

Opioids: Their History and Current Challenges

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PHARMACY


CLASSICS

BEST-SELLERS

NEW RELEASES



Introduction

- History of opioid development
 - Different opioids and their use in medicine
 - History of opioid abuse and addiction
 - The Opioid Epidemic
 - Opioid overdoses
 - Current opioids of abuse
 - A brief case study of an overdose
 - Opioid overdose reversal agents
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History of Opioid Development



It all starts with the Opium Poppy

History of Opioid Development



History of Opioid Development

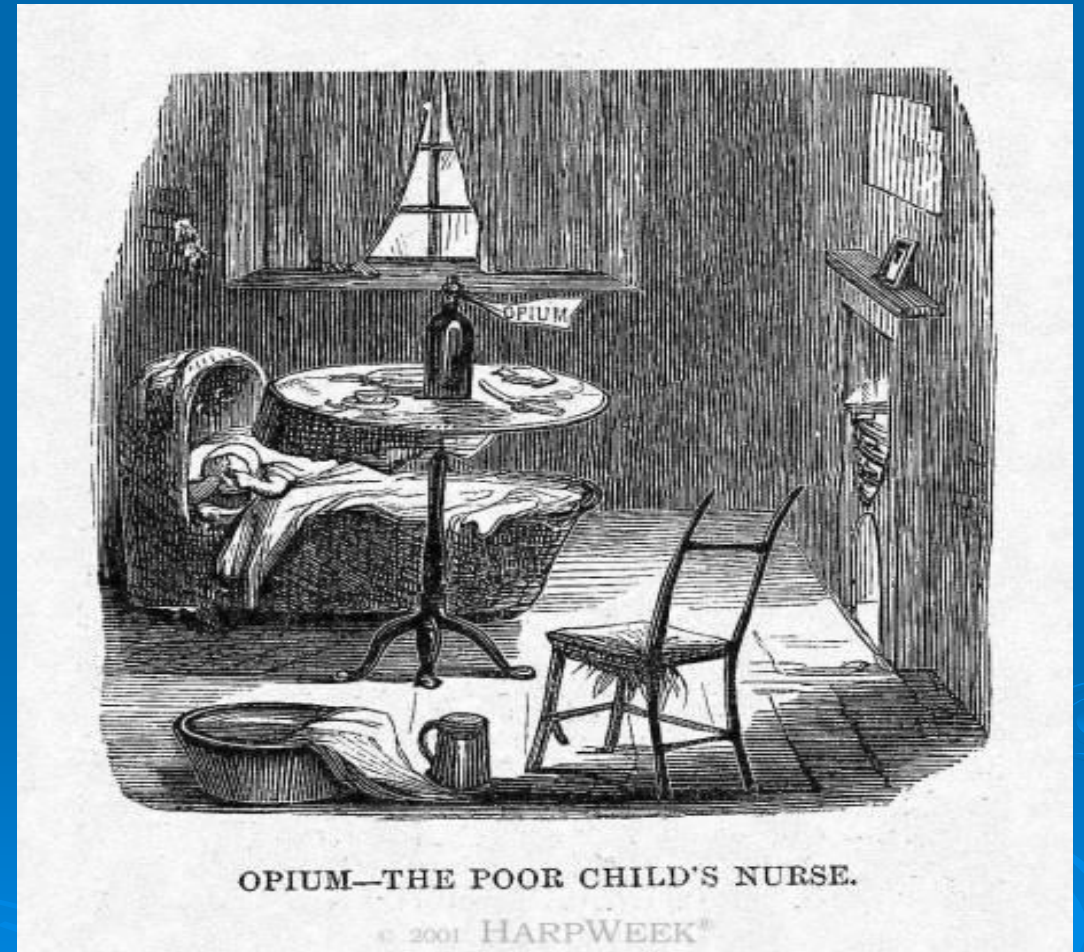
- The Opium Poppy is widely grown as an agricultural crop. Its latex contains alkaloids which have painkilling properties, including morphine, codeine and others. It is legally grown for medicine in 19 countries worldwide. Approximately 2000 tons of legal opium are produced annually (many times that illegally).



History of Opioid Development

- Use of the opium poppy predates history.
- Evidence of domestication predates 5000 BCE.
- It was first cultivated in the Mediterranean region and then spread to Asia, Afghanistan and Pakistan.
- Opium was a major colonial commodity in the colonial US.
- It is now extensively cultivated worldwide.
- Opium poppy cultivation is strictly illegal in most countries worldwide except for legitimate pharmaceutical purposes.

Opioids and Their Use in Medicine



Opioids and Their Use in Medicine

- Prescription opioids, when legally prescribed by a doctor and used as directed, can relax the body and relieve symptoms of an illness, an injury or a surgical procedure.
 - Pain due to trauma or disease (acute or chronic)
 - Post-surgical pain
 - Coughing
 - Diarrhea
 - Opioids may be given orally, via a skin patch, under the tongue or by injection.

Opioids and Their Use in Medicine

- Common medical opioids include the following.
 - Natural opioids – naturally occurring from opium poppy
 - Morphine, Codeine, Thebaine, Opium
 - Semi-synthetic opioids – modified naturally occurring
 - Heroin, Hydrocodone, Oxycodone, Hydromorphone, Buprenorphine
 - Synthetic opioids – made entirely in a lab
 - Fentanyl (and its analogues), Methadone, Tramadol, Meperidine

Opioids and Their Use in Medicine

- Opioids have been used in medicine for thousands of years.
- 3400 BCE - Sumerian references the opium poppy as the “joy plant”.
- 1552 BCE – Egyptians used opium as a sedative for children.
- Later use: Opium spread along trade routes, Arab traders bringing it to India and China. Widely used by Greek, Roman, and Islamic physicians for various ailments.

Opioids and Their Use in Medicine



Opioids and Their Use in Medicine

- 1803: Morphine was isolated from the opium poppy
 - German pharmacist Friedrich Serturner.
- 1832: Codeine was isolated from the opium poppy
 - French chemist Pierre-Jean Robiquet
- 1844: Hypodermic needle invented
 - Irish physician Francis Rynd
- 1874: Heroin was first synthesized from morphine
 - British chemist Charles Robert Alder Wright.

Opioids and Their Use in Medicine




Opioids and Their Use in Medicine



1861-1865 during the American Civil War
Opium and morphine were used extensively.

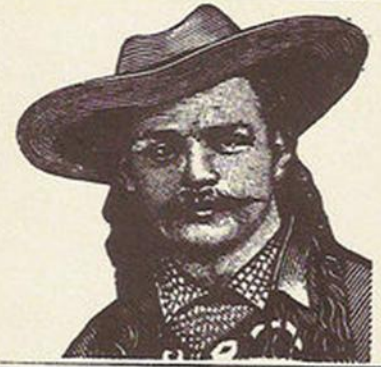
History of Opioid Abuse and Addiction

- The 19th and early 20th centuries were an era of minimal drug regulation, and opioids were common ingredients in many widely available products and “patent medicines”.
 - Common opioids used in these products included opium and morphine.
 - “Medicine Shows” in the US were ways to distribute these products to consumers.
- 



Medicine Show in Breckenridge Missouri

TEXAS CHARLEY.



CHAS. BIGELOW,

**GENUINE
KICKAPOO INDIAN SAGWA**

THE GREAT INDIAN MEDICINE!

Is a compound of the virtues of Roots, Herbs, Barks, Gums, and Leaves. Its elements are Blood-making, Blood-cleansing and Life-sustaining.

It is the the Purest, Safest, and Most Effectual Cathartic Medicine known to the Public.

The sciences of Medicine and Chemistry have never produced so valuable a remedy, nor one so potent to cure all diseases arising from an impure blood.

WILL CURE

Constipation, Liver Complaint, Dyspepsia,
Indigestion, Loss of Appetite, Scrofula,
Rheumatism, Chills and Fever,
or Any Disease

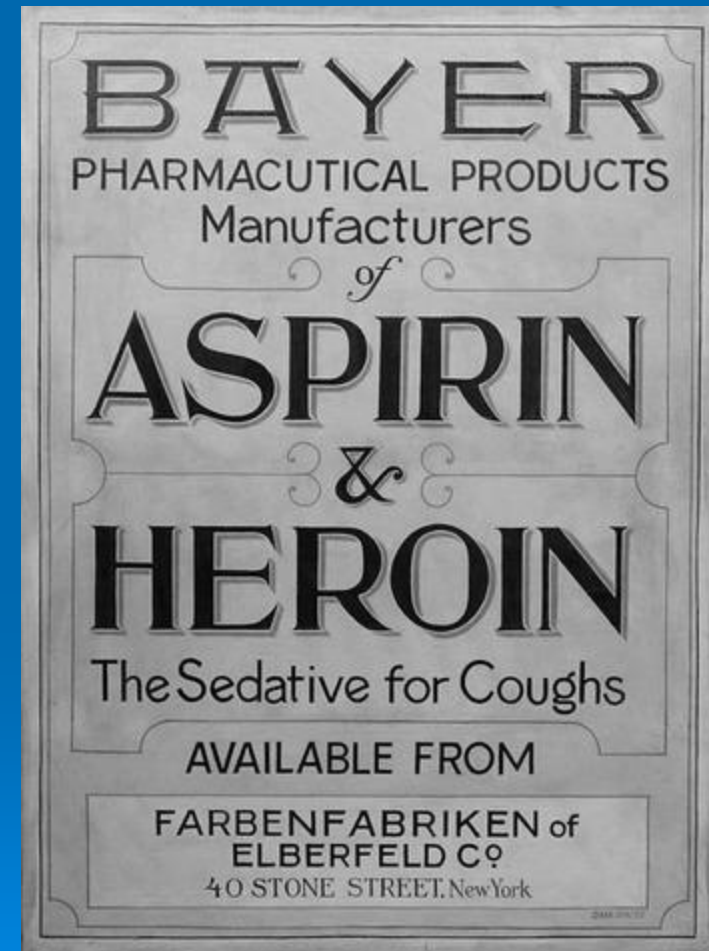
Arising from an Impure Blood or Deranged Liver.

FOR SALE BY ALL DRUGGISTS.

PRICE \$1.00 PER BOTTLE.

Bayer Heroin

- In 1897, the German pharmaceutical company Bayer marketed heroin as a cough suppressant and a less addictive alternative to morphine.



By the late 19th century, two-thirds of those battling opioid addiction at this point were likely upper- and middleclass white women who may have been initially prescribed the drugs for menstrual issues.



SAMHSA

Harrison Narcotic Act of 1914

- The Harrison Narcotic Act was a federal law enacted in the United States in 1914 that regulated and taxed the production, importation, and distribution of opiates and coca products.
- It required doctors, pharmacists, and other licensed professionals to register with the government and pay a special tax on their narcotics activities.
- It prohibited the sale of narcotics without a prescription from a registered physician.
- It established a system of federal inspections and controls over narcotics imports.

Harrison Narcotic Act of 1914

- The Harrison Narcotic Act was a landmark piece of legislation that had a lasting impact on the drug war in the United States. It is still considered one of the most important factors that shaped the current system of drug control in the country.
- However, it has been criticized for failing to effectively control the drug trade and for punishing drug users rather than drug dealers.

Harrison Narcotic Tax Stamp

•\$1•

UNITED STATES **SPECIAL TAX STAMP** INTERNAL REVENUE

71254

THIS STAMP EXPIRES JUNE 30, 1932
THIS STAMP IS NOT TRANSFERABLE ON CHANGE OF OWNERSHIP OF THE BUSINESS.

PRACTITIONER DISPENSING OPIUM, ETC.

YOUR REGISTRY NUMBER IS 1045

Issued by the Collector for the _____ District of **LOUISIANA**

S. J. Rosenthal, M. D.
205 Audubon Bldg,
New Orleans, La.

CLASS 4

UPON CHANGE OF ADDRESS NOTIFY COLLECTOR IMMEDIATELY

REGISTERED MAIL

Federal Agents Destroying Narcotics, 1920



Controlled Substances Act (CSA) of 1970

- Replaced the Harrison Narcotic Act
- Created a system of classifying drugs (I-V),
- Designed to prevent and treat addiction
- Serves as legal basis to combat abuse
- The DEA implements and enforces the CSA
- Drug classifications can be changed

Today - Substance Use in the USA

- 9.7% of Americans ages 12 and older had an alcohol use disorder in the past year. Over 50% of adult Americans have a family history of alcohol use disorders.
- 25% of children in America live in a household where at least one parent or primary caregiver has a substance use disorder (2023).
- Alcohol abuse has a significant impact on hospital admissions for a range of conditions, such as gastrointestinal diseases, injuries, and cardiovascular problems.
- Marijuana 2022 Data - 47% of adults in the US have used marijuana in their lifetime. 44% of young adults in the US, ages 19-30, have used marijuana in the past year. 23-28% of high school students in the US have used marijuana in their lifetime. (According to an AI Overview)
- Alcohol use is a major risk factor for many chronic diseases and contributes to premature death, making it a leading cause of death overall, alongside other factors like smoking, poor nutrition, and physical inactivity.

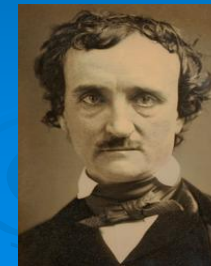
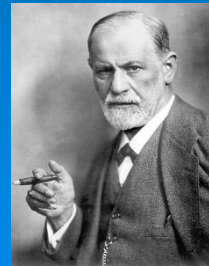
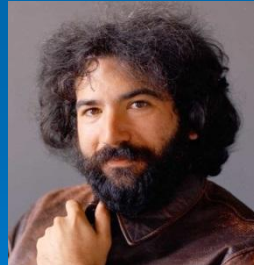
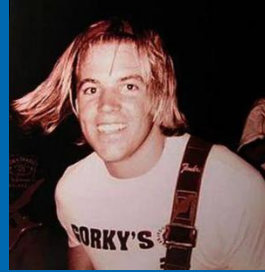
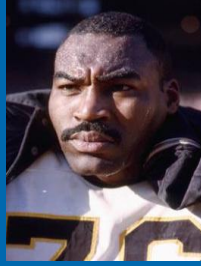
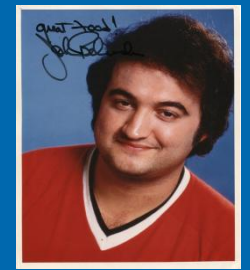
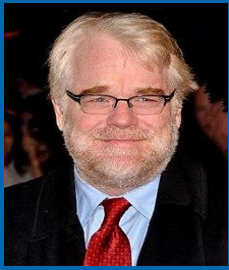
Today - Substance Use in the USA

- 51% of people in the US have used illicit drugs at least once.
- Substance use disorders contribute significantly to illness in each of the top two causes of death: heart disease and cancer.
- Approximately 1 in 184 U.S. citizens were confined in jail or prison in 2023. Alcohol is a factor in approximately 40% of all violent crimes: rape, sexual assault, robbery, aggravated and simple assault.
- Everyday, about 37 people in the US die in alcohol-impaired car crashes - that's one person every 39 minutes.
- Alcohol use during pregnancy is the leading preventable cause of birth defects and developmental disabilities (fetal alcohol spectrum disorders).

The Cost

- Substance use disorders cost the American economy an estimated **\$740 billion per year** in lost productivity, health care expenditures, crime, motor vehicle crashes and other conditions. Some estimates for the overall impact of addiction exceeds **\$820 billion per year**.
- Untreated substance use disorders are more expensive than heart disease, diabetes and cancer combined.
- Beyond the financial cost is the cost to individuals, families and society: *increased crime and homelessness, family dysfunction, social problems (unemployment, violence, lost productivity), medical problems (alcoholic hepatitis, cirrhosis, HIV AIDS, hepatitis C, fetal alcohol syndrome, cardiovascular problems, gastrointestinal problems) psychiatric problems (depression, anxiety, suicides) and unintentional injuries.*
- Deaths from overdoses. Overdose deaths are **the leading cause of preventable injury-related deaths** in the US.

The Opioid Epidemic



Drug Overdose Deaths

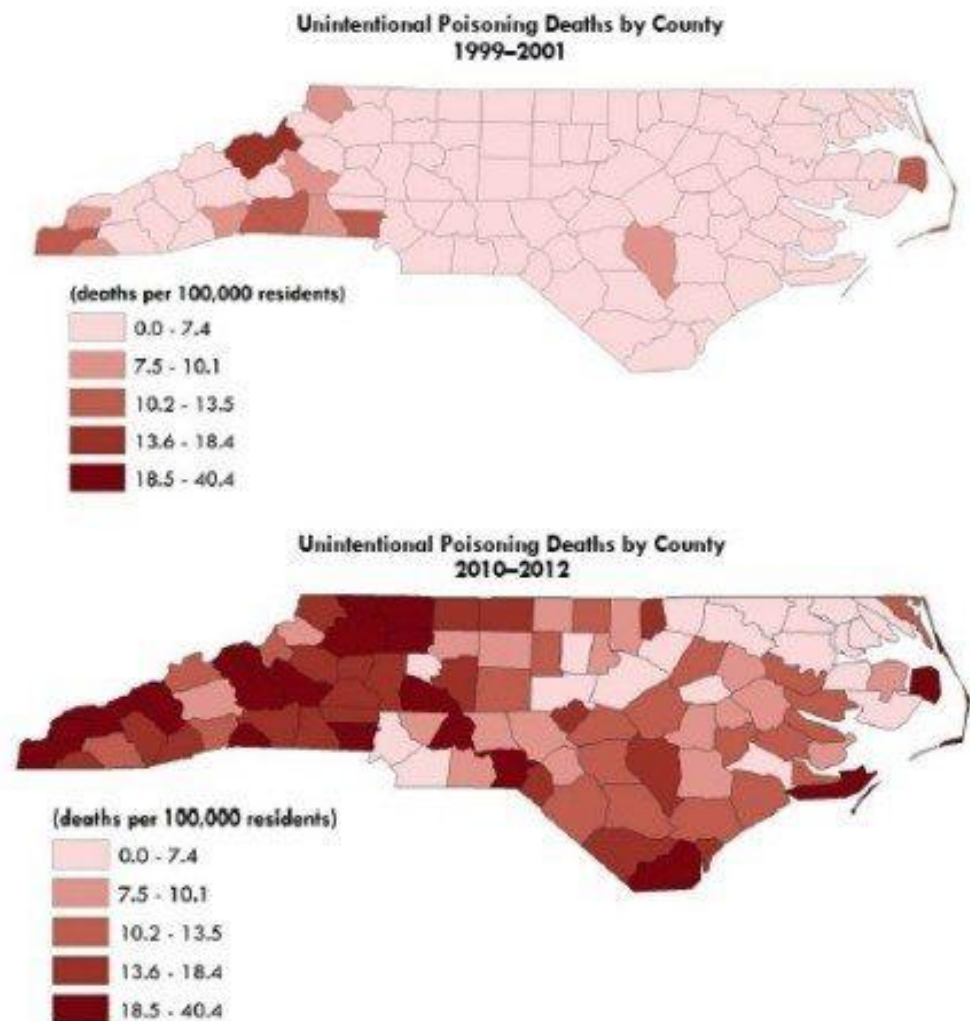
- In 2024, **80,391** drug overdose deaths occurred in the United States (220 daily). **68% were from opioids (48,422 from Fentanyl)**. This is a decline from **105,007** drug overdose deaths in 2023.
- More Americans died from drug overdoses each of the last nine years (2016-2024) than were killed in the entirety of the Vietnam War.
- A study published by the Recovery Research Institute and based on National Center for Health Statistics data shows that Tennessee experienced a 98% increase in drug overdose deaths in May 2020 compared to May 2019, one of the largest increases in the U.S. This was part of a larger national trend of surging overdose deaths in the first several months of the COVID pandemic. The rise in deaths continued into 2021.
- In 2024, **2565** drug overdose deaths occurred in Tennessee (provisional data). This is a 32.5% decrease from the **3799** estimated deaths in 2023, according to an AI Overview.

The Opioid Epidemic

Timeline

- **1996 – 2010** Annual prescription opioid use in the US increased dramatically as did annual prescription opioid overdoses.
 - **1996** - Purdue Pharma began to aggressively market OxyContin. Annual sales grew from \$48 million in 1996 to total sales reaching over \$40 billion by 2017.
 - **1996** - American Pain Society introduced “pain as the 5th vital sign” campaign. The VA adopted that campaign in 2000.
 - **2000** – Rx opioid ODs began to rise.
 - **2001** – Joint Commission issued standards requiring the use of a pain scale and stressing the safety of opioids.
 - **2010** - State and federal crackdowns to curb prescription opioid abuse began.
- **2011** - Heroin use began to rise along with a dramatic rise in heroin ODs. Heroin OD’s have continued to rise annually ever since.
- **2012** - Heroin OD’s surpassed Rx opioid ODs.
- **2013** - Fentanyl use began to rise along with a dramatic rise in Fentanyl ODs .
- **2015** - Fentanyl ODs surpassed heroin ODs.

Exhibit 1: Unintentional Poisoning Death Rates in North Carolina Have Increased in the Last Decade



Source: Program Evaluation Division based on data from the Department of Health and Human Services, Division of Public Health, Injury and Violence Prevention Branch.

2 The U.S. Centers for Disease Control defines an unintentional poisoning as a poisoning in which the individual exposed to the substance is not attempting to cause harm to himself or herself or others. These deaths include unintentional overdoses from prescription or recreational drugs. Other potential poisons include exhaust fumes and gases, pesticides, acids, organic solvents, and petroleum products.

Heroin Purity and Price (DEA Seizures)

➤ Purity (average street heroin)

- 1981 - 10%
- 2011 - 32%
- 2018 - 32%
- 2025 – 46% (Mexican black tar) 75% (Mexican white powder)

➤ Price per gram (pure heroin)

- 1981 - \$3260
- 2011 - \$500
- 2018 - \$75
- 2025 - \$60

Fentanyl

- Fentanyl is a synthetic opioid and is much more powerful than morphine or heroin.
- It is used for the treatment of severe, chronic pain.



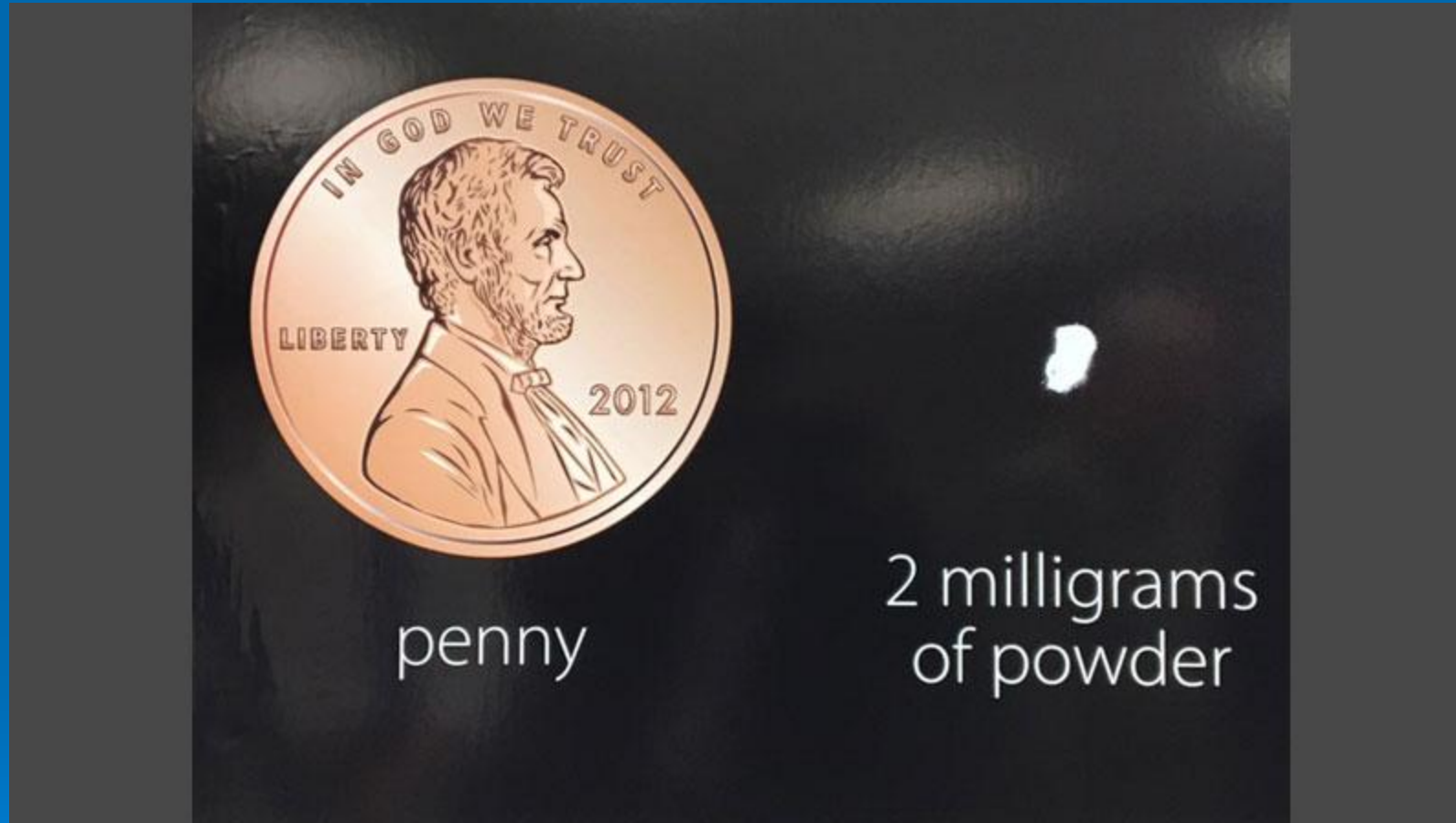
Fentanyl

- Fentanyl *50 times* stronger than heroin.
- Many Fentanyl analogues (i.e. Carfentanil, Lofentanil) are *5000-10,000 times* stronger than heroin.



Lethal Doses of Carfentanil, Fentanyl and Heroin

Fentanyl



penny

2 milligrams
of powder

2mg is a lethal dose of Fentanyl.

Fentanyl

DEA laboratory testing in 2024 revealed that five out of ten Fentanyl-laced, fake prescription pills contained a lethal dose of Fentanyl.



Fentanyl

- Fentanyl is cheaper and easier to manufacture than heroin.
- One kilo of heroin wholesales for approximately \$50,000. (\$200K RET)
- One kilo of Fentanyl wholesales for approximately \$4000. (\$10ml RET)
- 4 grams of Fentanyl (\$16 worth) will *double the strength* of one kilogram (1000 grams) of heroin.
- There are approximately 66 analogues of Fentanyl (i.e. Carfentanil, Lofentanil). Many are stronger than Fentanyl.
- Carfentanil (and other Fentanyl analogues) were not controlled substances in China until March 1, 2017. Until then, were manufactured legally and sold openly over the Internet, being actively marketed by several Chinese chemical companies.
- DEA – “Thousands” of clandestine labs in China.



“Drugs have taught an entire generation of American kids the metric system.”

– P.J. O'Rourke

Nitazenes

Nitazenes are a chemically defined class of substances derived from the parent compound nitazene. They were developed in the 1950's and never approved for human or veterinary medicine due to unacceptable side effects.



Nitazenes

- There are two primary reasons that the emergence of nitazenes in the street drug supply is alarming.
 - Their extreme potency. Some nitazenes are 10-40x stronger than fentanyl.
 - Researchers understand and are familiar with the range of potency of numerous fentanyl derivatives. However, researchers know little about nitazene derivatives. Scientists understand less about how modifications to their chemical structure will affect their potency, making nitazenes the “Wild West” of street drugs.
 - \$7000 for a kilo on the darknet – potentially 10,000,000 lethal doses.

Nitazenes

- Key facts regarding nitazenes in Tennessee
 - Rising death toll
 - Likely undercounted
 - Often hidden in other drugs
 - Highly potent
 - Response requires multiple naloxone doses
 - Middle Tennessee impacts



BUTYRFENTANYL FOR SALE

\$200.00 - \$8,000.00

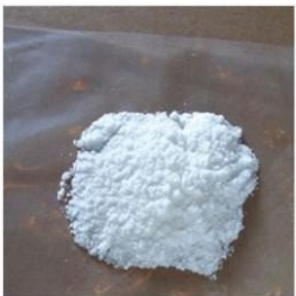
Select options



Buy 5-Aminoisotonitazene Online

\$200.00 - \$8,000.00

Select options



Buy butonitazene online

\$200.00 - \$8,000.00

Select options



Buy Carfentanil Wildnil Powder

\$200.00 - \$8,000.00

Select options



BUY 5-AMINOISOTONITAZENE ONLINE

\$200.00 - \$8,000.00

Choose quantity

\$1,050.00

1

Add to cart

Ask a Question

SKU: N/A Category: Opioids Tags: 5-Aminoisotonitazene sale, Buy 5-Aminoisotonitazene, ketamine hcl

Done

- Choose an option
- 5g
- 10g
- 50g**
- 100g
- 500g

Nitazenes

➤ Key types of nitazenes include:

- **Isotonitazene (ISO):** One of the most prevalent and potent nitazenes, ISO can be 250 to 900 times stronger than morphine. It has been detected in counterfeit pills resembling legitimate prescriptions.
- **N-Desethyl isotonitazene:** An active metabolite of isotonitazene that is now being produced and sold as a parent drug on its own. It is reported to be approximately 20 times more potent than fentanyl.
- **Protonitazene:** This nitazene has been found in confiscated street drug samples, including counterfeit pills, in various regions.
- **Etonitazepyne (N-pyrrolidino etonitazene):** A highly toxic nitazene that has been discovered in the illicit drug supply in places like Ottawa, Canada, where it was sold as counterfeit hydromorphone.
- **Metonitazene:** This nitazene has been reported in toxicology cases and drug seizures across North America.
- **Brorphine:** Identified in the unregulated drug supply as early as 2018, its derivatives continue to emerge, including **chlorphine** and **cychlorphine**.

7-OH

- "7-OH" is an abbreviation for **7-hydroxymitragynine**, a potent, opioid-like chemical found in the kratom plant. It is a substance of significant public health concern due to its potential for abuse and addiction.



7-OH

- **Effects:** At high concentrations, 7-OH binds to opioid receptors in the brain, producing strong pain-relieving (analgesic) and euphoric effects, which can be significantly more potent than morphine.
- **In Tennessee:** synthetic or concentrated forms of 7-hydroxymitragynine (7-OH) are illegal and classified as controlled substances. However, natural, botanical kratom (from which 7-OH is derived in small amounts) remains legal for individuals 21 and older, provided it is in its natural form and adheres to strict labeling and purity requirements.



Case Study



Naloxone



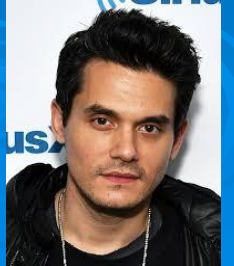
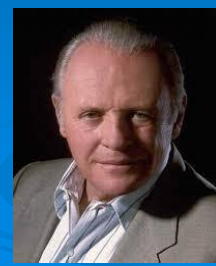
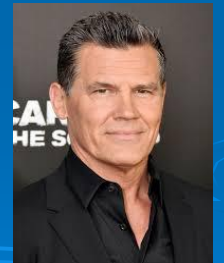
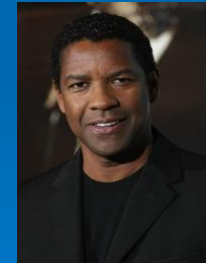
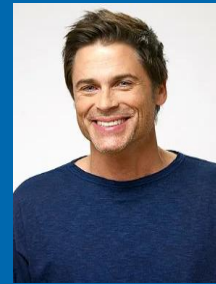
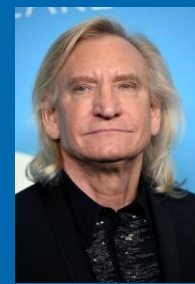
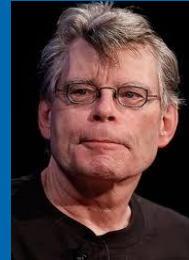
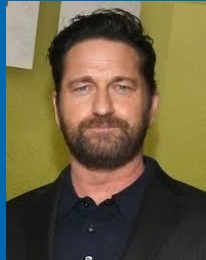
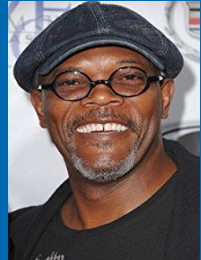
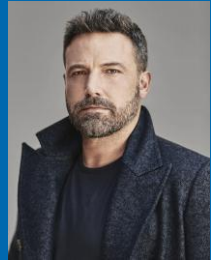
- Naloxone (Narcan) is a medication designed to rapidly reverse opioid overdose. It is an opioid antagonist—meaning that it binds to opioid receptors and can reverse and block the effects of opioids. It can very quickly restore normal respiration to a person whose breathing has slowed or stopped as a result of overdosing with heroin or prescription opioids.
- There are three FDA-approved formulations of naloxone:
 - Injectable (professional training required)
 - Auto Injectable (Evzio)
 - Prepackaged Nasal Spray (Narcan)

Surgeon General's 2018 Public Health Advisory



- “I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life.”
- The previous public health advisory from a Surgeon General was in 2005 and focused on drinking during pregnancy.

The Recovery Epidemic

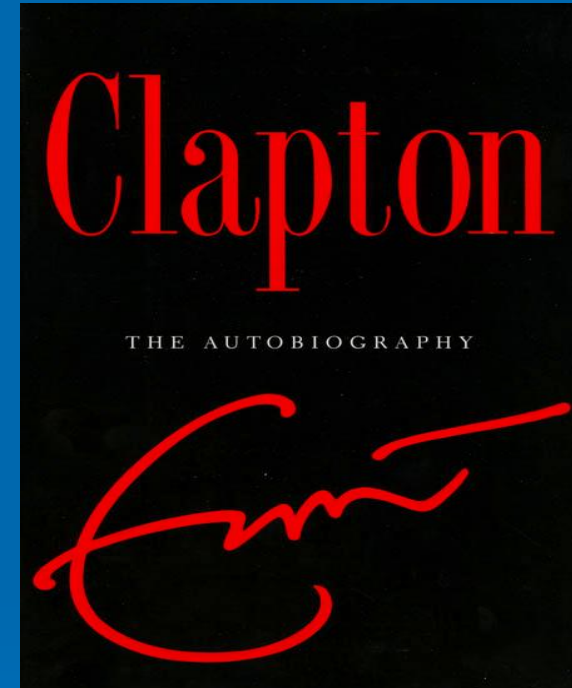




“Getting sober was the bravest thing I’ve ever done and ever will do in my life”

- Jamie Lee Curtis

Eric Clapton's past includes addictions to alcohol, cocaine, prescription drugs and heroin. The arrival of his son Conor, however, gave him the motivation to attempt sobriety. It was a sobriety he maintained even after Conor's tragic death in a 49-story fall at age 4.



“A woman came up to me after the meeting and said, ‘You’ve just taken away my last excuse to have a drink.’ I asked her what she meant. She said, ‘I’ve always had this little corner of my mind which held the excuse that, if anything were to happen to my kids, then I’d be justified in getting drunk. You’ve shown me that’s not true.’ I was suddenly aware that maybe I had found a way to turn this dreadful tragedy into something positive. I really was in the position to say, ‘Well, if I can go through this and stay sober, then anyone can.’ There was no better way to honor the memory of my son.”



That's all Folks!

Charles A. Odell, MSW, MAC, LCAS

Charles Odell has worked in the field of substance use disorder treatment since 1983. Mr. Odell is the Chief Executive Officer and President of Dilworth Center where he has worked since 1995. Dilworth Center is a private, non-profit organization providing substance use disorder treatment programs for adults, young adults, adolescents and families.

Mr. Odell received a Bachelor of Arts from the University of North Carolina at Charlotte and a Master of Social Work from the University of North Carolina at Chapel Hill. He is Master Addiction Counselor and a Licensed Clinical Addictions Specialist. Mr. Odell serves on the Board of Directors of the National Association of Addiction Treatment Providers (NAATP) and the NAATP Ethics Committee. He also serves on the Advisory Board of the Jonnie McLeod Institute on Substance Abuse at UNC-Charlotte. Mr. Odell is married to Sydney, and they have two sons, Alex and Andy.

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