Psychoactive Substance Use is Ancient
Psychoactive Substance Use is Ancient
Alcohol Through the Ages

Some 10 million years ago, a shared ancestor of humans and African apes evolved an enzyme that could more rapidly digest the alcohol in fermented fruit. That set the biological stage for the past 10,000 years—in which people all over the world have made alcoholic beverages by fermenting sugars in whatever fruits were available and even by finding ways to ferment starchy grains and roots.

Drinking locally, trading globally

In early civilizations, fermented beverages were made from whatever wild plants were available locally and later from domesticated plants. As trade between civilizations grew, technology and techniques for brewing and winemaking spread throughout the ancient world.
Fermented beverages of pre- and proto-historic China


*Museum of Science and Archaeology (MASCA), University of Pennsylvania Museum of Archaeology and Anthropology, Philadelphia, PA 19104; **Department of Scientific History and Archaeology, University of Science and Technology of China, Hefei, Anhui 230026, China; †Institute of Archaeology, Chinese Academy of Social Sciences, Beijing 100730, China; ††Institute of Cultural Relics and Archaeology of Henan Province, Zhengzhou 450000, China; ‡Institute of Evolutionary Studies, Peking University, Beijing 100871, China; †‡Institute of Human Evolution, Max Planck Institute for Evolutionary Anthropology, 44103 Leipzig, Germany; and †§Institute of Microbiology, Chinese Academy of Sciences, Beijing 10080, China

PNAS | December 21, 2004 | vol. 101 | no. 51
Seshat – Goddess of wisdom, knowledge, writing
Opioids: The Poppy Goddess
Demeter
Greek “Wine” and the Golden Mean

- Wine technologies in ancient Greece
- Molecular archaeology
- “Golden Mean” / “Moderation” reflected potency of other substance in wine more than avoidance of alcohol intoxication per se
Psychoactive Substance Use is Ancient

Drug Problems/Addiction, Modern Phenomena
William Hogarth’s *Gin Lane* 1751

King Alcohol and His Prime Minister c. 1820
Dr Benjamin Rush: Alcoholism is a medical condition
The victims to it [spirits] were pitied and compassionated, just as now are...other hereditary diseases.

In my judgment, such of us as have never fallen victims, have been spared more from the absence of appetite, than from any mental or moral superiority over those who have.

A. Lincoln, Address to Springfield Washington Temperance Society
February 22, 1842
COCAINE
TOOTHACHE DROPS
Instantaneous Cure!
Price 15 CENTS.
Prepared by the
LODDY MANUFACTURING CO.
218 Madison Ave., Albany, N.Y.
For sale by all Druggists.
(Registered March 1898.) See other side.

A Good Friend

Don't take Ayer's Sarsaparilla if you are well. Don't take it simply because you are sick. Take it for what the doctors recommend it and you will like it, become fond of it, for it gives health, strength, vigor.

"I suffered terribly for twelve years. The doctors said my blood was trying to water. I then tried Ayer's Sarsaparilla, and soon my health was restored."—Mrs. J. W. Bliss, Hadlby, Conn.

LAUDANUM—Poison
Each fluid ounce contains 12-20 grains of opium and 40% alcohol.

McCORMICK & CO., Baltimore, Md., U.S.A.
Within a few years many authorities have pointed out the danger of morphinism in women who come under treatment for gynecologic disorders. The impulse to secure relief from pain and to induce sleep is so imperative that morphin is taken without regard to its perils. The patient is both physiologically and psychologically impressed with the intense satisfaction of rapid relief, and ever after this impression becomes dominant in pain and suffering. All control of the will, feelings, and emotions is overcome by it. The desire to escape pain and suffering becomes in many cases a mania.

Capriciousness of mind, irritability, selfishness, restlessness, and excitability are the natural characteristics of many women, who quickly become morphinists, especially if under treatment for disorders of the generative organs. Such persons
Turn of the century treatment: Addiction is a disease

- Addiction – seen as medical condition and treated like one
  - Short acting opioids
  - Specialty clinics – detoxification and “maintenance”
  - 44 communities had morphine clinics (run by both public health and police departments) to care for “medically infirm addicts”
Early 20th Century

• 1914 Harrison Narcotics Tax Act
  – Regulated manufacture and distribution of opioids (and cocaine)
  – Licensing of pharmacists and physicians
  – Permitted dispensing opioids “to a patient in the course of [the physician’s] professional practice only”

• 1919 Supreme Court Cases – contesting/clarifying role of opioid prescribing for individuals with addiction
  – Rendered illegal the prescribing/dispensal of opioids for “maintenance” of opioid use disorders

• 1919 - 1935 c 25,000 physicians indicted for violation of Harrison Act

• All morphine maintenance clinics closed
The original New York World-Telegram and Sun caption reads: “Out of the paddy wagon and into the Police Headquarters go some of the 88 dope addicts and pushers rounded up last night in biggest mass drive against narcotics in the city’s history. They come from all over the city except Staten Island and in their possession cocaine, heroin, marijuana.” Photo by Ed Ford, November 12, 1955.
Eight men declineizophrenic drug addicts before a Lexington judge in order to be sent to farms to receive the six-month "cure." The original caption from the photograph reads: "Several times a week, the scene shown here is repeated in one of the courts. ... Like most groups of addicts, the group contains men from several cities who came here to seek help." The man in this photo came from New York, Chicago, Philadelphia, and Richmond, Virginia, in 1936.

The picture shows a group of men with their hands raised in a courtroom setting.
ATLANTA GEORGIAN

The Light of a New Day

PUBLIC ENLIGHTENMENT

With the federal government opening its two new facilities for the care of narcotic victims, historic progress is recorded in the humanitarian treatment of a serious problem. This movement should be carried rapidly on. There should be a narcotic-cure farm in every state of the Union. It is a deplorable fact that ONLY A FEW of the states have adopted the Uniform State Narcotic Law, which is necessary to build up the nation’s defenses against the “ dope” evil. Numerous legislators are now in session. In each of the laggard states (THE) IMMEDIATE adoption of the Uniform State Narcotic Law should be compelled by local public opinion. Failure to adopt the measure will be unconscionable.
Why do people take drugs?
Why do people take drugs?

• To feel good
• To feel better
• To do better
• To fit in
• Curiosity
If taking drugs makes people feel good or better, makes people do better, what’s the problem?
Substance Use Harms

• Substance use harms
  – Medical: biological and individual
  – Social
• Clinical Assessment
• Benefits?
Drinkers’ Pyramid

- At-risk drinkers: targeted group, most likely to respond to intervention and represents greatest savings in care use and prevention.
- Alcohol Dependant—5%
- At-risk drinkers—20%
- Low-risk drinkers—35%
- Abstainers—40%

Source: Center for Substance Abuse Treatment: Background Paper, Screening, Brief Intervention, and Referral to Treatment (SBIRT)
Different policies for levels of Severity

Addiction ~ 25,000,000
(Focus on Treatment)

“Unhealthy Use” – 68,000,000
(Focus on Early Intervention)

Little or No Use
(Focus on Prevention)
Harmful effects of Alcohol

Brain
- Strokes, seizures, coma, and death
- Addiction and withdrawal
- Brain shrinkage
- Learning and memory loss
- Loss of coordination
- Anxiety, depression, and personality disorders

Eyes
- Blurred vision

Mouth
- Stomatitis
- Risk of cancer

Throat
- Cancer
- Irritation, bleeding, and difficulty swallowing

Heart
- Cardiomyopathy (weakens heart muscle and ability to pump blood)
- Enlarged heart
- Irregular heart
- Weak and soft

Stomach
- Peptic ulcers, irritated lining, and bleeding lesions

Intestines
- Cancer
- Ulcers
- Abdominal pain, nausea, vomiting, and diarrhea
- Inflammation, irritation, and hemorrhaging

Liver
- Cirrhosis
- Fibrosis
- Hepatitis
- Liver failure
- Fatty liver

Pancreas
- Pancreatitis

Reproductive system
- Impotence in men
- Infertility, early menopause, and menstrual irregularity in women

Bones
- Early onset of Osteoporosis (bones are weak, soft, brittle, thin and more easily broken)
Harmful effects of Marijuana

Brain
- Addiction and withdrawal
- Lack of motivation
- Personality and mood changes
- Reduced ability to learn and remember

Lungs
- Increases risk of cancer
- Increases risk of Chronic Obstructive Pulmonary Disease which causes mucus build up in airways, chronic coughing, wheezing, and shortness of breath
- Increases risk of lung infections (like pneumonia)

Eyes
- Sleepy, blood shot eyes

Mouth
- Dry and burning

Throat
- Irritates lining of the esophagus
- Increases chance of cancer in the esophagus and larynx
- Coughing, burning, and phlegm

Heart
- Increases blood pressure and heart rate
- Increases risk of heart attack and stroke

Immune system
- Weakens immune system’s ability to protect the body against infections and diseases (like cancer)

Reproductive systems
- Reduces testosterone and male sex drive
- Increases risk of testicular cancer
- Reduces sperm count
- Irregular menstrual cycles and birth defects in women

Blood vessels
- Increases blood pressure leading to higher risk of strokes

Bones
- Bone marrow damage
Cannabis and the Development of Psychosis

10+ longitudinal studies – all show an association between cannabis use and psychosis

Risk in context:
Individual: Increase from 1-2%
Population: Additional 3,000,000 events
Harmful effects of Heroin

Brain
- Addiction and withdrawal
- Brain damage
- Overdose, coma, and death
- Loss of memory
- Depression
- Insomnia

Eyes
- Reduced vision and watery

Nose
- Irritated nostrils from snorting

Lungs
- Breathing may stop, then death
- Respiratory illnesses (like pneumonia and tuberculosis)

Liver
- Disease/damage caused by Hepatitis C and/or HIV from sharing contaminated needles

Heart
- Infections of the heart lining and valves
- Heart disease, heart failure, and death

Kidneys
- Disease and possible failure

Stomach
- Loss of appetite and weight loss
- Vomiting

Intestines
- Abdominal pain
- Diarrhea
- Nausea
- Chronic constipation

Blood vessels
- Scarred and/or collapsed arteries and veins
- Blood clots

Reproductive system
- Miscarriages
- Still births
- Birth defects
- Menstrual problems
- Inability to achieve orgasm (women and men)
- Impotence in men

 Bones
- Arthritic pain
Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014

Jon E. Zhodz, PhD, Alex K. Axten, PhD, Rejina C. Patel, MPH, Ben Kupont, MPH, Kashif Sjalal, MPH, John W. West, MD, and Deborah Holtzman, PhD

FIGURE 1—Reported Cases of Acute HCV Infection by Year: National Notifiable Disease Surveillance System, United States, 2004–2014
Harms – Operationalized:

Harms to people who use drugs vs. Harms to others

[Graph showing harm caused by drugs, with categories like Alcohol, Heroin, Crack Cocaine, Methamphetamine, Cocaine, Tobacco, Amphetamine, Cannabis, GHB, Benzodiazepines, Ketamine, Methadone, Mephedrone, Butane, Qat/Khat, Anabolic Steroids, Ecstasy, LSD, Buprenorphine, Mushrooms, with bars indicating harm to users and harm to others.]
## 2010 National and State Costs of Excessive Alcohol Consumption

Jeffrey J. Sacks, MD, MPH, Katherine R. Gonzales, MPH, Ellen E. Bouchery, MS, Laura E. Tomedi, PhD, MPH, Robert D. Brewer, MD, MSPH

### What Excessive Drinking Costs Us

- **$807 Per Person**
- **$249 Billion in 2010**
- **$2.05 Per Drink**

### Cost Breakdown

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Costs ($)</th>
<th>Government costs ($)</th>
<th>Binge drinking ($)</th>
<th>Underage drinking ($)</th>
<th>Drinking while pregnant ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>249,026.4</td>
<td>100,674.8</td>
<td>191,126.9</td>
<td>24,268.3</td>
<td>5,494.1</td>
</tr>
<tr>
<td>Health care</td>
<td>28,370.1</td>
<td>16,915.1</td>
<td>16,273.8</td>
<td>3,795.8</td>
<td>2,830.0</td>
</tr>
<tr>
<td>Specialty care for abuse/dependence</td>
<td>12,044.6</td>
<td>9,031.3</td>
<td>8,245.2</td>
<td>2,120.4</td>
<td>-</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>5,488.5</td>
<td>2,628.1</td>
<td>2,007.5</td>
<td>198.9</td>
<td>48.6</td>
</tr>
<tr>
<td>Ambulatory care</td>
<td>1,524.5</td>
<td>524.0</td>
<td>1,070.8</td>
<td>144.4</td>
<td>7.0</td>
</tr>
<tr>
<td>Nursing home</td>
<td>1,166.8</td>
<td>691.6</td>
<td>863.4</td>
<td>2.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Drugs/overdose</td>
<td>1,545.5</td>
<td>471.6</td>
<td>1,085.5</td>
<td>146.4</td>
<td>7.1</td>
</tr>
<tr>
<td>Fetal alcohol syndrome</td>
<td>2,750.0</td>
<td>1,248.5</td>
<td>1,160.5</td>
<td>449.5</td>
<td>2,750.0</td>
</tr>
<tr>
<td>Prevention and research</td>
<td>1,048.8</td>
<td>1,048.8</td>
<td>496.1</td>
<td>454.4</td>
<td>10.1</td>
</tr>
<tr>
<td>Training</td>
<td>34.8</td>
<td>11.5</td>
<td>16.4</td>
<td>6.3</td>
<td>-</td>
</tr>
<tr>
<td>Health insurance administration</td>
<td>2,315.6</td>
<td>1,059.7</td>
<td>1,328.5</td>
<td>273.3</td>
<td>6.7</td>
</tr>
<tr>
<td>Lost productivity</td>
<td>175,044.9</td>
<td>57,219.0</td>
<td>134,835.4</td>
<td>13,866.8</td>
<td>2,200.0</td>
</tr>
<tr>
<td>Impaired productivity at work</td>
<td>76,865.6</td>
<td>28,440.2</td>
<td>52,614.1</td>
<td>1,924.3</td>
<td>-</td>
</tr>
<tr>
<td>Impaired productivity at home</td>
<td>6,218.0</td>
<td>-</td>
<td>4,256.6</td>
<td>205.0</td>
<td>-</td>
</tr>
<tr>
<td>Absenteeism</td>
<td>4,619.9</td>
<td>1,529.2</td>
<td>4,019.9</td>
<td>201.5</td>
<td>-</td>
</tr>
<tr>
<td>Impaired productivity while in specialty care</td>
<td>1,983.4</td>
<td>656.5</td>
<td>1,386.8</td>
<td>349.1</td>
<td>-</td>
</tr>
<tr>
<td>Impaired productivity while in hospital</td>
<td>228.4</td>
<td>75.6</td>
<td>54.1</td>
<td>6.4</td>
<td>2.6</td>
</tr>
<tr>
<td>Mortality</td>
<td>75,204.5</td>
<td>24,892.7</td>
<td>58,312.4</td>
<td>6,044.2</td>
<td>170.7</td>
</tr>
<tr>
<td>Incarceration of perpetrators</td>
<td>9,150.5</td>
<td>3,028.8</td>
<td>9,150.5</td>
<td>3,855.3</td>
<td>-</td>
</tr>
<tr>
<td>Crime victims</td>
<td>2,704.8</td>
<td>895.3</td>
<td>2,704.8</td>
<td>734.7</td>
<td>-</td>
</tr>
<tr>
<td>Fetal alcohol syndrome</td>
<td>2,110.8</td>
<td>706.6</td>
<td>893.3</td>
<td>346.0</td>
<td>2,116.8</td>
</tr>
<tr>
<td>Other</td>
<td>41,662.5</td>
<td>26,540.7</td>
<td>40,817.7</td>
<td>6,080.0</td>
<td>374.1</td>
</tr>
<tr>
<td>Crime victim property damage</td>
<td>559.4</td>
<td>-</td>
<td>559.4</td>
<td>216.1</td>
<td>-</td>
</tr>
<tr>
<td>Criminal justice: corrections</td>
<td>15,865.9</td>
<td>15,865.9</td>
<td>15,865.9</td>
<td>1,842.0</td>
<td>-</td>
</tr>
<tr>
<td>Criminal justice: alcohol-related crimes</td>
<td>2,160.0</td>
<td>2,160.0</td>
<td>1,031.4</td>
<td>476.6</td>
<td>-</td>
</tr>
<tr>
<td>Criminal justice: violent and property crimes</td>
<td>5,998.8</td>
<td>5,998.8</td>
<td>5,998.8</td>
<td>2,117.6</td>
<td>-</td>
</tr>
<tr>
<td>Criminal justice: private legal</td>
<td>228.1</td>
<td>-</td>
<td>228.1</td>
<td>72.8</td>
<td>-</td>
</tr>
<tr>
<td>Motor vehicle crashes</td>
<td>13,461.9</td>
<td>-</td>
<td>13,461.9</td>
<td>1,402.0</td>
<td>-</td>
</tr>
<tr>
<td>Fire losses</td>
<td>2,914.3</td>
<td>2,142.0</td>
<td>2,914.3</td>
<td>527.5</td>
<td>-</td>
</tr>
<tr>
<td>Fetal alcohol syndrome (special education)</td>
<td>374.1</td>
<td>374.1</td>
<td>157.9</td>
<td>61.1</td>
<td>374.1</td>
</tr>
</tbody>
</table>
The Underestimated Cost of the Opioid Crisis

The Council of Economic Advisers
November 2017

Table 2: Estimated Cost of the Opioid Crisis in 2015 (2015 $)

<table>
<thead>
<tr>
<th>VSL Assumption</th>
<th>Fatality Costs</th>
<th>Non-fatality Costs</th>
<th>Total Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-dependent</td>
<td>$431.7 billion</td>
<td>$72.3 billion</td>
<td>$504.0 billion</td>
</tr>
<tr>
<td>Low</td>
<td>$221.6 billion</td>
<td>$72.3 billion</td>
<td>$293.9 billion</td>
</tr>
<tr>
<td>Middle</td>
<td>$393.9 billion</td>
<td>$72.3 billion</td>
<td>$466.2 billion</td>
</tr>
<tr>
<td>High</td>
<td>$549.8 billion</td>
<td>$72.3 billion</td>
<td>$622.1 billion</td>
</tr>
</tbody>
</table>
# Comparing and Contrasting Alcohol Use and Opioid Use During Pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Opioid Use During Pregnancy</th>
<th>Alcohol Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence of use</strong></td>
<td>1.6%-8.5% of pregnant women use opioids; however, it’s on the rise&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Approximately 8.5% of pregnant women drink alcohol at some point during pregnancy&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Likelihood of developing</strong></td>
<td>NAS is seen in 30-80% of infants born to women who used opioids in the third trimester&lt;sup&gt;2&lt;/sup&gt;</td>
<td>2-5% of school age children may have FASDs&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Negative effects/Disabilities</strong></td>
<td>Neonatal Abstinence Syndrome (NAS)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Fetal Alcohol Spectrum Disorders (FASDs)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Duration of effects</strong></td>
<td>Unknown&lt;sup&gt;4&lt;/sup&gt;</td>
<td>FASDs last a lifetime&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Comparing and Contrasting Alcohol use and Opioid use During Pregnancy (Continued)

<table>
<thead>
<tr>
<th>Cost of Care</th>
<th>Opioid Use During Pregnancy</th>
<th>Alcohol Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimate $1.2-2.5 million per case of FAS&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Average of $90,000 per case of NAS&lt;sup&gt;6&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Screening and Brief Intervention</th>
<th>Opioid Use During Pregnancy</th>
<th>Alcohol Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Universal screening using the 5 P’s tool, and brief intervention&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Universal screening using the AUDIT (US) tool, and brief intervention&lt;sup&gt;9&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethics</th>
<th>Opioid Use During Pregnancy</th>
<th>Alcohol Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid separation of mother and child&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Avoid separation of mother and child&lt;sup&gt;10&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Opioid Use During Pregnancy</th>
<th>Alcohol Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication-assisted therapy (MAT)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Appropriate treatment referral for alcohol use disorder *</td>
<td></td>
</tr>
</tbody>
</table>

*See treatment resource directories on ACOG website: https://www.acog.org/About-ACOG/ACOG-Departments/Tobacco--Alcohol--and-Substance-Abuse/Fetal-Alcohol-Spectrum-Disorders-Prevention-Program/Provider-Resources/FASD-Resource-Directory
Not everyone who uses drugs becomes addicted
What is the risk of opioid addiction among individuals prescribed opioids for pain?
What is the risk of opioid addiction among individuals prescribed opioids for pain?

Rates of misuse 12-29% (95%CI:13-38%)
Rates of addiction averaged between 8-12% (95% CI: 3-17%)
Why do some people become addicted and not others?
Why do some people become addicted and not others?

- Genetic
- Home environment/neighborhood
- Age of onset
- Psychiatric co-morbidities – Trauma
  - Childhood sexual and/or physical abuse (>60% of individuals w addiction)
  - PTSD (c 50% of individuals w PTSD lifetime addiction)
- Violence – history/current violent relationship
Reward/Reinforcement

- Reward/Reinforcement Pathway:
  - Ventral Tegmental Area (VTA)
  - Nucleus Accumbens with projections to Prefrontal Cortex
  - Dopaminergic system
Dopamine and the “Hijacked Brain” Hypothesis
Drugs release 2-10 times more dopamine than natural rewards such as eating and sex.
Prolonged drug use changes the brain: Functionally...

Dopamine D2 Receptors are Decreased by Addiction

Cocaine

Meth

Alcohol

Heroin

Control

Addicted

DA D2 Receptor Availability
Addiction Changes Biology

Decreased Brain Metabolism in Drug User

Decreased Heart Metabolism in Heart Disease Patient

Research supported by NIDA addresses all of these components of addiction.
THE METHADONE Maintenance Research Program \(^1\) began three years ago with pharmacoological studies conducted on the metabolic ward of the Rockefeller University Hospital. Only six addict patients were treated during the first year, but the results of this work were sufficiently impressive to justify a trial of maintenance treatment of heroin addicts admitted to open medical wards of general hospitals in the city.

Methadone therapy was started in low dosage (10 to 20 mg/day in divided portions) and increased slowly over a period of four to six weeks to avoid narcotic effects. After the patients had reached the stabilization level (80 to 120 mg/day) it was possible to maintain them with a single, daily, oral injection, without further increase in dose. At the end of the six weeks of hospitalization the patients were discharged to outpatient clinics where they received their daily

---

**Fig 1.**—Diagrammatic summary of functional state of typical "mainline" heroin user. Arrows show the repetitive injection of heroin in uncertain dose, usually 10 to 30 mg but sometimes much more. Note that addict is hardly ever in a state of normal function ("straight").

---

**Fig 2.**—Stabilization of patient in state of normal function by blockade treatment. A single, daily, oral dose of methadone prevents him from feeling symptoms of abstinence ("sick") or euphoria ("high"), even if he takes a shot of heroin. Dotted line indicates course if methadone is omitted.

---

**Fig 6.**—Employment of 77 male patients in the program for 3 to 27 months as of April 15, 1966, compared with their status before starting treatment.
Overtime Addiction from Reward Seeking to Relief Seeking

Figure 1 Conceptual framework placing common animal models along the trajectory of alcohol addiction. Alcohol dependence progresses over time from initial largely positively reinforcing pleasurable alcohol effects (reward), to be maintained by relief from a negative emotional state (negative reinforcement). The different animal models address distinct aspects of the addiction trajectory. Acute alcohol administration, e.g. for the development of conditioned place preference, or basic genetic models are mainly grounded on the positive reinforcing effects of alcohol but do not likely encompass neuroadaptations characterizing the progression into addiction. These are better modeled by long-term (several months and more) alcohol consumption or forced intoxication procedures, the former covering the spectrum of adaptive and maladaptive processes from drug initiation to relapse-like behaviors. Because rodents, in contrast to humans, rarely drink to intoxication and consequently do not develop noticeable withdrawal symptoms, forced chronic intermittent exposure leading to a post-dependent state has been instrumental for studying the emergence of negative motivational processes and their role in the pathophysiology of addiction. Both, long-term access and post-dependent models exhibit predictive validity for medication development in alcoholism.
If left untreated, addiction lasts a lifetime

• The natural history of addiction:
  – Relationship failure
  – Parenting failure
  – Inability to function in workforce
  – Incarceration
  – Homelessness
  – Untreated medical and psychiatric co-morbidities
  – HIV HCV acquisition and transmission
  – Overdose
  – Death
How effective is treatment?

**Similar Relapse (or Noncompliance) Rates for Drug Dependence Versus Other Chronic Diseases**

- **Drug Addiction**: 0, 20, 40, 60, 80, 100
- **Type 1 Diabetes**: 0, 20, 40, 60, 80, 100
- **Hypertension**: 0, 20, 40, 60, 80, 100
- **Asthma**: 0, 20, 40, 60, 80, 100

- Patients Who Relapse, %

Extended Abstinence is Predictive of Sustained Recovery

It takes a year of abstinence before less than half relapse.

After 5 years – if you are sober, you probably will stay that way.

Dennis et al, Eval Rev, 2007
Recovery is the Goal of Treatment

- Recovery is more than abstinence
- Building a life of integrity,
- Connection to others,
- Purpose and
- Serenity
- Recovery is fully compatible with the use of medications
Recovery Leads to Return of Normal Brain Structure and Function

DAT Recovery with prolonged abstinence from methamphetamine

Conclusion(s)

- Substance use is ancient, but harmful use, especially addiction, is a more recent phenomena
- Substance harms as health concerns – not new
- Harms of substances not limited to addiction
- The future is synthetic
Thank You

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