

## The Addicted Brain



Kirk Klemme MD FASAM  
906-360-0125  
kirkklemme@gmail.com

Gail Ploe BA, CADC, CPS  
906-482-7382 ext 103  
906-231-2799  
gploe@wuphd.org

---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

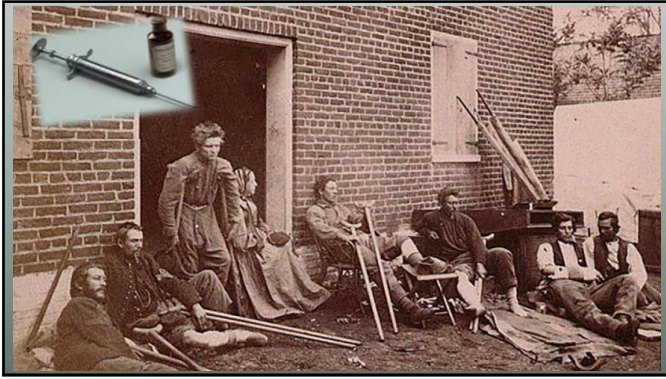
---

---

---

---

---




---

---

---

---

---

---

---

---

**1914 Harrison Narcotics Act**  
**1970 Controlled Substances Act**  
**1970 & 1974 Narcotic Tx Act**  
**DATA 2000**

---

---

---

---

---

---

---

---

**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<sup>1</sup> 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 no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,<sup>2</sup> 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.

JANE PORTER  
 HERSHEL JICK, M.D.  
 Boston Collaborative Drug  
 Surveillance Program  
 Waltham, MA 02154      Boston University Medical Center

1. Jick H, Mietinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.  
 2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

---

---

---

---

---

---

---

---



---

---

---

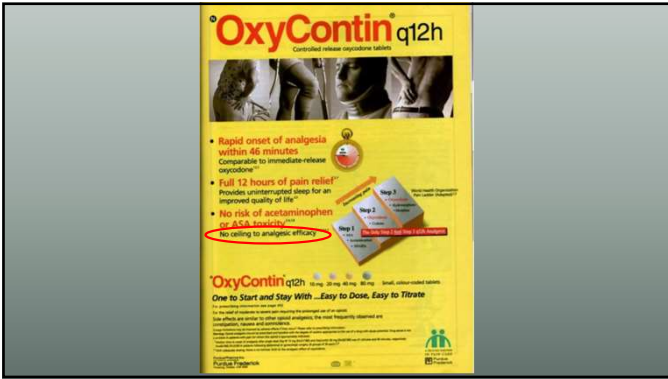
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

---

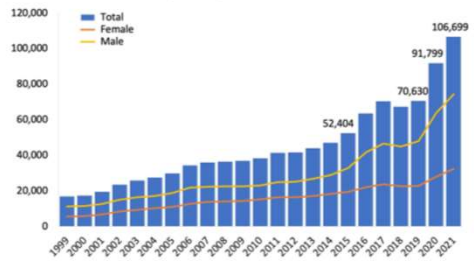
---

---

---

---

Figure 1. National Drug-Involved Overdose Deaths\*, Number Among All Ages, by Gender, 1999-2021



\*Includes deaths with underlying causes of unintentional drug poisoning (D60-D64), suicide drug poisoning (X60-X84), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10-Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

---

---

---

---

---

---

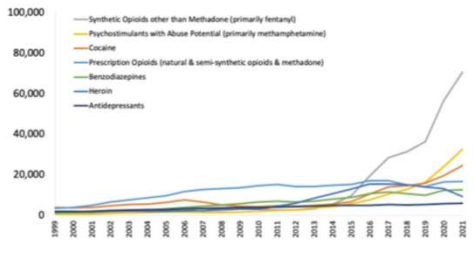
---

---

---

---

Figure 2. National Drug-Involved Overdose Deaths\*, Number Among All Ages, 1999-2021



\*Includes deaths with underlying causes of unintentional drug poisoning (D60-D64), suicide drug poisoning (X60-X84), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10-Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

---

---

---

---

---

---

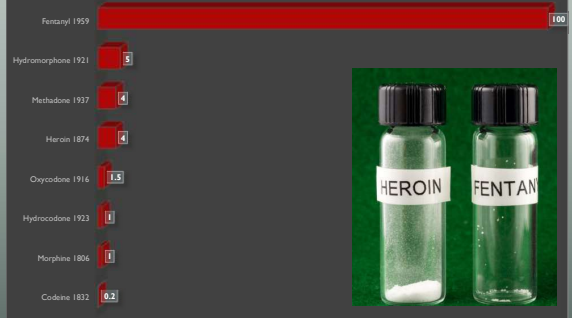
---

---

---

---

### Relative Opioid Potency



---

---

---

---

---

---

---

---

---

---




---

---

---

---

---

---

---

---




---

---

---

---

---

---

---

---




---

---

---

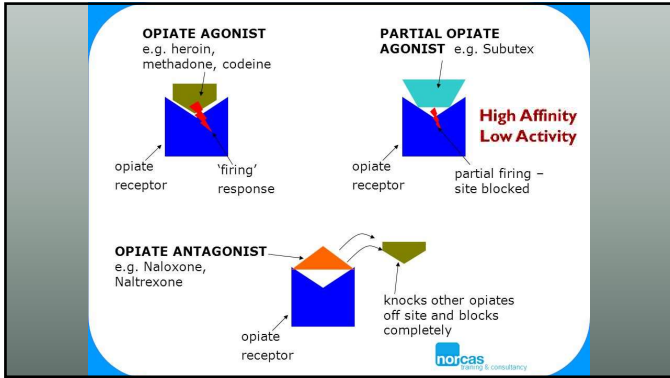
---

---

---

---

---




---

---

---

---

---

---

---

---

## MAT Treatment Effectiveness

- Reductions in overdoses and overall death rates
- Reductions in opioid use and other substance use/misuse
- Improved HIV and Hep C outcomes
- Increased likelihood that a person will remain in treatment
- Reduced criminal justice involvement
- Increased likelihood of employment
- Recent evidence suggesting cost effective and improved quality of life

(Norton et al 2017, Alice et al 1999, Kenworthy et al., 2017, Nosyk et al., 2015, Schwartz et al 2013, Sordo et al 2017)

---

---

---

---

---

---

---

---

**22 substances detected in street drug supply since late September 2023**

<p>1. <u>Fentanyl</u></p> <p>2. Heroin</p> <p>3. 4-ANPP</p> <ul style="list-style-type: none"> <li>o Non psychoactive substance created from improper processing/synthesis of fentanyl</li> </ul> <p>4. Cocaine</p> <p>5. Tropacocaine</p> <ul style="list-style-type: none"> <li>o cocaine-related alkaloid and a contaminant of street cocaine</li> </ul> <p>6. Ecgonine Methyl ester (EME)</p> <ul style="list-style-type: none"> <li>o Inactive metabolite of cocaine/crack</li> </ul> <p>7. Cinchonine/cinchona</p> <ul style="list-style-type: none"> <li>o Inactive metabolite of cocaine that becomes active when smoked/treated (crack)</li> </ul> <p>8. <u>Xylazine</u></p> <ul style="list-style-type: none"> <li>o Veterinary tranquilizer / CNS depressant not approved for human use, linked to chronic wounds, and lengthened/enhanced euphoric effects when mixed with opioids.</li> </ul> <p>9. Caffeine</p> <ul style="list-style-type: none"> <li>o Standard stimulant but it is cut into drugs so that the opioid will vaporize at a lower temperature. This causes a faster rush when smoked and the stimulant effect counterbalances the sedative effects.</li> </ul> <p>10. Tramadol</p> <ul style="list-style-type: none"> <li>o Medical-grade opioid</li> </ul>	<p>11. <u>Gabapentin</u></p> <ul style="list-style-type: none"> <li>o Anticonvulsant, treats nerve pain and partial seizures</li> </ul> <p>12. Methamphetamine</p> <ul style="list-style-type: none"> <li>o CNS stimulant</li> </ul> <p>13. Quinine</p> <ul style="list-style-type: none"> <li>o Cutting agent and was first used as a malaria drug. It is also present in tonic water.</li> </ul> <p>14, 5, 3. Oxycodone</p> <ul style="list-style-type: none"> <li>o Oxycodone fuel additive to boost octane index and reduce toxic gas emissions from diesel fuel</li> </ul> <p>15. N-butyl-aniline</p> <ul style="list-style-type: none"> <li>o Type of chemical dye. Shows up as an amber color. Severely irritates skin and eyes.</li> </ul> <p>16. N-allyl-noroxycodone (NAD)</p> <ul style="list-style-type: none"> <li>o Byproduct of when crack/cocaine is heated</li> </ul> <p>17. Benzoylecgonine (BE)</p> <ul style="list-style-type: none"> <li>o Inactive metabolite of cocaine</li> </ul> <p>18. 6-Acetyl-morphine (6-AM)</p> <ul style="list-style-type: none"> <li>o Heroin by product/metabolite, most often found in "black tar heroin"</li> </ul> <p>19. Lidocaine</p> <p>20. N-phenylpropanamide</p> <ul style="list-style-type: none"> <li>o Degradation product of Fentanyl</li> </ul> <p>21. P-fluorofentanyl</p> <ul style="list-style-type: none"> <li>o Also known as pFF (para-fluorofentanyl)</li> </ul> <p>22. Phorbol acetate</p> <ul style="list-style-type: none"> <li>o Fentanyl analog not intended for human use, illicit synthetic opioid</li> <li>o Also used as a cutting agent. Used to be a popular painkiller but was removed from the market years ago as they found it to be carcinogenic.</li> </ul>
--	--

---

---

---

---

---

---

---

---



### A step-by-step guide How to use a fentanyl test strip

**This is a fentanyl test strip**

- Add a tiny amount of substance (about the size of a half grain of rice) to a half ounce glass of water (about 15ml).  
*If you are testing with cocaine, ketone, or another compound, use a full ounce glass of water (30ml).*  
*You can use a 20ml medicine cup like the one in this kit.*
- Mix the powder into the water until it is completely dissolved.  
*If you are testing something that is not powder, crush it first.*
- Hold the solid blue end of the test strip and dip the other end in the water for about 10-15 seconds.
- Take the strip out of the water and lay it on a flat surface. Wait for about 60 seconds.
- Look at the strip under bright light. **Even very light red lines count!**  
**ONE (1) red line = FENTANYL PRESENT**  
**TWO (2) red lines = NO fentanyl present**  
Check the strip within 10 minutes of testing. Throw the strip away when done.

#### Interpreting the results

- Positive test:** One line means fentanyl detected.
- Negative test:** Two lines means no fentanyl detected.
- Unreadable / invalid test:** The top red line (closest to the solid blue) should always show up on the strip. If it doesn't, the test is invalid. Strips are sensitive above the solid line strip should be an invalid test.

Fentanyl test strips only tell you if fentanyl is present in the sample tested. They do not tell you how much fentanyl is present.  
A negative test result does not mean the substance is safe. Fentanyl test strips are not 100% accurate.  
**If you have symptoms or are overdosing, call 911 immediately and administer naloxone if available.**

**CDPH** OH 616-762-2200 • 1-833-6-4FAMILY

---

---

---

---

---

---

---

---

---

---

---

---

### What else can I do to lower my risk of overdose?

No drug is completely safe and there is always a risk of overdose. Try using the following tips:

- Use drugs with other people**, take turns, and avoid sharing needles and other devices.
- Go slow** by taking small amounts and waiting in between use.
- Get **naloxone** and use it if there is an overdose. Naloxone can be obtained at your local pharmacy or can be obtained free-of-charge through the mail by visiting: [naloxone.ohio.gov](http://naloxone.ohio.gov)
- Contact 988:** If you or someone you know is experiencing a non-life-threatening mental health or addiction-related crisis (thoughts of suicide, emotional distress, or substance use/addiction) **call, chat, or text 988** for free, 24/7, confidential support.

---

---

---

---

---

---

---

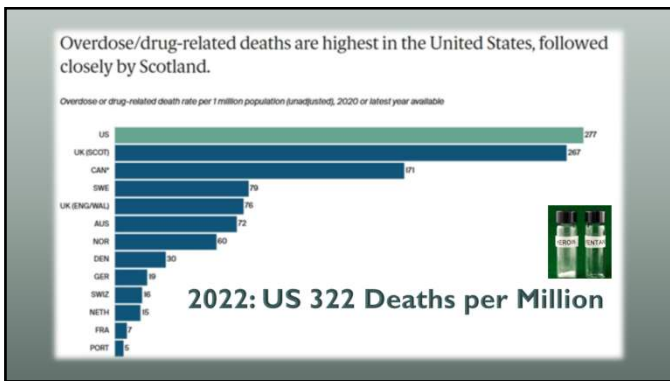
---

---

---

---

---




---

---

---

---

---

---

---

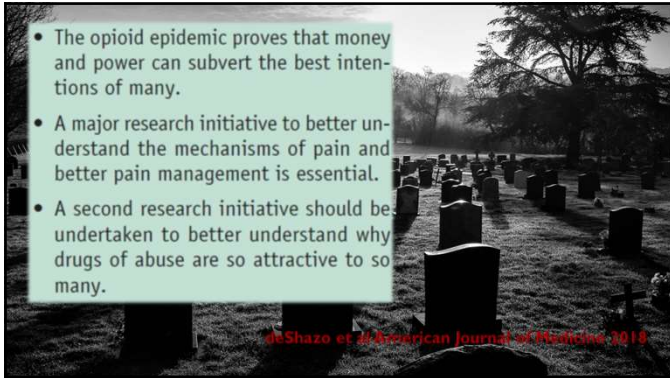
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

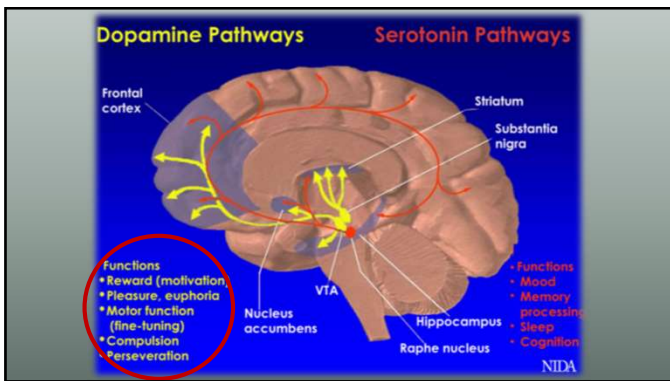
---

---

---

---

---



---

---

---

---

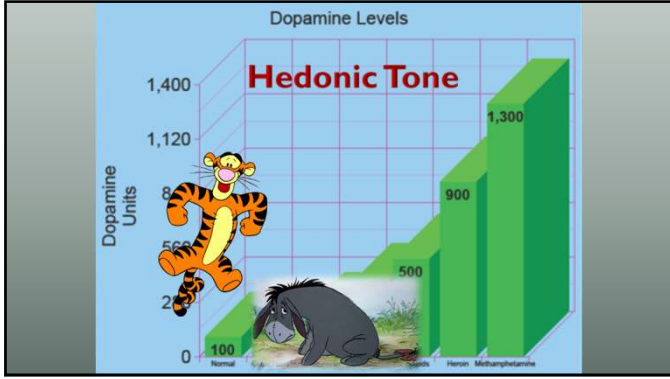
---

---

---

---





---

---

---

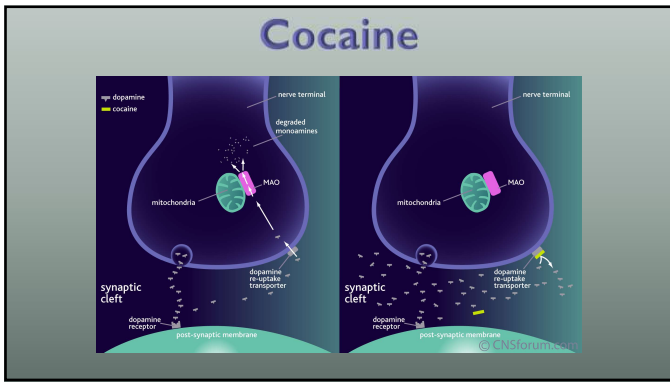
---

---

---

---

---



---

---

---

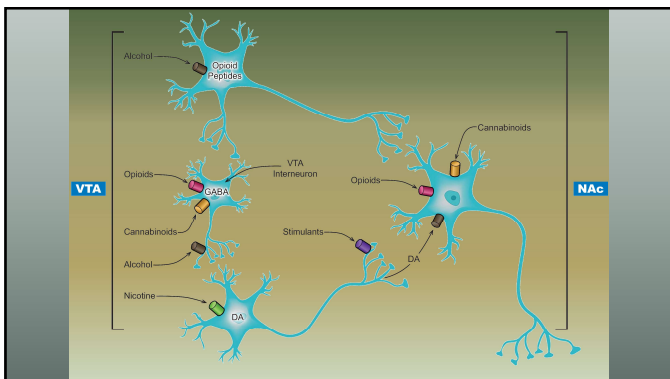
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

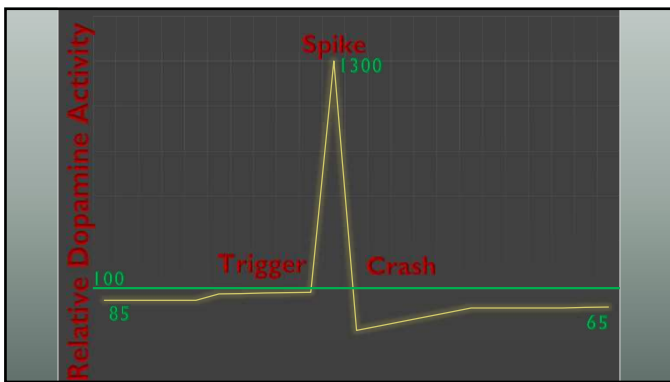
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

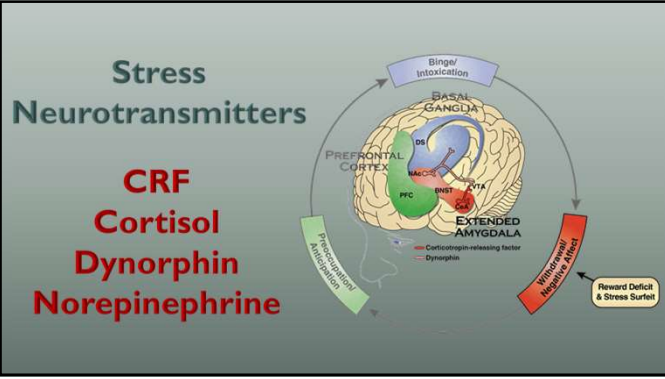
---

---

---

---

---




---

---

---

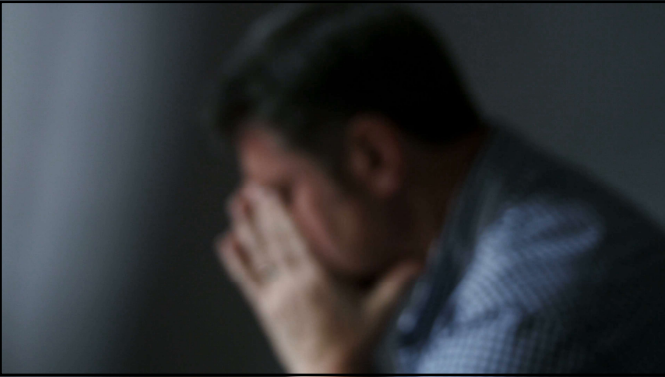
---

---

---

---

---




---

---

---

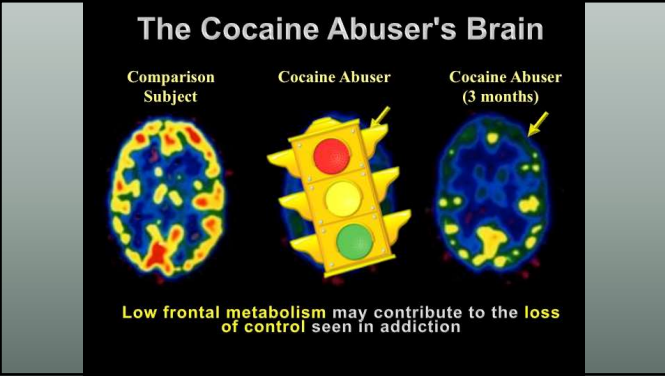
---

---

---

---

---




---

---

---

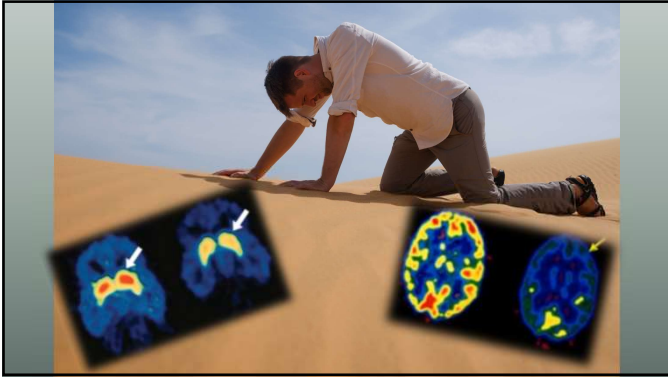
---

---

---

---

---



---

---

---

---

---

---

---

---

**Hijacked !**

Initial  
Massive  
Dopamine  
Reward  
Spike



Increased  
Stress  
Chemicals  
&  
Decreased  
Enjoyment  
in Daily Life

Susceptibility to Triggers  
Loss of "Executive" Function

---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

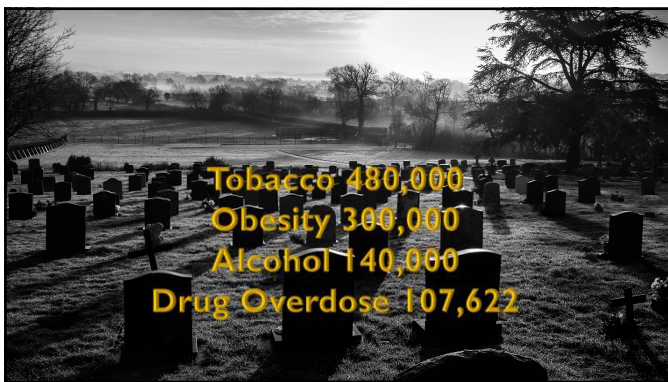
---

---

---

---

---



---

---

---

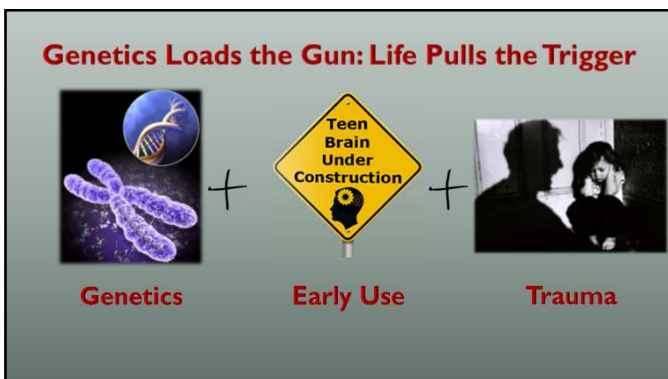
---

---

---

---

---



---

---

---

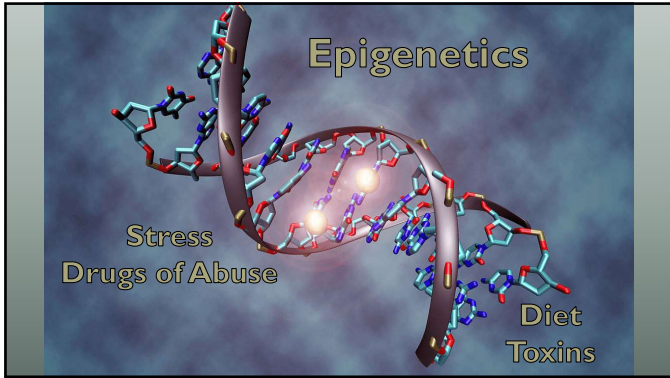
---

---

---

---

---




---

---

---

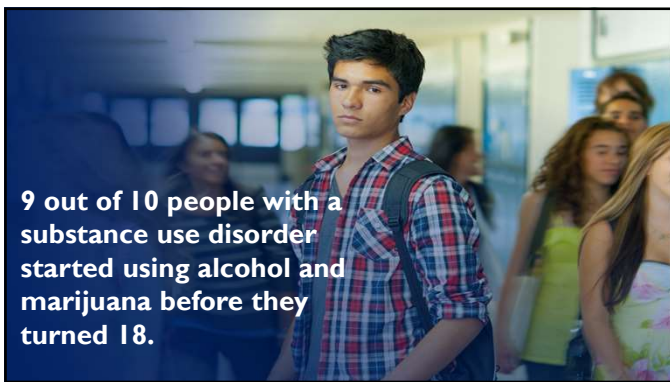
---

---

---

---

---




---

---

---

---

---

---

---

---

**Teen Alcohol Use Wires The Brain For Addiction**

Age (Years)	Percentage of Alcoholics
13	45
14	40
15	35
16	30
17	25
18	20
19	18
20	15
21	12

40% of kids who begin drinking at age 15 will become alcoholics.

Only 7% of those who begin drinking at age 21 become alcoholics.

Grant, RF and Dawson, DA. Journal of Substance Abuse 9:103-110, 1987  
\*Photo courtesy of NAAA and MADD

---

---

---

---

---

---

---

---



**Why is the adolescent brain so vulnerable?**

**DNA Uncoiling** 

**Underdeveloped PFC** 

**Lack of Coping Skills** 

**Endocannabinoid Neurodevelopment** 

---

---

---

---

---

---

---

---



---

---

---

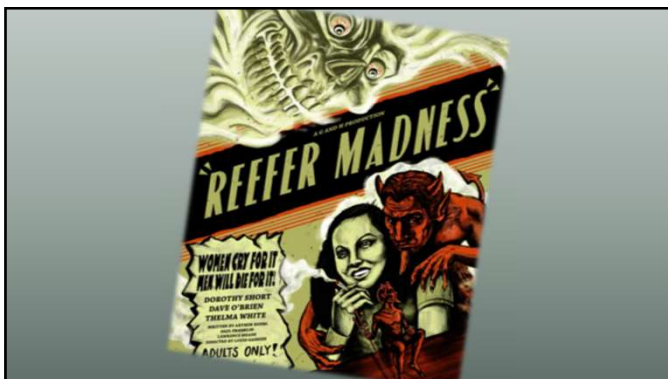
---

---

---

---

---



---

---

---

---

---

---

---

---




---

---

---

---

---

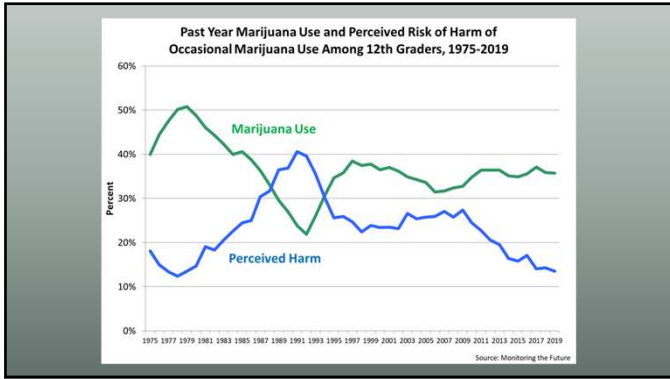
---

---

---

---

---




---

---

---

---

---

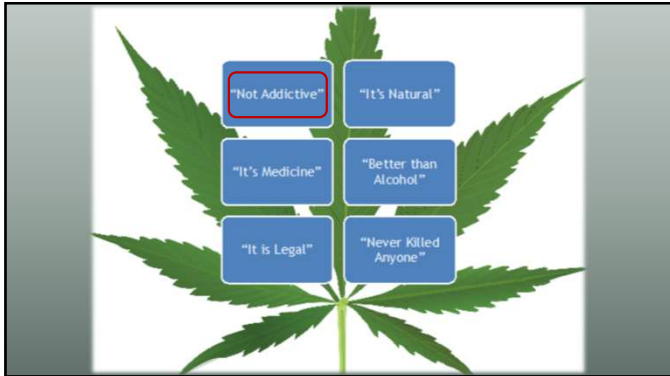
---

---

---

---

---




---

---

---

---

---

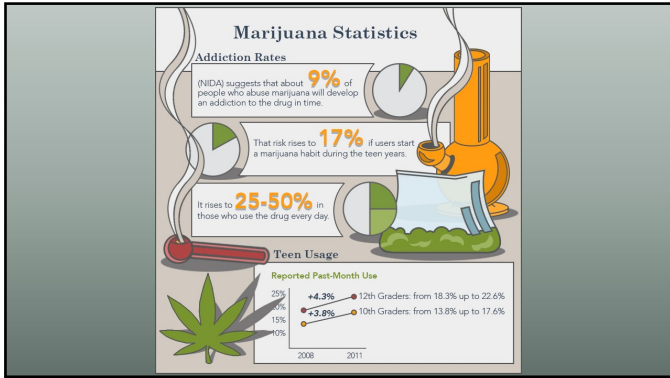
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

### CATEGORIES OF SUD SYMPTOMS

Symptoms of substance use disorders in the DSM 5 fall into four categories: 1) impaired control; 2) social problems; 3) risky use, and 4) physical dependence.

Impaired Control	Social Problems	Risky Use	Physical Dependence
Using more of a substance or more often than intended	Neglecting responsibilities and relationships	Using in risky settings	Needing more of the substance to get the same effect (tolerance)
Wanting to cut down or stop using but not being able to	Giving up activities they used to care about because of their substance use	<u>Continued use despite known problems</u>	Having withdrawal symptoms when a substance isn't used
Craving	<u>Inability to complete tasks at home, school or work</u>		
<u>Preoccupation</u>			

---

---

---

---

---

---

---

---

---

---

**Evidence on the acute and residual neurocognitive effects of cannabis use in adolescents and adults: a systematic meta-review of meta-analyses**

Authors: Laura Dell'Acqua<sup>1,2,3</sup>, Stéphane Potvin<sup>1,2</sup>, Sabrina Glavas<sup>1,2</sup>

**Genetic Variations in COMT Influences the Harmful Effects of Abused Drugs**

COMT genotype	Percentage of people with alcohol use disorders
Met/Met	~10%
Val/Met	~15%
Val/Val	~25%

**U.S. Surgeon General's Advisory: Marijuana Use and the Developing Brain**

U.S. Surgeon General Vivek Murthy, in expressing the importance of protecting our nation from the health risks of marijuana use in adolescents and young adults, stated that marijuana use during this critical period of brain development can have long-term effects on cognitive, social, and mental health.

**Background**

Marijuana, or cannabis, is the most commonly used drug in the United States. It acts by binding to a cannabinoid receptor in the brain to produce a variety of effects, including euphoria, relaxation, and altered perception. These same cannabinoid receptors are also critical for brain circuits important for decision-making, mood, and memory.

Research also has linked cannabis to an ability problem in children. These products can be addictive, and regular use can lead to dependence. These products can be addictive, and regular use can lead to dependence. These products can be addictive, and regular use can lead to dependence.

**Is cannabis use associated with an increased risk of onset and persistence of alcohol use disorders? A three-year prospective study among adults in the United States**

Authors: H. M. ...

---

---

---

---

---

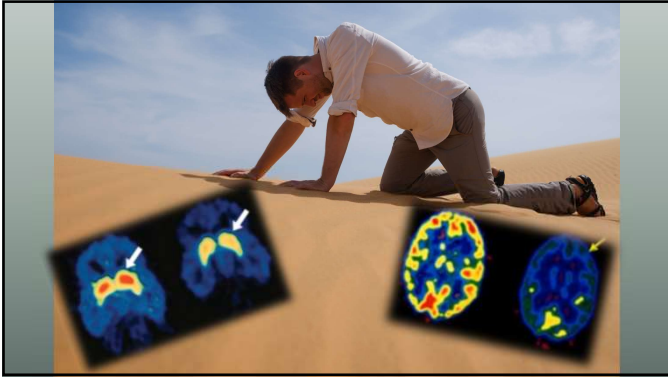
---

---

---

---

---



---

---

---

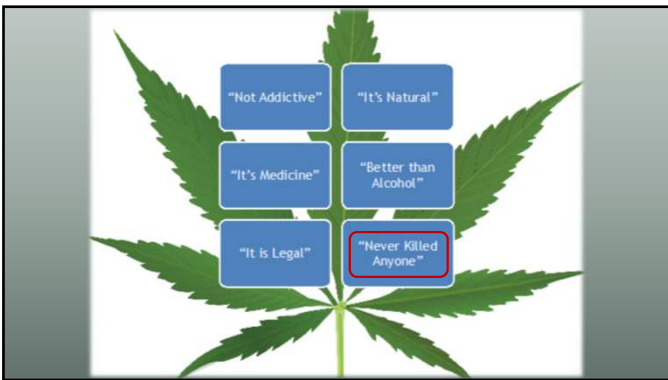
---

---

---

---

---



---

---

---

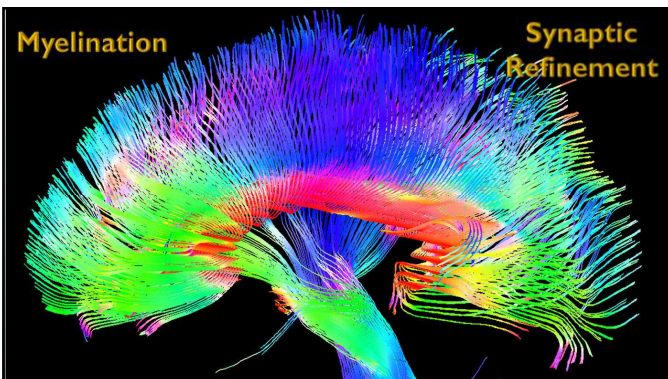
---

---

---

---

---



---

---

---

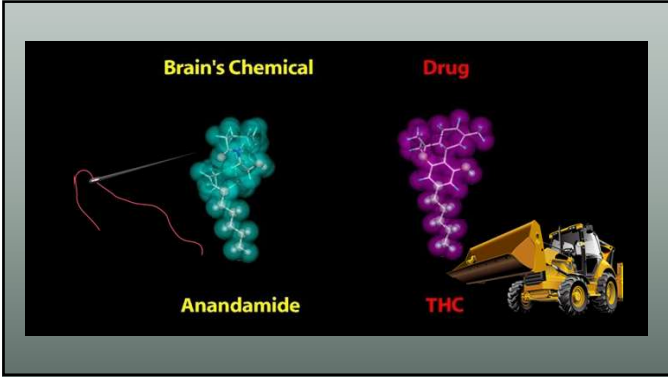
---

---

---

---

---




---

---

---

---

---

---

---

---




---

---

---

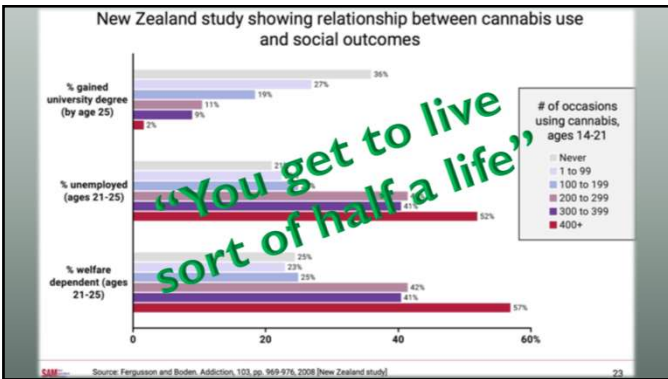
---

---

---

---

---




---

---

---

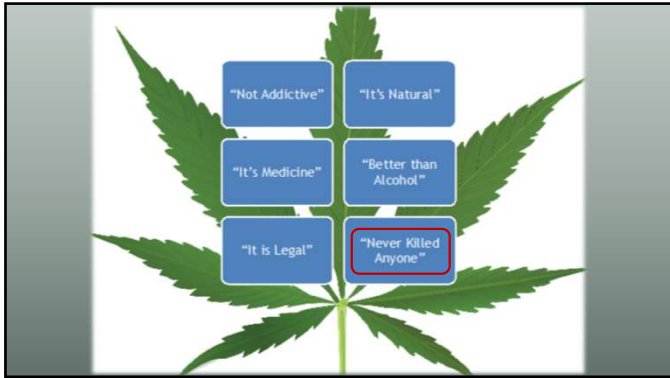
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

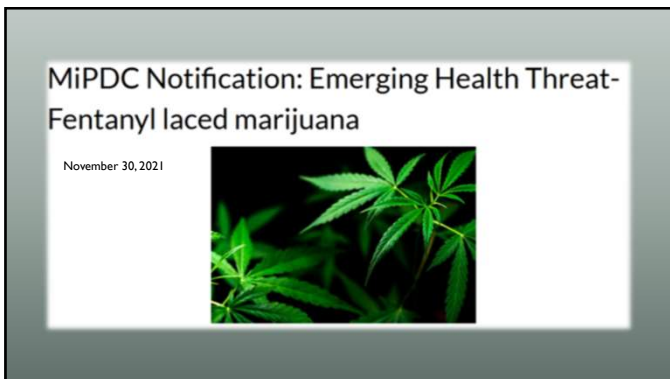
---

---

---

---

---



---

---

---

---

---

---

---

---



### Sharp Increase in Fake Prescription Pills Containing Fentanyl and Methamphetamine

September 27, 2021



DEA Warns that International and Domestic Criminal Drug Networks are Flooding the United States with Lethal Counterfeit Pills

---

---

---

---

---

---

---

---

DEA LAB TESTING REVEALS THAT  
**4 OUT OF EVERY 10 PILLS**  
WITH FENTANYL CONTAIN A POTENTIALLY  
**LETHAL DOSE**



Counterfeit pills often contain fentanyl  
and are more lethal than ever before.

---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---

**A step-by-step guide**  
**How to use a fentanyl test strip**

**This is a fentanyl test strip**

- 1** Add a tiny amount of substance (about the size of a half grain of rice) to a half ounce glass of water (about 1.5oz).  
 If you are testing pills, capsules, tablets or another substance, use a half ounce glass of water (150ml).  
 You can use a 20ml medicine cup like the one in this kit.
- 2** Mix the powder into the water until it is completely dissolved.  
 If you are testing something that is not powder, crush it first.
- 3** Hold the solid blue end of the test strip and dip the other end in the water for about 10-15 seconds.
- 4** Take the strip out of the water and lay it on a flat surface. Wait for about 60 seconds.
- 5** Look at the strip under bright light. Every tiny light red line counts!  
**ONE (1) red line = FENTANYL PRESENT**  
**TWO (2) red lines = NO fentanyl present**  
 Check the strip within 10 minutes of testing. Throw the strip away when done.

**Interpreting the results**

- Positive test**  
 One line means fentanyl detected.
- Negative test**  
 Two lines means no fentanyl detected.
- Unreadable / invalid test**  
 The top red line (closest to the solid blue) should always show up on the strip. If it doesn't, the test is invalid. Discard or retest above the solid blue strip shown in an invalid test.

Fentanyl test strips only tell you if fentanyl is present in the sample tested. They do not tell you how much fentanyl is present.

A negative test result does not mean the substance is safe. Fentanyl test strips are not 100% accurate.

If you have concerns or questions, call 911 immediately and administer naloxone if available.

**CDPH** 1st & 10th - Sacramento • 1-833-9-4FRESH

---

---

---

---

---

---

---

---

---

---

Not Addictive

It's Natural

It's Medicine

Better than Alcohol

It is Legal

Never Killed Anyone

---

---

---

---

---

---

---

---

---

---

Facebook

Instagram

NBC

McDonald's

Amazon

Playboy

---

---

---

---

---

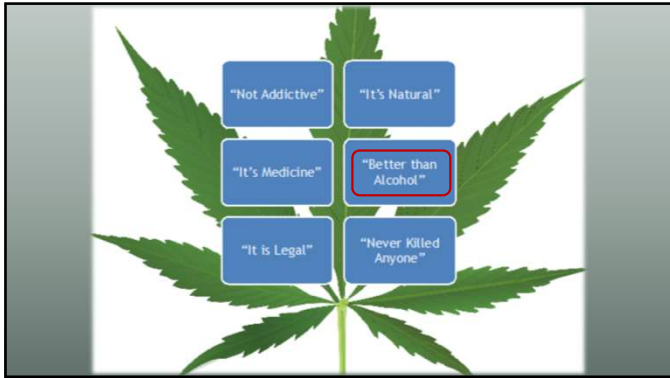
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---

INCONSISTENT RESULTS* - ANALYTE DETECTED BUT NO CORRESPONDING MEDICATION REPORTED		
DETECTED ANALYTE	DETECTION WINDOW <sup>1</sup>	COMMENTS
cTHC (Marijuana metabolite)	Single use: 2-3 days; Moderate use (4 times/wk): 5-7 days; Heavy use: 10-15 days; Chronic use: 19-40 days; Oral ingestion: 1-5 days	cTHC was detected and is found in marijuana. Marijuana is a DEA Schedule I controlled substance with very limited pharmaceutical application. Historical cTHC creatinine-corrected levels may be useful when monitoring for abstinence from marijuana. Consider contacting a toxicologist for assistance with interpretation of historical levels.

ILLCITS				
Methamphetamine	LC-MS/MS	Negative	-	100
Cocaine metabolite	LC-MS/MS	Negative	-	50
cTHC (Marijuana metabolite)	LC-MS/MS	POSITIVE	> 1,000	N/A
MDMA	LC-MS/MS	Negative	-	100
6-AMM (Heroin metabolite)	LC-MS/MS	Negative	-	10
Phencyclidine	LC-MS/MS	Negative	-	10

---

---

---

---

---

---

---

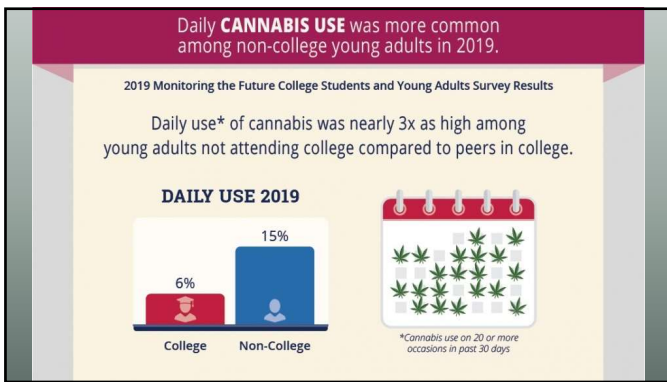
---

---

---

---

---




---

---

---

---

---

---

---

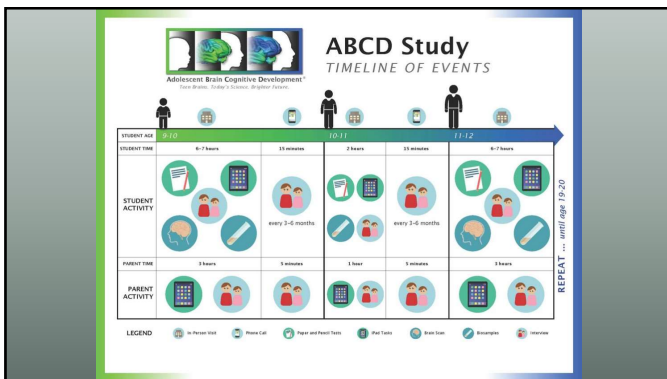
---

---

---

---

---




---

---

---

---

---

---

---

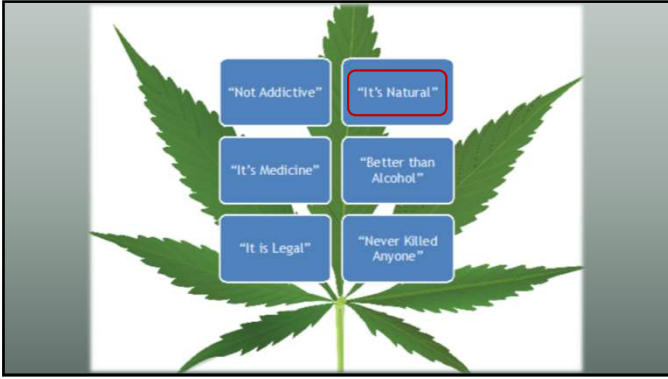
---

---

---

---

---




---

---

---

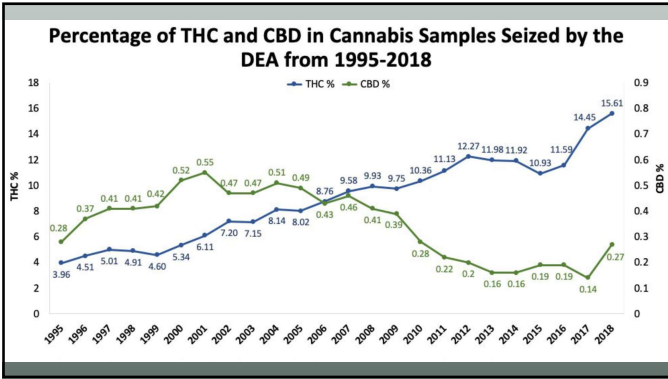
---

---

---

---

---




---

---

---

---

---

---

---

---




---

---

---

---

---

---

---

---

- The ~~opioid~~ epidemic proves that money and power can subvert the best intentions of many.
- A major research initiative to better understand the mechanisms of pain and better pain management is essential.
- A second research initiative should be undertaken to better understand why ~~drugs of abuse~~ are so attractive to so many.

**Alcohol**  
**Tobacco**  
**Cannabis**  
**Illicits**  
**Gambling**  
**Food**  
**Sex**  
**Pornography**  
**Media**  
**Shopping**

---

---

---

---

---

---

---

---

### Genetics Loads the Gun: Life Pulls the Trigger

**Genetics**      **Early Use**      **Trauma**

---

---

---

---

---

---

---

---

**Verbal abuse**    **Sexual abuse**    **Physical abuse**    **Emotional neglect**    **Physical neglect**  
**Mental illness**    **Domestic violence**    **Problem drug and alcohol use**    **Parental incarceration**    **Parental separation**

---

---

---

---

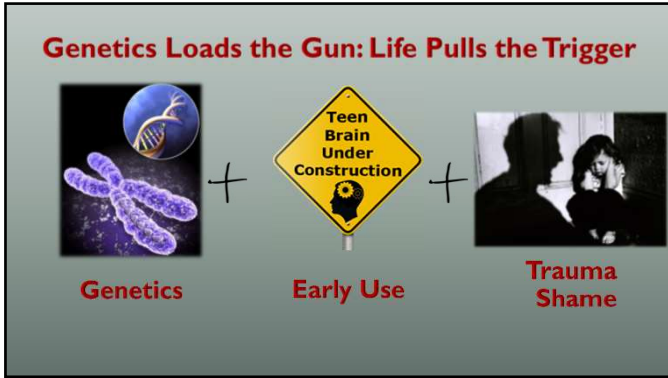
---

---

---

---





---

---

---

---

---

---

---


---

--Guilt says "I made a mistake". Shame says "I am a mistake".

--Shame is one of the root factors leading to addiction.

--As the cycle of addiction continues, it can of course deepen the sense of shame and self-loathing.

--Stigma is defined as a set of negative (and potentially unjustified) beliefs that a person or group of people may have regarding a particular individual, circumstance or condition.



---

---

---

---

---

---

---


---

--People with substance use disorders may be perceived as making "poor choices" or having "weak morals."

--Internal shame combined with external stigma is a deadly combination. It may result in people not seeking or leaving treatment.

**"They treated me like an addict."**

Which by the way says a lot more about the person doing the judging than it says about the person being judged.



---

---

---

---

---

---

---

---

--MAT patients may be stigmatized by the recovery community. "You're not really sober!"

--SUD or MAT patients may be stigmatized by law enforcement or even other members of the healthcare community.

--Societal stigma may lead to a society being less likely to dedicate resources to the treatment of addiction.



---

---

---

---

---

---

---

---



---

---

---

---

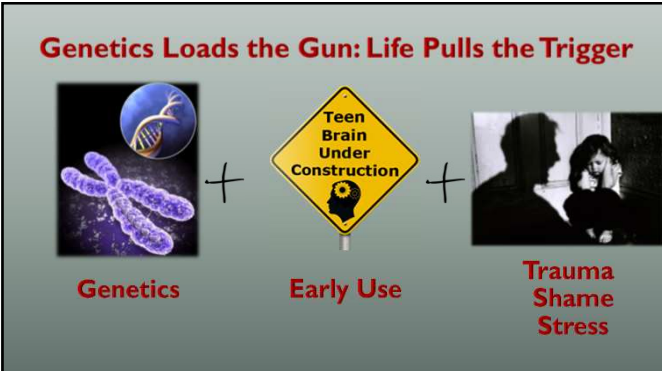
---

---

---

---

**Genetics Loads the Gun: Life Pulls the Trigger**



**Genetics**

**Early Use**

**Trauma  
Shame  
Stress**

---

---

---

---

---

---

---

---



---

---

---

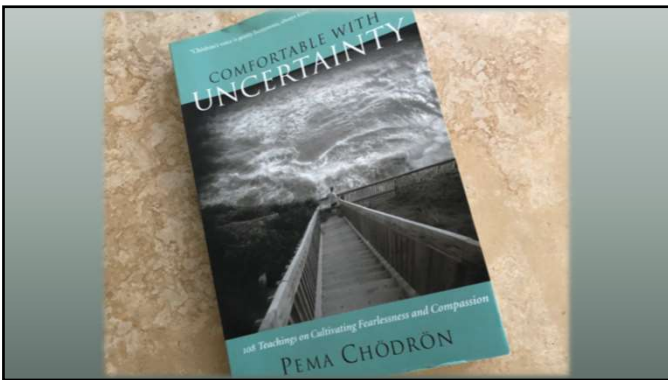
---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---