

# **Substance Abuse**

**Herbert Kleber, M.D.**

**Part 1**

# Key Points

- Addiction is both a chronic relapsing disorder & a treatable condition, comparable to adult onset diabetes & hypertension
- There is no one treatment for addiction – some individuals recover with behavioral interventions & 12-step programs, while others require medications on an acute or chronic basis
- The most effective medications currently are for treatment of alcohol or opioid dependence. There are no approved medications for stimulant or marijuana dependence

Outline  
Substance Abuse  
Herbert D. Kleber, M.D.

- I. Epidemiology
  - a. Social problems and their cost
  - b. Magnitude of problem
  - c. Substance related health effects
- II. Substance Related Drug Problems
  - a. Problems by drug category
  - b. Diagnosis of substance abuse/dependence
  - c. Definitions of tolerance and withdrawal
- III. Comorbidity - Extent and by Substance
- IV. Drugs & Adolescence
- V. Making an Addict
  - a. Addicting drug
  - b. Susceptible person
  - c. Mechanism to bring them together
- VI. Diagnostic Issues
- VII. Pharmacological Treatment – Acute & Chronic
  - a. Alcohol
  - b. Opioids
  - c. Stimulants
  - d. Nicotine
- VIII. Ethical Issues

# Pre-Lecture Exam

## Question 1

- 1. Which of the following statements is false:**
  - A.** Physical dependence is synonymous with addiction.
  - B.** One can be addicted without being physically dependent.
  - C.** Once a patient has met criteria for Substance Dependence, they should not be diagnosed in the future with Substance Abuse.
  - D.** A critical feature of addiction is compulsive use in spite of harm.

## Question 2

- 2. Which of the following statements is false:**
- A.** Psychiatric disorders can cause substance abuse.
  - B.** Substance abuse can cause psychiatric disorders.
  - C.** If both substance abuse and a psychiatric disorder are present, treating the psychiatric disorder is usually not necessary.
  - D.** Treating an underlying psychiatric disorder usually does not adequately treat the substance abuse.

## Question 3

- 3. The most common comorbid psychiatric diagnosis in patients with substance abuse is:**
- A. Schizophrenia**
  - B. Antisocial Personality Disorder**
  - C. Anxiety Disorder**
  - D. Major Depression**

## Question 4

- 4. Which one of the following is false:**
- A.** Cocaine decreases negative symptoms in schizophrenics.
  - B.** When cocaine free, schizophrenics have more negative symptoms.
  - C.** Chronic cocaine use increases depression in schizophrenics.
  - D.** Chronic cocaine decreases positive symptoms of schizophrenia.

## Question 5

- 5. Which of the following are considered “Gateway Drugs”?**
- A. Alcohol**
  - B. Marijuana**
  - C. Nicotine**
  - D. A & C only**
  - E. A, B, & C**



## Question 6

- 6. Adolescent substance abuse is associated with:**
- A. Increased school dropout**
  - B. Increased depression and suicidality**
  - C. Premature involvement in sexuality**
  - D. All of the above**

## Question 7

- 7. The proportion of users who ever became dependent is as follows (from high to low):**
- A.** Nicotine, alcohol, heroin, cocaine, marijuana.
  - B.** Alcohol, nicotine, cocaine, heroin, marijuana.
  - C.** Nicotine, heroin, cocaine, alcohol, marijuana.
  - D.** Nicotine, alcohol, marijuana, cocaine, heroin.

## Question 8

- 8. Which of the following is not used as a maintenance agent in heroin addiction:**
- A. Methadone
  - B. Clonidine
  - C. LAAM
  - D. Naltrexone
  - E. Buprenorphine

## Question 9

- 9. Which category of medications is not yet available for treatment of heroin addiction:**
- A. Agonists**
  - B. Antagonists**
  - C. Partial agonists**
  - D. Anti-craving agents**
  - E. Anti-withdrawal agents**

## Question 10

- 10. Which of the following statements are true:**
- A.** Naltrexone blocks the effects of alcohol.
  - B.** Drinking while on naltrexone can make one very ill.
  - C.** Benzodiazepines are the usual agents used for alcohol withdrawal.
  - D.** All of the above

# The Leading Causes of Disability in the World, 1990

		Total (Millions)	Percent of Total (%)
	All Causes	473	100
1	Unipolar Major Depression	51	11
2	Iron-Deficiency Anemia	22	5
3	Falls	22	4
4	Alcohol Use (+ other drugs)	16	3
5	Chr. Obstructive Pulmonary Dis.	15	3

# Total Dollars (Billions) Spent or Lost Due to Alcohol and Drug Disorders, 1990

	Total AD	% of Total	Mental Health	Alcohol	Drug
AIDS/Fetal Alcohol	\$ 8.4	2.7	\$ 0.0	\$ 2.1	\$ 6.3
Crime	67.8	21.6	6.0	15.8	46.0
Loss of Productivity	157	50	75	370	12
Health Care Costs	80.8	25.8	67.0	10.6	3.2
Dollars Lost	313.6	100.0	147.9	98.7	66.9

# Categories of Drugs

- Depressants
- Stimulants
- Opiates
- Cannabinoids
- Hallucinogens
- Phencyclidine (PCP)
- Inhalants/solvents
- Others



## **\*Magnitude of Problem (USA)**

- Nicotine - over 50 million dependent
- Alcohol - 12 - 18 million alcoholics and problem drinkers
- M.J. - over 3 million dependent
- Cocaine - 2-3.5 million dependent
- Heroin - 800,000 - 1 million dependent
- Prescription opioids – 2-4x heroin number

# Health Effects of Drugs

## (1) Infections

- Hepatitis (heroin, cocaine, alcohol)
- AIDS (heroin, cocaine, inhalants)

## (2) Gastrointestinal Pain and Bleeding

- Ulcers (alcohol)

## (3) Brain and Peripheral Neuron Damage

- Dementia (alcohol, stimulants, inhalants)

## (4) Cardiovascular

- Stroke and heart attack (stimulants)

# \*Continuum of Drug Use

- Initiation/intoxication
- Harmful use/abuse
- Dependence/withdrawal
- Relapse and craving
- Recovery and persisting deficits

# Definitions

- Psychological dependence/addiction
- Physical dependence/addiction
- Tolerance
- Dependence syndrome

# Considerations Each Clinician is to Review

- Overdose/toxic reaction
- Abstinence syndrome/state of withdrawal
- Organic Brain Syndrome (OBS)
- Psychosis
- Depression/anxiety

# \*Clinically Significant Drug Problems by Category

	Panic	Flashbacks	Overdose	Psychosis	OBS	Withdrawal
Depressants	-	-	++	++	++	++
Stimulants	+	-	+	++	+	++
Opiates	-	-	++	-	+	++
Cannabinoids	+	+		+	+	+
Hallucinogens	++	++	+	-	+	-
Solvents	+	-	+	-	++	-
PCP	+	?	++	a	a	?
OTC	-	-	+	-	++	-

+ = the syndrome (eg., panic) is likely to be seen with the drug  
 ++ = the syndrome can be very intense  
 a = absence of syndrome

# MAJOR SUBSTANCE DIAGNOSES (I)

<u>Substance</u>	<u>Intoxication</u>	<u>Withdrawal</u>	<u>Persisting</u>	<u>Abuse</u>	<u>Depend</u>
Alcohol	X	X	X	X	X
Amphetamine	X	X		X	X
Caffeine	X				
Cannabis	X	X		X	X
Cocaine	X	X		X	X
Hallucinogen	X		X	X	X

# Substance Intoxication

- Reversible syndrome
- Maladaptive behavior (anger, depression, cognitive impairment)
- Not due to medical condition



# Substance Abuse (DSM-IV)

....made only in the absence of dependence or history of dependence

One or more of the below:

- Failure to fulfill major role obligations
- Use in hazardous situations
- Legal problems
- Use despite problems

# \*Substance Dependence

- Maladaptive pattern of use including 3 or more of the below in the same 12 month period:
  - With tolerance or withdrawal
  - More use than intended
  - Unsuccessful attempts to cut down
  - Reduce other activities
  - Great deal of time spent on drug use
  - Continued use despite adverse consequences

# Tolerance

- Occurs after prolonged (usually weeks), regular (daily), heavy use
- Increased amounts for desired effect
- Diminished effects

# Withdrawal

- Requires regular (at least daily) use for prolonged period
- Specific physiological syndromes by drug
- Substance taken to avoid syndrome
- Not due to general medical condition

## **\*Possible Relation Between Substance Use and Psychiatric Disorder**

- Psychiatric disorder causes substance abuse
- Substance abuse causes psychiatric disorder
- Both caused by common underlying disorder
- Both occur independent of the other

# Lifetime Comorbid Substance Use Disorder Prevalences - ECA (I)

	Any Substance		Alcohol Diagnosis		Other Drug Diagnosis	
<b>Schizophrenia</b>	<b>47.0%</b>	<b>4.6</b>	<b>33.7%</b>	<b>3.3</b>	<b>27.5%</b>	<b>6.2</b>
<b>Antisocial PD</b>	<b>83.6%</b>	<b>29.6</b>	<b>73.6%</b>	<b>21.0</b>	<b>42.0%</b>	<b>13.4</b>
<b>Anxiety Disorder</b>	<b>23.7%</b>	<b>17.9</b>	<b>17.9%</b>	<b>1.5</b>	<b>11.9%</b>	<b>2.5</b>
<b>Phobia</b>	<b>22.9%</b>	<b>1.6</b>	<b>17.3%</b>	<b>1.4</b>	<b>11.2%</b>	<b>2.2</b>

# Lifetime Comorbid Substance Use Disorder Prevalences - ECA (II)

	Any Substance		Alcohol Diagnosis		Other Drug Diagnosis	
<b>Panic Disorder</b>	<b>35.8%</b>	<b>2.9</b>	<b>28.7%</b>	<b>2.6</b>	<b>16.7%</b>	<b>3.2</b>
<b>OCD</b>	<b>32.8%</b>	<b>2.5</b>	<b>24.0%</b>	<b>2.1</b>	<b>18.4%</b>	<b>3.7</b>
<b>Bipolar I</b>	<b>60.7%</b>	<b>7.9</b>	<b>46.2%</b>	<b>5.6</b>	<b>40.7%</b>	<b>11.1</b>
<b>Maj Dep</b>	<b>27.2%</b>	<b>1.9</b>	<b>16.5%</b>	<b>1.3</b>	<b>18.0%</b>	<b>3.8</b>

# Categories of Drugs Most Likely to Produce Psychopathology

- Stimulants
  - all forms of amphetamines and all forms of cocaine
- Depressants
  - alcohol
  - benzodiazepines
  - barbituates
  - carbamates
    - (i.e. meprobamate)



# \*Substance-Induced Disorders

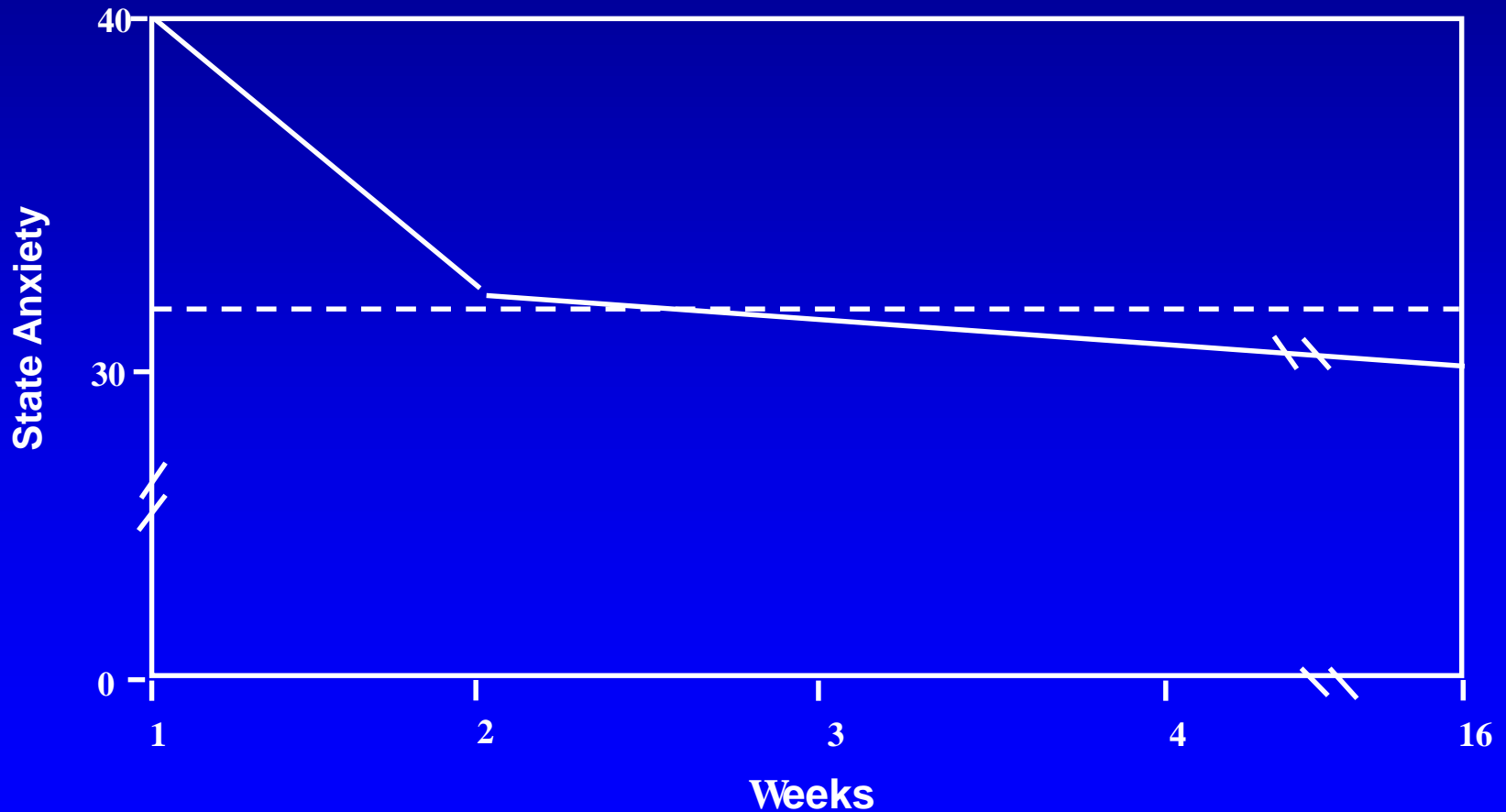
- Development of a substance-specific syndrome which is usually reversible.
- Symptoms are:
  - not due to general medical condition
  - not better accounted for by another mental disorder
- There is evidence obtained from:
  - history
  - physical exam
  - toxicologic analysis of body fluids

# **\*Drugs of Abuse are Known to Exacerbate Prior Psychiatric Disorders**

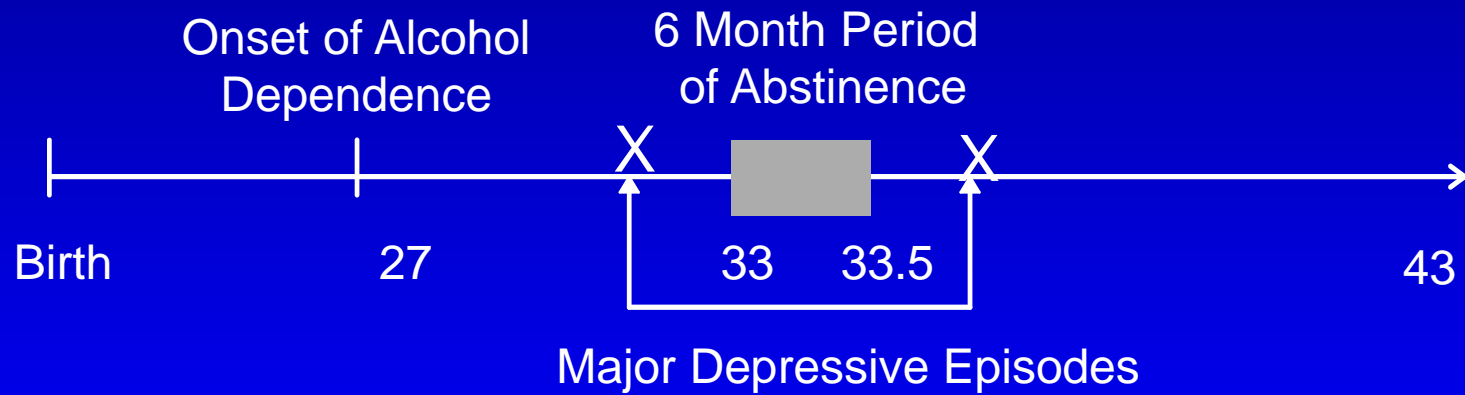
*by increasing:*

- Mood swings
- Anxiety
- Paranoia
- Hallucinations
- Confusion

# X Spielburger State Anxiety During Alcohol Withdrawal



# Time Line Example



# \*Psychostimulants and Negative Symptoms of Schizophrenia

- Negative symptoms reduced in laboratory studies using amphetamines (0.25mg/Kg/day)
- Fewer negative symptoms in ER presentations of cocaine abusing schizophrenics
- At four-week cocaine free follow-up, more negative symptoms in cocaine abusing schizophrenics
- Chronic cocaine increases anxious, agitated depression in schizophrenics

# \*Psychostimulants and Positive Symptoms of Schizophrenia (I)

- More paranoia (Brady, Satel)
- Hallucinations specifically intensified (Serper)
- Global psychotic symptoms may be lower in stimulant abusing schizophrenics, when abstinent

# \*Psychostimulants and Positive Symptoms of Schizophrenia (II)

- Stimulant abusing schizophrenics hyposensitive to amphetamine effects (Kornetsky 1976)
- Psychotomimetic cocaine effects last hours to days; may relate to sleep deprivation
- Regular stimulant use for over 6 years associated with psychosis induction (McLellan 1979)

## \*SUBSTANCE-INDUCED DISORDERS (I)

	<u>Delirium</u>	<u>Dementia</u>	<u>Amnestic</u>	<u>Psychotic</u>
<b>Alcohol</b>	I/W	P	P	I/W
<b>Amphetamine</b>	I			I
<b>Caffeine</b>				
<b>Cannabis</b>	I			I
<b>Cocaine</b>	I			I
<b>Hallucinogens</b>	I			I

I= intoxication, W= withdrawal



## \*SUBSTANCE-INDUCED DISORDERS (II)

	<u>Mood</u>	<u>Anxiety</u>	<u>Sex</u>	<u>Sleep</u>
Alcohol	I/W	I/W	I	I/W
Amphetamine	I/W	I	I	I/W
Caffeine		I		I
Cannabis	I	I		
Cocaine	I/W	I	I	I/W
Hallucinogen	I	I		

## \*SUBSTANCE-INDUCED DISORDERS (III)

	<u>Delirium</u>	<u>Dementia</u>	<u>Amnestic</u>	<u>Psychotic</u>
Inhalant	I	P		I
Nicotine				
Opioid	I			I
PCP	I			I
Sedative	I/W	P	P	I/W
Other	I/W	P	P	I/W

## \*SUBSTANCE-INDUCED DISORDERS (IV)

	<u>Mood</u>	<u>Anxiety</u>	<u>Sex</u>	<u>Sleep</u>
Inhalant	I	I		
Nicotine				
Opioid	I		I	I/W
PCP	I	I		
Sedative	I/W	W	I	I/W
Other	I/W	I/W	I	IW

# \*Gateway Drugs and Later Dependence

- Alcohol, nicotine, marijuana
- Use before age 15
- Earlier use more likely to result in dependent young adults
- Risk of dependence varies by drug used

# \*Normal Growth and Development and Substance Abuse

- Hormonal control: growth hormone, testosterone
- Drugs disrupt hormone release/effects
- Adolescent struggle for independence
- Pseudoindividuation of drug abuse
- Experimentation vs. dependence on drugs

# **\*Drug Abuse and Adolescent Development**

- Drug use as integral to growing up
- Premature involvement in work and sexuality
- Deviant behavior and crime
- Poor social integration and education
- Cognitive processes disrupted

# **\*Adolescent Social Disruption With Drug Abuse**

- Early family formation and divorce
- Increased stealing
- Reduced job stability
- Increased high school dropout
- Increased depression and suicidality

# Adolescent Social Forces in Hard Drug Use

- Not peer pressure
- Distress and alienation
- Vary by type of drug (alcohol vs. cocaine)



# **\*It takes 3 things to make an addict**

- Addicting drug
- Susceptible person
- Mechanism to bring them together

## \*Addicting drugs

Drug	Proportion of users that ever became dependent
Nicotine	32%
Heroin	23%
Cocaine	17% - 22%
Alcohol	15%
Marijuana	9%
Anxiolytics	9%

# \*Susceptible Person

- Genetic issues
- Psychological issues
- Psychosocial issues

# \*Mechanism to Bring Drug/person Together

- Availability - physical, economic, psychological, legal status
- Role of poverty

# Effective Identification of Substance Use Disorders

- Recognize prevalence problem
- Drop stereotypes
- Always screen for disorders
- Corroborate results

# **M.A.S.T.**

## **Michigan Alcoholism Screening Test**

- 25 item self-administered questionnaire
- Self-report of alcohol (and perhaps drug) problems
- Paper and pencil test
- Helpful, but not diagnostic

# \*CAGE - AID

- Have you felt you ought to **C**ut down on your drinking or drug use?
- Have people **A**nnoyed you by criticizing your drinking or drug use?
- Have you ever felt bad or **G**uilty about your drinking or drug use?
- Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover (**E**ye-opener)?

*(Brown, R.L., & Rounds, L.A. (1995). Conjoint screening questionnaires for alcohol and other drug abuse: Criterion validity in a primary care practice. Wisconsin Medical Journal, 94, 135-140)*

# **\*Sharing the Diagnosis (Confrontation or Intervention)**

- Give specific findings
- Remember patient is responsible
- Watch for signs of denial
- Repeat as needed



# \*Stimulant Intoxication (I)

- Euphoria
- Agitation/retardation
- Weakness, respiratory depression
- Chest pain, cardiac arrhythmia
- Confusion, seizures, coma
- Dystonias, dyskinesias

## \*Stimulant Intoxication (II)

- Tachycardia
- Pupillary dilation
- Elevated blood pressure
- Perspiration/chills
- Nausea/vomiting
- Weight loss

# \*Opioid Intoxication

- Pupillary constriction
- Drowsiness
- Slurred speech
- Impaired attention

# \*Sedative and Alcohol Intoxication

- Maladaptive behavior (aggression/depression)
- Slurred speech/incoordination
- Nystagmus/unsteady gait
- Impaired attention (stupor)

# \*Hallucinogen Intoxication

- Perceptual changes (intensified, depersonalization)
- Maladaptive behavior (paranoia, anxiety, ideas of reference)
- Pupillary dilation, blurred vision
- Tachycardia, sweating, tremors
- Incoordination

# Optimize Levels of Physical Functioning

- Careful physical examination
- Appropriate detoxification procedures when needed
- Efforts to reverse physical pathology

# Detoxification

## for Depressants, Stimulants, and Opiates

- Physical exam
- Educate, reassure
- Vitamins, etc.
- Meds?

# Rehabilitation for Substance-Use Disorders

- Use best data
- Establish realistic goals
- Change is the patient's responsibility
- Use all resources
- Agree on goals



# Maximize Motivation for Abstinence

- Lectures
- Discussion groups with patients
- Discussion groups with family members
- Using counselors in recovery
- Self-help groups
- Motivational Enhancement Therapy (MET)

# Rebuild a Life Without Substances

*Substances have been a very important part of life and are very difficult to give up.*

*Lectures and discussion groups to talk about issues.*

- Appropriate use of free time
- Interaction with relatives and friends now that you are sober
- Appropriate interaction with or avoidance of substance-using friends
- Saying no to substances when offered (refusal skills)

# \*Relapse Prevention

- Avoid high risk situations
- Anticipate minor relapses
- Recovering from relapses
- Identify triggers

# Aftercare

- Lessons learned can be reinforced
- Provides opportunity to apply knowledge to everyday situations

# \*Recovery from Dependence

- Early remission - no symptoms for one to 12 months
- Full remission - no symptoms for one year
- On agonist therapy (e.g., methadone)
- In controlled environment (e.g., T.C.)
- Relapse vs. slip

# Treatment of Intoxication

- Hallucinogens - benzodiazepines
- Stimulants - benzodiazepines, haloperidol

# \*Stimulant Relapse Prevention Investigational Agents

- Antidepressants
  - tricyclics
  - serotonin reuptake inhibitors
- Anti-epileptics (mood stabilizers)
  - Topiramate
- Dopamine agonists
- Disulfiram
- Modafinil
- Vaccines - antibodies against cocaine

# **\*Possible Medications**

## *For Opiate Rehabilitation*

- Methadone
- LAAM
- Buprenorphine
- Naltrexone



# **\*Possible Medications**

## *For Alcohol Rehabilitation*

- Disulfiram
- Naltrexone
- Serotonin re-uptake inhibitors
- Acamprosate

# Medical Disorders and Symptoms Mimicked by Substance Abuse

- Intoxication: thyroid, brain dysfunction
- Withdrawal:
  - a) metabolic delirium
  - b) non-specific symptoms; fatigue, weakness, nausea, diarrhea

# Basic Pharmacology

- Medications and abused drugs affect multiple organs in body
- Neuron receptors altered by abused drugs
- Neuron receptors bind medications to reverse abnormalities induced by abused drugs
- Metabolism by liver - damaged by abused drugs
  - impair efficacy of medications

# Pharmacotherapy

- Alcohol and sedatives
- Opioids – heroin & prescription opioids
- Stimulants - cocaine/amphetamines
- Nicotine
- Hallucinogens

# \*Pharmacotherapy Targets

- A. Overdose reversal (flumazenil or naloxone)
- B. Detoxification (chloridiazepoxide)
- C. Relapse Prevention
  - Substitution (methadone)
  - Blockade (naltrexone for opioids)
  - Aversion (disulfiram)
  - Anti-craving (naltrexone for alcohol)

# \*Reversal of Overdoses

- Stimulants - benzodiazepines  
- haloperidol
- Opioids - naloxone “IV drip”
- Benzodiazepines - flumazenil “IV drip”
- Hallucinogens - benzodiazepines

# \*Detoxification Principles

- Oral medication
- Long duration of action
- Clear target symptoms/signs
- No metabolic or toxic interactions with other detox medications for polydrug abusers

# \*Alcohol and Sedative Detoxification

- Benzodiazepines
  - chlordiazepoxide
  - oxazepam
- Barbiturates – Phenobarbital
- Carbamazepine

## Investigational

- Valproate
- Adrenergic blocker augmentation



# **\*Benzodiazepines for Alcohol Detoxification**

- Titrate dose to symptoms- chlordiazepoxide
- Peak symptoms at day 3, last 7 days
- Oxazepam in older or liver impaired alcoholics
- May supplement with adrenergic blockers

# **\*Carbamazepine for Alcohol Detoxification**

- Non-abusable, prevents seizures
- Equal efficacy to benzodiazepines
- Loading dose of 1200 mg orally
- Taper dose days 3 to 7
- Anticonvulsives may be first line agents for patients with history of withdrawal seizures

## **\*Adrenergic Blockers for Alcohol Detoxification**

- Beta blocker (atenolol) - 50-100 mg QD improves vital signs and agitation
- Alpha adrenergic agonist (clonidine) -0.1–0.3 mg works with benzodiazepines to control anxiety and vital signs
- Both agents do not prevent seizures and need to be augmenting agents not sole therapy

# \*Alcohol Relapse Prevention

- Naltrexone
- Depot Naltrexone
- Disulfiram
- Acamprosate

## Investigational

- Serotonin reuptake inhibitors
- Buspirone
- Tricyclic antidepressants

# **\*Alcohol Relapse Prevention**

## **Disulfiram**

- Aversive with alcohol use: vomit, hypotension
- Inhibit acetaldehyde breakdown
- Need enforced compliance
- Contraindications: liver failure, psychosis, unwilling patient

# **\*Alcohol Relapse Prevention**

## **Naltrexone**

- Anti-craving, decreases priming effect
- No aversive effect if alcohol used
- Daily oral dose of 50 mg for 6 to 12 months
- New depot injection can last 1 month
- Contraindications: opioid dependence  
severe liver disease
- Side effects (5-10%): nausea, headache

# \*Risks vs. Benefits for Naltrexone in Alcoholism

## Risks

- ✓ 6-10% initial dropout due to vomiting, nausea, and anxiety, which does not persist after discontinuation

## Benefits

- ✓ Approximately 50% reduction of relapse risk
- ✓ Improved ratings of employment problems
- ✓ Benefits for preventing relapse persist for six months after discontinuation
- ✓ Improved abstinence rates at endpoint and follow-up

# Naltrexone for Alcoholism Cases

## Mr. A - Clear Cut Effect

### Course in Treatment

- Immediate subjective reduction in craving
- Challenged effect on day 1 at liquor store, bar
- Abstinent for 10 weeks on medications
- Randomized to placebo at 10 weeks
- Returned unused medications at 14 weeks stating that it is placebo
- Resumed pre-treatment drinking weeks 18-24
- Returned to treatment/naltrexone week 24
- Abstinent x1 year while on naltrexone



# Naltrexone for Alcoholism Cases

## Mr. A - Clear Cut Effect

### Alcohol History

38 year old married white man

- Drinking 1.5 pints vodka/night 4x weekly for 10 years
- Cocaine dependence in late 20's
- 1 prior inpatient stay with rapid relapse
- Seeking treatment under pressure from 2nd wife
- Family History+++ Alcoholic father, 2 brothers, 2 grandfathers, 1 grandmother

# \*Opioid Detoxification

- Methadone tapering
- Clonidine or Lofexidine
- Buprenorphine

## Investigational

- Clonidine/naltrexone - rapid
- Benzodiazepine/clonidine/naltrexone - ultra-rapid

# \*Opioid Detoxification Methadone Tapering

- Standard starting dose of 25-35 mg for “street addict” on heroin
- Methadone patient may be over 100 mg QD
- Day 2 dose same or higher, if withdrawal seen
- Day 3 reduce 5 mg/day to 10 mg, then 2-3 mg/day reduction
- Inpatient 5-10 days, outpatient up to 30 days

## \*Opioids: Clonidine Detoxification

- Adrenergic anti-hypertensive
- Non-abusable, oral use
- Dose titration, start 0.1 mg TID
- Heroin - 7 days, Methadone - 14 days
- Targets autonomic symptoms
- Anxiety, diarrhea not well relieved
- Side effects - sedation, orthostatic hypotension

# **\*Opioid Detoxification: Rapid Clonidine/Naltrexone**

- Inpatient or day hospital procedure - 3 days
- Clonidine preload day 1: 0.2-0.3 mg
- Naltrexone 12.5 mg, 1 hour after clonidine
- Continue clonidine TID on first day
- Day 2: clonidine + naltrexone 25 mg
- Day 3: clonidine + naltrexone 50 mg
- Augmenting agents helpful: oxazepam 30 mg

## **\*Opioid Detoxification: Ultra Rapid**

- Precipitates withdrawal using naltrexone or naloxone or nalmefene
- Benzodiazepine induced sedation
- Or agents such as propofol for anesthesia
- Takes 6 hours to one day
- Risk of severe complications/death with anesthesia detox
- High costs
- Should be considered experimental

# \*Opioid Detoxification: Buprenorphine

- Partial opioid agonist: low dose relieves withdrawal, high dose may precipitate withdrawal
- Once daily sublingual dosing
- Transition from street heroin onto 2-8 mg buprenorphine
- Transition from methadone at more than 40 mg methadone
- Mild withdrawal during dosage taper
- Can combine with clonidine/naltrexone rapid detoxification

# \*Opioid Relapse Prevention Pharmacotherapy

- Methadone
- Levo alpha acetyl methadol (LAAM)
- Naltrexone
- Buprenorphine



## \*Opioids - Methadone Maintenance

- Agonist - relieves withdrawal
- Cross-tolerance to opioids
- Starting dose 30 mg, then escalate
- Dose - over 70 mg once daily orally
- Duration - one to over 20 years

# \*Opioids: Methadone Limitations

- Side effects - constipation, sedation
- Diversion to street abuse of “take homes”
- Alcohol and cocaine abuse
- Difficult to discontinue
- Medication interactions
- Dosing for rapid metabolizers

# \*Opioids: Levo Alpha Acetyl Methadol (LAAM)

- Long acting opioid agonist
- 3 x per week dosing
- 70 mg - 70 mg - 120 mg (M - W - F)
- Lower abuse potential than methadone
- Slow onset, poorer retention than methadone
- Mostly discontinued because of risk of Torsade de Pointes

# **\*Opioid Relapse Prevention**

## **Naltrexone**

- Pure opioid antagonist, need detox before start
- Heroin use not aversive, just blocked
- Oral dosing - either 50 mg / day or 100 mg Monday and Wednesday, 150 mg Friday
- Duration: 6-12 months
- Maintain abstinent state
- Need enforced compliance, e.g. parolees, significant others; otherwise retention poor
- New 1 month depot injection may improve compliance

# **\*Opioid Relapse Prevention: Naltrexone Limitations**

- Lower preference than methadone by addicts
- Poorer treatment retention than methadone
- Requires opioid detoxification before starting
- Lacks negative reinforcement when not taken (e.g. no withdrawal symptoms if stopped)
- Potential liver toxicity at higher doses (300 mg)
- Blocks opioid pain medications for up to 72 hours

# \*Opioid Relapse Prevention

## Buprenorphine

- Partial opioid agonist, cross tolerance, at 12 mg daily has about 75% blockade of heroin high
- Maintenance dose of 8-24 mg sublingual daily
- Two forms – buprenorphine alone or in combination with naloxone
- Comparable to methadone in treatment retention and reduced illicit heroin abuse
- Lower overdose potential and abuse liability than methadone
- Less severe withdrawal than methadone when discontinued
- Combo form used in pregnancy & at times for induction
- Unlike methadone, can be prescribed in office-based setting

# \*Stimulant Relapse Prevention

- Only Investigational Agents
- Antidepressants
  - tricyclics
  - serotonin reuptake inhibitors
- Mood stabilizers, e.g., Topiramate
- Dopamine agonists
- Disulfiram
- Modafinil
- NMDA antagonists
- Glutamate antagonists
- Vaccine

# \*Nicotine Detoxification/Relapse Prevention

- Nicotine gum
- Nicotine patch
- Nicotine aerosol
- Bupropion

## Investigational

- Tricyclic antidepressants
- Clonidine
- Naltrexone



# Ethical Issues in Treatment

- Personal relationships
- Confidentiality
- Dangerousness to self and others
- Informed consent
- Financial conflict of interest

# Ethical Issues: Confidentiality I

- Interdisciplinary treatment teams
- Supervision in and outside of program
- Outside agencies/practitioners
- Family members
- Teaching/sharing experiences

# Ethical Issues: Confidentiality II

- Legal protection of records
- Illegal activities by patients and reporting to police
- Drug use itself as illegal activity
- Group and family meeting risks

# Ethical Issues: Personal Relationships

- No sexual relationships with patients
- Meetings outside treatment program
- Group versus individual meetings
- Ongoing contacts after patient leaves treatment

# Ethical Issues: Dangerous

- Duty to inform threatened persons
- Conflict with confidentiality
- Who and when to notify
- Medical emergencies - limited disclosure
- High risk behaviors - AIDS

# Ethical Issues: Informed Consent I

- Written informed consent
- Release of written records
- Oral communication - dangerousness
- Need to document released information
- Program policies, HIV testing

# Ethical Issues: Informed Consent II

- Capacity to provide consent
- Surrogate consent (e.g. family members)
- Full disclosure of risks and benefits
- Parole, probation and criminal justice reports

# Ethics: Conflict of Interest

- Financial most common with treatment extension or discharge due to insurance
- Favoring one easily available treatment mode
- Pre-treatment relationship to patient
- Dual reporting to criminal justice, employer, etc.



# Ethics: HIV Testing

- Negative consequences: medical services, housing, employment, school admission
- Contact tracing and partner notification
- Associated sexual diseases, tuberculosis

# Ethics: Methadone Programs

- Retention vs discharge: non-compliance
- Blind withdrawal only on request
- Pregnancy and continued drug use
- Child protective services

# Post Lecture Exam

## Question 1

- 1. Which of the following statements is false:**
  - A.** Physical dependence is synonymous with addiction.
  - B.** One can be addicted without being physically dependent.
  - C.** Once a patient has met criteria for Substance Dependence, they should not be diagnosed in the future with Substance Abuse.
  - D.** A critical feature of addiction is compulsive use in spite of harm.

## Question 2

- 2. Which of the following statements is false:**
- A.** Psychiatric disorders can cause substance abuse.
  - B.** Substance abuse can cause psychiatric disorders.
  - C.** If both substance abuse and a psychiatric disorder are present, treating the psychiatric disorder is usually not necessary.
  - D.** Treating an underlying psychiatric disorder usually does not adequately treat the substance abuse.

## Question 3

- 3. The most common comorbid psychiatric diagnosis in patients with substance abuse is:**
- A. Schizophrenia**
  - B. Antisocial Personality Disorder**
  - C. Anxiety Disorder**
  - D. Major Depression**

## Question 4

- 4. Which one of the following is false:**
- A.** Cocaine decreases negative symptoms in schizophrenics.
  - B.** When cocaine free, schizophrenics have more negative symptoms.
  - C.** Chronic cocaine use increases depression in schizophrenics.
  - D.** Chronic cocaine decreases positive symptoms of schizophrenia.

## Question 5

- 5. Which of the following are considered “Gateway Drugs”?**
- A. Alcohol**
  - B. Marijuana**
  - C. Nicotine**
  - D. A & C only**
  - E. A, B, & C**

## Question 6

- 6. Adolescent substance abuse is associated with:**
- A. Increased school dropout**
  - B. Increased depression and suicidality**
  - C. Premature involvement in sexuality**
  - D. All of the above**



## Question 7

- 7. The proportion of users who ever became dependent is as follows (from high to low):**
- A.** Nicotine, alcohol, heroin, cocaine, marijuana.
  - B.** Alcohol, nicotine, cocaine, heroin, marijuana.
  - C.** Nicotine, heroin, cocaine, alcohol, marijuana.
  - D.** Nicotine, alcohol, marijuana, cocaine, heroin.

## Question 8

- 8. Which of the following is not used as a maintenance agent in heroin addiction:**
- A. Methadone
  - B. Clonidine
  - C. LAAM
  - D. Naltrexone
  - E. Buprenorphine

## Question 9

- 9. Which category of medications is not yet available for treatment of heroin addiction:**
- A. Agonists
  - B. Antagonists
  - C. Partial agonists
  - D. Anti-craving agents
  - E. Anti-withdrawal agents

## Question 10

- 10.** Which of the following statements are true:
- A. Naltrexone blocks the effects of alcohol.
  - B. Drinking while on naltrexone can make one very ill.
  - C. Benzodiazepines are the usual agents used for alcohol withdrawal.
  - D. All of the above

# Answers to Pre & Post Competency Exams

1. A

6. D

2. C

7. C

3. B

8. B

4. D

9. D

5. E

10. C