BEHAVIORAL HEALTH TELE-ECHO CLINIC

NOVEMBER 9TH
NOON-1PM

OPIOIDS

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2021 MAT UPDATE

I have no financial interests, arrangements, or relationships that could be perceived as a conflict of interest within the context of this presentation.

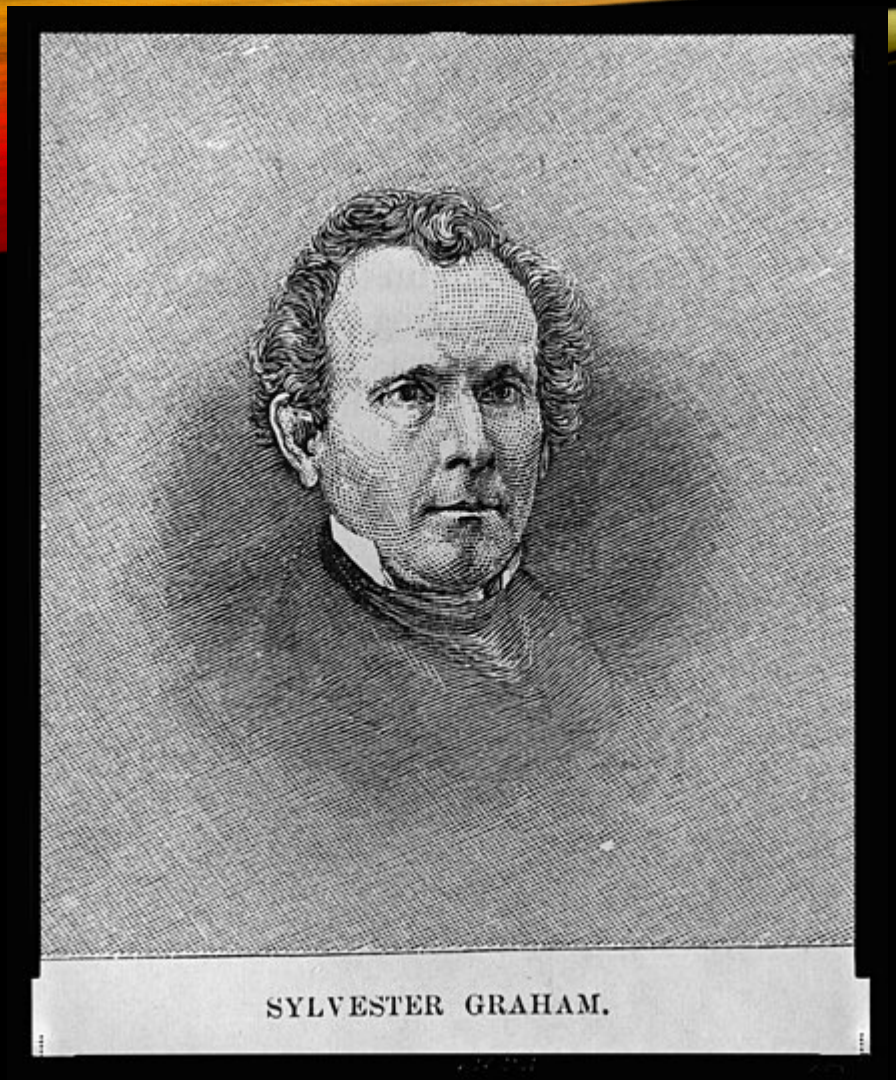
DISCLOSURE STATEMENT

1. Participants will describe the fundamental psychophysiology of Substance Use Disorder (SUD).

2. Participants will competently identify currently medications approved by the U.S. Food and Drug Administration for SUD.

3. Participants will be able to articulate the clinical intervention opportunities for these medications.

OBJECTIVES



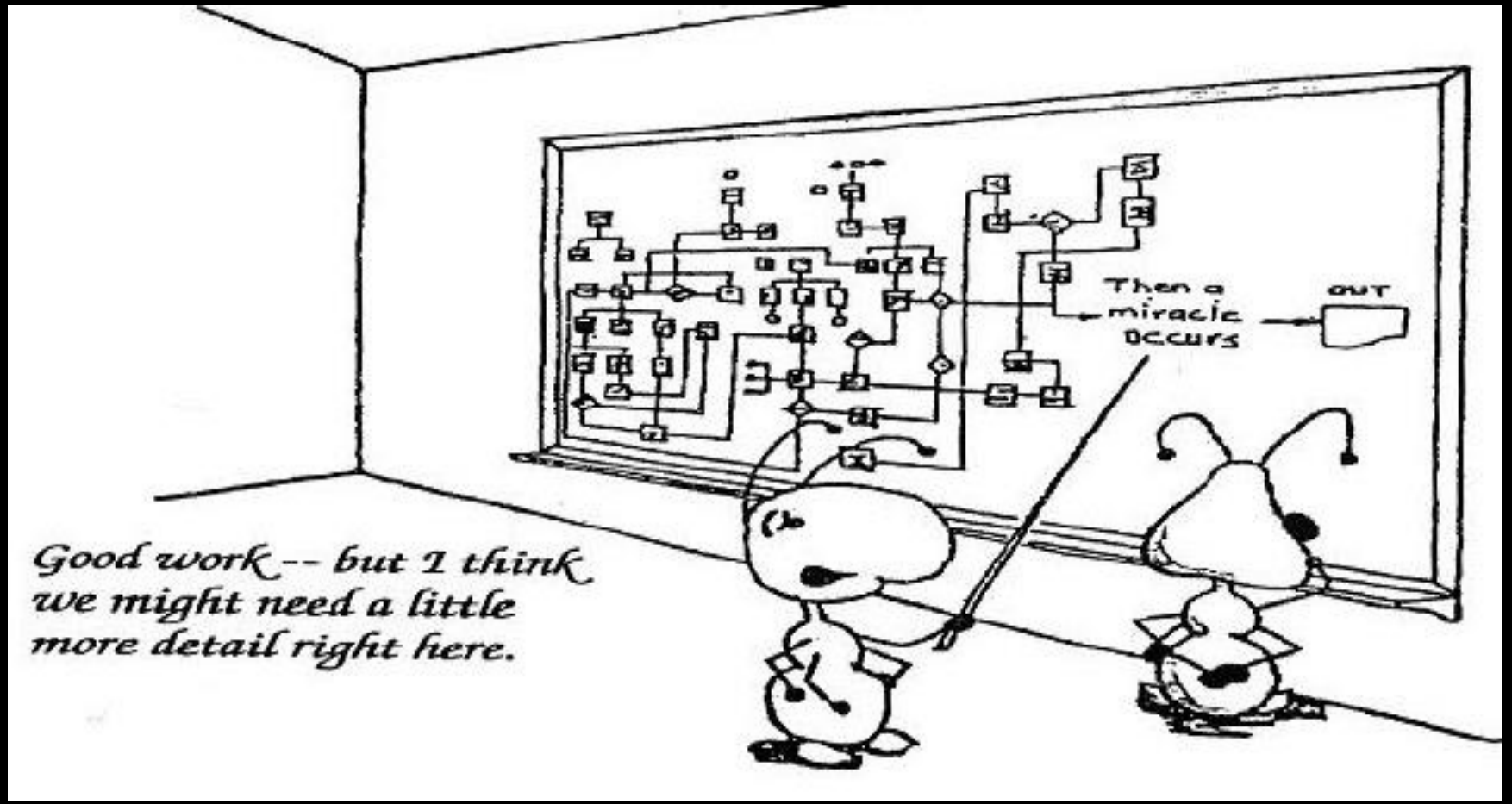
1820 – Philadelphia Temperance Movement

HISTORICAL PERSPECTIVE

- SUD - chronic, progressive, fatal brain disease
  - compulsive drug craving, seeking and use despite harmful consequences
  - MAT – Medication Assisted Treatment
    - AKA TREATMENT

DEFINITIONS

Sources-(National Institute on Drug Abuse, 2008) (Monroe, Kenaga, Dietrich, Carter, & Cowan, 2009) (DuPont, McLellan, White, Merlo, & Gold, 2013)



- Pharmacotherapies
- Professional Behavioral Therapies
- Mutual Assistance Groups/Programs

BEST PRACTICE

Source-(National Institute on Drug Abuse, 2019)

- Abstinence Based
- Harm Reduction Model
- Hybrid Programs

- Mutual Assistance Groups/Programs

Source-(National Institute on Drug Abuse, 2019)

- Cognitive-Behavioral Therapy (Alcohol, Marijuana, Cocaine, Methamphetamine, Nicotine)
- Contingency Management Interventions/Motivational Incentives (Alcohol, Stimulants, Opioids, Marijuana, Nicotine)
- Community Reinforcement Approach Plus Vouchers (Alcohol, Cocaine, Opioids)
- Motivational Enhancement Therapy (Alcohol, Marijuana, Nicotine)
- The Matrix Model (Stimulants)
- Family Behavior Therapy

Professional Behavioral Therapies

Source-(National Institute on Drug Abuse, 2019)

- Tobacco – nicotine replacement, varenicline, buPROPion
- Alcohol – disulfiram, acamprosate, naltrexone
- Opioid – methadone, buprenorphine, naltrexone

FDA APPROVED PHARMACOTHERAPIES

Source-Douaihy, A. B., Kelly, T. M., & Sullivan, C. (2013). Medications for substance use disorders. Social work in public health, 28(3-4), 264–278. doi:10.1080/19371918.2013.759031

- Nicotine patches/gum/lozenges
- **Chantix** (varenicline)-nicotine antagonist
  - high affinity and high selectivity for binding at the a4ß2 receptor
- **Zyban (bupropion)-** NDRI
  - MOA unclear in tobacco cessation

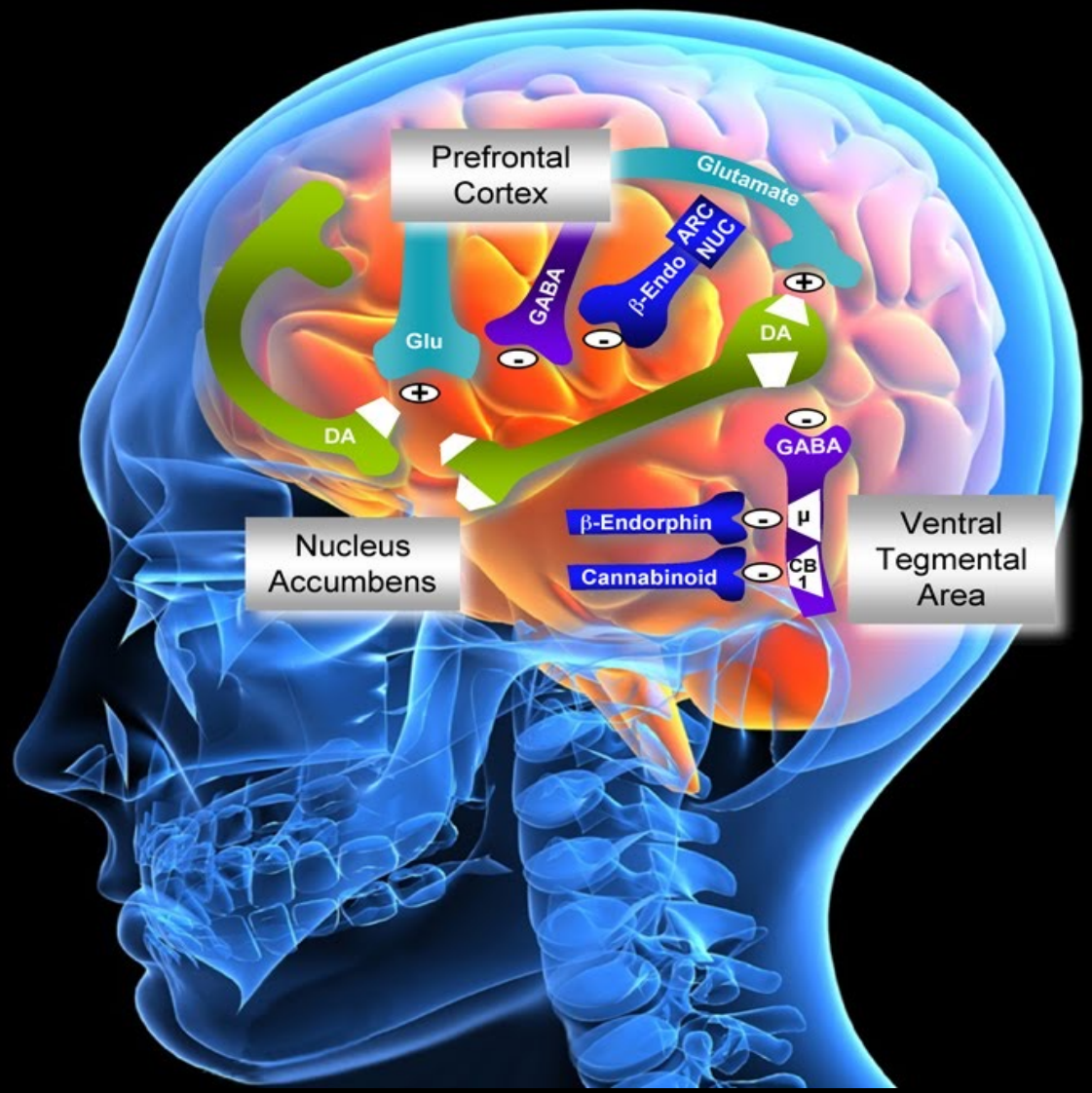
PHARMACOLOGICAL ASSISTANCE - TOBACCO

PHARMACOLOGICAL ASSISTANCE - ALCOHOL

- Vivitrol® (injectable **naltrexone**)
  - 30 day IM injection (compliance)
- Revia® (oral **naltrexone**)
  - Mu-opioid receptor antagonist
- Campral® (**acamprosate**)
  - Possible GABA receptor agonist
- Antibuse® (**disulfiram**)
  - Blocks acetaldehyde dehydrogenase

PHARMACOLOGICAL ASSISTANCE - OPIOIDS

- Vivitrol® (injectable **naltrexone**)
  - 30 day IM injection (compliance)
- Suboxone® (buprenorphine and naloxone)
  - Mu and kappa opioid receptor modulators
  - Partial agonist
  - Used for pain control also
- Methadone
  - Mu receptor agonist – no "ceiling effect"



System Structure

Sources- (Abuse., 2008; McClure & Bickel, 2014; National Institute on Drug Abuse (NIDA), 2015)

- Addictive substance enters body
  - Inject, drink, IV/IM, Intranasal
- Reward System Activated (dopaminergic pathways)
- Reward system "hijacked"
  - Nucleus Accumbens flooded
  - Hippocampus retains patterning
  - Amygdala establishes Conditioned Response

PATHOLOGY REVIEW

Sources- (Abuse., 2008; McClure & Bickel, 2014; National Institute on Drug Abuse (NIDA), 2015)

Opiate (n)

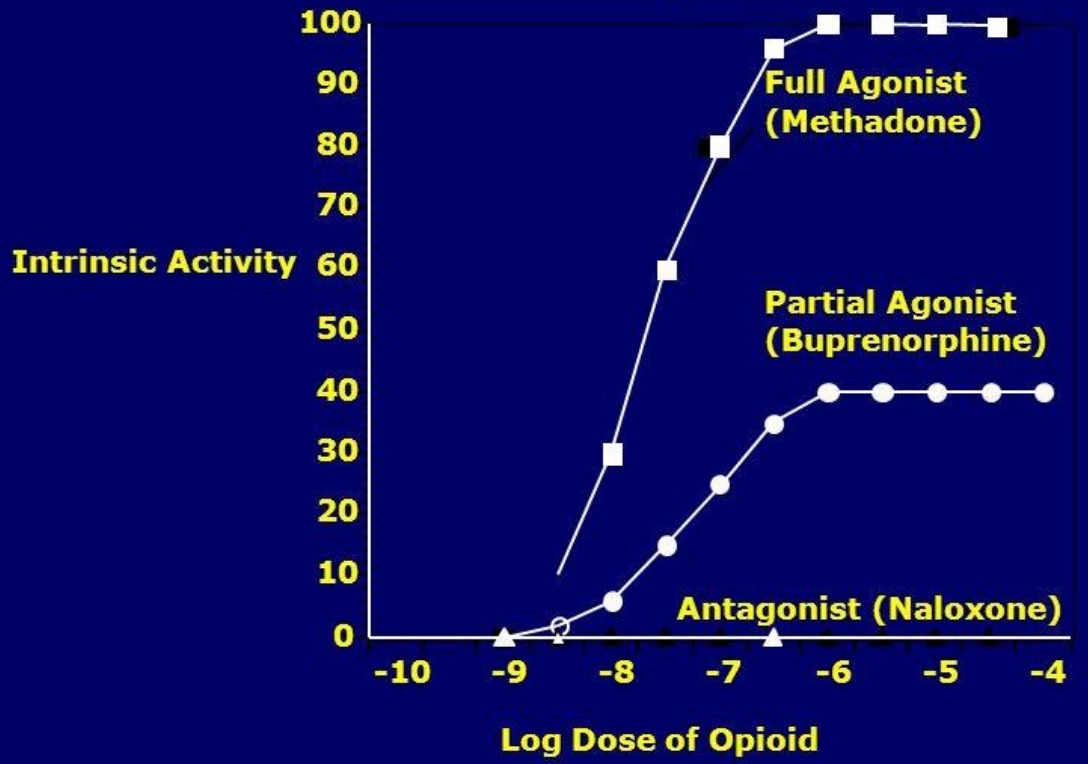
"An unlocked door in
the prison
of identity.
It leads to the
jail yard."

Ambrose Bierce
The Devil's Dictionary (1906)

Papaver somniferum
Photo by Eric Clausen, © 2000 Erowid.org

OPIOIDS

Intrinsic Activity: Full Agonist, Partial Agonist and Antagonist



DO NOT CONFUSE

NALOXONE

Can be bought without a prescription in many states

NALTREXONE

Cannot be bought without a prescription

[USES]

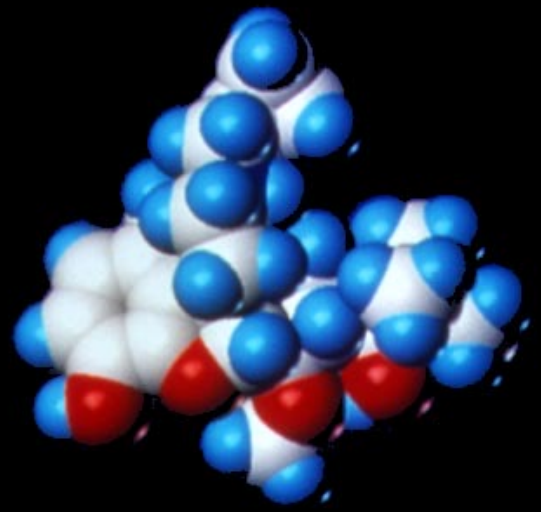
NALOXONE

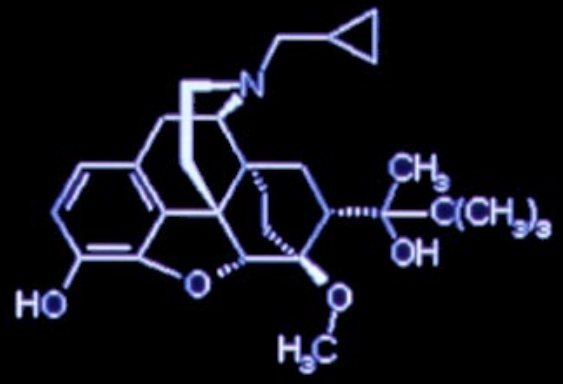
- Injected into a patient suffering from an opioid overdose
- Works rapidly to take the effect of the drug away
- It's now offered as a take-home kit for Fentanyl overdose

NALTREXONE

- Is primarily used as alcohol and drug recovery treatment
- It has been in use for over 30 years
- Injected and slowly released into the body

BUPRENORPHINE





FORMULATIONS

Formulation	Route	Indication
Buprenorphine + naloxone		
Suboxone	Sublingual film	Opioid use disorder
Zubsolv	Sublingual tablet	Opioid use disorder
Bunavail	Buccal film	Opioid use disorder
Buprenorphine		
Subutex	Sublingual tablet	Opioid use disorder
Belbuca	Buccal film	Pain management
Buprenex	Intravenous	Pain management
Butrans	Transdermal patch	Pain management
Probuphine	30-day subcutaneous implant	Opioid use disorder

Company: Reckitt Benckiser
Approval Status: Approved October 2002
Specific Treatments: Opiate Dependence
Off Patent: 2018

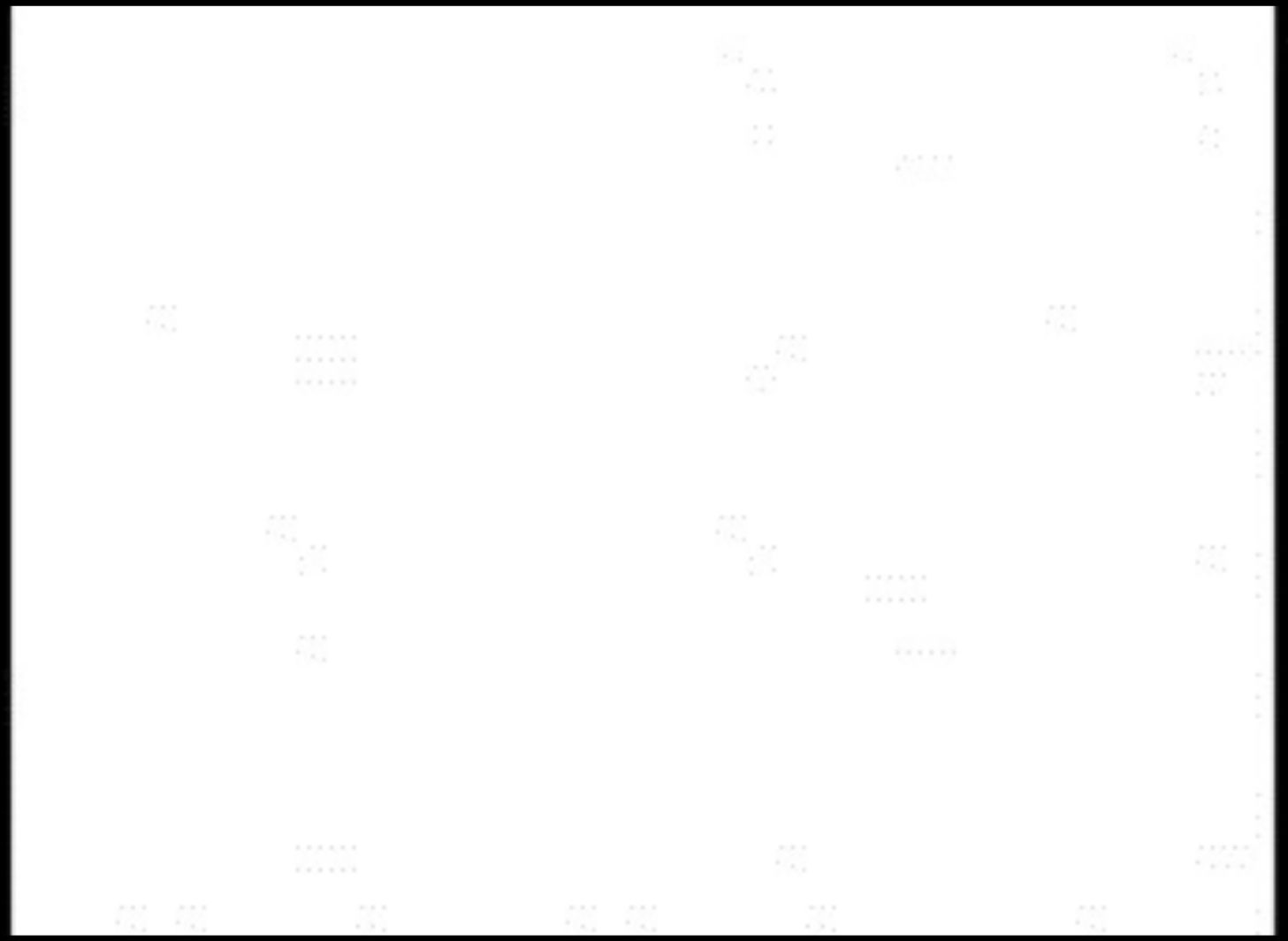
SUBOXONE® - BUPRENORPHINE/NALOXONE

Sublocade™
(buprenorphine extended-release)
injection for subcutaneous use
100mg·300mg

Probuphine®
(buprenorphine) implant

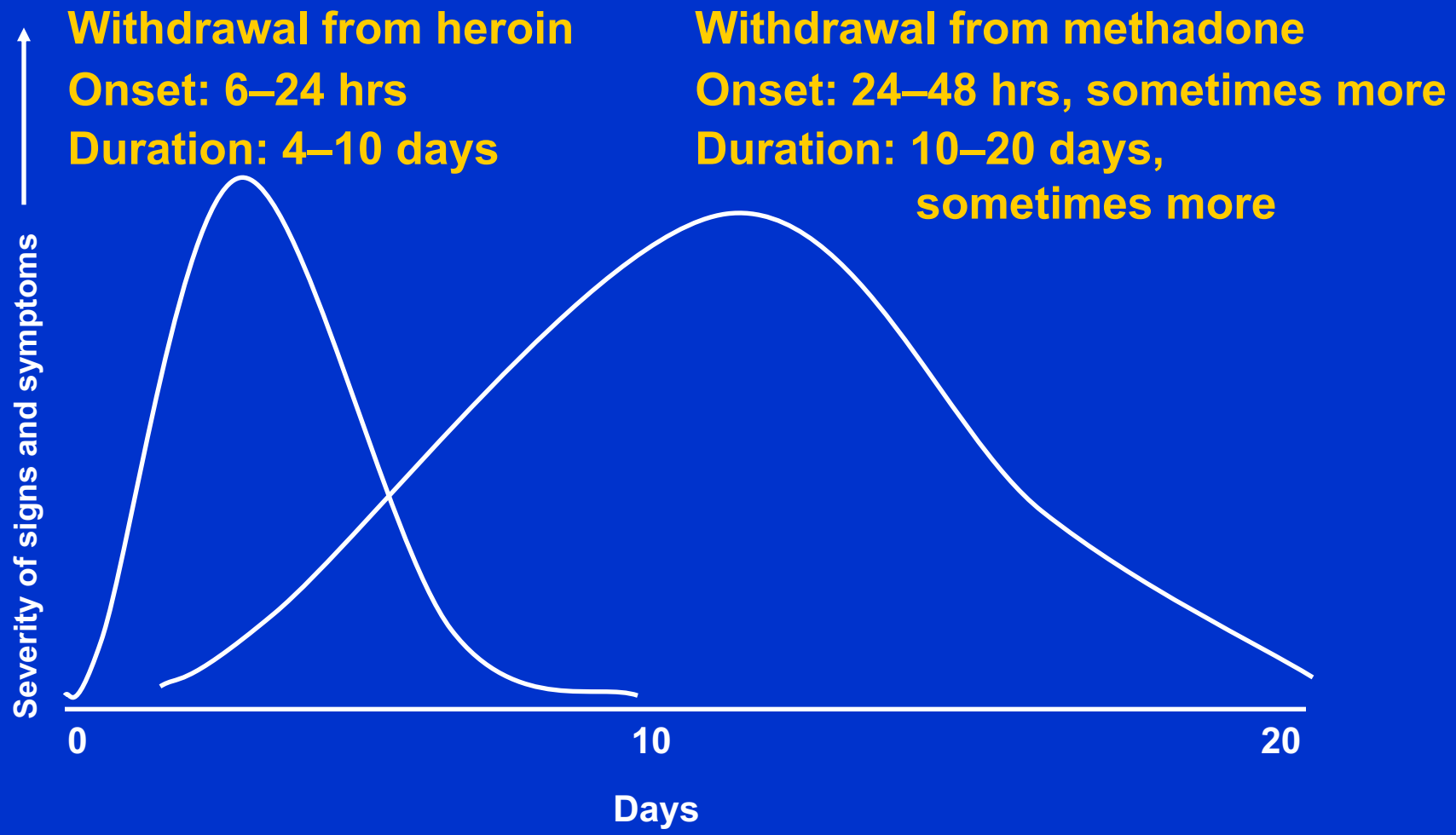
300 mg monthly for the first 2 months following induction and dose adjustment with transmucosal buprenorphine

SUBLOCADE® & PROBUPHINE



MOA

Progress of the Acute Phase of Opioid Withdrawal Since Last Dose



deCrespigny & Cusack (2003)
Adapted from NSW Health Detoxification Clinical Practice Guidelines (2000-2003)

INDUCTION

- Measure withdrawal, several scales available such as:
  - Clinical Opioid Withdrawal Scale (COWS 12–16 is mild/moderate and appears sufficient to avoid precipitated withdrawal
- Hours of abstinence since last full mu opioid use
- 12-16 short-acting, 17-24 intermediate-acting, 30-48 methadone
- BUP dose: 2 – 4mg initial, 16mg max day #1
- Monitor: 1+ hours
- Follow-up: phone + visit in 3 – 4 days

- Treatment contract
- Sole provider for Scheduled medications
- Staged interval increasing
- Random UDS with mass spectrometry confirmation
- Dose range usually 8mg to 24 mg per day
- Consider long term therapy benefit

MAINTENANCE

TAPERING

- Shared decision-making
- Support systems in place
- Criteria for returning to previous dose
- Consider other psychoactive medications to treat comorbidities as they appear
- What is desired outcome (abstinence v harm reduction)

THE SYSTEMS VIEW

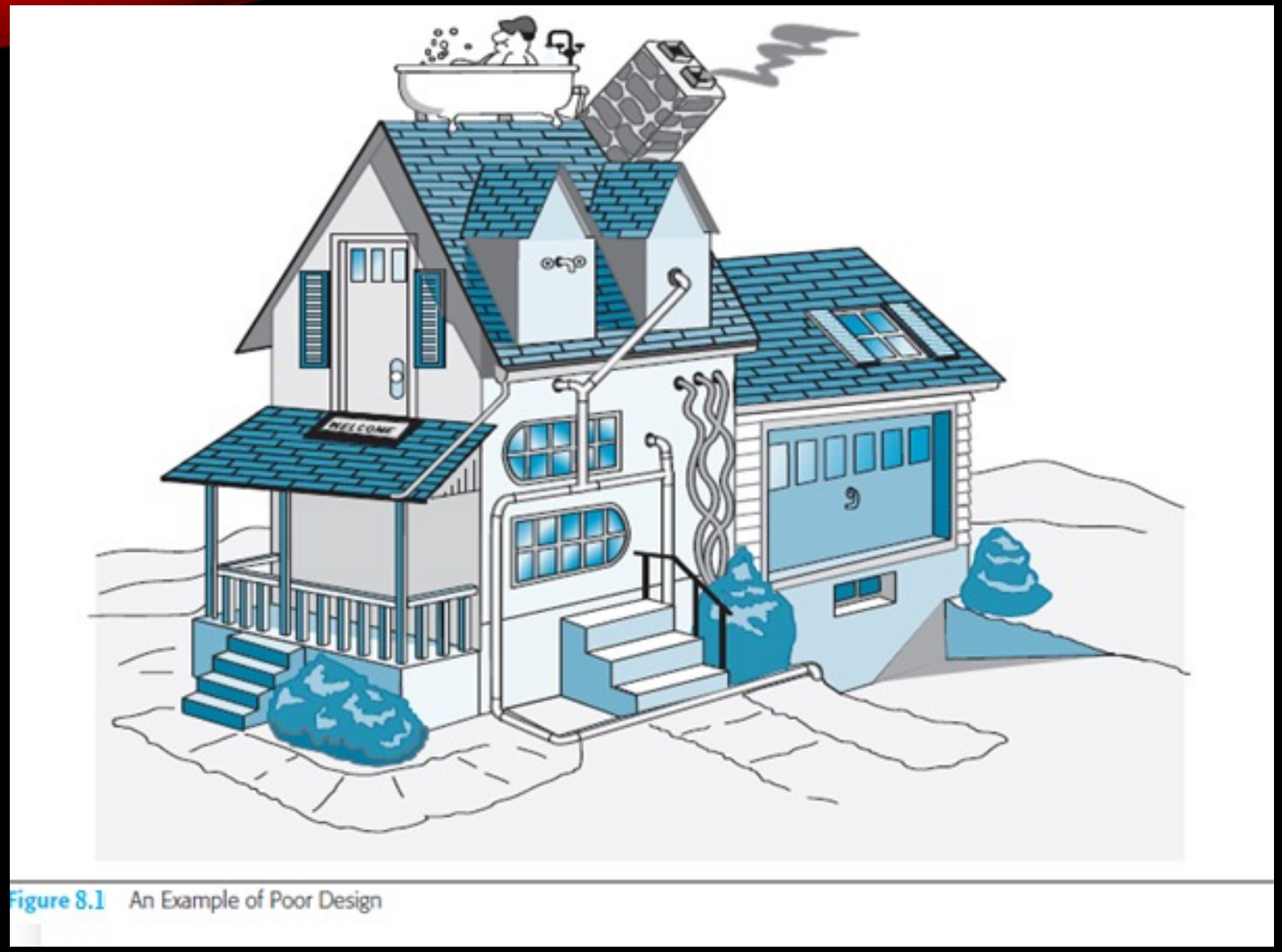


Figure 8.1 An Example of Poor Design

- Each piece needs to be well-designed, but the pieces also need to work well *together*

ANCILLARY MEDICATIONS-----PLEASE!

Chlordiazepoxide – Detox BZO

Librium (chlordiazepoxide HCl) has antianxiety, sedative, appetite-stimulating and weak analgesic actions. The precise mechanism of action is not known. The drug blocks EEG arousal from stimulation of the brain stem reticular formation, RESULTING IN DECREASED SEIZURE RISK.

SHORT TERM USE ONLY – DANGER OF USE WITH ALCOHOL

Drowsiness, dizziness, nausea, constipation, blurred vision, or headache may occur

May use fixed, symptom triggered, or tapering dosage.

ANCILLARY MEDICATIONS

Ondansetron – antiemetic

- MOA - serotonin (5-HT3) receptor antagonist, which decreases vagal stimulation
- First line antiemetic for most withdrawal syndromes
- Adverse effects
  - QT prolongation
  - serotonin syndrome
  - headache
  - constipation

ANCILLARY MEDICATIONS

Folic Acid - Vitamin

Folic acid supplementation has been postulated to be a therapeutic option for correcting hyperhomocysteinemia and therefore for reducing the risk of seizures in patients undergoing **alcohol withdrawal.**

An important mechanism in alcohol-induced injury is biomolecular oxidative damage. Folic acid is supplied to chronic alcoholic patients in order to prevent this situation, as this is the main vitamin deficiency that they suffer from. The decreased concentration of serum folic acid may occur in 80% of alcoholics.

ANCILLARY MEDICATIONS

Thiamine - Vitamin

Routine use of thiamine is recommended because the development of Wernicke encephalopathy or Wernicke-Korsakoff syndrome is disastrous in these patients and can remain unrecognized.

Role in axonal conduction, particularly in acetyl cholinergic and serotoninergic neurons. A reduction in the function of these enzymes leads to diffuse impairment in the metabolism of glucose in key regions of the brain, resulting in impaired cellular energy metabolism.

Rare ADR

Dosage: 100 mg tab, 1 tab po qd

Thiamine has no effect on the symptoms or signs of alcohol withdrawal or on the incidence of seizures or DTs.

ANCILLARY MEDICATIONS

Hydroxyzine Pamoate (Not HCL) - Antihistamine

MOA for anxiety - competes with histamine for binding at H1-receptor sites on the effector cell surface. The sedative properties of hydroxyzine occur as a result of suppression of certain subcortical regions of the brain. Secondary to its central anticholinergic actions, hydroxyzine may be effective as an antiemetic

ADR/SE - Dry mouth (pilocarpine?)

- Drowsiness (usually transitory, improves with tolerance
- Involuntary motor activity (tremor, convulsions) usually with doses considerably higher than those recommended
- Clinically significant respiratory depression has not been reported at recommended doses

ANCILLARY MEDICATIONS

Topiramate – Anti-seizure WITHDRAWAL and MOOD MANAGEMENT – OFF LABEL!

1. Blocks voltage-dependent sodium and calcium channels.
2. Inhibits the excitatory glutamate pathway while enhancing the inhibitory effect of GABA.
3. Moreover, it inhibits carbonic anhydrase activity. (The relevant mechanism of action responsible for efficient migraine prophylaxis remains to be determine)

Tiredness, drowsiness, dizziness, loss of coordination, tingling of the hands/feet, loss of appetite, bad taste in your mouth, diarrhea, and weight loss may occur

MANY CURRENT RESEARCH STUDIES ON OTHER USES FOR THIS MEDICATION. IT IS ALREADY SHOWING PROMISE IN WEIGHT LOSS, ALCOHOL/OPIOID/BENZO WITHDRWAL AND MOOD DISORDERS

ANCILLARY MEDICATIONS

Topiramate – Anti-seizure WITHDRAWAL and MOOD MANAGEMENT – OFF LABEL!

- Alprazolam is successful in reducing anxiety but has a high addictive/misuse potential.
- Topiramate is a novel anticonvulsant which has been used as a mood stabilizer.
- Other anticonvulsants, such as carbamazepine and valproate, have been used in alcohol and benzodiazepine withdrawal.
- Topiramate has recently been used in alcohol, cocaine and opiates withdrawal.
- There has been also one report of topiramate use in midazolam withdrawal.
- (In our case of a patient with recurrent major depressive disorder, subthreshold anxiety disorder and addiction to alprazolam, topiramate appears to be efficient and safe in alprazolam withdrawal)

ANCILLARY MEDICATIONS

Alprazolam - benzodiazepine

Alprazolam (Xanax) is a psychoactive drugs that work to slow down the central nervous system by activating GABA receptors. This provides a variety of useful tranquilizing effects. Aside from relieving symptoms of alcohol withdrawal, benzodiazepines are also commonly prescribed to treat insomnia, muscle spasms, involuntary movement disorders, anxiety disorders, and convulsive disorders.

ADR/SE - Drowsiness, dizziness (these effects will be less pronounced after a few days, avoid driving a car or engaging in other dangerous activities if these occur); GI upset (take drug with food); fatigue; depression; dreams; crying; nervousness

Although benzodiazepines have gotten their reputation tarnished over the past 15 years, they are still useful in many cases. As with opioids, I never start a person on benzodiazepines without an exit strategy. When I have a polysubstance abuser, I generally try to address all substance recovery at the same time, including nicotine. The transition from one benzo to another using topiramate is beyond the scope of this lecture, he may see me afterwards as it is off label.

ANCILLARY MEDICATIONS

- All FDA approved medications are to be used as PART of a comprehensive treatment program that includes and mutual support groups
- Buprenorphine and Naltrexone both show promise in multiple harm reduction studies
- Buprenorphine treatment may be initiated by any prescriber who completed special training required by the DATA 2000 (stay tuned for COVID driven changes

SUMMARY

The End!