Components of Substance Use Disorder Epidemiology

- **Host** - The User
- **Agent** – The Substances
- **Environment** - Social, Economic, and Geographic Conditions

Contributing Factors – Supply Vectors

- **Production**
- **Patterns of Trafficking**
- **Price**
- **Purity**
- **Profit**
- **Availability**
- **Poisonous Contamination**

Contributing Factors – Demand Vectors

- **Attitudes:**
  - Perceived Harmfulness
  - Perceived Wrongfulness
  - Acceptance by others
- **Desired Effects**
- **Withdrawal** – “Dope Sick”
- **Public Consensus**
- **Cost**
- **Rapid Onset of Action**
- **Access**
Cycles of Change
Reoccurring Patterns of Substance Use Disorder Epidemics 1880 – 2018

DEFINITION OF OPIOID
“Similar to opium”
Morphine and similar drugs derived from opium
All substances, both natural and synthetic, that bind to opioid receptors in the brain and body

The Morphine Molecule
- Binding to and activating the opioid μ receptors in the brain and spine
- Principal effect on the central nervous system and gastrointestinal tract
- Primary actions are analgesia and sedation.

Types of Opioids
- Illegal Heroin
- Legal Prescription Opioid Pain Relievers (e.g., Oxycodone, Hydrocodone, Methadone, Morphine, Rx Fentanyl, et al)
- Illicitly manufactured Opioid Analogues (e.g., Fentanyl, U-4700, et al sold as Heroin or adulterants to Heroin, Cocaine or other drugs, and counterfeited prescription pills)

History of Opioids
- Opium the first drug from early agricultural civilizations
  - Assyrians invented slicing the poppy pod
  - Sumerians - The “Joy Plant”
  - Egyptians first produced opium as a drug – Thebaine
  - Greeks
  - Indian Subcontinent
  - Medieval Trade spread the drug
- 1804 German pharmacist first isolated Morphine
  - Named after the Greek god of sleep and dreams, Morpheus
- 19th Century 330 Wars forced production of Morphine
  - Heavily used in US Civil War
  - Leaving many addicted ???
Epidemic

November 29, 2018

Jim Hall         upfrontin@aol.com

History of Opioids in the U.S.

• In 1874, Heroin was created in Germany and sold in the United States as a “safe, non-addictive” substitute for morphine.

• From the late 1800’s to the 1900’s, drug companies sold over-the-counter drug kits containing glass barreled hypodermic needles and vials of morphine or heroin.

• Heroin, morphine and other opiates were sold legally in the U.S. until controlled by Harrison Narcotic Tax Act in 1914 and made illegal in the 1920’s

• 200,000 heroin addicts in the U.S. by 1925

History of Opioids in the U.S.

• 1950’s – Drug Advertising and Direct Marketing to Physicians – antibiotic Terramycin

• 1960’s – Valium becomes first $100 million drug

• 1980’s – NEJM Porter and Jick Letter to Editor

  Purdue Pharma releases MS Conti
  WHO Ladder of Pain treatment

• 1996 – Purdue Pharma releases OxyContin

  Nation’s first “Pill Mill South Shore, KY
  American Pain Society – Pain as 5th Vital Sign

**ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS**

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients’ who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had a history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients, Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

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Fentanyl: A Particularly Potent Opioid

• Schedule II synthetic and short-acting opioid. About 80 to 100 times more potent than morphine, 25 to 40 times more potent than heroin

• Introduced into medical practice as an intravenous anesthetic in the 1960s and approved for pain associated with advanced cancer

• It is a μ-opioid receptor agonist with a rapid onset and short duration of effects. Similar to other μ-opioid receptor agonists (like morphine or oxycodone) in its pharmacological effects

High Levels of Opioid Prescriptions have Facilitated Diversion & Contributed to Overdose Deaths

Near Tripling of Opioid Prescriptions from U.S. Retail Pharmacies, 1991-2013

Total Rx Opioid Tablets Dispensed in Retail Pharmacies in the USA:

• 2013  15,972,304,698
• 2014  15,606,882,755

Source:  Jones CM, et al. JAMA Internal Medicine 2015; Jul 20:2799
Symptoms of Opioid Withdrawal

- nausea
- sweating
- cramps
- vomiting
- diarrhea
- insomnia
- loss of appetite
- agitation
- irritability
- mood swings
- depression
- anxiety
- muscle soreness
- aching bones
- fever
- runny nose
- twitching

“Dope Sick”
Addiction is the Affliction

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**Fentanyl**: A Particularly Potent Opioid

Most overdoses are from non-pharmaceutical fentanyl (i.e. illicit manufacture), BUT mortality statistics include fentanyl deaths in analgesic category (misclassification?)
**Epidemic of Opioid Addiction and Deaths**

*The Perfect Storm*

For Pain
Rx

Pill Mills Street

For Pleasure

Tolerance
Need More

“Dope Sick”

Mexican Heroin

Polysubstance Abuse

Abstinence
Relapse

OUD

Counterfeit Pills

“Dope Sick”

Fentanyl Analogues
el al IM Opiates

In 10-state study, almost 57% of people who died from an overdose which tested positive for fentanyl and/or fentanyl analogs also tested positive for cocaine, methamphetamine, or heroin.

**Fentanyl-Contaminated Cocaine Headlines**

Ft. Lauderdale

DEA warns of deadly contaminated cocaine in South Florida

Philadelphia

Fentanyl-Laced Cocaine Becoming A Deadly Problem Among Drug Users

New Jersey

Man faces charges in 3 fentanyl-laced crack cocaine deaths

**Number of Crime Lab Reports of Fentanyl Alone and in Combination with Other Drugs in the USA: 2016**

- Fentanyl Alone: 22,278
- Fentanyl & Heroin: 8,067
- Fentanyl & Opioids: 1,341
- Fentanyl & Cocaine: 496
- Fentanyl & Other Substances: 577
- Fentanyl & Heroin & Cocaine: 492

Source: DEA – National Forensic Laboratory Information System Data Queried August 2017
Cocaine – The Origin

- Since 15th Century – Andean South American native people chewed coca leaves to relieve hunger and dispel fatigue
- 1859 – Alkaloid cocaine isolated by German pharmacist, Albert Niemann
- Dr. Theodore Aschenbrandt - Bavarian Army cocaine water solution for exhausted collapsed soldier who cheerfully resumed the march
- Dr. Sigmund Freud: “a magical drug” * recommended to friends and colleagues
- Because of numbing effects became a standard treatment for eye disorders and local anesthetic for minor surgery and dentistry
- By 1863 Vin Mariani – coca leaves and Bordeaux wine

The First Cocaine Epidemic 1880 -1920

Introduction Phase - the Drug Rapidly Gains Acceptance

- 1884 – Purified cocaine commercially available in USA
- Wholesale cost very high $5-10 per gram but fell to 25 cents a gram until WW I compared to average wage at 20 cents per hour. Retail price $2.50 per gram
- Popular in the US: sold from drug and grocery stories, saloons and patent-medicine vendors
The First Cocaine Epidemic 1880-1920

**Introduction Phase**

- Freud published 5 papers about Cocaine
- Some physicians believed cocaine reduced cravings for opiate addicts and alcoholics
- Encouraged by medical authorities and entrepreneurs as an elixir for the masses
- Touted as a panacea for melancholia, neuralgia, hysteria and nervous afflictions

**The First Cocaine Epidemic 1880-1920**

**Middle Period - Use Spreads, Adverse Effects Revealed**

- 1885 – John Pemberton registers a trademark for: "*French Wine Coca - Ideal Nerve and Tonic Stimulant*
- 1886 - Renamed as "*Coca-Cola*
- 1887 – Noted neurologist William Hammond’s cocaine wine 2 grams/pint instead of ½ gram in Vin Mariana

**The First Cocaine Epidemic 1880-1920**

**Middle Period - Use Spreads, Adverse Effects Revealed**

- 1890s – Decade of Hedonism and Creativity
- Reports of cocaine addiction becoming common in medical literature
- Late 19th and early 20th Century – Era of Bacteriology
  - Allowed prescribing of specific medications for more illnesses
  - Thus, fewer general elixirs with cocaine and opioids

**The First Cocaine Epidemic 1880-1920**

**Middle Period - Use Spreads, Adverse Effects Revealed**

- 1903 - Commission on the Acquisition of the Drug Habit declared cocaine, once favored by upper-class professionals, was being used mostly by "bohemians, gamblers, prostitutes, burglars, racketeers, and pimps."
- As use of cocaine increased so did abuse.
- Chronic abuse led to paranoid delusions, insomnia, malnutrition and nasal septum ulcerations.

**The First Cocaine Epidemic 1880-1920**

**Middle Period - Use Spreads, Adverse Effects Revealed**

- 1906 – Pure Food and Drug Act only required cocaine listed as an ingredient in Over-the-Counter remedies
- 1914 - All 48 States had anti-cocaine laws
- The journal *Medical Record* reported: "There is no such thing as an occasional or moderate cocaine user. The line is very sharply drawn between the total abstainer and the fiend...."
- The Harrison Act passed, Nation’s first major anti-narcotic law
  - Cocaine classified as a narcotic, along with opium, morphine and heroin. Permitted sale of cocaine only by prescription.
  - Banned any trace of cocaine in patent meds.
The Calm Between Epidemics: 1930s to late 1960s

Nonmedical Use of Cocaine Nearly Non-Existent

References to cocaine rarely appeared in movies, music and literature if so portrayed negatively. In Cab Calloway's 1931 song "Minnie, the Moocher," Minnie was a "low-down hoochy coocher," but she took up with a "cokey" named Smokey. It didn't take long for Smokey and Minnie to wind up in the county jail. And it wasn't too long after that "poor old Min" was "kickin' up daisies."

• Public's attitude toward all drugs was downright antagonistic.
• 1930s-1940s – Mandatory drug education gradually disappeared

The Calm Between Epidemics: 1950s

Nonmedical Use of Cocaine Nearly Non-Existent

• 1950s - Antidrug laws increased in severity: Era of drug intolerance
• Cocaine use dwindled reaching 50,000 by the late 1950s
• Personal knowledge of a "dope fiend" was unusual for the vast majority of Americans during the 1950s.
• Cocaine Prohibition worked because of strong public consensus
• Cocaine: A problem we used to have and has now been almost eliminated

The Modern Epidemics: 1975 to 2018

The noted drug historian Dr. David Musto stated, "The people who had lived through the nation’s first cocaine epidemic knew that the euphoria induced by the drug was a dangerous delusion," "When cocaine reappeared in the 1970s, few people remembered the previous American experience, because the earlier generations that had learned a hard lesson about cocaine were no longer around. Cocaine's notorious reputation died with them. By the 1970s, America was ready for another fling with this most seductive and dangerous drug."

Those in denial of History tend to repeat it

1971 – Law enforcement seizures of cocaine surpass those for heroin. The number of users and consequences of abuse would steadily climb until the late 1980s

Cocaine’s Second Epidemic

Escalating cocaine use among young adult users of other illicit drugs in the late 1970s and adolescents in the early 1980’s led to the outbreak of a second national cocaine epidemic

Cocaine in the early 1980’s

• Chic
• Expensive
• "Non-addictive"
• Relatively “Safe”
• ...But really expensive

Hurricane Crack

• The Ether Factor
• Coca Paste – “basuco”
• Netherlands Antilles and Caribbean Trafficking Nations
• Benzine-Washed Cocaine
• “baking soda base” introduced to Caribbean populations in South Florida

Crack accelerates all the consequences of cocaine abuse and escalates the cocaine epidemic
Cocaine in the mid 1980s

- Killer Cocaine
- Addiction from Hell
- Crack Monsters
- Nation’s #1 Drug Problem
- By 1986: Nation’s #1 Problem

September 1986

By 1986:

- Nation’s #1 Problem

First Time Users

- 1.1 million

New Initiates in (000s) - Stimulants

- Total Past Year Stimulant Initiates: 2,395,000
- Ox Stimulants: 1,200,000
- Methamphetamine: 185,000
- Cocaine: 1,000,000

Past Years Users in (000) - Stimulants

- Total Past Year Stimulant Use: 13,415,000
- Ox Stimulants: 5,819,000
- Methamphetamine: 1,633,000
- Cocaine: 5,943,000

HIDTA Cocaine Seizures 2011-2017

- 0
- 2,000
- 4,000
- 6,000
- 8,000
- 10,000
- 12,000
- 14,000
- 16,000
- 18,000
- 2011
- 2012
- 2013
- 2014
- 2015
- 2016
- 2017

HIDTA Cocaine/Crack Seizures 2017

Source: National Survey on Drug Use and Health and United States Government
Pharmaceutical Amphetamines

- 1887 – First produced in Germany
- 1919 – Japan makes more powerful version: methamphetamine
- 1929-1945 - First US Epidemic generated by pharmaceutical industry and medical profession
- Gordon Alles seeking substitute for ephedrine as a decongestant and bronchodilator focused on activity of beta-phenylisopropylamine (soon to be known as amphetamine)
- 1933 - Smith, Kline and French (SKF) patented amphetamine SKF marketed it as the Benzedrine Inhaler (325 mg of oily amphetamine base). Sold as OTC until 1948

1937 AMA “Seal of Approval” for Benzedrine Sulfate amphetamine tablets for narcolepsy, Parkinsonism, and minor depression (first antidepressant)

“bennies”
Pharmaceutical Amphetamines

World War II

- USA and British military supplied 5-mg Benzedrine tablets
- Germany and Japan supplied methamphetamine
- Increase in use for weight lost during war years not as approved indication but off-brand manufacturers started clinics
- 1945 supply for 1/2 million Americans with 2 tablets daily
- Abused by eating the contents of Benzedrine Inhalers
- Benzedrine abuse was multiplied many times by military exposure

As World War II neared its conclusion, a request was sent from high command for a drug that would boost morale and fighting ability, and Germany’s scientists responded with a pill called D-IX that contained equal parts cocaine and painkiller (5 mg of each), as well as Pervitin (3 mg). The war ended before it reached the general military population.

Pharmaceutical Amphetamines

Post World War II

- 1949 AMA approval for weight lost advertisement
- 1952 Food and Drug Administration placed production of amphetamine & methamphetamine salts at nearly 4 times the 1949 estimate
- 1950 SKF intro’s Dexamyl (dextroamphetamine + amobarbital) for mental and emotional distress and weight lost remedy
- In the early 1960s, amphetamines consumed at a higher rate than tranquilizers.
- Largest age group among the medical users were those aged 36 to 45 years, and 85% of all amphetamine patients were women

In the 1950s, competition among pharmaceutical firms boosted amphetamine consumption dramatically, after expiration of the Alles and Smith, Kline and French patent in 1949. Source: Journal of the American Medical Association 147 (1951): 19 (advertising section).

Pharmaceutical Amphetamines

Post World War II

- At the end of the 1950s, monoamine oxidase inhibitors and tricyclic antidepressants were introduced and quickly acclaimed by psychiatrists as superior to amphetamines for depression.
- In the United States, however, prescribing rates for amphetamines did not decline significantly in the 1960s. Mostly prescribed by Primary Care rather than psychiatric specialists
- By about 1960, widespread consumption had begun to make amphetamine’s negative health consequences more evident.
- Flat retail prescription sales from 1964 to 1970
Pharmaceutical Amphetamines
Post World War II

• By the late 1950s and early ’60s, it was becoming harder for the medical community to ignore the growing number of professionals-turned-speed-freaks who had become hopelessly hooked on Benzedrine and Dexedrine.

• American serviceman in the Vietnam War consumed on average 30 to 40 amphetamine tablets each year of the conflict.

Pharmaceutical Amphetamines
Post World War II

• Amphetamine psychosis could happen to anyone, and eventually would, given enough of the drug.

• Evidence emerging around 1960 that amphetamine is truly addictive, instead of merely “habituating” like caffeine, as leading pharmacologists had asserted when the drug was first introduced.

• 1970 - 9.7 million Americans were past-year users of amphetamines.

• In 1970, 80%-90% of amphetamines seized on the street were pills manufactured by US pharmaceutical firms.

• In the United States, medical amphetamine use declined only after 1970, when new laws restricted prescribing.

Pharmaceutical Amphetamines
1970s

• Early 1970s - BNDD (forerunner of DEA) moves all amphetamine products to Schedule II, including methylphenidate (Ritalin) and the diet drug phentermine (Preludin), both of which had proved attractive to high-dose injection abusers.

• Prescription sales of amphetamines and related drugs shot up when the new restrictions were announced and then plummeted 60% below their original level when they came into effect.

• Only narcolepsy and “hyperkinetic disorder of childhood” (today’s attention deficit disorder, then rare) remained approved usages.

• Because of FDA & BNDD controls, amphetamines became relatively minor drugs of abuse by the late 1970s, while illicit cocaine use exploded.

Pharmaceutical Amphetamines
1970s

• The first amphetamine epidemic was created by the pharmaceutical industry and (mostly) well-meaning prescribers.

• Current amphetamine resurgence began through a combination of recreational drug fashion cycles and increased illicit supply since the late 1980s.

• Striking similarity between present and past epidemics relates to the role of pharmaceutical amphetamines.

• Since 1995, medical consumption of amphetamine-type attention deficit medications, such as Ritalin (methylphenidate) and Adderall (amphetamine) has more than quintupled.

Pharmaceutical Amphetamines

![Graph showing prescription rates for stimulants](Source: DEA Production Quota figures)
Reoccurring Patterns of Stimulant Epidemics: 1880 - 2018

- Illicit Methamphetamine

Methamphetamine

- 1919 - Crystallized methamphetamine was first produced from ephedrine using iodine and red phosphorus. Methamphetamine was easier to make than amphetamine and more potent.

- Nazi leaders distributed millions of doses of methamphetamine in tablets called Pervitin to their infantry, sailors and airmen in World War II.


Methamphetamine

- 1938 - Pervitin first sold to the German public over the counter and became quite popular. When supplies ran low on the war front, soldiers would write to their families requesting shipments of speed.
- Hitler himself consumed vast quantities of drugs during the war, including cocaine, an early version of oxycodone and crystal meth
- Stimulants went a long way toward the Nazi dream of creating super-soldiers.

Methamphetamine

• 1969: Rolling Stones Concert – Altamont Springs, California

The Hells Angels acted as security though they were loaded on drugs, cheap red wine and totally uncontrollable.

Methamphetamine

• Early 2000s, meth made from pseudoephedrine, the decongestant in drugstore products like Sudafed, poured out of domestic labs like those in the early seasons of “Breaking Bad.”
• Narcotics squads became glorified hazmat teams.
Methamphetamine

• 2005 Congress passed the **Combat Methamphetamine Act**, which put pseudoephedrine behind the counter. Although some meth makers tried “smurfing,” meth cases plummeted.

• With no more meth lab explosions on the nightly news, the public forgot about the drug.

• Mexican drug cartels stepped in

Methamphetamine

• The market is inundated with so much pure, low-cost meth that dealers have more of it than they know what to do with.

• 2018 - United States border agents seizing 10 to 20 times the amounts they did a decade ago.

• Methamphetamine, experts say, has never been purer, cheaper or more lethal.

• 2012 – 2018 Fentanyl-Contaminated Meth and Cocaine
**Designer Stimulants**

- **1970s - MDA**
  - 3,4-Methylenedioxyamphetamine
  - “Mellow Drug of America”
- **1982 - MDMA – “Ecstasy” or XTC**
  - 3,4-Methylenedioxymethamphetamine
- **1985 - Place in Schedule I**
- **Often Adulterated and Substituted**
- **Mid-1990s – September 12, 2001**
  - MDMA “All the Rave”
- **Decline and Fall of Ecstasy**
  - Stacking
  - Tuesday Blues

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**MAJOR Synthetic Cathinones**

- **Cathinones – Synthetic Khat**
  - MDPV
  - 4 MEC
  - Methylone
  - Alpha-PVP
  - Ethylone
  - Dibutylene
  - N-Ethylpentylone
  - Others

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**Number of National Crime Lab Reports for MDMA and Synthetic Cathinones: USA 2004-2014**

Source: US DEA - National Forensic Laboratory Information System (NFLIS) 2014 Annual Data

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**New Psychoactive Substances (NPS)**

- **Buy Online from China**

- **Worldwide Delivery Services to Your Hometown**
Designer Stimulants

Looking for Molly

She Makes Me Want to Dance

“Flakka”

- **Flaca** – Skinny
- **Flaka** – Beautiful, elegant woman who charms all
- Elsewhere called “Gravel” **alpha-PVP**

Toxic Effects:

- Tachycardia,
- Agitation,
- Psychosis,
- Violent behavior,
- Excited Delirium
  - Hyperthermia
  - Kidney failure
  - Death

“Flakka”

Molly’s Enigma

- Need for Laboratory Confirmation
- Need for Accurate public information:
  - Content, Purity, Potency
- Forecasted Paradigm Shift in 21st Century Drug Production and Trafficking
- Non Cartel, mid-level Online Dealers
- Illicitly Manufactured Non-Pharmaceutical Fentanyl Analogues from foreign clandestine labs
Pharmacology of Synthetic Cannabinoids

- Effects almost immediate
- Onset of action is seconds to minutes
- Duration of effects: last 30 minutes – 1 hour
- Tolerance and Dependency develops
  - More drug needed for same effect
- Full and potent agonists at CB1 Receptors
- Greater receptor affinity than THC (3 - 10 Xs)
- As compared to THC, synthetic cannabinoids produce much more intense responses with smaller amounts of the drug

Quest Diagnostics
www.questdiagnostics.com

25I-NBOMe

- AKA
  - 25I
  - “N-Bomb”
  - “Smiles”
- Cheap, High Potency Hallucinogen
- Used Sublingual, Thus sold on Blotter Paper
- Fake LSD
- Small quantities = Large number of Doses

Binge Drinking Rates Steady After Decades of Decline

Binge drinking appears to have leveled off this year, but is significantly lower than peak years.

Teens More Likely to Use Marijuana Than Cigarettes

Daily use among 12th graders

Past Year E-Vaporizer Use and What Teens are Inhaling

Nearly 1 in 3 students in 12th grade report past-year use of E-vaporizers, raising concerns about the impact on their long-term health.
“Budder” Beware: Dangers of Marijuana Wax

- Marijuana Wax
- “Budder,” or
- Butane hash oil, or even
- “ear wax hash”

Produced by soaking marijuana plant material in a solvent such as butane which extracts various cannabinoids of the plant.

DABBING

Just a Little Dab will do you....in

Kratom

- Large tree indigenous to Thailand and Malaysia
- Leaves are usually chewed but it can be found in a dried form to create powder, tinctures and resins and is sold in the US as a powder, or in capsules, and as liquid.
The National Opioid Epidemic Has Progressed to

The National Addiction Epidemic
Or Simply:

THE EPIDEMIC

Substance Use Disorder Epidemiology

Provides the tools to identify contributing factors as both

Supply Vectors
Demand Vectors

These critical factors may then be targeted to:

• Direct Prevention Strategies
• Reach Populations in Need of Behavioral Health Services
• Determine the Best Use of Criminal Justice Resources

We Can
End the Epidemic