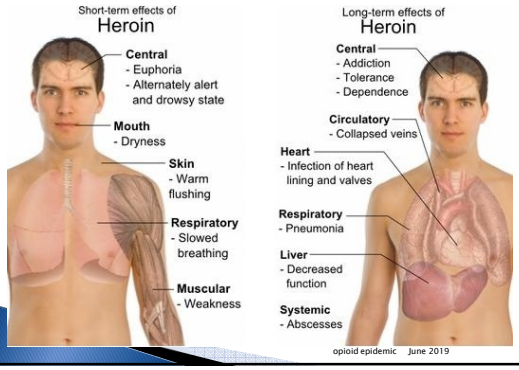


https://ndews.umd.edu/sites/ndews.umd.edu/files/dea-2016-national-drug-price-purity-data.pdf

Street Heroin

- H
- Smack
- Dope
- China White
- Horse
- Skag
- Junk
- Black Tar
- Big H
- Brown Sugar
- Mud
- Dragon
- Boy
- Mexican Brown
- Thunder
- Skunk
- Scag

Effects of Heroin



Heroin Overdose

- Risk factors
  - Variable drug purity
  - Loss of tolerance
- Mechanism of death
  - Severe respiratory depression
  - Pulmonary edema
  - Arrhythmia

Fentanyl

Pharmaceutical Fentanyl

- Synthetic opioid introduced as IV anesthetic in 1960s
- Various formulations
- 100 times more potent analgesic than morphine
- For breakthrough cancer pain or chronic pain

Pharmaceutical Fentanyl

- Injection
- Sublingual tablet
- Lozenge "lollipop"
- Transdermal patch
- Buccal tablet
- Nasal spray
- Sublingual spray

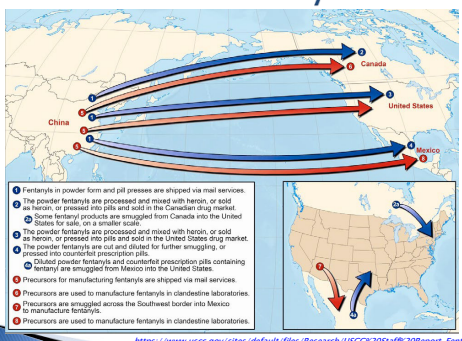
Pharmaceutical Fentanyl Abuse

- Abused since 1970s for intense euphoric effect
- Injecting or ingesting gel contents of patches
- Illicit distribution
  - Pharmacy theft
  - Fraudulent prescriptions
  - Distributed by patients, physicians, pharmacists
  - Theft from nursing homes, LTCF

Illicit Fentanyl

- Produced in clandestine laboratories mainly in Mexico and China
- Mixed with or substituted for heroin
- Counterfeit pills (e.g. Oxycontin/oxycodone)

Flow of Illicit Fentanyl



https://www.uscc.gov/sites/default/files/Research/USCC%20Staff%20Report_Fentanyl-China%E2%80%99s%20Deadly%20Export%20to%20the%20United%20States020117.pdf

Profitability of Fentanyl

Drug	Cost Per 1 Kg to DTO	Approximate Number of Kgs Produced from Original Drug Procurement	Wholesale Price per Kg in Massachusetts	Revenue to DTO from 1 Kg
Heroin	$5,000 - 7,000 (Purchased from Colombia)	1 kg	$80,000	$80,000
Pure Fentanyl (99%)	$3,300 -5,000 (Purchased from China)	16-24 kgs	$80,000	$1,280,000 - 1,920,000

https://www.dea.gov/sites/default/files/2018-07/DIR-040-17_2017-NDTA.pdf

Street Fentanyl ± Heroin

- Apache
- China Girl
- China White
- Dance Fever
- Friend
- Goodfella
- Jackpot
- Murder 8
- TNT
- Tango and Cash

Fentanyl Effects

- Onset of action is IMMEDIATE.
- Maximal analgesic and respiratory depressant effects take only a few minutes.
- Usual duration of action of analgesic effect is 30 to 60 minutes after IV dose of 100 mcg.
- It only takes 50 mcg to equal the effects of 10 mg of morphine.

Fentanyl (Opioid) Toxicity

- Respiratory depression
- Skeletal muscle flaccidity
- Cold, clammy skin
- Reduction in BP, HR
- Coma
- Respiratory arrest
- Death

Toxicology Testing

Why toxicology alone is not enough!

Postmortem Drug Levels

- Survival interval
- Fluid resuscitation
- Postmortem interval
- Specimen type, source, storage
- Postmortem redistribution

Redistribution from Reservoirs

Organs	Proposed Mechanisms	Molecules Concerned
Redistribution from the stomach	↗ concentrations in the left cardiac cavities > base of the left lung > right cardiac cavities	Ethanol, fluoxetine, amitriptyline
Redistribution from the lungs	↗ concentrations in the pulmonary vessels, left cardiac cavities and aorta	Lipophilic weak bases
Redistribution from the myocardium	Release of molecules concentrated in the myocardium toward the cardiac cavities	Digitalis, betablockers, quinidines, calcium inhibitors, amphetamine, amitriptyline, doxepine, maprotiline, some synthetic cannabinoids
Redistribution from the liver	↗ concentrations in the right cardiac cavities, peripheral venous blood, adjacent organs (esophagus, stomach, proximal duodenum)	Ethanol, fluoxetine, tricyclic antidepressants
Redistribution toward fatty tissue	↗ concentrations in fatty tissue	Lipophilic molecules (tricyclic antidepressants, anesthetics, volatiles, THC)

Sastre et al. 2017

Agonal and Cadaveric Phenomena

Phenomena	Proposed Mechanisms	Potential Consequences
Cell autolysis	Release in the vascular sector of enzymes and xenobiotics concentrated in the cells	↗ concentrations in the vascular sector (particularly lipophilic weak bases) Persistence of the activity of certain enzymes
Blood movements	Reflux of blood towards the superficial vessels as rigor mortis sets in	↗ concentrations in the subclavian vessels ?
Coagulation and hemolysis	Impossibility of separating plasma from erythrocytes → measurement in whole blood	Variations in the ratios of whole blood/plasma concentrations
Hypostasis	Variations in hematocrit Albumin extravasation	Change in free fraction/bound fraction balance
Putrefaction	Neoformation Degradation	Ethanol Ethanol, nitrobenzodiazepines, fluoxetine, chlorpromazine, thioridazine, risperidone, paliperidone, morphine glucuronides

Sastre et al. 2017

Biochemical & Pharmacological

Parameters	Proposed Mechanisms	Potential Consequences
Absorption route	Redistribution from drug reservoirs (particularly stomach and lungs) varies according to absorption route	Variations in concentration in the cardiac compartments
Metabolic phase	Occurrence of death before the end of the distribution phase (phenomenon more marked after overdose)	Variations in concentration according to arterial or venous site (heroin, 6-MAM)
Volume of distribution (Vd)	Marked tissue distribution of molecules with a high Vd	Release in the vascular compartment during cell autolysis?
Lipophilicity (partition coefficient, Kp)	Marked tissue distribution of molecules with a high Kp	Release in the vascular compartment during cell autolysis?
State of ionization (dissociation constant, pKa)	Marked tissue binding of molecules in an ionized form (high pKa)	Release in the vascular compartment during cell autolysis?

Sastre et al. 2017

Heroin Blood Levels

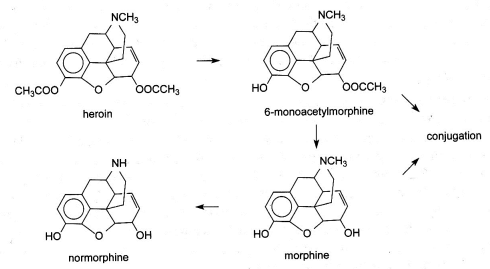
Route	Dose (mg)	6-MAM (µg/L)	Morphine (µg/L)
Nasal	12	14	19
IV	150-200	---	300
Oral	400	---	1035

Baselt 2017

	Therapeutic /Nontoxic	Toxic	Lethal
6-MAM	0-20		0-530
Morphine	10-230		10-1700

Molina 2010

Heroin Metabolism



Fentanyl Blood Levels

Route	Dose	Peak Plasma (µg/L)
Transdermal	25-100 ug/hr	0.3-3.8
Oral	800 ug	1.4-3.0
IV	2 ug/kg	11

Baselt 2017

Therapeutic/ Nontoxic	Toxic	Lethal
0.3-10	3-20	3-210

Molina 2010

Drug Death Diagnosis

- Postmortem drug levels may not reflect antemortem drug levels
- Drug level may not correlate with toxicity (e.g. tolerance, metabolism)
- History + Autopsy + Toxicology

Investigating Acute Drug Intoxication Deaths

Drug Administration Routes

- Oral ingestion
- Parenteral (IV, IM, SQ)
- Nasal insufflation/snorting
- Inhalation/smoking
- Transdermal
- Par rectum

History & Scene Investigation

- Circumstances surrounding death
  - How found?
  - Recent complaints?
  - Last known alive?
- Scene indicators of drug use
  - Prescription, OTC, illicit drugs (bottles, baggies)
  - Injection materials (syringes, spoons, lighters, tourniquets)
  - Smoking materials (pipes/tubes, foil, steel wool)
  - Snorting materials (tubes/straws, razors, mirrors)
- Medical history

Postmortem Findings

External

- Nothing
- Foam cone
- If insufflation
  - Residue in nares
- If ingested
  - Residue in gastric contents
- If parenteral
  - Recent injection sites
  - Track marks
  - Infection

Internal

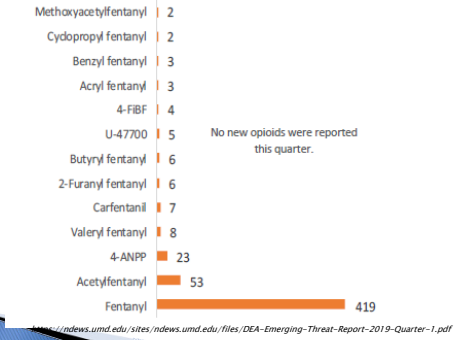
- Nothing
- Pulmonary edema
  - Granulomas
  - FB emboli
- Urinary retention
- Cerebral edema
- Infection

Fentanyl Related Drugs

FENTANYL	BUTYRFENTANYL	NORFENTANYL
BETA.-HYDROXYTHIOFENTANYL	CARFENTANIL	ORTHO-FLUOROFENTANYL
3-METHYLFENTANYL	DEPROPIONYL FLUOROFENTANYL	P-FLUOROFENTANYL
4-FLUOROBUTYRFENTANYL	DEPROPIONYLFENTANYL	REMIFENTANIL
4-FLUOROISOBUTYRYLFENTANYL	FURANYLFENTANYL+	SUFENTANIL
4-METHOXYBUTYRFENTANYL	ISOBUTYRFENTANYL	
ACETYLFENTANYL	METHOXYACETYLFENTANYL	
ACRYLFENTANYL	METHYLFENTANYL+	
ALFENTANIL	NORALFENTANIL	

https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_03-508.pdf

Emerging Threat Report 2019



https://ndews.umd.edu/sites/ndews.umd.edu/files/DEA-Emerging-Threat-Report-2019-Quarter-1.pdf

Drug Death Diagnosis

- Postmortem drug levels may not reflect antemortem drug levels
- Drug level may not correlate with toxicity (e.g. tolerance, metabolism)
- History + Autopsy + Toxicology

Autopsy Required

- B3.1 the death is known or suspected to have been caused by apparent criminal violence.
- B3.2 the death is unexpected and unexplained in an infant or child.
- B3.3 the death is associated with police action.
- B3.4 the death is apparently non-natural and in custody of a local, state, or federal institution.
- B3.5 the death is due to acute workplace injury.*
- B3.6 the death is caused by apparent electrocution.*
- B3.7 the death is by apparent intoxication by alcohol, drugs, or poison, unless a significant interval has passed, and the medical findings and absence of trauma are well documented.
- B3.8 the death is caused by unwitnessed or suspected drowning.*
- B3.9 the body is unidentified and the autopsy may aid in identification.
- B3.10 the body is skeletonized.
- B3.11 the body is charred.
- B3.12 the forensic pathologist deems a forensic autopsy is necessary to determine cause or manner of death, or document injuries/disease, or collect evidence.
- B3.13 the deceased is involved in a motor vehicle incident and an autopsy is necessary to document injuries and/or determine the cause of death.

https://name.memberclicks.net/assets/docs/684b2442-ae68-4e64-9ecc-015f8d0f849e.pdf

NAME Accreditation Checklist

- Is the medical staff of sufficient size that no autopsy physician is required to perform more than 250 autopsies/year?
- Is the medical staff of sufficient size that no autopsy physician is required to perform more than 325 autopsies/year?

https://www.thename.org/assets/docs/NAME%20Accreditation%20Checklist%202019%20-%202024.pdf

Projected 2018 Drug Deaths