



WEST VIRGINIA INTEGRATED BEHAVIORAL HEALTH CONFERENCE

Medication Assisted Treatment: Tools of the Trade

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Dr. James H. Berry

Objectives

- *The participant will be able to articulate how addiction is a disease.*
- *The participant will be able to discuss the rationale behind using medications to assist treatment.*
- *The participant will learn what medications are available and be able to confidently discuss these options.*



Overview

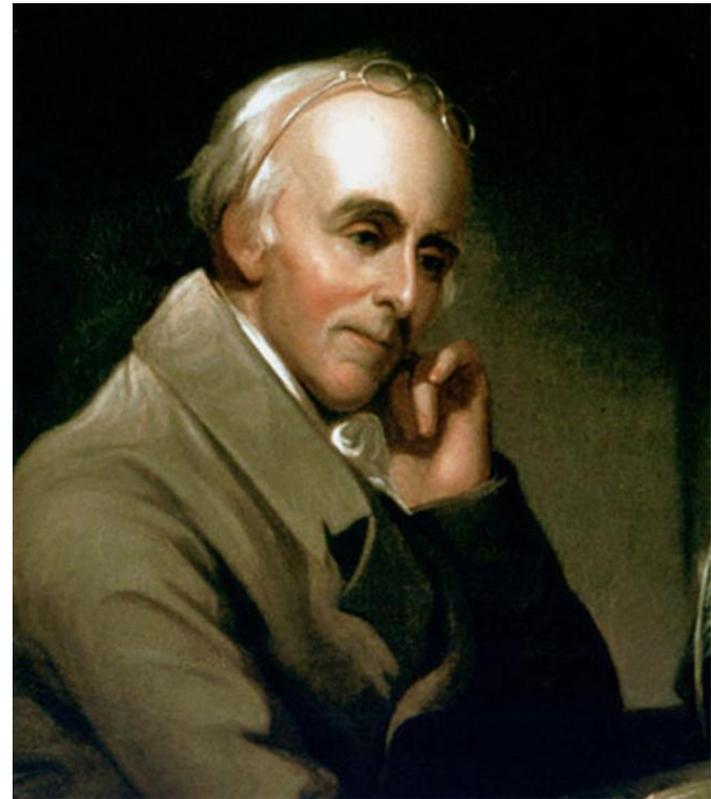
- Introduce the disease concept of addiction
- Define goals for using medications in SUD
- Describe intoxication and withdrawal patterns
 - Opioids
 - Alcohol
 - Nicotine
- Discuss management of above



Dis-Ease

“My observations authorize me to say, that persons who have been addicted to them, should abstain from them suddenly and entirely. 'Taste not, handle not, touch not' should be inscribed upon every vessel that contains spirits in the house of a man, who wishes to be cured of habits of intemperance...

habitual drunkenness should be regarded not as a bad habit but as a disease"



Chronic Disease

Percentage of Patients Who Relapse

TYPE I DIABETES



DRUG ADDICTION



HYPERTENSION



ASTHMA



Disease

- **Addiction** is a primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations.
- The disease is often progressive and fatal
- Characterized by
 - impaired control over use
 - preoccupation with the substance
 - use despite adverse consequences
 - distortions in thinking (e.g. denial)
- Symptoms may be continuous or periodic

Medications



Philosophy for Medication

- Treatment is often multi-*phasic*
 - Detox
 - Recovery
- Treatment is often multi-*disciplinary*
 - Psychiatrist, PCP, etc.
 - Therapist, clergy, etc.
 - PT, dietician, trainer, etc.
- Treatment is often multi-*dimensional*
 - Bio-psycho-social-spiritual
- Collaborate with the patient
- NO Miracles in pill form!



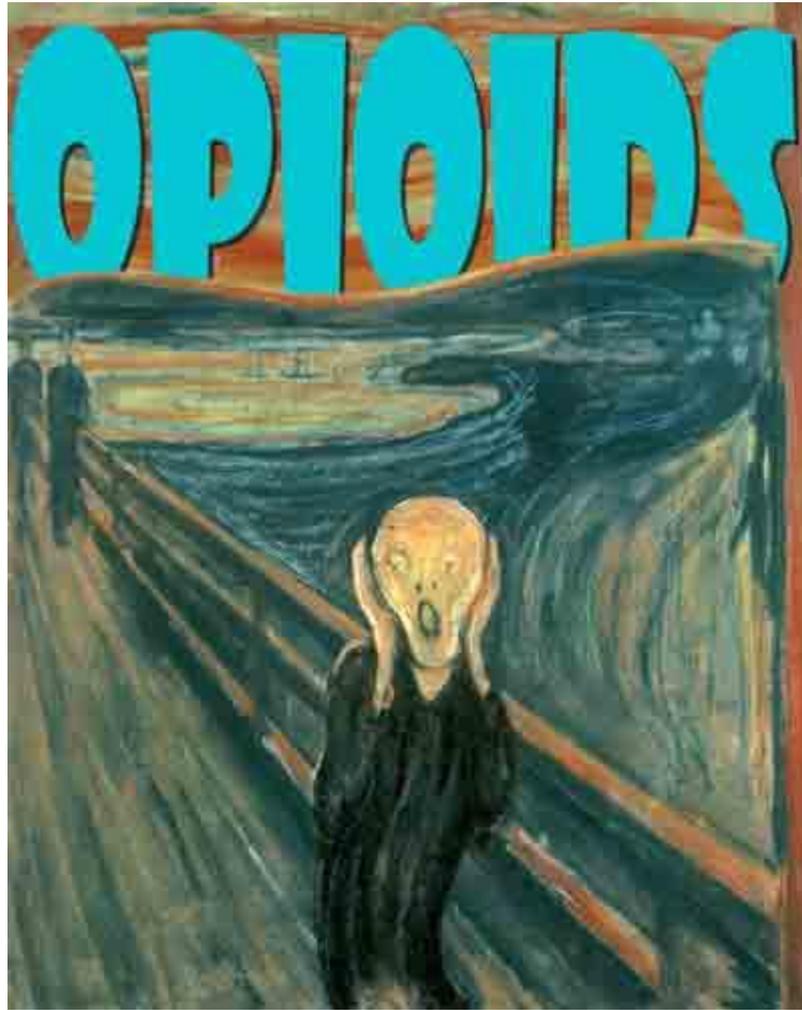
TOOL

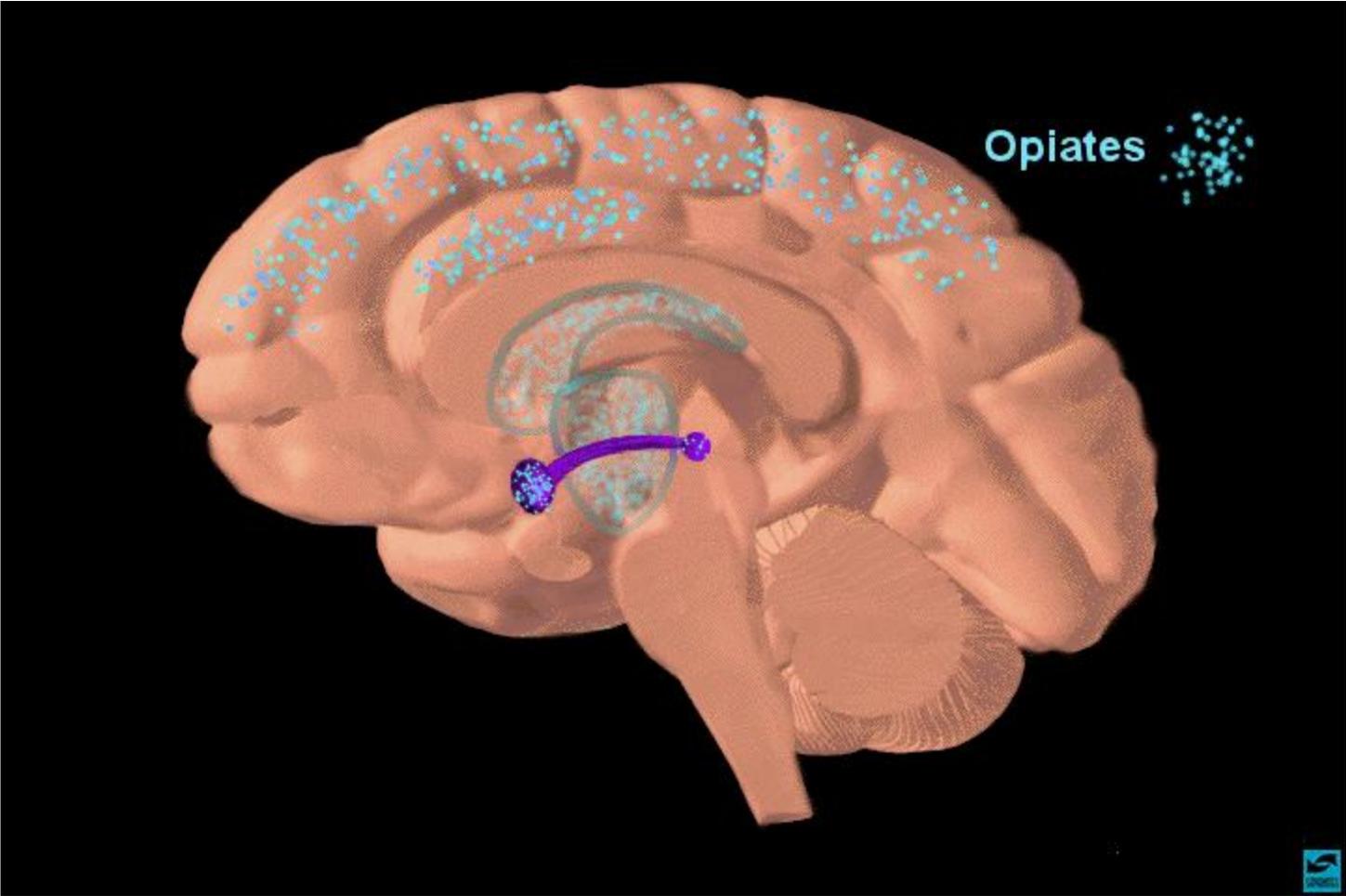


Goals for Medication

- Treat or prevent withdrawal
- Reduce urges/cravings to use
- Block the effects of a substance
- Diminish pleasure associated with use
- Associate discomfort with use
- Treat co-morbid disorders that may interfere with recovery process







Opioid Effects

- Near instantaneous euphoria/rush
- hits opioid receptors in the brain, a massive release of DA occurs in Ventral Tegmental Area (VTA) to Nucleus Accumbens
- feels relaxed, sedated, drowsy
- Brain stem effects: respiratory depression, vomiting



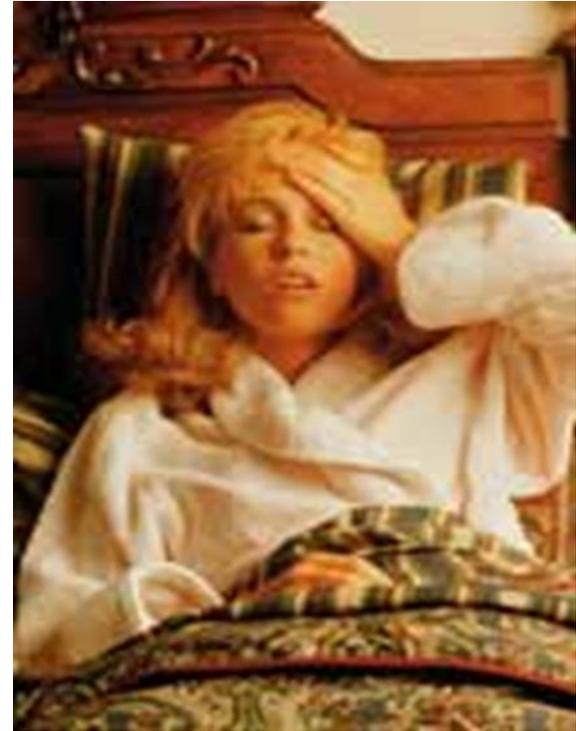
Opioid Toxicity

- Influenced by purity, loss of tolerance, alcohol/sedative mix
- clouded consciousness to coma
- Severe respiratory depression
- Constricted pupils
- Pulmonary edema
- Severe hypotension, cardiovascular collapse (hypoxia may lead to dilated pupils)
- Reversed by naloxone (narcan)



Opioid Withdrawal

- Effects begin within 4-24 hrs
- Typical sx's (flu-like and leaky):
 - nausea/vomiting,
 - cramps (abd & muscular),
 - sweating,
 - goose bumps/piloerection,
 - rhinorrhea, diarrhea, mydriasis
- Insomnia
- Typically NOT life-threatening



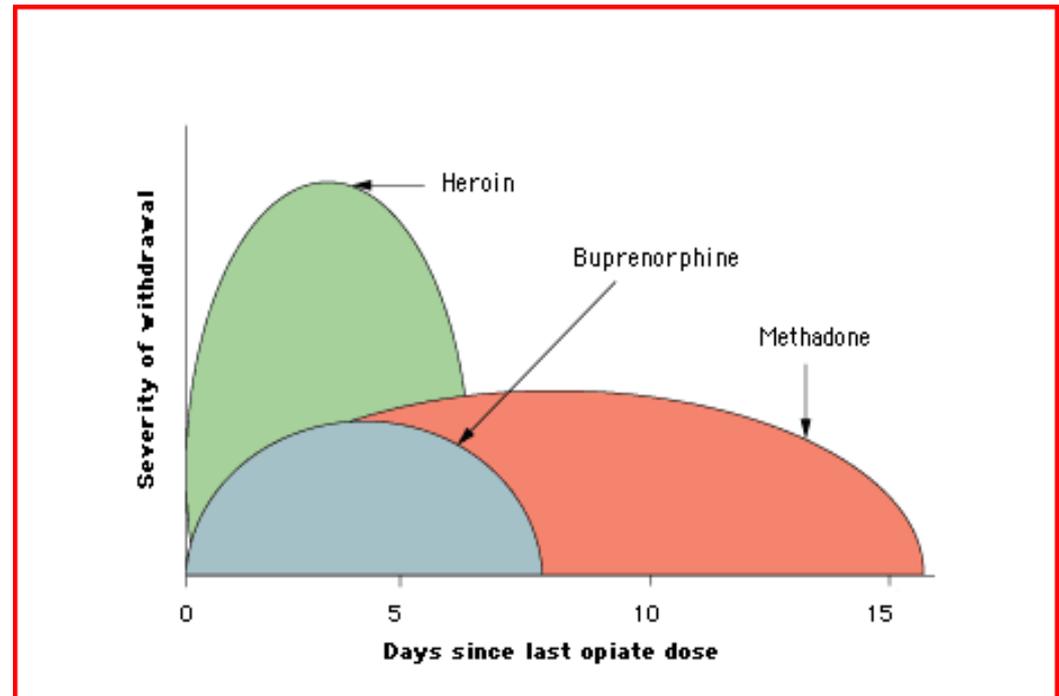
OPIATE WITHDRAWAL

Heroin

- short $\frac{1}{2}$ life
- 4-6h after last use

Methadone

- long $\frac{1}{2}$ life
- 24-36h after last use



Severity of opioid-withdrawal symptoms after abrupt discontinuation of equivalent doses of heroin, buprenorphine, and methadone Peak withdrawal symptoms are most severe after discontinuation of heroin. Such symptoms last longest with methadone, which has a somewhat later peak of severity. Buprenorphine has milder peak withdrawal symptoms than does methadone; the duration of symptoms is intermediate between those for methadone and those for heroin. Reproduced with permission from: Kosten, TR, O'Connor, PG. Management of drug and alcohol withdrawal. N. Engl J Med 2003; 348:1786. Copyright © 2003 Massachusetts Medical Society.

Opiate WD: Measurement

- Opiate WD scale (OWS)- 32 item
- Short Opiate WD scale (SOWS)- 10 item
- Clinical Opiate Withdrawal Scale (COWS)
 - Most recent
 - 11 item
 - Mild: 5-12; Moderate: 13-24; Moderately Severe: 25-36; Severe: >36



Opiate WD: Treatment

- Detoxification
 - or
- Maintenance
 - Methadone
 - Methadone Clinic
 - Buprenorphine
 - Office based



Detoxification from heroin is good for many things – but staying off heroin is not one of them.

- Walter Ling



Opiate WD: Detox

- Four major detoxification options:
 1. Opiate agonists
 2. Nonopioids
 3. Rapid
 4. Ultrarapid



Opiate WD: Agonist Detox

- General principle: substitute abused opiate with one that is tapered under supervision
- Methadone, Buprenorphine, Codeine
- 24-48 hr amt of opioid is estimated and begin substitute to alleviate withdrawal
- Taper over shortest period of time with least discomfort



Opiate Withdrawal: Supportive

- Bentyl 10mg qid for diarrhea
- Immodium 4mg; 1-2 q hr prn NTE 8qd
- Motrin 600mg one q 6 prn bone pain
- Compazine 10mg TID prn nausea
- Benadryl 25mg two q 6 prn nasal cong.
- Clonidine 0.01 to 0.2mg/kg; up to 1.2mg q d
- Check vitals; clonidine patch



Opiate WD: Rapid & Ultra-rapid Detox

- Rapid
 - Precipitate wd with antagonist
 - Follow with naltrexone maintenance and adjuvant meds (e.g. antiemetics, analgesics)
- Ultra-Rapid
 - Precipitate wd with antagonist
 - Under general anesthesia or heavy sedation
 - High cost and risk



Opioid Maintenance Treatment

- Dole and Nyswander introduced using methadone in 1960s
 - “Harm Reduction”
- Negative attitudes
 - “just substituting one drug for another”
- Involves stabilization of endogenous opioid system (Dole 1988)
- Decrease cravings and prevent withdrawal
- Engage in recovery and improve functioning



Opioid Maintenance Treatment

- Hope of most is to use as transition to no medication
- However, long term use is the norm
- GOAL: Get life back and avoid consequences of the disease!



Methadone Maintenance

- Schedule II
- Use is restricted to non-residential narcotic treatment facilities (Methadone Clinics)
- Pain relief is the only legitimate medical reason in the office setting



Methadone Maintenance

- Mu opioid agonist
- NMDA
- Federal regulations limit initial dose to 30mg and no more than 40mg on first day
- Tricky to start and stop
- Stabilization dose of 20-120mg daily w/ avg 60mg



Methadone Induction

- 6.7 times more likely to die than untreated heroin addicts (Caplehorn & Drummer, 1999)
- 42% of drug-related deaths occurred during first week (Zador & Sunjic 2000)
- Requires knowledge of steady-state pharmacologic principles (Drummer, Opeskin 1992)



Methadone Maintenance

- No established “ceiling dose”
- Dose may vary between people
- Metabolism
- Medications
 - Induce or inhibit CYP450
- Pregnancy
- Diet



Buprenorphine

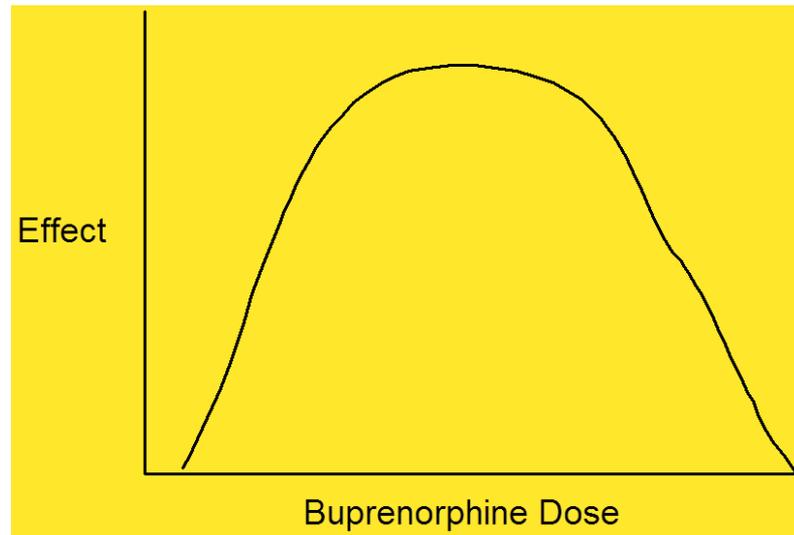
- Schedule III
- Partial agonist of mu receptor
- Drug Abuse Treatment Act of 2000: can prescribe any schedule III-V
- 2002 FDA approved for narcotic addiction tx
- Subutex (bup. only) & Suboxone (bup./naloxone)



Buprenorphine

- 2 & 8 mg SL tabs/film
- 10-16 mg usual daily dose (12 avg)
- Pros: lower abuse potential, far less respiratory depression (safer in OD), less physical dependence & milder w/d





Forms of Buprenorphine

- Suboxone Film[®] —buprenorphine/naloxone
- Buprenorphine Tablets – Generic
- Buprenorphine/naloxone Tablets – Generic
- Buprenex – IM/IV shot
- Probuphine – 6m implant



Naltrexone

- Opioid Antagonist
- 50-150mg day (Oral)
- 3 forms
 - Oral
 - Injection
 - Implant



ALCOHOL



COMPLICATIONS

- Alcoholism causes 100,000 deaths annually
- Alcoholics lose 12 years of their expected life span
- Alcohol intoxication is present in most cases of suicide, homicide, rape, and other acts of physical abuse
- Alcohol intoxication is responsible for nearly one-half of all fatal car accidents
- 15% - 25% Healthcare Budget
 - 90% of Liver Disease
 - 72% of Pancreatitis
 - 41% of Seizure Disorders
 - 13% of Breast Cancers



Domains of Pathology with Progressive Alcohol Dependence

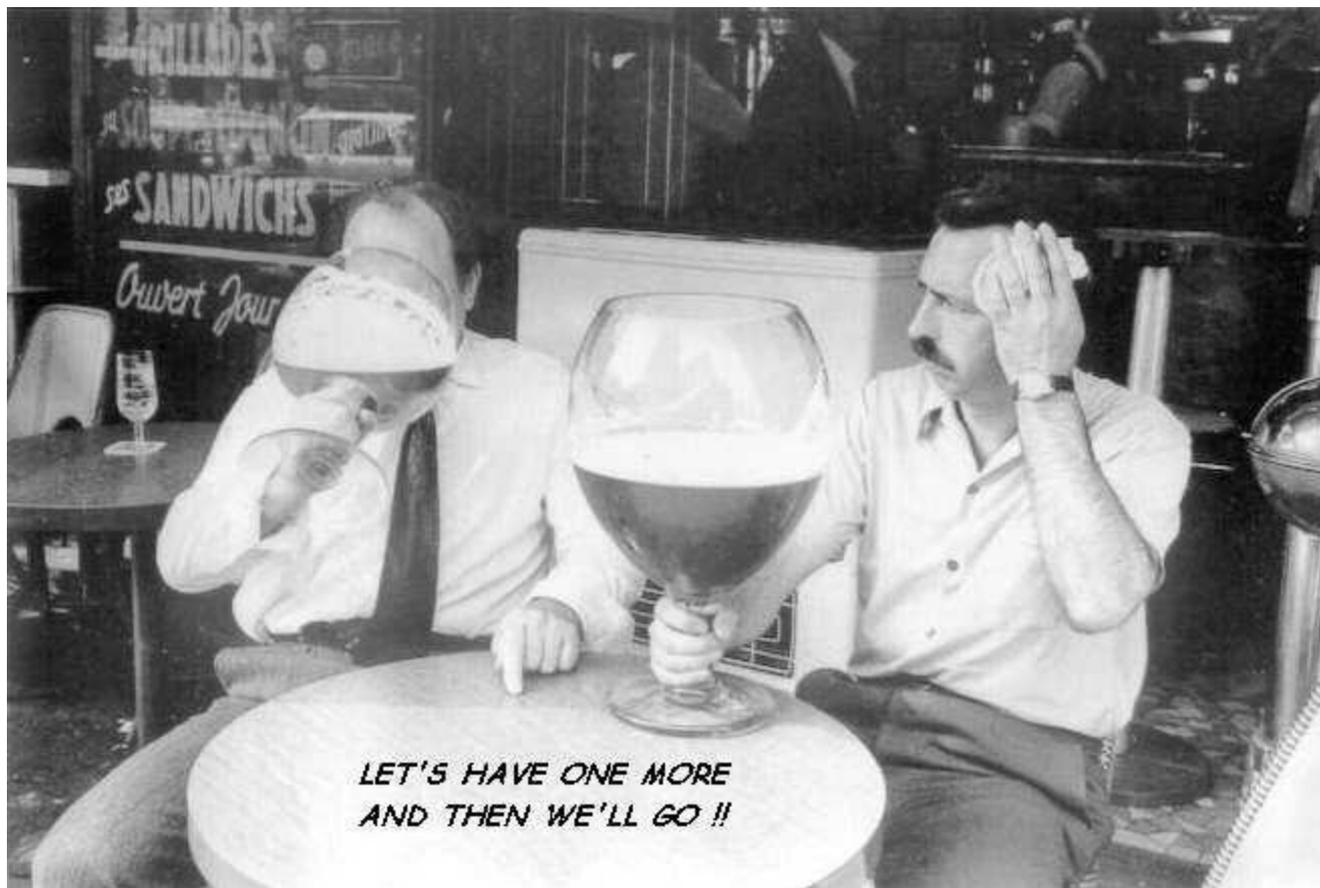
- Hepatic
- Cardiac
- Pancreatic
- Neurologic
- Psychiatric
- Oncologic



SCREEN

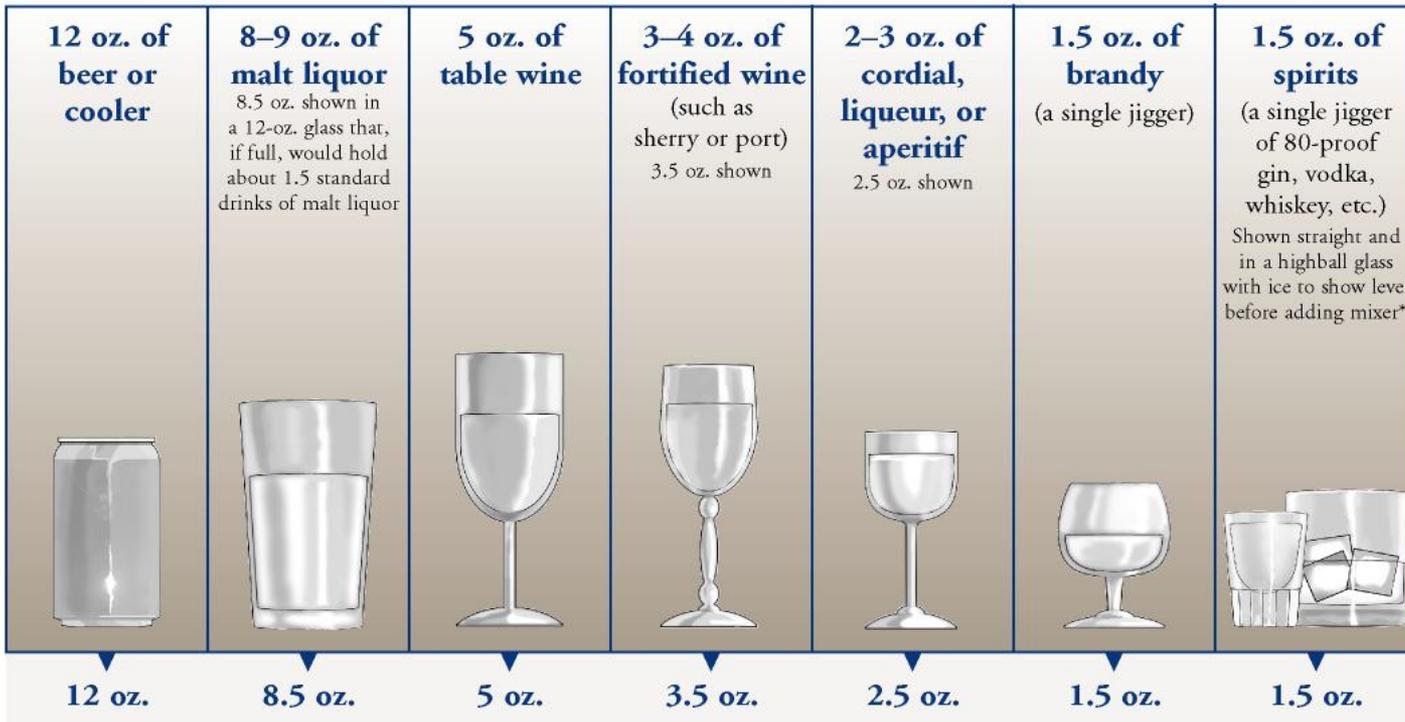
- “How much alcohol do you drink?”
- “How many days per week do you drink?”
- “On a day when you drink alcohol, how many drinks do you have?”





**LET'S HAVE ONE MORE
AND THEN WE'LL GO !!**

Standard Drink



Concentration-Effect Relationship

BAC [%]	Effects
0.02-0.03	Mood elevation. Slight muscle relaxation.
0.05-0.06	Relaxation and Warmth. Increased reaction time. Decreased fine muscle coordination.
0.08-0.09	Impaired balance, speech, vision, hearing, muscle coordination. Euphoria.
0.14-0.15	Gross impairment of physical and mental control.
0.20-0.30	Severely intoxicated. Very little control of mind or body.
0.40-0.50	Unconscious. Deep coma. Death from respiratory depression



AT-RISK DRINKING

	<u>Per Week</u>	<u>Per Occasion</u>
Men	>14 drinks	>5 drinks
Women	>7 drinks	>3 or 4 drinks
Elders	>7 drinks	>1 drink

(NIAAA Physicians Guide, 1995)



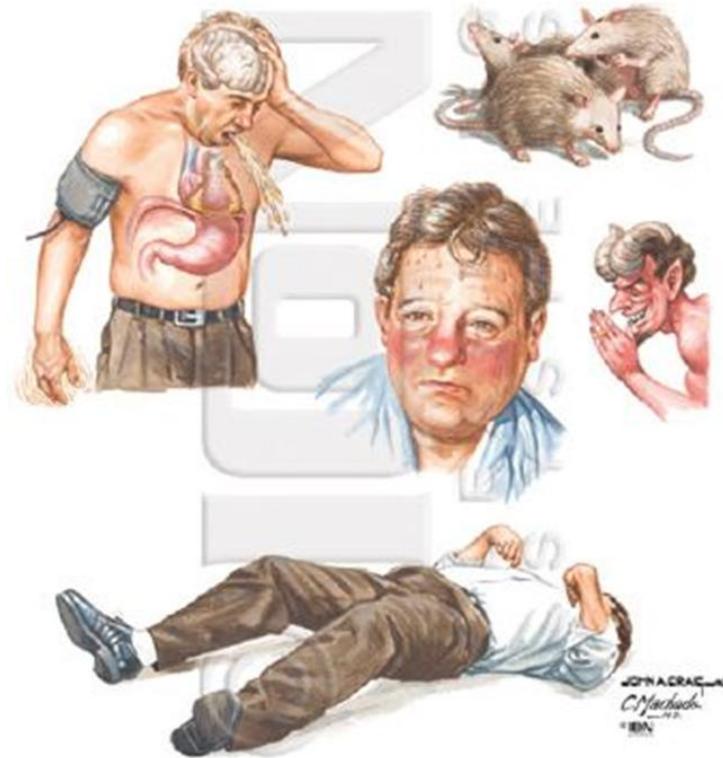
Alcohol Withdrawal

- **Stage 1:** Minor (early) withdrawal symptoms:
 - Onset 6-7 hours after last drink
 - Anxiety
 - Mild nausea
 - Decreased appetite
 - Sweating, a flushed face, and insomnia
 - Fluctuating tachycardia and hypertension
 - Mild disorientation



Alcohol Withdrawal

- Stage 2: Major withdrawal symptoms:
 - Onset 24-72 hours after the last drink
 - Moderate tremor and constant eye movement
 - Increase in psychomotor activity
 - Nausea and vomiting
 - Vivid hallucinations
 - Marked tachycardia and hypertension
 - Pulse > 120 and SBP > 160
 - Profound disorientation
 - Increased autonomic activity and fever
 - Seizures may occur



Delirium Tremens

- Stage 3 Symptoms:
 - 72 to 96 hrs after last drink
 - Fever
 - Sever tachycardia and hypertension
 - Delirium
 - Drenching sweats
 - Marked tremulousness
- Causes of death:
 - Cardiovascular
 - Infections
 - Aspiration
 - Pneumonia
 - Fluid and electrolyte



Withdrawal Management Overview

- Distinction between detox and treatment
- Outpatient vs. Inpatient
 - Medical Criteria
 - Absence of serious medical problems
 - No hx of withdrawal delirium, seizures, or psychosis
 - Abstinence Criteria
 - Agrees to abstinence and treatment
 - Agrees to random testing
 - Psychosocial Criteria
 - Support of sober family and friends



Withdrawal Management

- Supportive Care
 - Fluids
 - Mg, Thiamine, MVI, folic acid, lytes
 - Reassurance
 - Respect



ALCOHOL WD Management

- Benzos
- Anticonvulsants (AEDs)
- Barbiturates
- Neuroleptics
- Sympatholytics
- ETOH

=>Benzos are the preferred method b/c prevent stage 2,3 withdrawal, partially protect against seizures, easy transition, and rapid induction



RECOVERY



Shown at Funny-games.biz



Naltrexone (Revia)

- Opiate antagonist
- Works best in motivated patients with a shorter hx who describe intense craving
- Positive response w/i 7-10d (DC if none)
- Contraindicated in acute hepatitis or liver failure (or pts taking opiates)
- Good Evidence: Reduces relapse and drinking days
- Some Evidence: Reduces cue-induced cravings and enhances abstinence
- Safe if relapses



Acamprosate (Campral)



- FDA approved Sept 2004
- Made from taurine
- Dose: 333mg two pills three times a day
- Targets Relapse Prevention
 - Good evidence for enhancing abstinence
 - Minimal evidence for craving
- Most Common Side Effects: Diarrhea, rash.



Disulfiram (Antabuse)

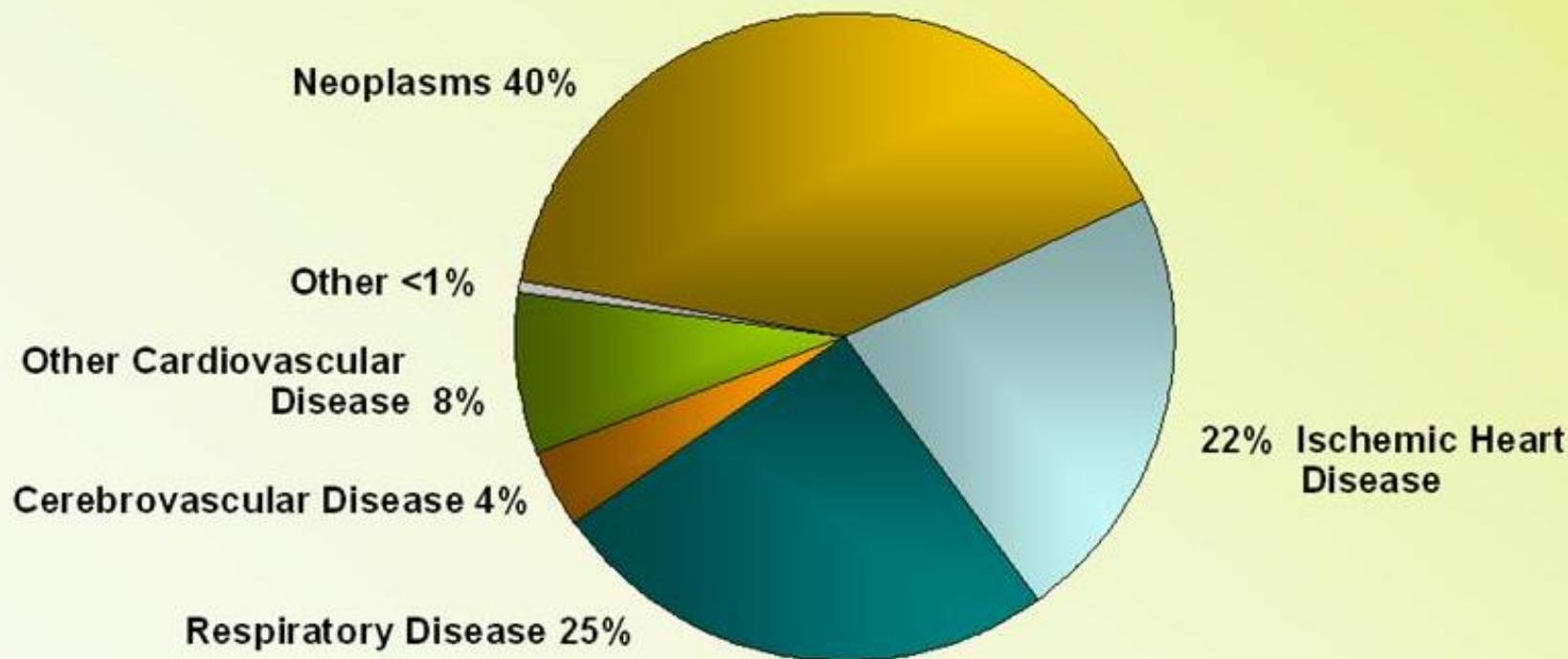
- Inhibits enzyme aldehyde dehydrogenase
- Leads to a very bad experience
- 250mg orally
- Works best in older, stable, motivated pts with close follow-up



Nicotine



Smoking-Related Disease Mortality*



* Percentage of deaths attributable to specific smoking-related diseases, 1997 – 2001 based on estimates using smoking-attributable fraction and relative risk estimations

- More than 399,000 US deaths annually are attributable to cigarette smoking
- Every eight seconds, someone dies from tobacco use

1. Adapted from CDC. *MMWR*. 2005;54:625-628. 2. WHO. Fact Sheets Smoking Statistics. http://www.wpro.who.int/media_centre/fact_sheets/fs_20020528.htm. Accessed on May 18, 2006.

Cessation Statistic

- 70% of smokers want to quit
- 81% of smokers have tried to quit at least once
- 35% try to quit each year
- It may require ~10 attempts to quit successfully
- Only 7% of smokers attempting to quit remain smoke free at one year



Addictive Aspects of Nicotine

- The addictive characteristics of nicotine are believed to be the result of its rapid effects on dopamine release in the brain
- Like other psychoactive drugs (cocaine, heroin, or alcohol) nicotine serves as a reinforcer of its use
- Inhaled nicotine reaches the brain within 10 seconds
- Nicotine's $T^{1/2}$ is approximately 2 hours



Withdrawal Symptoms

<u>Symptom</u>	<u>Duration</u>	<u>%</u>
• Irritability/aggression	<4 wks	50
• Depression	<4 wks	60
• Restlessness	<4 wks	60
• Poor concentration	<2 wks	60
• Increased appetite	>10 wks	70
• Light-headedness	<48 hrs	10
• Night-time awakening	<1 wk	25
• Craving (not in DSM)	>2 wks	70

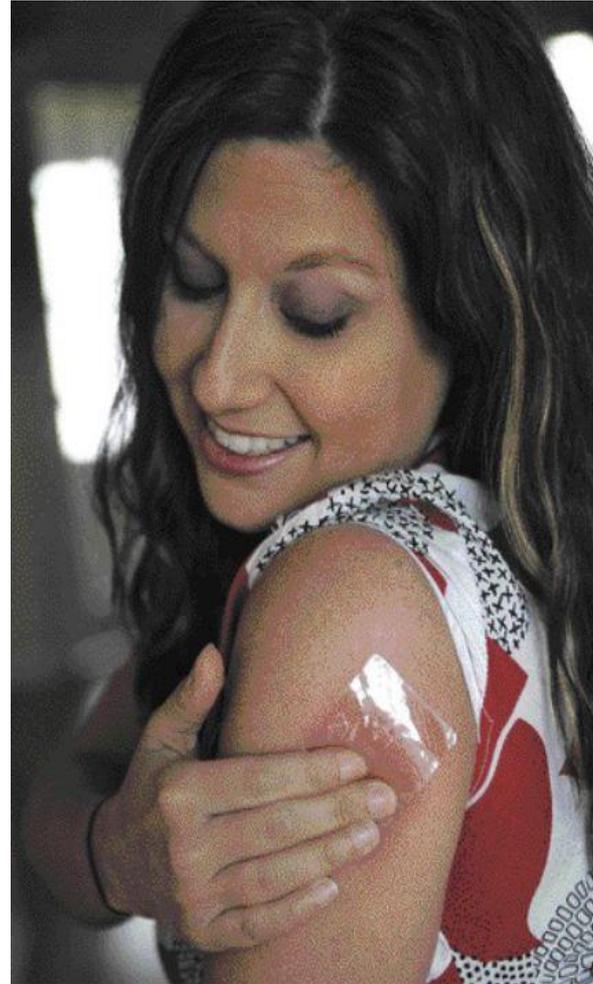
Nicotine Polacrilex Gum

- Improves smoking cessation rates
- Poor compliance
- Available OTC (2 mg & 4 mg)



Nicotine Patch

- 2 to 3 times more effective than placebo
- High compliance
- Retains effectiveness with minimal support
- Available OTC



Nicotine Inhaler



- Produces a nicotine vapor when air is drawn through tube into mouth
- Nicotine absorption is in mouth and throat
- Nicotine levels peak in 20 minutes, approach levels of nicotine polacrilex



Nicotine Nasal Spray

- More rapid rise in nicotine levels than other NRT: Peaks within 10 minutes
- Potential for dependence liability
- May be best suited for higher levels of nicotine dependence



Nicotine Polacrilex Lozenge

- Use is similar to gum
- Use 2mg if you smoke after 30 minutes of waking
- Use 4mg if you smoke within 30 minutes of waking
- Move side to side for no more than 30 minutes
- Don't drink or eat 15 minutes before using (pH)
- No more than 5 lozenges in a 6hr period



Zyban, Bupropion SR



- Antidepressant believed to exhibit both dopaminergic and noradrenergic activity
- Can use safely while smoking and preparing to quit
- Begins to affect dopamine reward pathway cycle while still smoking
- May provide help with dysphoria after nicotine withdrawal and tends to be weight neutral



Chantix, Varenicline tartrate

- Only the second nicotine-free smoking-cessation drug to gain FDA approval
- Dosing is twice-daily for 12 weeks, a period that can be doubled in patients who successfully quit to increase the likelihood they remain smoke-free
- The most common adverse side effects include: nausea, headache, vomiting, gas, insomnia, abnormal dreams, and a change in taste perception
- Cost is \$125 per month

<http://www.lungusa.org/site/pp.asp?c=dvLUK900E&b=33566>



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Tobacco consumption and related illnesses represent a great human and financial cost to West Virginia and its residents. With the help of health care providers, we can offer a healthier lifestyle to thousands of West Virginians and improve the future wellness of our state. One of the most important actions that West Virginia health care providers can take for their patients is to increase their awareness of the West Virginia Tobacco Quitline.

Since July 1, 2000, more patients are visiting their physician to obtain tobacco cessation advice. Your professional referral to the West Virginia Tobacco Quitline can be monumental in your patient's decision to enlist support for a smoking cessation plan.

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Questions?

