



U.S. Opioid Crisis

21st Century

Substance Use Disorders (Addicts)

1. (Prescription) **Opioid** Use Disorder
2. (Illicit) **Heroin** Use Disorder
3. **Benzodiazepenes** Use Disorder
4. **Cigarette** Use Disorder
5. **Alcohol** Use Disorder
6. **Tranquilizer** Use Disorder
7. **Stimulant** Use Disorder
8. **Marijuana** Use Disorder
9. **Methamphetamine** Use Disorder
10. **Cocaine** Use Disorder
11. **Other Illicit Drug** Use Disorders

Hul Gil - The 'Joy Plant'

- ▶ ~4,000 B.C. (About 6,000 years ago) – First known written records :
- ▶ Opium poppy was cultivated in lower Mesopotamia.
- ▶ Sumerians called the opium poppy flower:

***Hul Gil,
The 'joy plant'***





1300 B.C. Egyptian Eber papyrus (About 3300 years ago)

- ▶ Advises using condensed juice of the unripe poppy seed pod "to prevent the excessive crying of children".



Physicians believed over the Centuries that:

- ▶ **Poppy plant** was of divine origin;
- ▶ **Opium** was variously called:
 1. *Sacred Anchor Of Life,*
 2. *Milk Of Paradise,*
 3. *Hand Of God,*
 4. *Destroyer Of Grief.*





~1200 B.C. – ‘Sea Peoples’



- Around 1200 B.C., migrations/invasions by **sea of peoples** overwhelmed the political states of **Crete and Cyprus** and attacked the **Egyptian Empire** by sea from the north.
- The Pharaoh's armies stopped the invasion of Egypt Proper.
- The **Pharaoh** allowed the invaders to settle in the peripheral territories of Egypt, in Canaan, what is now Israel and Palestine.
- These settlers were the **Philistines of the Bible**. The name ***Palestine*** is derived from the name **Philistine**.

Island of Cyprus, 1100 B.C. (About 3100 years ago)



- ▶ “Sea Peoples”
- ▶ Crafted surgical-quality culling knives to harvest
- ▶ **Opium**, which they would cultivate, trade and smoke before battle.

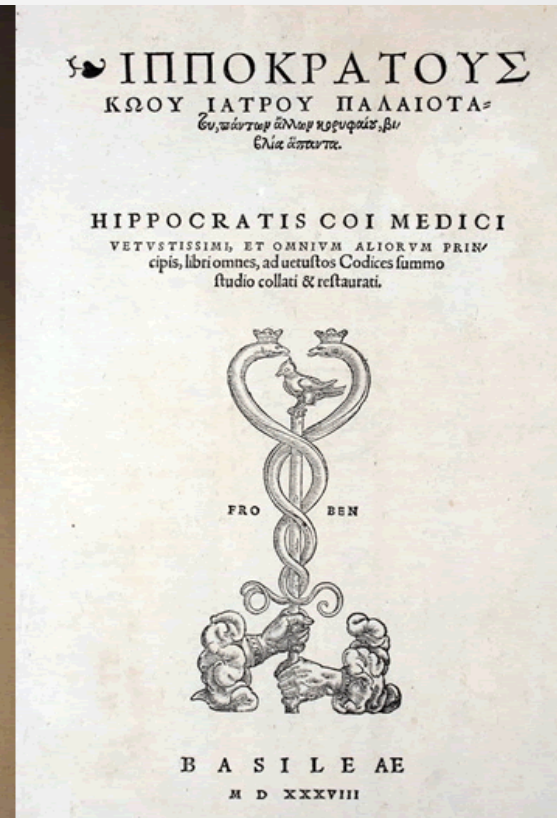
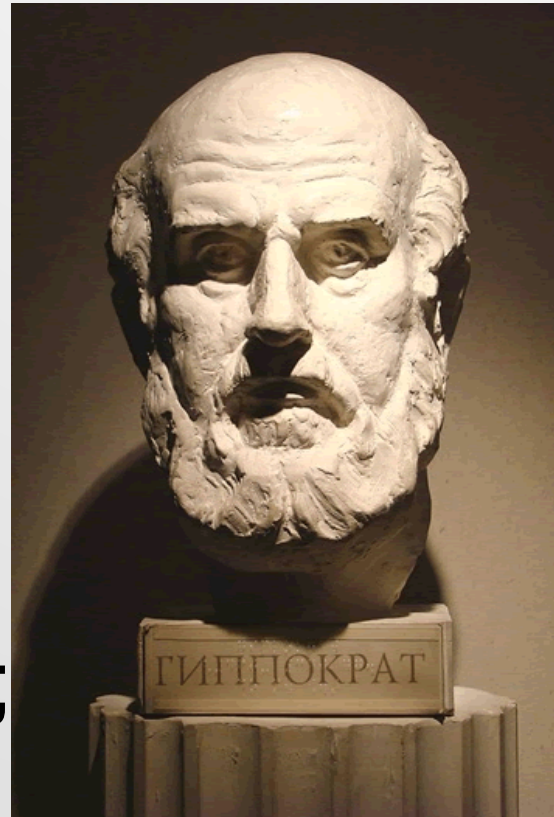


Hippocrates, 460 BC – 370 BC

Greek Dr. "the father of medicine"

Opium useful as:

- ▶ Narcotic;
- ▶ styptic – stop bleeding;
- ▶ Treating internal disorders;
- ▶ Women Diseases;
- ▶ Epidemics.



330 B.C., Alexander the Great , Greek Military Leader

- ▶ Introduced **opium** to Persia and India.



Galen



- ▶ **Greek physician, writer, and philosopher**
- ▶ **129–216 AD**
- ▶ **Born in Pergamum, Mysia, Anatolia [now Bergama, Turkey]**

Galen, physician, listed medical indications for opium ~ 200 A.D.

- ▶ "...resists poison and venomous bites, cures chronic headache, vertigo, deafness, epilepsy, apoplexy, dimness of sight, loss of voice, asthma, coughs of all kinds, spitting of blood, tightness of breath, colic, the lilac poison, jaundice, hardness of the spleen stone, urinary complaints, fever, dropsies, leprosies, the trouble to which women are subject, melancholy and all pestilences."

400 A.D. *Opium* from Egyptian fields at Thebes was introduced by Arab traders to China.



1020 A.D., Dr. Avicenna of Persia called Opium 'the most powerful of the estupefacients' (Narcotic/Hypnotic)



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

~1300 A.D. Opium disappeared for 200 Years from European historical record

- ▶ Opium was a *taboo* subject for those in circles of learning during the **Holy Inquisition**, in the eyes of which **anything from the East was linked to the Devil**.



Holy Inquisition

1527 A.D. Paracelsus, Swiss physician, alchemist, and astrologer

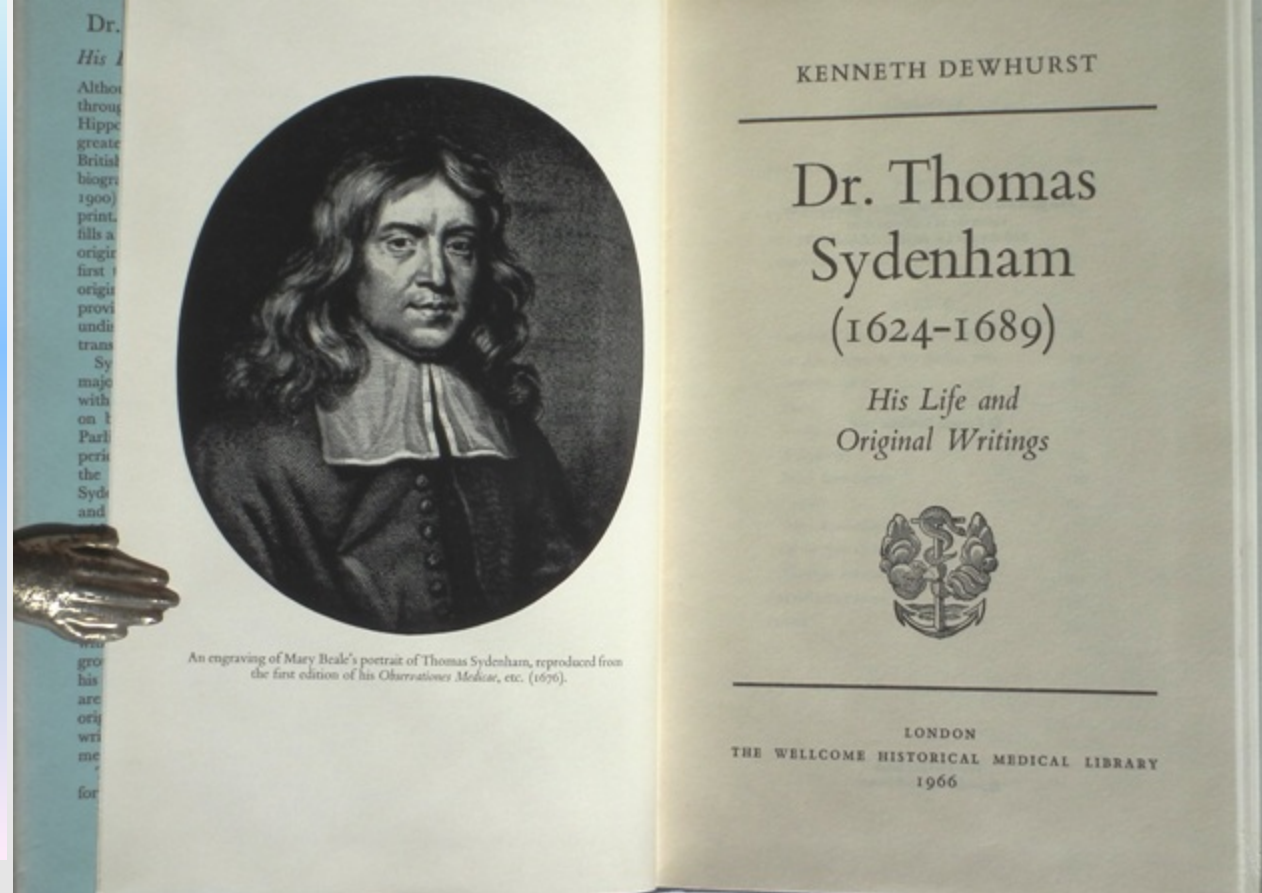
- ▶ Reintroduced **Opium** as laudanum into European medical literature, during the height of the Reformation.
- ▶ **Black pills**, or "Stones of Immortality", were made of **opium thebaicum**, citrus juice and quintessence of gold and were prescribed as 'painkillers'.



Dr. Thomas Sydenham

1624- 1689]

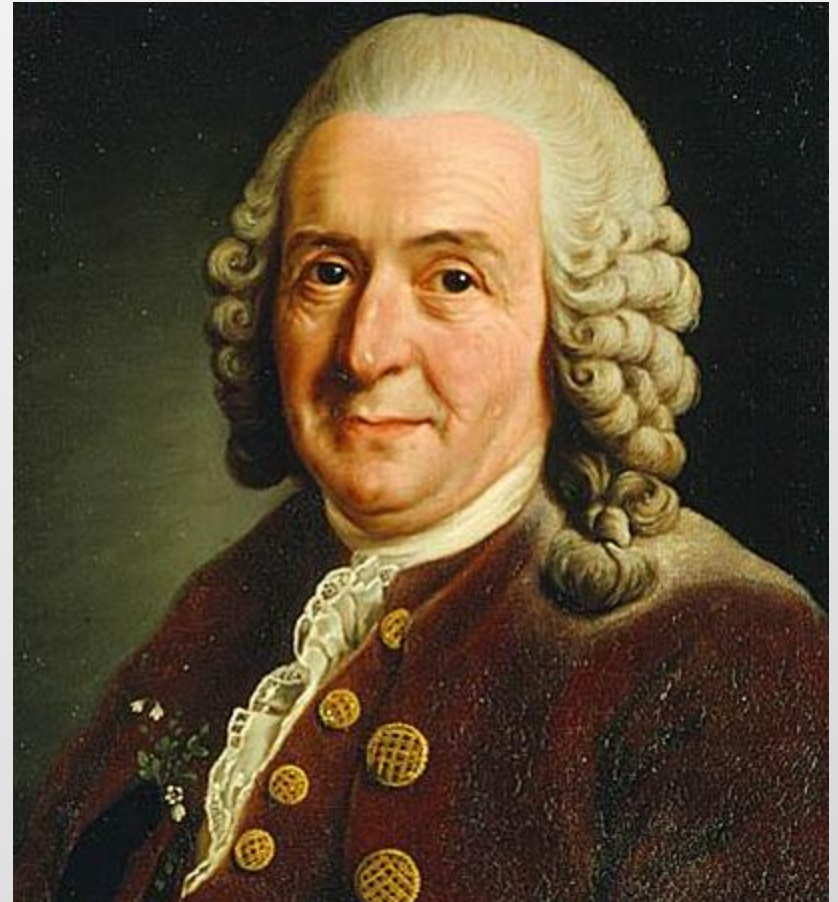
'the English Hippocrates'
'Shakespeare of medicine'



"Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium."

1753 Dr. Carl A.D. Linnaeus, [1707-1778 A.D.]

- ▶ Swedish physician
- ▶ Father of botany
- ▶ First classified poppy in his book
Genera Plantarum, as
Papaver somniferum
– 'sleep-inducing'



Spread of Opium to China

- ▶ 1700 A.D. Dutch exported shipments of opium from India to China.
- ▶ 1729 A.D. Chinese emperor, Yung Cheng, issued an edict prohibiting the smoking of opium and its domestic sale, except under license for use as medicine.



Opium to China

- ▶ 1750 A.D. British East India Co. assumed control of Bengal and Bihar, opium-growing districts of India.



Spread of Opium to China

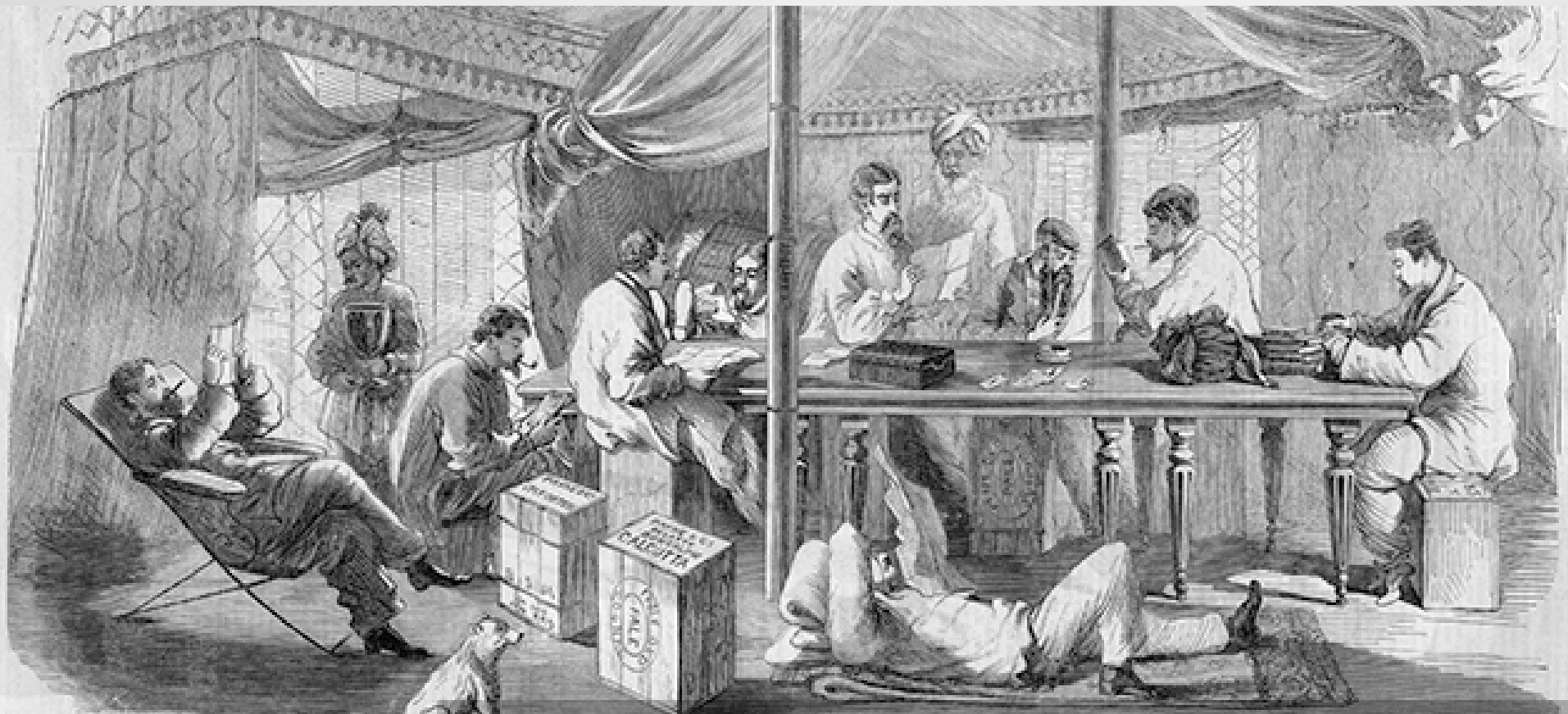
- ▶ 1750 A.D. British East India Company shipping dominated trade, and had their own armies.
- ▶ **Shipped** opium out of Calcutta to China.

Armies of the East India Company 1750–1850



Opium import to China

- ▶ 1796 A.D. – **Import of opium into China** becomes a contraband trade. Silver was smuggled out to pay for smuggling opium in.



Opium import to China

- ▶ 1799 A.D.
China's emperor,
Kia King,
banned opium
completely,
making trade and
poppy cultivation
illegal.



First Opium War

British v. Chinese

- ▶ 1841 – British defeated the Chinese during the **First Opium War**.



Second Opium Wars

British v. Chinese

- ▶ 1856 – British and French renewed hostilities and defeated China in the **Second Opium War**.
- ▶ **Importation of opium to China was legalized.**



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

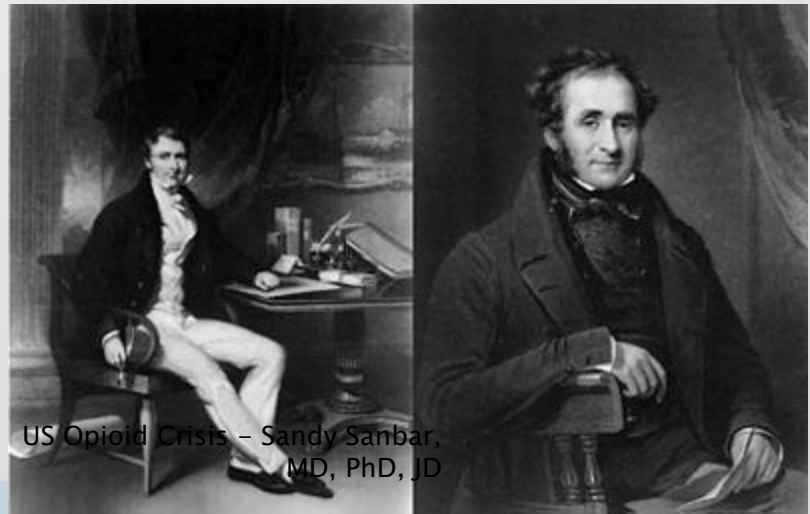
Opium import to Europe and U.S.

- ▶ 1800 A.D. – **British Levant Company** purchased nearly half of all of the opium coming out of Smyrna, Turkey, strictly for importation to Europe and the **United States**.



1830 - British Dependent on Opium

- ▶ For medicinal and recreational use
- ▶ Reached an all time high.
- ▶ 22,000 pounds of opium imported from Turkey and India.
- ▶ **Jardine–Matheson & Company of London** inherit India Co. and its opium from the British East India Company.



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

1827 - E. Merck & Company of Darmstadt, Germany, began commercial manufacturing of morphine.

- ▶ Morphine was named after **Morpheus**, the Roman god of dreams.
- ▶ Used in World Wars I & II, and U.S. Civil War.



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

U.S. Civil War (1861-65)

Close to 800,000 soldiers died

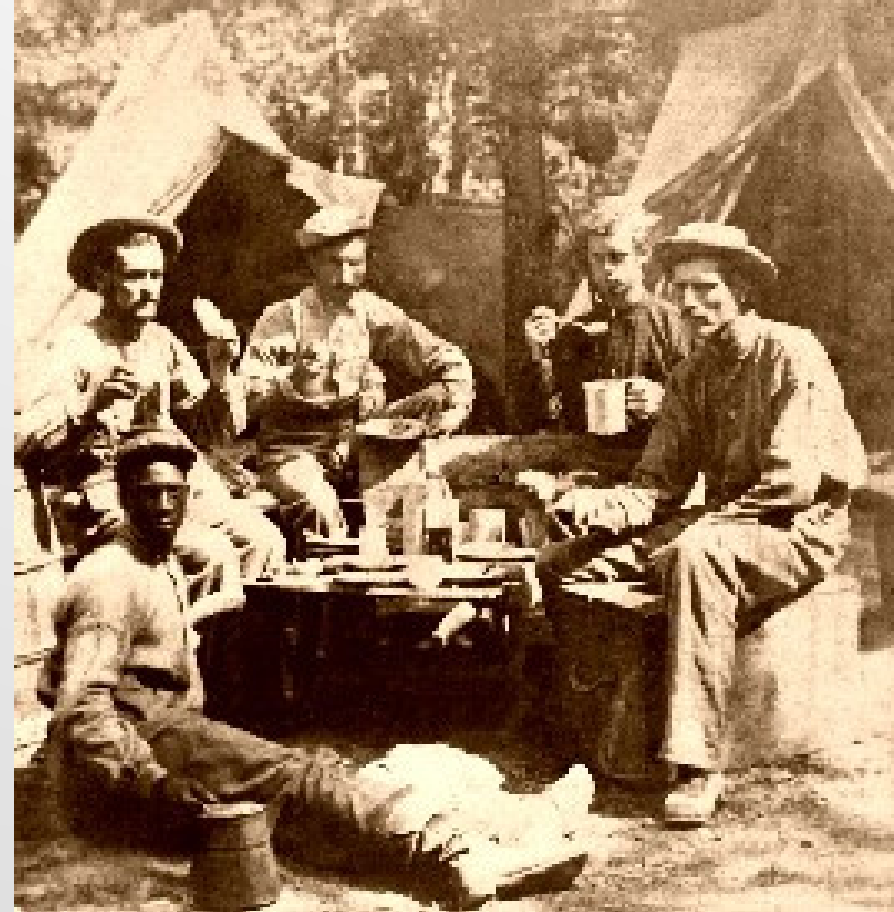


US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

“Soldier’s disease”

addiction to morphine

- Civil War pivotal to the history of drug use in the US.
- The Union cut off of Northern **coffee** to the South, and
- 10 million **opium pills** were distributed to Northern soldiers.



1st US Opioid Crisis (1865)

- ▶ U.S. experienced its first major **OPIUM** drug epidemic/crisis
- ▶ About 150 years ago .



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

“Soldier’s disease”

Epidemic: addiction to morphine

Civil War soldiers were given morphine for pain from war injuries and many became addicted.

- ▶ About 400,000 soldiers of the U.S. Civil War became addicted.



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

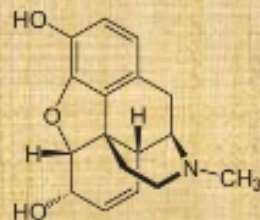
Morphine + Alcohol 11%



1874 C.R. Wright, Englishman, first synthesized 'heroin.'



• Heroin was first synthesized by C.R. Alder Wright in 1874 by adding two acetyl groups to the morphine molecule.

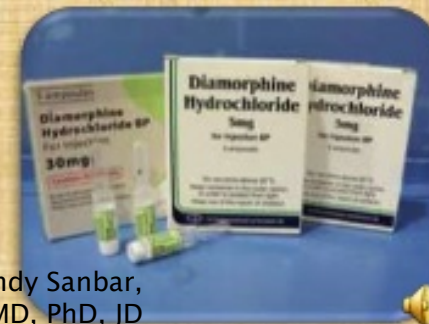


• When used in medicine it is typically used to treat severe pain, such as that resulting from a heart attack or a severe injury.

• The name "heroin" is only used when being discussed in its illegal form.



• When it is used in a medical environment, it is referred to as Diamorphine and comes in tablet or injectable form for the same indications as morphine and is often being preferred over morphine due to its lower side-effect profile



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

COUGH

The Sum of Clinical Experience Designates Glyco-Heroin (Smith) as a Respiratory Sedative Superior in All Respects to the Preparations of Opium, Morphine, Codeine and Other Narcotics and without devoid of the toxic or depressing effects which characterize the latter when given in doses sufficient to reduce the reflex irritability of the bronchial, tracheal and laryngeal mucous membranes.

THE PROBLEM
of administering Heroin in proper doses in such form as will give the therapeutic virtues of this drug full sway, and will suit the palate of the most exacting adult or the most capricious child
HAS BEEN SOLVED BY
the pharmaceutical compound known as

GLYCO-HEROIN (Smith)

The results attained with GLYCO-HEROIN (SMITH) in the alleviation and cure of cough are attested by numerous clinical studies that have appeared in the medical journals within the past few years.

Scientifically Compounded, Scientifically Conceived, GLYCO-HEROIN (SMITH) simply stands upon its merits before the profession, ready to prove its efficacy to all who are interested in the advances in the art of medication.

NOTES.

GLYCO-HEROIN (SMITH) is supplied to the druggist in sixteen ounce dispensing bottles only. The quantity ordinarily prescribed by the physician is two, three or four ounces.

DOSE.

The adult dose of GLYCO-HEROIN (SMITH) is one teaspoonful, repeated every two hours or at longer intervals, as the case may require. Children of ten or more years, from a quarter to a half teaspoonful. Children of three years or more, five to ten drops.

SOLE BRITISH AGENTS:
THOMAS CHRISTY & CO.,
OLD SWAN LANE, UPPER THAMES ST., LONDON, E.C.

MARTIN H. SMITH & CO., Chemists,
NEW YORK CITY.

Samples and Literature

Supplied on Request.



Sirop-Zed

Le Sirop du D^r Zed (Codéine et Tolu) est précieux pour les Enfants dans les cas de *Coughluche*, *Injonnie*; *Toux des Phtisiques*, *Catarrhes*, *Rhumes*, etc.

PARIS, 12, rue Drouot, et les Ph^{ies}.

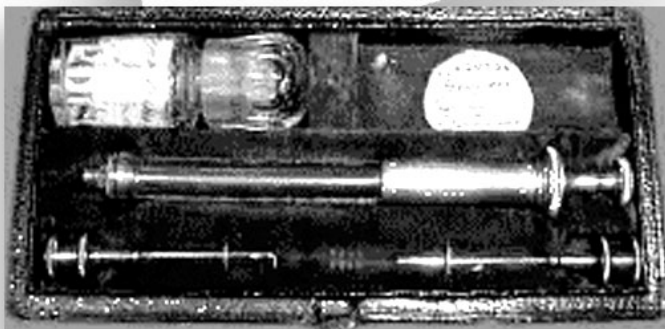


**Sold by Bayer
along with Aspirin**



1898 - 1910

fact medicinehistory rosalulita





COCAINE TOOTHACHE DROPS

Instantaneous Cure!

PRICE 15 CENTS.

Prepared by the

LLOYD MANUFACTURING CO.

219 HUDSON AVE., ALBANY, N. Y.

For sale by all Druggists.

US Opioid Crisis - Sandy Sanbar,
MD, PhD JD
(Registered March 1880.)

See other side.



MORPHINA-CURA

\$2.00 PER BOTTLE

An infallible remedy for the cure of Drug Habits of all kinds.
Sent postpaid at \$2 per bottle. Morphina-Cura is prepared
for Hypodermic or Internal use. Delta Chem. Co., St. Louis.
For sale by W. H. White & Co.

19th century, Morphine was a panacea. Used for surgery, and in Medicines to treat as many as 54 diseases, including insanity, diarrhea, dysentery, menstrual and menopausal pain, and even nymphomania. “An infallible remedy for the cure of Drug Habits of all kinds.”

Tax Opium to U.S.

- ▶ 1840
New Englanders brought 24,000 pounds of opium into the United States.
- ▶ That caught the attention of U.S. Customs.
- ▶ Promptly puts a **duty fee on the import.**





OPIUM DENS IN U.S.

Prior to 1875,
narcotics were
widely available
and essentially
unregulated in
America.

A NEW AND MAGNIFICENT CLIPPER FOR SAN FRANCISCO.

MERCHANTS' EXPRESS LINE OF CLIPPER SHIPS!

Loading none but First-Class Vessels and Regularly Dispatching the greatest number.

THE SLENDID NEW OUT-AND-OUT CLIPPER SHIP



CALIFORNIA

HENRY BARNES, Commander, AT PIER 13 EAST RIVER.

This elegant Clipper Ship was built expressly for this trade by Samuel Hall Esq., of East Boston, the builder of the celebrated Clippers "Scorpion," "Hammock," "Jenny Green," and others. She will fully equal them in speed! Commonly prompt dispatch and a very quick trip may be relied upon. Engagements should be completed at once.

Agents, in San Francisco,
HARRIS, WHEAT, SMITH & CO.

RANDOLPH M. COOLEY, 88 Wall Street, Tontine Building.

REGISTERED & PATENTED

California Gold Rush of 1848–1855
Chinese, Opium smoking

Opium den in Chinese lodging house in San Francisco, California



FIRST LAW

1875

**ANTI-OPIUM
ORDINANCE
BANNED
SMOKING
OPIUM IN
SAN FRANCISCO
CITY LIMITS
(NOT IN
CHINATOWN
DENS)**



OPIUM DENS



Federal laws (1875–1895) barred Chinese people from trafficking in opium, outlawed opium dens altogether, or made it illegal to possess opium, morphine and heroin *without a physician's prescription*.



1890 Heroin & Opiates

- ▶ In 1890, the first Congressional Act regarding heroin and other opiates was enacted.
- ▶ Focus was not on consumption or use.
- ▶ Federal taxes be levied on each sale of morphine and opium.



- From 1879–1906, ~ 100 bills introduced in Congress to regulate food and drugs.
- Opium use increased.
- Legal opiates by physicians and pharmacist to women with **"female problems"** (painful menstruation).
- In the late 19th century, about **150,000 to 200,000 opiate addicts** lived in the United States and **over two-thirds of these addicts were women.**



**Poppy, or Opium
Poppy,
Papaveraceae,
Papaver
somniferum L.**



President Theodore Roosevelt



Food and Drug Act of 1906

Sec. 8. "Misbranded" drugs

required
**Accurate
Labeling
of**

Alcohol
Cocaine
Heroin
Morphine
Cannabis





President Woodrow Wilson Board of Food and Drug Inspection 1907



Smoking Opium Exclusion Act of 1909



- ▶ First Federal law banning *non-medical use* of a substance.
- ▶ Banned the importation, possession and use of "smoking opium".
- ▶ *Did not regulate opium-based "medications".*

United States v. Forty Barrels and Twenty Kegs of Coca-Cola

241 U.S. 265 (1916)



- ▶ 1911 - Coca-Cola adulterated with caffeine & misbranded;
- ▶ Coca-Cola won.
- ▶ 1912 - Caffeine "habit-forming" and "deleterious" listed on product's label.



Harrison Narcotics Act (1914)

(Public Law 223, 63rd Cong., 3rd sess., Dec. 17)

- ▶ **Criminalized** nonmedical use of drugs;
- ▶ Outlawed nonmedical use of opium, morphine, and cocaine;
- ▶ **Illegal to prescribe narcotics to a patient who was addicted to opioids;**
- ▶ Required **Registration** was by MDs, DDS, PharmD, and Manufacturers.

THE "WAR ON DRUGS" INTENSIFIES...

FREEZE,
DIRT BAG!



US Opioid Crisis: Sandy Sanbar,
MD, PhD, JD



Prosecutions: 1914–1938

- ▶ 1914–1928 – U.S. attorneys prosecuted >77,000 people, mostly medical professionals, for violating the Harrison Narcotic Act.
- ▶ 1914–1938 – ~25,000 doctors arrested for giving narcotic prescriptions to addicts.

Harrison Act Prosecutions

- Doctors put on trial.
- Lost reputations, careers, or life savings.
- Clinics closed; addicts abandoned.
- By 1928, sentence 1 year & 10 mos.
- >19 % of prisoners – for narcotics.
- Black market for narcotics.





President Franklin D. Roosevelt **1938**

Food, Drug, and Cosmetic Act
(Replaced 1906 Food & Drug Act)

Elixir Sulfanilamide with DEG



War on Drugs



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

WAR ON DRUGS INTENSIFIED



Drug Abuse Prevention and Control Act (DAPCA) - 1970



- ▶ DAPCA replaced the Harrison Narcotics Act.
- ▶ Title II of DAPCA – is the Controlled Substances Act (CSA).
- ▶ Potent weapon as the war on drugs intensified.



CSA Schedules of drugs

Schedule I: high abuse potential -- no accepted use (heroin, marijuana)

Schedule II: high abuse potential and severe dependence liability (morphine, codeine, percocet etc.)

Schedule III: Moderate dependence liability (Tylenol #3, Vicodin)

Schedule IV: Limited dependence liability (benzodiazepines, fioricet)

Schedule V: Limited abuse potential (Lomotil)

Federal intractable pain policy

- ▶ Federal Regulation: CSA
- ▶ Federal Government does not Regulate the Practice of Medicine; States do.
- ▶ Practitioner & Pharmacists *Responsible.*



Drug Enforcement Administration (DEA) - 1973

- ▶ Established by President Richard M. Nixon;
- ▶ Part of the Justice Department;
- ▶ United federal drug agencies that had often worked at cross-purposes.



Drug Enforcement Administration

Administers federal laws;

1. Maintains opioid records;
2. Registers health professionals;
3. Sets quotas;
4. Enforces violations of the CSA.



United States v. Moore

(423 U.S. 122, 124 [1975])

- ▶ U.S. Supreme Court affirmed legality of DAPCA's CSA (& the Harrison Narcotic Act) to criminalize doctors who treat addicts by prescribing controlled drugs.



Substance Use Disorders (Addicts)

1. (Prescription) **Opioid** Use Disorder
2. (Illicit) **Heroin** Use Disorder
3. **Cigarette** Use Disorder
4. **Alcohol** Use Disorder
5. **Tranquilizer** Use Disorder
6. **Stimulant** Use Disorder
7. **Marijuana** Use Disorder
8. **Methamphetamine** Use Disorder
9. **Cocaine** Use Disorder
10. **Other Illicit Drug** Use Disorders

2017 National Survey on Drug Use and Health in U.S. - SAMHSA

In 2017, about 2.1 million people (0.64 %) had **opioid use disorders** (addicts):

1. 1.7 million prescription opioids, and
2. 0.7 million with a heroin use disorder.

**In 2018, U.S.
Population was
327.2 million**



US Opioid Crisis – Sandy Saito
MD, PhD



Opiates and Opioids

Natural Opiates

opium
morphine
codeine

Semi-Synthetic Opioids

heroin
hydromorphone
hydrocodone
oxycodone

Fully Synthetic Opioids

Fentanyl
Carfentanyl
Methadone

The Opioid Crisis Should be Declared a *State of Emergency*

Over
140



Americans die each day
from an *opioid overdose*

That means every
3 WEEKS,
death tolls from the
U.S. *opioid crisis*
equal those from 9/11



2017

The Tragic State of Opioid Addiction in the U.S.



More than
47,000
Americans
died from an
opioid overdose
in 2017

(including prescription
and illicit opioids).

46
PEOPLE

... die every day from
overdoses involving
prescription opioids.

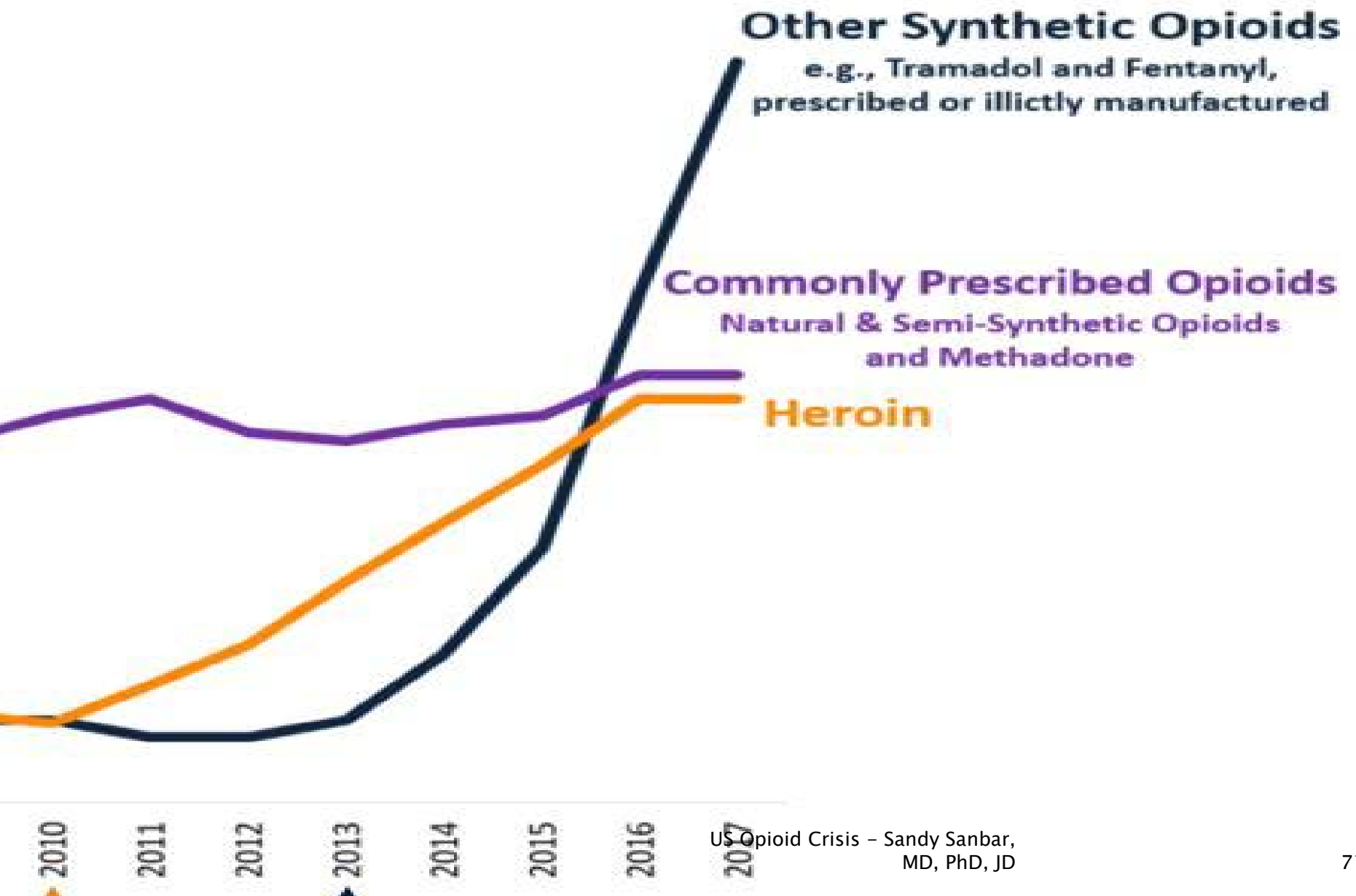


www.cdc.gov

US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD



Opioid Overdose Deaths



Deadly fentanyl bought Online from China, shipped by mail

- ▶ “Fentanyl” is 50 times more potent than Heroin, and up to 100 times more potent than morphine. (?Pay back time?)
- ▶ 300 grams of Fentanyl powder could deliver a fatal dose to 150,000 people.



China Is Poisoning America With Fentanyl

- ▶ Sen. Tom Cotton holds up a salt shaker with an amount of powder that he said approximates a volume of fentanyl that could kill thousands of people.



Deadly Carfentanyl bought Online from China, shipped by mail

- ▶ 'Carfentanyl', derivative of Fentanyl, is used by veterinarians to tranquilize elephants.
- ▶ It is 100 times more potent than Fentanyl, and 10,000 times more potent than Morphine. Only five grams of powder could deliver a fatal dose to over 250,000 people.

▶ (?Pay back time?)

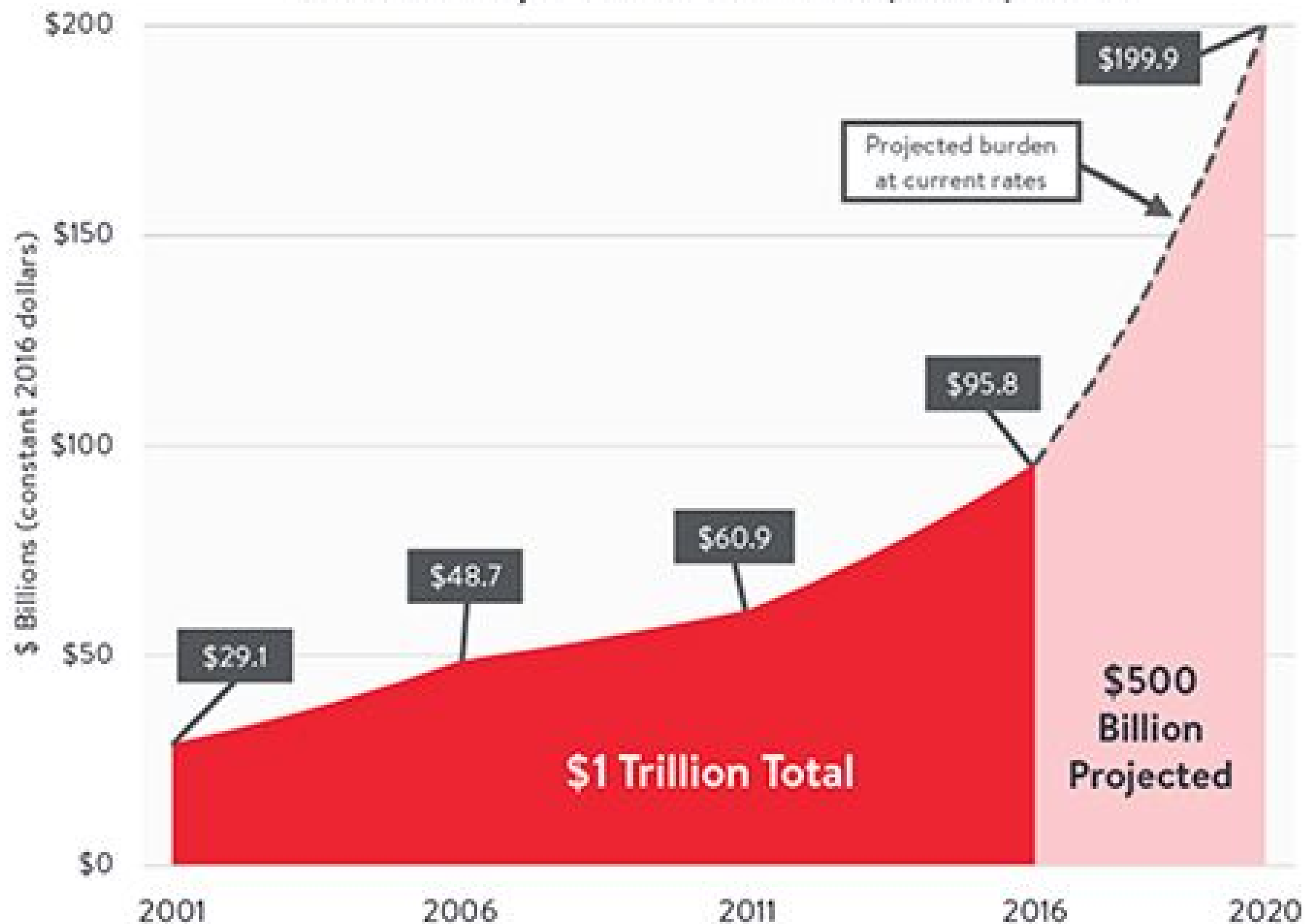


Opioid Overdose Deaths

STAT forecast

- ▶ Even the more middle-of-the-road of 10 forecasts suggest that by 2027, the annual U.S. death toll from opioids alone will be nearly 500,000 deaths over the next decade.
- ▶ **Average 50,000 opioid deaths per year**
 - ▶ *BY* MAX BLAU, JUNE 27, 2017

Total and Projected Costs of the Opioid Epidemic



* Data between labeled estimates interpolated using constant growth rates

Solutions for Opioid Crisis in U.S.

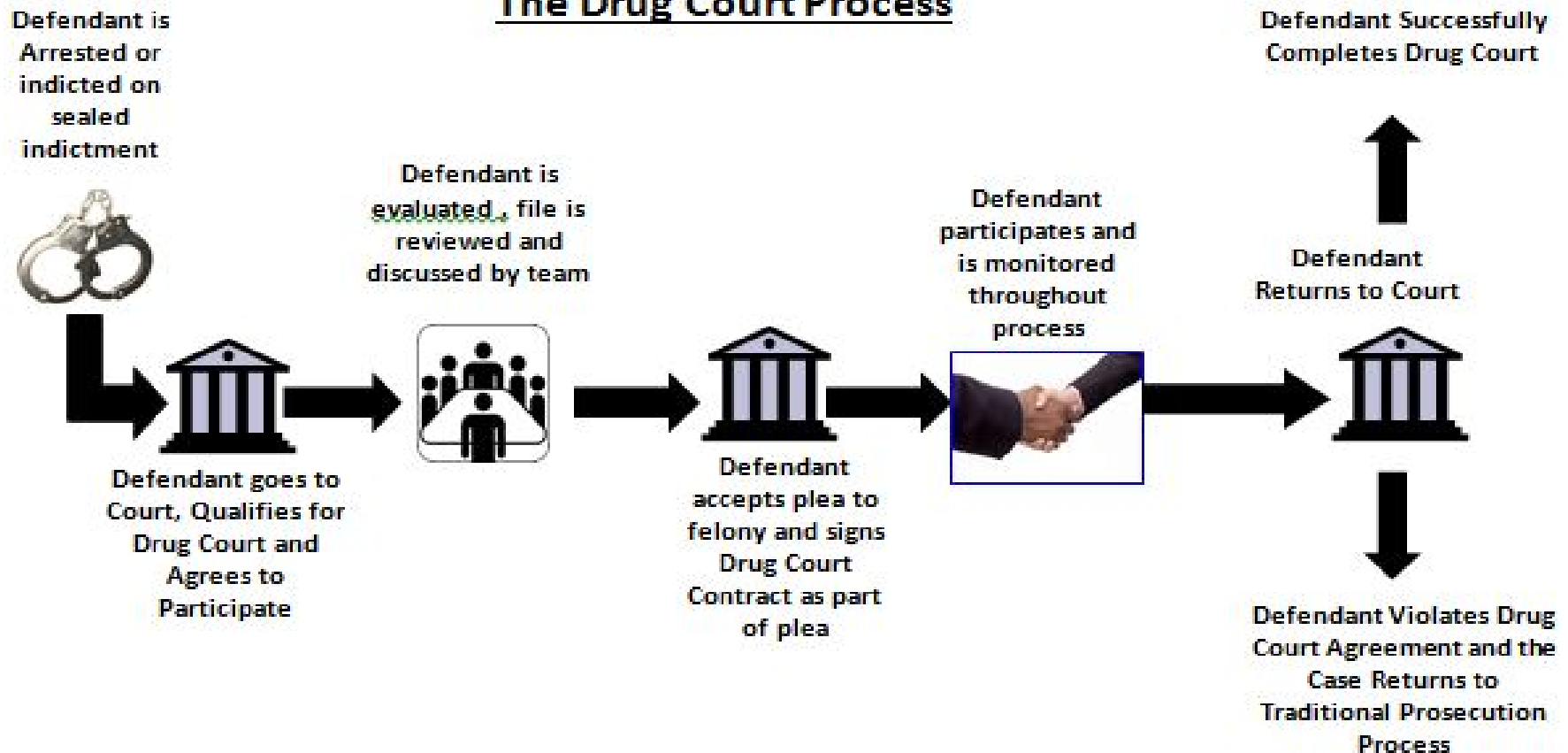
1. Sue Manufacturers, Distributors, Doctors, Pharmacists, Nurses, and Other Health Care Providers



Solutions for Opioid Crisis in U.S.

2. Drug Courts instead of incarceration

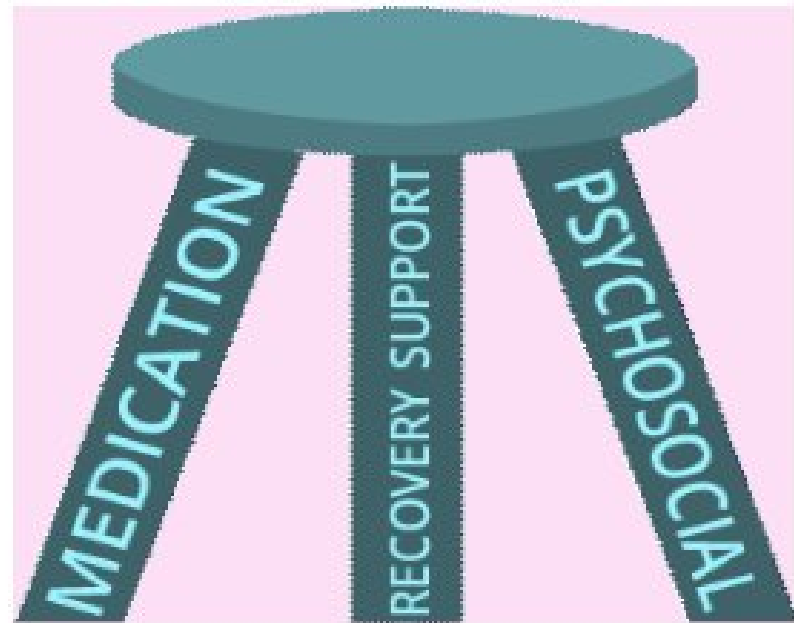
The Drug Court Process



Solutions for Opioid Crisis in U.S.

3. Medication Assisted Treatment

Welcome MAT



Solutions for Opioid Crisis in U.S.

4. Education Patient and Public about Naloxone use for opioid overdose

Naloxone Could Prevent More Than 20,000 U.S. Overdose Deaths, WHO Says

Reuters

Posted: 11/04/2014 6:57 am EST | Updated: 01/04/2015 5:59 am EST



Opioid actions against manufacturers and distributors

- ▶ 2007, Purdue Pharma – Penalty > \$630 million
- ▶ 2008, McKesson – Fine > \$13 million
- ▶ 2017, McKesson – Settlement \$150 mil.
- ▶ Kentucky – settled with Purdue and Janssen – combined total \$40 million
- ▶ 2019, Oklahoma – Pharma settled \$278 millions.

Opioid Lawsuits by Other States

- ▶ 2018 – New York, Nevada, Texas, Florida, North Carolina, North Dakota, Tennessee, Florida, and Many Other States
- ▶ Current Lawsuits total over 1,000

Allegations v. Defendants (2019)

- ▶ False and Deceptive Statements;
- ▶ Misrepresented Risks And Benefits;
- ▶ Targeted Prescribers And Patients;
- ▶ Fraudulently Concealed Their Misconduct;
- ▶ Fueled The Opioid Epidemic And Devastated Oklahoma Communities;
- ▶ Substantial Economic Injury To State Agencies; and
- ▶ Record Profits.

Manufacturers and Distributors Defenses to Opioid Lawsuits

1. merely manufacture and sell opioids;
2. no direct contact with patients;
3. Drs. learned intermediaries treat patients;
4. opioids known to be addictive;
5. Informed consent;
6. Treatment agreement;
7. Illicit drug use.

Opioid prescription lawsuits against healthcare providers

- A. Liability for Underprescribing:
 - 1. Negligence (Malpractice);
 - 2. Elder Abuse;
 - 3. State Board Disciplining;
 - 4. Quality of Care.

Opioid prescription lawsuits against healthcare providers

B. Liability for Overprescribing

1. Addiction
2. Overdose death
3. Third party liability–Duty to Warn
4. Criminal liability
5. Federal DEA license revocation
6. State Board Disciplining

California Death Certificate Project -2015

- ▶ About 2,700 death certificates from 2012–2013
- ▶ 522 prescribers were investigated – (450 MDs; 12 DOs; 60 NPs and PAs).
- ▶ 46 accused of overprescribing
- ▶ 13 MDs cases are pending

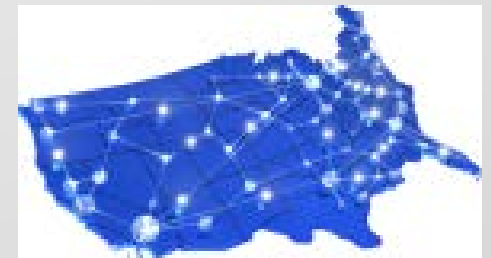
2019 Appalachian Regional Prescription Opioid (ARPO) Strike Force resulted indictment of 60 doctors, pharmacists and nurses.





Model Policy for Safe Opioid Prescribing:

1. Patient evaluation
2. Treatment plan
3. Informed consent & agreement for Rx
4. Periodic review
5. Consultation
6. Medical Records
7. Compliance with Controlled Substances Laws and Regulations



- ▶ **"Chasing the dragon" (CTD)**
- ▶ Inhaled Heroin
- ▶ Users heat heroin over aluminium foil with a lighter and then chase the fumes
- ▶ Tied to Peculiar, Often Catastrophic Brain Damage



OD – Response

1. Alert EMS
2. CPR – Rescue breathing
3. Administer Naloxone



US Opioid Crisis – Sandy Sanbar,
MD, PhD, JD

If an OD is Suspected

Step 1: Assess victim's signs & Sx - Call EMS support

Step 2: Stimulate person - sternal rub

- If no pulse, start CPR

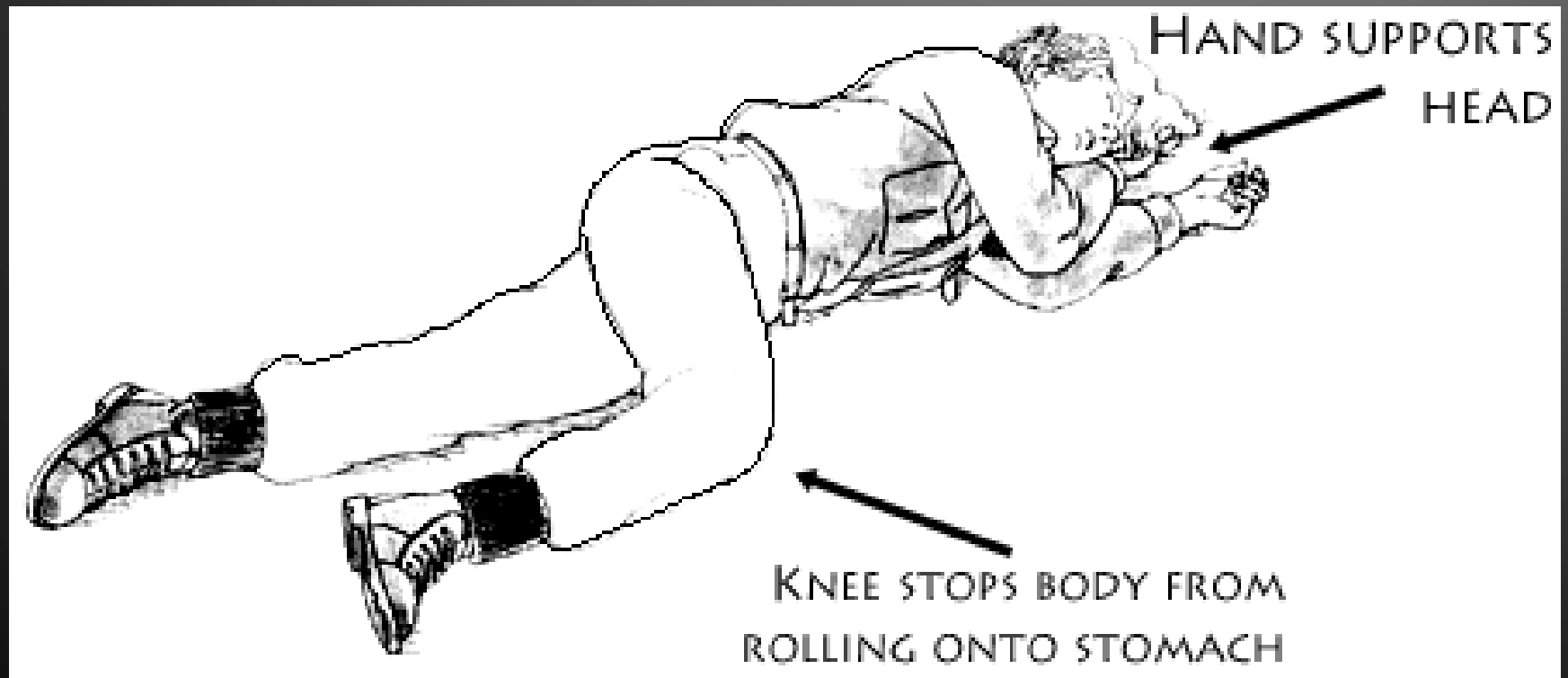
Step 3: Rescue breathing

Step 4: Administer Naloxone

Step 5: Monitor and Support

- If no pulse, start CPR. If breathing remains absent or slow (< 8 per minute), continue rescue breathing + administer 2nd dose of Naloxone.
- If breathing restored, place recovery position and observe for at least 2 hours.

Recovery Position



Know the Products

➤ Naloxone solution for injection



➤ Off-label intranasal kit



➤ Evzio[®] auto-injector



➤ Narcan[®] nasal spray





EVZIO



EVZIO



**EVZIO
Outer Case**



