Substance Related Disorders

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Lecture Outline

1. Definitions & Diagnostic Criteria
2. Etiologic/pathogenic factors (Biopsychosocial theories)
3. Components of Comprehensive Assessment and Treatment
4. Intoxication and Withdrawal of Psychoactive Substances

CME Financial Disclosure Statement

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Vignette: Office Presentation

- John is an 18-year-old male with past h/o non-verbal LD and ADHD, inattentive type. With hard work and academic support, he graduated high school in the middle of his class.
- He lives with his parents and 2 younger siblings. He will be the first member of his family to attend college.
- He reports occasional drinking with friends at parties, but denies ever using illicit drugs.
- Current medication is Ritalin SR 20 mg QAM.
Vignette: Management

- You refer John to his PCP for a meningococcal vaccine.
- You discuss prescribing of his stimulant medication while away at college.
- You discuss student support services available at the college.
- You congratulate him on admission to college, and encourage him to continue to work hard and stay away from drugs.

Vignette: Epilogue

- Three days later, John attends an end-of-summer party with some high school friends.
- While driving home, John’s car crosses over the median and strikes another vehicle head on.
- John is pronounced dead at the scene. His blood alcohol concentration at autopsy is 0.24.

In memory of…

JOHN PAUL S.
(May 9, 1983 - Oct 16, 2004)

Substance-Related Disorders: Definitions & Diagnostic Criteria
Substance Related Disorders

- **Substance Use Disorders**
  - A- Abuse (social)
  - B- Dependence (physiological/medical & LOC)

- **Substance Induced Disorders**
  - Intoxication
  - Withdrawal
  - Delirium
  - Persisting Dementia
  - Persisting Amnestic Disorder
  - Psychotic Disorder
  - Mood Disorder
  - Anxiety Disorder
  - Sexual Disorder
  - Sleep Disorder
  - (Hallucinogen) Persisting Perception Disorder

Substance Abuse & Dependence:
According to DSM IV…

“A *maladaptive* pattern of substance use leading to clinically significant impairment or distress, as manifested by --- or more of the following, occurring within a **12 month period**…”

**Substance Abuse**

**Any 1 OF 4:**
- Major role failure
- Arrests/recurrent legal problems
- Physically hazardous use
- Social/interpersonal problems
**Substance Dependence**

3 or > in 12 months, *maladaptive* w/distress/impairment

1. Tolerance* - absolute (or relative)
2. Withdrawal* - characteristic symptoms
   (or avoided through substance use)
3. Larger amounts or periods of use than intended
4. Persistent desire or unsuccessful cutting down
5. Excessive time obtaining, using or recovering
6. Activities given up
7. Continued use despite knowledge of problem

* Specify if: with or without physiological dependence

**The 3 C’s of Addiction**

- **Craving**
- **Compulsion**
- **Loss of Control**

"First a man takes a drink, then the drink takes a drink, then the drink …

... takes the man."

-Native American saying

**Dependence: Course Specifiers**

- Early Partial Remission: 1m < **12m**; some criteria for abuse or dependence met
- Early Full Remission: 1m < **12 m**; no criteria
- Sustained Partial Remission: >**12m**; some criteria for abuse or dependence met
- Sustained Full Remission: > **12m**; no criteria
- On Agonist Therapy
- In a Controlled Environment
Substance Intoxication

- Reversible substance-specific syndrome due to recent ingestion/exposure
- Significant maladaptive behavior or psychological changes due to the effects of the substance on the central nervous system (CNS)
- Not due to a general medical condition or another mental disorder

Substance Withdrawal

- Reversible substance specific syndrome
- State of hyperexcitability due to decline in blood level of substance
- Significant distress or impairment
- Not due to general medical condition or another mental disorder

Withdrawal: Signs & Symptoms

- Opposite to direct pharmacological effects of a drug
- Same symptoms with substances in a given pharmacologic class (reversal with cross-tolerant drug)
- Variable in onset, duration, and intensity
- Dependent on:
  - agent used
  - duration of use
  - degree of neuroadaptation
  - half life & active metabolites: Alprazolam (Xanax) vs. Chlordiazepoxide (Librium)

Polysubstance Dependence

- Using at least 3 groups of substances (not including caffeine & nicotine) in 12 month period but no predominating substance
- Dependence criteria met for substances as a group but not for any specific substance
- Same pharmacological class → effects are additive
- Different pharmacologic class → detoxification strategy must accommodate each drug class
Polysubstance Dependence

- Opiate and sedative-hypnotic dependence: most complex; both require medication treatment
- Stimulants and opiates: managed as opiate withdrawal; no specific medication regimen for stimulants
- Traditionally, not advisable to withdraw both drugs at the same time (opiates and sedative-hypnotic symptoms overlap. Thus confusion about which drug is causing the symptoms).

Models of Addictive Behavior

A. Psychological & Behavioral Models
B. Social Models
C. Biological Models

Psychological Models

1. Addictive Personality - not substantiated
2. Psychopathologic Model - increased comorbidity w/ Conduct Disorder, ASPD, Bipolar I, Schizophrenia
3. Self-Medication Hypothesis
4. ? Role of “dysfunctional family” of origin
Behavioral Model

<table>
<thead>
<tr>
<th>Addictive Component</th>
<th>Behavioral construct</th>
<th>Treatment Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleasure</td>
<td>+ reinforcement</td>
<td>Motivation</td>
</tr>
<tr>
<td>Self medication</td>
<td>- reinforcement</td>
<td>Detox, Motivation, mutual-help, Rx</td>
</tr>
<tr>
<td>Habit</td>
<td>Conditioned +</td>
<td>Cognitive/behavioral relapse prevention</td>
</tr>
<tr>
<td></td>
<td>reinforcement</td>
<td>CBT, relapse prevention</td>
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<tr>
<td>Habit</td>
<td>Conditioned -</td>
<td></td>
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<tr>
<td></td>
<td>reinforcement</td>
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Social Model: Availability & Social Norms

1. Subcultures evolve specific drug use patterns -
   “Hippies” & marijuana
   Truckers & amphetamines
   Performers & cocaine
   * Crystal Meth mainly in West and Midwest
2. Vietnam Vets, 3 yrs later…
   50% used opioids in Vietnam; 20% dependent
   95% remitted in U.S.

Biological Models

1. Pharmacologic basis of dependence:
   a. Pharmacokinetics (faster is worse)
   b. Pharmacodynamics (tolerance at the receptor, i.e. BZs)
2. Genetic vulnerability confers > =50% of risk
3. Neuropharmacology: all addictive drugs (except LSD) affect mesocorticlimbic dopaminergic reward thresholds
Less yellow means less normal activity occurring in the brain— even after the cocaine abuser has abstained from the drug for 10 days.

Endogenous Opioids
- Noradrenaline
- Glutamate
- Serotonin

• Release
• Storage
• Blockade

Simulate actions of NT’s
Interfere in Normal Function
Altering/Blocking:
- * Storage
- * Release

Reuptake Blockade

Course of Addiction As An “Illness”
- Disease w/o a cure but with effective treatments
- Most severe during the first 3 to 18 months of sobriety
- Lifelong tendency of symptoms to return during times of physical or psychosocial stress.
- Chronic nature and the risk of relapse are reasons why the diagnosis of Substance Dependence should be maintained, even when sobriety is maintained over long periods of time.
Principles of Treatment

- Sobriety is the FIRST priority (re-evaluate when sober)
- Relapse is an expectation, not a failure
- If dual diagnosis, the more severe the disorders, the more important is integrated treatment (pharmacologic & behavioral)
- Progress, not perfection
- If the system is not ready for you, be ready for the system

Ostacher, 2005

Motivation to Enter / Sustain Treatment

- Effective treatment need not be voluntary
- Sanctions/enticements (family, employer, criminal justice system) can increase treatment entry/retention
- Treatment outcomes are similar for those who enter treatment under legal pressure vs voluntary

Don’t

- Use scare tactics: “scared straight” doesn’t work
- Judge: “If you keep doing this you’re going to become a druggie.”
- Punish: “We’re not going to give you anything to make this more comfortable for you, that way you won’t do this again.”

Do

- Be supportive: Provide medications to minimize withdrawal symptoms and a supportive physical and emotional environment
- Be aware of your biases and park them at the door
- Use brief interventions (BI):
  - Small steps, large gains… “one day at a time”

Interviewing Style (Not Preferred)

Sergeant Friday

- How much?
- How often?
- Where did you get it?
- Closed ended questions
- Cold, distant, interrogational
- “Just the facts…”

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Interviewing Style (Preferred)

Lieutenant Columbo

- What happened?
- How did that make you feel? Why?
- Open ended questions
- Mutual discovery and problem solving
- Empathy
- “Can you help me out here…”

CAGE vs. CRAFFT

- Cut down
- Annoyed
- Guilty
- Eye Opener
- Car Intoxicated
- Relax / fit in / peer influence
- Alone
- Forget / blackouts / dep risk
- Family / friends worry
- Trouble because of use

The CRAFFT Questions*

A Brief Screening Test for Adolescent Substance Abuse

C - Have you ever ridden in a CAR driven by someone (including yourself) who was “high” or had been using alcohol or drugs?
R - Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?
A - Do you ever use alcohol or drugs while you are by yourself, ALONE?
F - Do you ever FORGET things you did while using alcohol or drugs?
F - Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?
T - Have you ever gotten into TROUBLE while you were using alcohol or drugs?

*Two or more yes answers suggest a serious problem. Comprehensive assessment is available through the Adolescent Substance Abuse Program (ASAP) at Children’s Hospital Boston. For appointments call 617-355-ASAP or 1-800-225-8384.

TRAPPED Mnemonic

- Treatment History (inpt/outpt/MM, etc.)
- Route of administration (IV, IN, smoked)
- Amount (used, types, Spent; grams, bags, pints)
- Pattern (W/ changes over time)
- Prior Abstinence (why, helped, mood, relapse)
- Effects (O.D., withdrawal, consequences)
- Duration of use (incl. most recent & fam hx)
Matching Patients to Individual Needs

- No single treatment is appropriate for all individuals
- Effective treatment attends to multiple needs of the individual, not just his/her drug use
- Treatment must address medical, psychological, social, vocational, and legal problems

Medical Detoxification

- Removal of toxins / management of w/d
- Three immediate goals
  1. To provide a safe withdrawal and enable the patient to become free of substances
  2. To provide a withdrawal that is humane and that protects the patient's dignity
  3. To prepare the patient for ongoing treatment of his or her dependence (CSAT, 1995a):
- Detox alone, does little to change long-term drug use!
Cost-Effectiveness of Drug Treatment

- Drug treatment is disease prevention
- Drug treatment is opportunity for screening, counseling, and referral
- Reduced interpersonal conflicts, improved workplace productivity, fewer drug-related accidents
- Reduces HIV infection by 6 fold in IV users
- Treatment is less expensive than not treating or incarceration ($4,700 = 1 yr methadone vs. $18,400 for imprisonment)
- Every $1 invested in treatment yields up to $7 in reduced crime-related costs; 12:1 when health care costs included

Adherence and Relapse Rates

- Treatment reduces drug use by 40-60%
- Reduces crime by 40-60%
- Increases employment by 40%
- As successful as treatment of diabetes, asthma, and hypertension

Motivational Enhancement Therapy

- Helps people recognize and do something about their present or potential problem
- Useful in people who are reluctant to change and ambivalent about changing
- Intended to resolve ambivalence and aid an individual along a path of change
- Used as a brief “boost” for those who have the skills and resources to make a lasting change
- Prelude to treatment creating an openness to change that is key to further therapeutic work

Psychotherapy for Addictions

Motivational Enhancement Therapy

CBT
12 Step Programs
Motivational Interviewing

- A counseling style that creates conditions favorable to behavioral change
- Core assumptions:
  - Motivation is NOT an innate character trait
  - Motivation IS a product of interpersonal interaction
  - Ambivalence to change is normal and acceptable

Stages of Change

Precontemplation → Contemplation → Determination → Action → Maintenance

Source: Prochaska and DiClemente

Stage Specific Strategies

<table>
<thead>
<tr>
<th>Stage</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRE</strong></td>
<td>Develop therapeutic relationship; empathy; raise doubt, increase awareness of risks and problems</td>
</tr>
<tr>
<td><strong>CONTEMPLATION</strong></td>
<td>Acknowledge ambivalence, evoke reasons to change, tip the balance, success stories</td>
</tr>
<tr>
<td><strong>DETERMINATION</strong></td>
<td>Help find best course of action (timelines)</td>
</tr>
<tr>
<td><strong>ACTION</strong></td>
<td>Assist in moving forward (referrals, reassurance despite “rollercoaster”)</td>
</tr>
<tr>
<td><strong>MAINTENANCE</strong></td>
<td>Relapse prevention strategies, positive reinforcement</td>
</tr>
<tr>
<td><strong>RELAPSE</strong></td>
<td>Avoid demoralization, enhance movement back to action, assist in learning process</td>
</tr>
</tbody>
</table>

CBT Vs. Motivational Interviewing

**CBT Approach**
- Assumes patient is motivated (action stage)
- No direct strategies used for building motivation
- Seeks to *identify* and *modify* maladaptive cognitions
- *Prescribes* and teaches specific coping strategies
- Uses modeling, directed practice, and feedback
- Specific problem solving strategies are taught

**MI Approach**
- Employs specific strategies for building patient motivation for change
- *Explores* and *reflects* perceptions without labeling or correcting them
- *Elicits* possible change strategies from the patient and significant others
- Responsibility for change is left with the patient, no training, modeling, or practice
- Natural problem solving processes are elicited
Things do not change:
we change.

– Henry David Thoreau, Walden Pond

12 Step Programs: AA

- AA founded in 1935
- 2 million members worldwide
- Adapted to a variety of other addictions
- Features – open to all, apolitical, non-professional, self-supporting, non-denominational, multiracial.
- Addiction is an illness which can only be controlled by lifelong abstinence

12 Step Programs - AA

- Philosophy to obtain and maintain sobriety
  - Mutual help; positive role modeling
  - Group affiliation
  - Identification
  - Spirituality – “higher power” defined by the person & represents faith & hope in recovery
  - Pragmatism – belief in doing “whatever works”
  - Cognitive restructuring – “alcoholic thinking” = emotional immaturity, self centeredness, and irresponsibility = cognitive distortion
Types of Drug Tests

- **Breath:**
  - Good reflection of the blood alcohol level at time of test.
  - Available for alcohol only.
  - Not generally useful in primary care.

- **Saliva:**
  - Available for alcohol and other drugs.
  - Reflects blood level of drugs.
  - Not standardized, “cut-off levels” for positive tests varies between products.

- **Blood:**
  - Gives accurate assessment of acute intoxication.
  - More useful in emergency situations than in primary care.

- **Sweat:**
  - Patch worn for up to 14 days
  - High rate of false positives from “environmental contact”

- **Hair:**
  - Gives up to 90 day “history” of drug use.
  - Cannot determine when use occurred.
  - Ability to “hold” chemicals dependent on hair type.
  - Marijuana test not considered reliable.

- **Urine (Immunoassays):**
  - Well studied, standardized, quick, inexpensive.
  - Multiple drugs screened at once
  - Drug concentrations relatively high.
  - Drugs and metabolites are excreted in the urine for a period of time after acute intoxication.
  - Positive results require confirmation
Definitive (Confirmatory) Testing
Gas chromatography/Mass spectrometry (GCMS)
- Gold standard in drug testing
- Highly specific, can be used to confirm positive screen
- Can give quantitative levels
- Can test for substances not detected by a screen

Department of Transportation Protocol
Patient is required to:
- Show picture identification
- Empty pockets/ wash hands
Facility:
- No running water
- Toilet water is dyed blue
- Temperature is checked immediately

Urine Drug Testing Pitfalls
Defeating Drug Tests
- Urine drug testing is easy to evade.
- A sample of products are available on the Internet:
  - Synthetic urine
  - Urine “detoxifier” (in-vitro adulterant)
  - Real powdered urine

Urine Drug Testing Pitfalls
False Negatives
Adulterants:
- In vivo:
  - Large fluid volume + creatine + vitamin B
- In vitro:
  - Gluteraldehyde, potassium nitrate, pyridinium chlorochromate, hydrogen peroxide
  - Household products: bleach, salt, Visine, soap
The Urinator

… a one of a kind, state of the art, electronic urine testing device that will maintain testing temperature for a minimum of 4 hours with one set of batteries.

“The NIDA 5”

- Marijuana
- Cocaine
- Opiates
- Amphetamines
- PCP

Urine Drug Testing

- Cocaine, Opiates = 3 days
- Amphetamines = 1-2 days
- Alcohol = loose detection of 1 oz/hour
- Cannabis (THC)
  - Casual user = 3 days
  - Heavy user = 2 weeks - months

Detection Windows

<table>
<thead>
<tr>
<th>Substance</th>
<th>Detection Window</th>
</tr>
</thead>
<tbody>
<tr>
<td>THC</td>
<td>3-30 days</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>2-3 days</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>1-3 days</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1-7 days</td>
</tr>
<tr>
<td>Cocaine &amp; metabolite</td>
<td>6 hours – 3 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>7-9 days</td>
</tr>
<tr>
<td>PCP</td>
<td>8 days</td>
</tr>
<tr>
<td>Opiates</td>
<td>1-3 days</td>
</tr>
</tbody>
</table>
Alcohol Testing

- Alcohol has a short half life in urine
- Blood alcohol level: determines whether patient is acutely intoxicated or has been drinking recently.
- Breath and saliva tests: reflective of the blood alcohol level
- Ethyl glucuronide (ETG): longer half life* and may improve sensitivity up to 5 days
- Carbohydrate Deficient Transferrin (CDT): helps detect HEAVY alcohol consumption

Question: Which of the following converts alcohol into acetaldehyde?

A. Alcohol dehydrogenase
B. Aldehyde dehydrogenase
C. Both A & B
D. Glucose-6-Phosphatase
E. Acetate dehydrogenase

Question: Which of the following is inhibited by Disulfiram?

A. Alcohol dehydrogenase
B. Aldehyde dehydrogenase
C. Both A & B
D. Glucose-6-Phosphatase
E. Acetate Dehydrogenase
Question: Which of the following converts acetaldehyde into acetic acid?

A. Alcohol dehydrogenase
B. Aldehyde dehydrogenase
C. Both A & B
D. Glucose-6-Phosphatase
E. Acetate Dehydrogenase

Question: Which of the following is decreased in Asian people?

A. Alcohol dehydrogenase
B. Aldehyde dehydrogenase
C. Both A & B
D. Glucose-6-Phosphatase
E. Acetate Dehydrogenase

Question: Which of the following laboratory tests is not useful in making the diagnosis of alcohol abuse or dependence?

A. GGT
B. MCV
C. Triglycerides
D. Reticulocyte count
E. AST

Question: Which of the following three diagnoses are most likely to predate alcohol abuse or dependence and be considered true comorbid conditions?

A. Antisocial personality disorder, schizophrenia, and bipolar I disorder
B. Antisocial PD, panic disorder, and bipolar I disorder
C. Bipolar I disorder, major depression, and schizophrenia
D. Major depressive disorder, agoraphobia, and obsessive-compulsive disorder
E. None of the above
Question: Mr. Van Damme is a 79 y/o male admitted to the Orthopedic service for scheduled hip replacement surgery. Four hours after his procedure, you are paged to his bedside by his nurse who just witnessed him having a seizure. His daughter, who was also in the room tells you “the same thing happened the last time he stopped drinking cold turkey” prior to his last surgery. All of the following statements about seizures associated with alcohol withdrawal are true except:

A. They are tonic-clonic in character.
B. They usually recur 3 to 6 hours after the first seizure.
C. They often progress to status epilepticus.
D. They do not respond to anticonvulsants.
E. They may be associated with hypomagnesemia.

Defining the “Standard Drink”

A standard drink = 14 g ethanol
- 12 oz of regular beer or cooler (5% alcohol)
- 5 oz of table wine (12% alcohol)
- 1.5 oz of hard liquor (40% alcohol, 80 proof)

American Medical Association: Consumption Guidelines

- Standard Drink = 0.6 oz (14 grams)
  - 12 oz beer (5%)
  - 5 oz wine (12%)
  - 1.5 oz spirits (40%)

- Limits:
  - Men: < 14 per week or < 4 max/day
  - Women: < 7 per week or < 3 max/day

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wwwBeatTheBoards.com 877-225-8384
Morbidity and Mortality

- 9-31% of chief complaints
- D.A.W.N. (Drug Abuse Warning Network): drugs alcohol: 34% (204,524) cases in 2000
- 100,000 annual unexpected deaths
- 15% of all MVA’s
- 50% deaths in MVA’s
- Liver cirrhosis: 8% of all deaths due to medical causes (50% alcohol related)

Psychosocial Impact

- 15% of heavy ETOH users missed work due to “illness”/injury and...
- 12% missed work due to drinking ...in previous 30 days
- Suicide
- Domestic violence
- Abuse and neglect of minors
- Annual cost US economy 1998: $184.6 bill; $26.3 bill health care

Prevalence of Alcohol Use

NIAAA – National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

Any Alcohol Disorder 17.6 million (8.5%)

Alcohol Abuse 9.7 million (4.7%)

Alcohol Dependence 7.9 million (3.8%)


Alcohol Dependence: Natural History

Early: Drinking behavior similar to peers

Early to mid-20s: Difficulties with alcohol use escalate

Mid-20s to early 40s: 1st major alcohol-related life problem emerges

Established dependency: Exacerbations and remissions

Long-term abstinence:
- Without formal treatment or self-help groups: 20% chance long-term abstinence
- With treatment: 50% to 66% maintain abstinence ≥ 1 year

- ETOH use d/o's, including intoxication, abuse and dependence, are major causes of physical and behavioral morbidity and mortality and require emergency intervention.
- Studies conducted in ER settings find anywhere from 9-31% of all ER visits are ass w/ ETOH use.
- ETOH also involved w/other drug use and abuse; DAWN (monitors drug emergencies) reported ETOH in combo w/other drugs mentioned in 34% (204,524) of ER drug episodes in yr 2000
- ETOH use causes considerable impact on health care and on society in general
- Estimated to cause 100,000 excess deaths annually
- Approx 15% of all MVA’s and 50% of fatal car crashes estimated to be ETOH related
- Liver cirrhosis accounts for 8% of all deaths and 1/2 of these are directly due to ETOH

Slide 82
- Psychosocial impact of ETOH is also considerable
- Survey data show that 15% of heavy ETOH users missed work bc of illness/injury in previous 30 days and 12% skipped work b/c drinking in previous 30d.
- ETOH use is commonly ass w/ suicide, community and domestic violence and child abuse.
- Total annual costs to US economy in 1998 estimatd to be $184.6 billion, w/ $26.3 billion incurred b y health care costs

Ximena Sanchez Samper, 9/24/2004
Alcohol Intoxication

- Recent ingestion of alcohol
- Maladaptive behavior/psychological changes: (inappropriate sexual/aggressive behavior, poor judgment, mood lability)
- One or more:
  1. Slurred speech
  2. Incoordination
  3. Unsteady gait
  4. Nystagmus
  5. Impairment in attention or memory
  6. 6- stupor or coma

Substance (Alcohol) Induced Disorders

- Alcohol Intoxication
- Alcohol Withdrawal
- Alcohol Intoxication Delirium
- Alcohol Withdrawal Delirium (Delirium Tremens)
- Alcohol Induced Persisting Dementia
- Alcohol Persisting Amnestic Disorder (Wernicke’s Encephalopathy & Korsakoff’s Syndrome)
- Alcohol Induced Psychotic Disorder (with del. / hall.)
- Alcohol Induced Mood Disorder
- Alcohol Induced Anxiety Disorder
- Alcohol Induced Sexual Disorder
- Alcohol Induced Sleep Disorder

Alcohol Intoxication

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Treatment</th>
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<tbody>
<tr>
<td><strong>Mild-Moderate:</strong></td>
<td></td>
</tr>
<tr>
<td>Poor coordination, ataxia, conjunctival injection, slurred speech, gastrointestinal bleeding, orthostatic hypotension</td>
<td>Observation and supportive care, protect airway, position on side to avoid aspiration</td>
</tr>
<tr>
<td><strong>Severe:</strong></td>
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</tr>
<tr>
<td>Respiratory depression, coma, death (Chronic – pancreatitis, cirrhosis)</td>
<td>Ventilatory support, intensive care</td>
</tr>
<tr>
<td><strong>Pathologic:</strong></td>
<td></td>
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<tr>
<td>Belligerent, excited, combative, psychotic state</td>
<td>Physical restraint, Benzodiazapine (lorazepam 1-5 mg prn) or haloperidol</td>
</tr>
</tbody>
</table>
Alcohol Assessment

- Lab tests: complete blood count, TGL, electrolytes, magnesium, liver enzymes, (GGT, AST >ALT), urine drug screen, pregnancy test, and Breathalyzer or blood alcohol level.

- Others: skin test for tuberculosis, chest x-ray, electrocardiogram, and tests for viral hepatitis, HIV, or other STD’s.

* CDT, ETG

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Alcohol Withdrawal

- Cessation or reduction in alcohol use
- Two or more within hours or days:
  1. Autonomic hyperactivity (sweating; HR>100)
  2. Increased hand tremors
  3. Insomnia
  4. Nausea or vomiting
  5. Transient visual, auditory, tactile hallucinations
  6. Psychomotor agitation
  7. Anxiety
  8. Grand mal seizures

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Alcohol Withdrawal

- **Seizures:** within 48 hours of cessation
  1. Stereotyped, generalized, tonic-clonic
  2. Repeat within 3-6 hours
  3. Status epilepticus rare (< 3%)
  4. Consider head tx, CNS infections,
  5. Neoplasms, CV disease
  6. Treat w/ Benzo’s (not anticonvulsants)

  OTL: “Out The Liver”:
  Oxazepam/Temazepam/Lorazepam

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Substance (Alcohol) Withdrawal Delirium

- Disturbance of consciousness (focus, sustain, shift attention)
- Cognition impaired (memory, orientation, language, perception)
- Acute & fluctuating course
- Consequence of substance withdrawal
Alcohol Withdrawal Delirium (Delirium Tremens)

- 48-72 hrs after cessation
  - Preceded by early withdrawal symptoms
- Masked or delayed by illnesses or medications
  - 5% of hospitalized Alcohol Dependent patients
- Medical emergency!
  - Mortality: up to 20%
  - Increases w/ delayed diagnosis, inadequate treatment & concurrent medical conditions

Alcohol Withdrawal Delirium (Delirium Tremens)

- Sympathetic Hyperactivity
  - Tachycardia, hypertension, fever, diaphoresis, hallucinations, delusions
- Treatment: Prevention!
  - Benzo’s, hydration, caution with neuroleptics & restraints, support

Predictors of Delirium Tremens

- Prior history of severe withdrawal symptoms
- High blood alcohol level w/o signs of intoxication
- Withdrawal signs with high blood alcohol level
- Concurrent use of sedative-hypnotics
- Medical problems (hepatitis, pancreatitis)

Alcohol Induced Persisting Amnestic Disorder

- Wernicke’s Encephalopathy
  - Impaired short term memory due to prolonged/heavy ETOH use
  - Thiamine deficiency (poor nutrition or malabsorption)
  - Rare < 35 y/o
  - Acute symptoms
  - Reversible with treatment
- Triad: Ataxia, Nystagmus, Ophthalmoplegia

- Tx: Thiamine 100mg IM/IV x 3d; 100mg PO tid x 2 wks

- Korsakoff’s Syndrome
  - Chronic condition
  - 20% recovery rate
  - Anterograde amnesia in alert, responsive pt
  - +/- confabulation
  - Tx: 100mg tid 3-12 months
The mammillary bodies are atrophic and discolored brown, which is associated with vitamin B1 (thiamine) deficiency. Microscopically there is capillary proliferation, gliosis and, in severe cases, neuronal loss and hemorrhage. It is commonly seen in chronic alcoholics but may also be found in other nutritionally deprived populations.

Pharmacotherapy for Alcohol Dependence

- **Disulfiram**: 125-500 mg PO daily
- **Acamprosate**: 666 mg PO tid
- **Naltrexone (PO)**: 50 mg PO daily
- **Naltrexone (IM)**: 380 mg IM monthly

Undertreatment of Alcohol Use Disorders

Comprehensive Alcohol Dependence Treatment
Challenges of Current Therapies

- High relapse rate w/ psychosocial support alone: 50% at 12 months
  - 90% at 48 months
- Poor medication adherence is common and associated w/ higher relapse rates
- NIAAA guidelines: consider adding medication in active ETOH dependence or if stopped but experiencing cravings.slips

Disulfiram

- Inhibits metabolism (ALDEHYDE DEHYDROGENASE) → accumulation of acetaldehyde → unpleasant physical symptoms on exposure to alcohol (aversive agent)
- Serious side effects include hepatotoxicity, depression, and psychosis.
- Use in motivated & reliable patients only

Fuller et al, 1986
Acamprosate

- Glutamate receptors & transmission
- Moderation of prolonged withdrawal
  - Insomnia, fatigue, mood lability, anxiety
  - Possible effect on attenuating cravings
- European data > 3000 subjects, superior to placebo in maintaining abstinence
- Optimal treatment → combination with naltrexone, psychosocial therapy, 12 step

Features of Alcohol Dependence

<table>
<thead>
<tr>
<th>Normal</th>
<th>Acute Alcohol Intake</th>
<th>Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Normal Diagram" /></td>
<td><img src="image2.png" alt="Acute Alcohol Intake Diagram" /></td>
<td><img src="image3.png" alt="Tolerance Diagram" /></td>
</tr>
</tbody>
</table>

Relapse and Conditioning

Repeated alcohol use has caused "conditioning" to occur in related circuits
- Now “cues” associated with alcohol use can activate the reward and withdrawal circuit
- This can evoke anticipation of alcohol or feelings similar to withdrawal that can precipitate relapse in an abstinent patient

Pathophysiology of Potential Relapse

- Glutamate
- NMDA Receptor
- mGluR5
- Ca²⁺

Source: Fox et al, 2003
Source: Ali-Daoud et al, 2003
Source: De Witte, Addict Behav. 2004;29(7):1325-1339.
Acamprosate: Indications and Usage

- Maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation
- Should be part of a comprehensive management program that includes psychosocial support

*Precaution: Acamprosate does not eliminate or diminish acute withdrawal symptoms.

Acamprosate: Dosage and Administration

- Initiate as soon as possible after alcohol withdrawal when patient achieves abstinence
  - Maintain treatment if patient relapses
- Recommended dose: two 333-mg tablets tid
- Patients with moderate renal impairment
  - Starting dose of 1 x 333 mg tid
- Can be taken with or without meals

*Creatinine clearance of 30-50 mL/min.
Acamprosate: Pharmacokinetics

- **Bioavailability**: 11%
- **$T_{1/2}$**: 3-8 hours
- **$C_{max}$**: 180 ng/mL
- **$C_{max}$ (steady state)**: 350 ng/mL (5 days)
- **Food Effect**: Minimal (can be taken with food)
- **Plasma Protein Binding**: Negligible
- **Metabolism**: None (eliminated via kidneys)
- **$t_{1/2}$ (steady state)**: 20-33 hours
- **Volume Distribution**: 72-109 L (approx. 1 L/kg) (following IV administration)

---

Acamprosate: Safety

**Acamprosate is Safe to Use With Medications Commonly Used in This Population**

- **Acute Detoxification**
- **Co-occurring Psychiatric Disorders and Detoxification**
- **Alcohol Dependence***

**Hypnotics/Sedatives** (including benzodiazepines)
- **Antidepressants**
- **Anxiolytics**
- **Nonopioid Analgesics**

**Ethanol Disulfiram Naltrexone**

---

Naltrexone

- Synthetic opioid antagonist: FDA (1994) approved as adjunct to psychotherapy in alcohol dependence
- World Health Organization (1996): “safe and effective treatment for alcohol dependence”
  - Reduces drinking frequency
  - Reduces likelihood of relapse to heavy drinking
  - Reduces reinforcing response to ETOH
- Safety & efficacy: > 8 double-blind RCT
- Adverse events: nausea, anorexia
- Contraindicated: severe liver damage

---

Naltrexone

- Can be used safely without prior detox
- Effective even if only taken when drinking is expected
- 50mg/day effective, if compliant, w/ psychosocial therapy
- Monthly intramuscular preparation (Vivitrol)
  - Improved compliance, enhanced steady state plasma levels, fewer GI side effects

---

*Srisurapanont et al. 2003
Naltrexone: Oral vs. IM

- Once-monthly injection (Vivitol)
- Elimination of daily decisions to take oral medications = tmt adherence
- Consistent and measurable plasma levels of the active drug naltrexone
- I.M. = reduction first pass hepatic metabolism

Naltrexone: Oral vs. IM

- Medical alert card carried at all times
- Emergency pain management (IM/Vivitrol): regional analgesia, conscious sedation w/ a benzo and non-opioid analgesic, general anesthesia
- * Comprehensive management w/ psychosocial support

Naltrexone IM: Potential Side Effects

- Nausea/Vomiting
- Headache
- Fatigue/Dizziness
- Injection Site Reaction
- Contraindicated in acute hepatitis, liver failure & opioid dependent pt’s (min. 7-10 days opioid free)
- Eosinophilic Pneumonia (rare; dyspnea; hypoxemia)
- No significant change in LFT’s

Alcohol Dependence: Subtypes

- **Type I/A** = less severe dependence, later onset > 25, fewer childhood problems, fewer alcohol related problems, less psychopathology
  - Sertraline…?

- **Type II/B** = more severe dependence, early onset < 25, childhood risk factors, family history, polydrug use, psychopathology, life stress
  - Ondansetron…?

Pettinati et al, 2000

Johnson et al, 2000
Question: Which of the following converts alcohol into acetaldehyde?

A. Alcohol dehydrogenase  
B. Aldehyde dehydrogenase  
C. Both A & B  
D. Glucose-6-Phosphatase  
E. Acetate Dehydrogenase

A. Alcohol dehydrogenase  
B. Aldehyde dehydrogenase  
C. Both A & B  
D. Glucose-6-Phosphatase  
E. Acetate Dehydrogenase

Question: Which of the following is inhibited by Disulfiram?

A. Alcohol dehydrogenase  
B. Aldehyde dehydrogenase  
C. Both A & B  
D. Glucose-6-Phosphatase  
E. Acetate Dehydrogenase

Question: Which of the following converts acetaldehyde into acetic acid?

A. Alcohol dehydrogenase  
B. Aldehyde dehydrogenase  
C. Both A & B  
D. Glucose-6-Phosphatase  
E. Acetate Dehydrogenase

Question: Which of the following is decreased in Asian people?

A. Alcohol dehydrogenase  
B. Aldehyde dehydrogenase  
C. Both A & B  
D. Glucose-6-Phosphatase  
E. Acetate Dehydrogenase
Question: Which of the following laboratory tests is not useful in making the diagnosis of alcohol abuse or dependence?

A. GGT  
B. MCV  
C. Triglycerides  
D. Reticulocyte count  
E. AST

---

Question: Which of the following three diagnoses are most likely to predate alcohol abuse or dependence and be considered true comorbid conditions?

A. Antisocial personality disorder, schizophrenia, and bipolar I disorder  
B. Antisocial PD, panic disorder, and bipolar I disorder  
C. Bipolar I disorder, major depression, and schizophrenia  
D. Major depressive disorder, agoraphobia, and obsessive-compulsive disorder  
E. None of the above

---

Question: Mr. Van Damme is a 79 y/o male admitted to the Orthopedic service for scheduled hip replacement surgery. Four hours after his procedure, you are paged to his bedside by his nurse who just witnessed him having a seizure. His daughter, who was also in the room tells you “the same thing happened the last time he stopped drinking cold turkey” prior to his last surgery. All of the following statements about seizures associated with alcohol withdrawal are true except:

A. They are tonic-clonic in character.  
B. They usually recur 3 to 6 hours after the first seizure.  
C. They often progress to status epilepticus.  
D. They do not respond to anticonvulsants.  
E. They may be associated with hypomagnesemia.
Question: Lolita is a 39 y/o nurse with GAD whom you suspect has been “taking more than the prescribed amount” of Klonopin. She arrives to your office 5 days early and says she has “run out of medications early this month due to increased stress at work”. The symptoms of benzodiazepine withdrawal that you would expect to see include all of the following except?

A. Dysphoria  
B. Intolerance for bright lights  
C. Nausea  
D. Muscle twitching  
E. Pinpoint Pupils

---

Sedative, Hypnotic, Anxiolytic Intoxication

- Recent ingestion
- Maladaptive behavior/psychological changes (inappropriate sexual/aggressive behavior, poor judgment, mood lability)
- One or more:
  1. Slurred speech
  2. Incoordination
  3. Unsteady gait
  4. Nystagmus
  5. Impairment in attention or memory
  6. Stupor or coma

---

Sedative, Hypnotic, Anxiolytic Withdrawal

A. Cessation or reduction in use
B. Two or more within hours or days:
   1. Autonomic hyperactivity (sweating; HR>100)
   2. Increased hand tremors
   3. Insomnia
   4. Nausea or vomiting
   5. Transient visual, auditory, tactile hallucinations
   6. Psychomotor agitation
   7. Anxiety
   8. Grand mal seizures

---

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild-Moderate:</td>
<td></td>
</tr>
<tr>
<td>CNS sedation, pupillary constriction, disorientation, slurred speech, staggering gait</td>
<td>Observation and supportive care, protect airway, position on side to avoid aspiration</td>
</tr>
<tr>
<td>Severe:</td>
<td></td>
</tr>
<tr>
<td>Respiratory depression, hypothermia, coma, death</td>
<td>Acute overdose – gastric lavage; Supportive – ventilator, warming blanket, ICU Care; Flumazenil</td>
</tr>
<tr>
<td>Pathologic:</td>
<td></td>
</tr>
<tr>
<td>Paradoxical disinhibition, hyporesponsibility</td>
<td>Symptoms pass in a matter of hours; physical restraint, lo</td>
</tr>
</tbody>
</table>

---
Sedative, Hypnotic, Anxiolytic Withdrawal

- Long-acting sedative-hypnotic (diazepam, chlordiazepoxide, clonazepam, or phenobarbital)
- Drug of dependence may be gradually tapered by 10% daily
- May need anticonvulsant for smooth & gradual withdrawal

Cannabis Intoxication

- Recent cannabis use
- Maladaptive behavior or psychological changes (impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawal)
- Two or more within 2 hours of use:
  1. Conjunctival injection
  2. Increased appetite
  3. Dry mouth
  4. Tachycardia

Cannabis Intoxication

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute:</strong></td>
<td>Reassurance and observation</td>
</tr>
<tr>
<td>Euphoria, sensory stimulation, pupillary</td>
<td></td>
</tr>
<tr>
<td>constriction, conjunctival injection,</td>
<td></td>
</tr>
<tr>
<td>photophobia, diplopia, increased appetite,</td>
<td></td>
</tr>
<tr>
<td>autonomic dysfunction, temporary bronchodilation</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic:</strong></td>
<td>Discontinuation of use, symptomatic treatment/care (bronchodilators for wheezing)</td>
</tr>
<tr>
<td>Gynecomastia, reactive airway disease,</td>
<td></td>
</tr>
<tr>
<td>decreased sperm count, weight gain, lethargy</td>
<td></td>
</tr>
<tr>
<td><strong>Intoxication:</strong></td>
<td>Psychosis: neuroleptic medication</td>
</tr>
<tr>
<td>Panic, delirium, psychosis</td>
<td></td>
</tr>
</tbody>
</table>
Cannabis Withdrawal

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical:</strong> mild increases in heart rate, blood pressure, and body temperature</td>
<td>Reassurance; symptoms disappear in 3-4 days (sometimes longer)</td>
</tr>
<tr>
<td><strong>Psychological:</strong> anxiety, depression, irritability, agitation, insomnia, tremors, and chills</td>
<td></td>
</tr>
</tbody>
</table>

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A. Dysphoria  
B. Intolerance for bright lights  
C. Nausea  
D. Muscle twitching  
E. Pinpoint Pupils

Question: An 18-year-old high school senior was brought to the ER by police after being picked up wandering through traffic. He was agitated and aggressive, and talked of people who were deliberately trying to confuse him with misleading directions. His story was rambling and disjointed, but he admitted that he had used speed. In the ER he had difficulty focusing his attention and had to ask that questions be repeated.

He was disoriented to time and place and was unable to repeat the names of 3 objects after 5 minutes. His family gave a history of patient’s regular use of pep pills over the last 2 years, during which time he was frequently high and did poorly in school.
Question: Which of the following would not be a clinical effect of amphetamine intoxication in this patient?

A. Increased libido
B. Formication
C. Delirium
D. Catatonia
E. Pupillary dilation

Question: The abrupt discontinuation of amphetamine in this patient would produce all of the following except?

A. Fatigue
B. Dysphoria
C. Nightmares
D. Agitation
E. Appetite decrease

Question: Which of the following is true about Cocaine?

A. Competitively blocks dopamine reuptake by the dopamine transporter
B. Does not lead to physiological dependence
C. Induced psychotic disorders are most common in those who snort cocaine
D. Has been used by 40 percent of the United States population since 1991
E. Is no longer used as a local anesthetic

Question: Amphetamines and cocaine are similar in which of the following ways?

A. Their mechanisms of action at the cellular level
B. Their duration of action
C. Their metabolic pathways
D. The induction of paranoia and production of major cardiovascular toxicities
Question: In distinguishing schizophrenia from amphetamine-induced toxic psychosis, the presence of which of the following is most helpful?

A. Paranoid delusions
B. Auditory hallucinations
C. Clear consciousness
D. Tactile or visual hallucinations
E. Intact orientation

Question: Pharmacologic agents that have been confirmed to reduce cocaine use include:

A. Dopaminergic agonists
B. Bupropion
C. SSRIs
D. Desipramine
E. None of the above
Cocaine/Amphetamine Intoxication

A. Recent cocaine/amphetamine use
B. Maladaptive behavioral or psychological changes (euphoria or affective blunting; sociability changes; hypervigilance; interpersonal sensitivity; anxiety, tension or anger; stereotyped behaviors; impaired judgment)
C. Two or more of the following:
   1. Tachycardia or bradycardia
   2. Pupillary dilation
   3. Elevated or lowered blood pressure
   4. Perspiration or chills
   5. Nausea or vomiting
   6. Evidence of weight loss
   7. Psychomotor agitation or retardation
   8. Muscular weakness, respiratory depression, chest pain or cardiac arrhythmias
   9. Confusion, seizures, dyskinesias, dystonia or coma

Cocaine/Amphetamine Withdrawal

- Cessation or reduction in use
- Dysphoric mood & 2 or more of the following:
  1. Fatigue
  2. Vivid, unpleasant dreams
  3. Insomnia or hypersomnia
  4. Increased appetite
  5. Psychomotor retardation or agitation

### Signs & Symptoms

<table>
<thead>
<tr>
<th>Chronic users:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe depression with suicidal/ homicidal ideation, exhaustion, prolonged sleep, voracious appetite</td>
</tr>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Close observation, reassurance; symptoms disappear in 3-4 days</td>
</tr>
</tbody>
</table>
Methamphetamines

- Chemically related to amphetamines
- More potent, long-lasting and harmful to CNS (damages DA and serotonin nerve terminals)
- White, odorless, bitter-tasting crystalline powder (easily dissolves in water or alcohol)
- Schedule II stimulant (high abuse potential; available only through a prescription (ADHD, Narcolepsy))

Methamphetamines

- Referred to as: "speed,” "meth,” "chalk “, “ice,” "crystal,” "glass,” and "tina."
- Taken orally, intranasally, IV, or by smoking (rapidly addictive); varies by geographical region and use varies through time
- Approx. 10 million people in the United States > age 12 (4.3%) have tried at least once (2005 NSDUH)
Methamphetamine

- Smoking/ I.V.: intensely pleasurable rush or “flash”
- Snorting: “high” 3-5 m.
- Oral ingestion: 15 to 20 m.
- “Binge and crash” pattern: maintain high by taking more drug
- “Run”: foregoing food and sleep for several days.

**Short-term effects:**
- Increased attention and decreased fatigue
- Increased activity and wakefulness
- Decreased appetite
- Euphoria and rush
- Increased respiration
- Rapid/irregular heartbeat
- Increased BP
- Increased risk for stroke
- Hyperthermia
- ↑ libido & disinhibition
- Unsafe, risky behaviors
- Seizures and death

**Long-term effects:**
- Addiction
- Paranoia/hallucinations
- Repetitive motor activity
- Changes in brain structure and function
- Memory Loss
- Aggressive or violent behavior
- Mood disturbances
- Severe dental problems
- Weight loss
- Increased transmission of HIV and Hepatitis

**Recovery of Brain Dopamine Transporters in Chronic Methamphetamine (METH) Abusers**

**HOW TO GET HELP**

*The Matrix Model:* combines behavioral therapy, family education, individual counseling, 12-Step support, drug testing, and encouragement for nondrug-related activities

*Contingency management interventions:* tangible incentives in exchange for engaging in treatment and maintaining abstinence

No specific medications to counteract effects or prolong abstinence
(Bupropion: reduced the methamphetamine-induced “high” as well as drug cravings)
Stimulants: Management

- β-Blockers/Nitroprusside (hypertensive crisis)
- Risk of relapse is high during early withdrawal
- Drug craving is easily triggered by encounters with or thinking of drug-associated stimuli.
- Psychosocial treatment → behavioral therapy, desensitization & cue extinction

(Gawin and Ellinwood, 1988).

Stimulants: Management

- “Dopamine deficiency” hypothesis: not consistently supported
- Dopamine agonists: bromocriptine and amantadine → inconsistent results
- Short-acting benzodiazepines: for agitation or sleep
- Typical Neuroleptics: contraindicated (dysphoric side-effects may increase drug craving)
- Atypical neuroleptics – no data but clinically may be of benefit.

Question: An 18-year-old high school senior was brought to the ER by police after being picked up wandering through traffic. He was agitated and aggressive, and talked of people who were deliberately trying to confuse him with misleading directions. His story was rambling and disjointed, but he admitted that he had used speed. In the ER he had difficulty focusing his attention and had to ask that questions be repeated. He was disoriented to time and place and was unable to repeat the names of 3 objects after 5 minutes. His family gave a history of patient’s regular use of pep pills over the last 2 years, during which time he was frequently high and did poorly in school.

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Question: Pharmacologic agents that have been confirmed to reduce cocaine use include:

A. Dopaminergic agonists
B. Bupropion
C. SSRIs
D. Desipramine
E. None of the above

Question: Which of the following drugs is not an opioid antagonist?

A. Naloxone
B. Naltrexone
C. Nalorphine
D. Apomorphine
E. Oxycodone

Question: Opioid intoxication is generally characterized by:

A. Pupillary dilation
B. Piloerection
C. Increased blood pressure
D. Depressed respiration
E. Increased body temperature
History

- Opioids have been used for 6000 years (pain)
- Hippocrates: treatment of headaches, coughing, asthma, melancholy, etc.
- Unfortunately, increased potency (stronger) has increased physical and psychological dependence

Fact...

- Use of prescription painkillers (OC’s, Percocet, Vicodin) and heroin has increased in 10 years
- 2000: 810,000-1 million Americans addicted
- 2003: 1.5 million Americans
- 2006: 2.4 million (4X the population of Boston)

Concerns...

- Almost half (44%) of new recreational use of prescription painkillers in 2001 was by people under younger than age 18.
- The number of 18- to 25-year-olds admitted to treatment for prescription painkillers more than doubled between 1993 and 2002.

- Heroin today is almost 7 times stronger than in the 70’s…more addictive FASTER!!!
- Loss of control and inability to stop despite problems or consequences
- Through time, tolerance and dependence develop, and physical/or psychological symptoms can occur if the opioid use is reduced or stopped abruptly.
Medical & Social Problems
- HIV/AIDS
- Hepatitis B and C
- Tuberculosis
- Fetal effects
- Crime
- Violence
- Family problems
- Workplace
- School
- Economy ($100 billion in unemployment, missed work, criminal activities, medical care and social welfare)

Barriers to treatment
- Number seeking treatment is greater than resources available
- Stigma limits people from seeking help
- Only 1 in 5 receive treatment
- Opioid dependence is a MEDICAL problem, not a moral issue!
Opioid Intoxication

A. Recent opioid use
B. Maladaptive behavior (euphoria followed by apathy, dysphoria, psychomotor agitation/retardation, impaired judgement)
C. Pupillary constriction & one or more:
   1. Drowsiness
   2. Slurred speech
   3. Impairment in attention or memory

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<thead>
<tr>
<th>Signs &amp; Symptoms</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Acute:</td>
<td>Euphoria, pupillary constriction, depression of respirations and gag reflex, bradycardia, hypotension, constipation</td>
</tr>
<tr>
<td>Chronic:</td>
<td>Complication of IV use include hepatitis B, HIV/AIDS, endocarditis, brain abscesses</td>
</tr>
<tr>
<td>Intoxication/overdose:</td>
<td>Acute overdose may cause respiratory arrest and death</td>
</tr>
</tbody>
</table>

Opioid Withdrawal

A. Either of the following:
   1. Cessation or reduction in opioid use
   2. Administration of opioid antagonist after period of opioid use
B. Three or more of the following:
   1. Dysphoric mood
   2. Nausea or vomiting
   3. Muscle aches
   4. Lacrimation or rhinorrhea
   5. Pupillary dilation, piloerection or sweating
   6. Diarrhea
   7. Yawning
   8. Fever
   9. Insomnia
“Quitting Cold Turkey” and…

“Kicking the Habit”…

Relief of Opioid Withdrawal Symptoms

- Headache, muscle pain, joint or bone pain: *Ibuprofen* 600-800 mg q6-8h or *acetaminophen* 650 mg q4h.
- Muscle spasm: *Quinine Sulfate* 325mg q 6h prn
- Anxiety: *Hydroxyzine* 25-50 mg or *lorazepam* 1-2 mg or *chlordiazepoxide* 25 mg q6-8h.
- Insomnia: *Lorazepam* 2 mg or *chlordiazepoxide* 25 mg or *trazodone* 50-100 mg or *doxepin* 10-20 mg.
- Abdominal cramps: *Dicyclomine* 10-20 mg q6h.
- Nausea: *Phenergan* 25 mg PO/IM q6h or *metoclopramide* 20 mg q6h.
- Loose stool: *Bismuth subcarbonate* (Pepto-Bismol) 30 cc or *Imodium* 2 mg after each loose stool, up to 8 doses total.

Clonidine

- Reduces opiate withdrawal signs & symptoms → decreases sympathetic outflow
- Suppresses autonomic mediated signs & symptoms of withdrawal (less effective for other subjective symptoms).
- **Side effects**: Drowsiness & orthostatic hypotension common (monitor BP)
- Oral and transdermal presentations

Methadone

- Synthetic opioid agonist
- Acute Opioid Withdrawal in Detox Centers
- Most researched treatment for opioid replacement therapy (1970’s)
  - Better treatment retention rates
  - Reduces morbidity and mortality
  - Curbs spread of infectious disease
  - Work best if program is numerous, accessible, and flexible
- ***Approved in pregnancy***

*Mattick et al. 2003

**Single, 2000
**Buprenorphine / Suboxone**

- Newer medication; approved in US since early 2000’s
- Can be given in primary care offices by physicians who have completed brief training and obtained a waiver
- Good first choice for adolescents

---

**What Is Suboxone?**

- Suboxone is a combination of two medicines: buprenorphine and naloxone

---

**Buprenorphine/Suboxone**

- Long acting, potent, partial (mu) agonist
- Subutex/Suboxone safe & effective in treatment, use reduction/craving
- Mixed agonist/antagonist (kappa): decrease risk of respiratory depression, fewer autonomic withdrawal symptoms, less euphoria

---

**How Does Buprenorphine / Suboxone Work?**
Partially vs. Full Opioid Agonist

<table>
<thead>
<tr>
<th>Opiate</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Agonist</td>
<td>(e.g., methadone)</td>
</tr>
<tr>
<td>Partial Agonist</td>
<td>(e.g., buprenorphine)</td>
</tr>
<tr>
<td>Antagonist</td>
<td>(e.g., Naloxone)</td>
</tr>
</tbody>
</table>

With ongoing, escalated use, tolerance develops, upregulation of receptors occurs and patients need larger doses in order to get “high”.

Following abrupt discontinuation (or marked reduction in use), withdrawal symptoms begin.

However, even after patients stop withdrawing, the brain can still interpret this situation as “something not being quite right”.

Opioid receptor satisfied with a full-agonist opioid. The strong opioid effect of heroin and painkillers stops the withdrawal for a period (e.g., 2-3 hours). Initially, euphoric effects can be felt. However, as up-regulation occurs, tolerance and physical dependence can develop. Now, instead of producing a euphoric effect, the opioid is primarily just preventing withdrawal symptoms.
How does Buprenorphine / Suboxone work?

- Replacement/Substitution Therapy
- Curbs Opioid withdrawal symptoms
- Decreases cravings

Opioids replaced and blocked by Buprenorphine. Buprenorphine competes with the full agonists opioids for the receptor. Since buprenorphine has a higher affinity than the full agonists, it expels existing opioids and blocks others from attaching. As a partial agonist, the buprenorphine has a limited opioid effect, enough to prevent withdrawal but not enough to cause intense euphoria.

Over time (24-72 hours) buprenorphine dissipates, but still creates a limited opioid effect (enough to prevent withdrawal) and continues to block other opioids from attaching to the opioid receptors.

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Buprenorphine

- Must be started when patients are in withdrawal (or clean)
- Buprenorphine displaces other opioids from the receptor; if this occurs, opioid withdrawal symptoms will soon follow.

Buprenorphine Blocks Other Opioids

- Buprenorphine has a high affinity for opioid receptors.
- Other opioids cannot bind to the receptor if buprenorphine is there.

What Does Naloxone Do?

- Naloxone also binds to the opioid receptor, but as an ANTAGONIST!
- If Suboxone is injected, rather than taken SL, the patient will immediately begin to withdraw.

Naloxone Is A Safety Feature

- When Suboxone is taken SL as prescribed, the body absorbs only the buprenorphine, NOT the Naloxone
- If Suboxone is injected, rather than taken SL, the patient will immediately begin to withdraw.
Buprenorphine/Suboxone

- In combination w/ naloxone 4:1 (2 mg & 8 mg)
- No effect unless administered parenterally
  - S.L. only
    - decrease IV abuse/diversion/O.D
    - less tightly controlled
  - M.D. waiver needed (8 hrs ASAM training); no longer 30 patient limit

---

Buprenorphine/Suboxone

- **Unique pharmacologic properties**
  - Ceiling effect, safer in overdose, less addictive than full agonists, easier in w/d vs. methadone (agonist effect at low doses)
  - High mu rct affinity blocks rct activation by other full agonists or displaces them

---

Buprenorphine/Suboxone

- **Unique pharmacologic properties**
  - Quick onset of action (100 vs 150 min), slow dissociation rate, less frequent dosing (option of alternative day dosing)
  - SE’s: HA/ nausea/constipation/monitor LFT’s/CYP 450 3A4 metab (decrease dose if on azoles or protease inhibitors)

---

Question: Which of the following drugs is not an opioid antagonist?

A. Naloxone  
B. Naltrexone  
C. Nalorphine  
D. Apomorphine  
E. Oxycodone
Question: Opioid intoxication is generally characterized by:

A. Pupillary dilation
B. Piloerection
C. Increased blood pressure
D. Depressed respiration
E. Increased body temperature

The Action of Anabolic Steroids

Potential Negative Side Effects

Headaches  Strokes and blood clots
Baldness  High blood pressure and heart disease
Severe acne on face and back  Nausea
Liver damage  Bloating
Development of breasts  Impotence
Mood swings  Reduced sperm count
Urinary and bowel problems  Aching joints
Enlarged prostate  Aggressive behavior
Shrinkage of the testicles  Increased risk of tendon injuries

PROBLEMS IN WOMEN:
- Reduced breast size
- Enlarged clitoris
- Increase in facial and body hair
- Deepened voice
- Menstrual problems

Anabolic Steroid Intoxication

Signs and Symptoms

Evidence suggests that steroid use has effects on mood and emotional functioning including anxiety, exhilaration, agitation, and depression, psychotic reactions can occur
Anabolic Steroid Withdrawal

**Signs and Symptoms**

Mood swings, depression with suicidal behavior, and aggression with violent and assaultive behavior, sometimes-dramatic reductions in size and strength.

---

Question: An 18 y/o male is brought to the ER with extreme agitation. He needs to be held down by 4 security officers. He has prominent drool which is getting on everyone. When he is subdued you note the presence of vertical nystagmus and tachycardia. Which substance is this patient most likely intoxicated with?

A. Alcohol  
B. Cocaine  
C. Inhalant  
D. LSD  
E. Phencyclidine

---

Question: The patient in the previous question should *not* be treated with which of the following?

A. Diazepam (Valium)  
B. Reduction of environmental stimulation  
C. Phentolamine (Regitine)  
D. Phenothiazines (Chlorpromazine)  
E. Supportive measures (cardiopulmonary resuscitation)
Question: Current recommendations state that the patient in the previous question should **not** have his urine acidified. Why not?

A. Diazepam will be inactivated
B. Pt intoxicated with PCP is more likely to display violent behavior
C. Pt intoxicated with PCP is at high risk of aspirating the cranberry juice
D.Pts intoxicated with PCP are at risk for acidosis and rhabdomyolisis

---

**Hallucinogen Intoxication**

1. Recent hallucogen use
2. Maladaptive behavior/psychological changes (anxiety or depression, ideas of reference, fear of losing one’s mind, paranoid ideation, impaired judgement)
3. Perceptual changes in a state of full wakefullness & alertness (depersonalization, derealization, illusions, hallucinations, synesthesias)
4. Two or more of the following:
   1. Pupillary dilation
   2. Tachycardia
   3. Sweating
   4. Palpitations
   5. Blurring of vision
   6. Tremors
   7. Incoordination

---

**LSD/Acid**

- One of the strongest mood-altering drugs
- Sold: tablets, capsules, liquid, absorbent paper
- Psychological Effects
  - unpredictable
  - delusions and visual hallucinations with high doses
- Physical Effects
  - hyperthermia, tachycardia, HTN, insomnia and loss of appetite
- 2005 MTF study: 1.8% of 12th graders used

Source: NIDA Infosfacts: High School and Youth Trends.

---

**Ketamine**

- Currently used in human anesthesia and veterinary medicine
- Diverted from veterinarians' offices (evaporated to form a powder; snorted or compressed into pills)
- Chemical structure, mechanism of action & effects similar to PCP but less potent & of shorter duration.
- Range of sensations range: pleasantly floating to sensory detachment: “K-hole.”
- Odorless and tasteless = amnesia = date-rape drug

Source: NIDA Infosfacts: High School and Youth Trends.
Dextromethorphan

- "DXM" or "robo"; cough-suppressing ingredient in a variety of over-the-counter cold / cough medications.
- NMDA receptor antagonist
- At doses recommended for coughs, it is safe and effective.
- Effects similar to PCP and ketamine (vary with dose)
- Distorted visual perceptions to complete dissociation (for 6 hours)
- Often contain antihistamine and decongestant ingredients

PCP/ Phencyclidine

- Illegally manufactured in labs
- Variable routes of administration (snorted, smoked, P.O.)
- Developed in the 1950s as an IV anesthetic
- Street Names: angel dust, ozone, wack, rocket fuel
- Effects: overdose; unpleasant psychological effects; increased violence/suicidality
- NIDA’s 2005 MTF study: 2.4% of high school seniors/lifetime

PCP/ Phencyclidine Intoxication

A. Recent use
B. Maladaptive behavior (belligerence, assaultiveness, impulsiveness, agitation, impaired judgement)
C. Two or more within an hour:
   1. Vertical or horizontal nystagmus
   2. Hypertension or tachycardia
   3. Numbness or diminished response to pain
   4. Ataxia
   5. Dysarthria
   6. Muscle rigidity
   7. Seizures or coma
   8. Hyperacusis

Hallucinogen/PCP Treatment

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute:</td>
<td>Reassurance and observation (some symptoms may be more severe depending upon type of hallucinogen)</td>
</tr>
<tr>
<td>Perceptual distortion and hallucinations, mild nausea, tremors, tachycardia, hypertension, hyperreflexia</td>
<td>*PCP: Diazepam for seizures or agitation; NO Ammonium Chloride, Ascorbic Acid, Cranberry juice to acidify urine as leads to metabolic acidosis, rhabdomyolysis, etc); Phentolamine for HTN</td>
</tr>
<tr>
<td>Chronic:</td>
<td>Discontinuation of use</td>
</tr>
<tr>
<td>Flashbacks</td>
<td></td>
</tr>
<tr>
<td>Intoxication/overdose:</td>
<td>Psychosis: close observation in quiet room, benzodiazepines: NO Phenothiazines (anticholinergics worsen effects/seizure risk)</td>
</tr>
<tr>
<td>Panic, paranoia, psychosis</td>
<td></td>
</tr>
</tbody>
</table>

Sanchez © 2010
Hallucinogen/PCP Withdrawal

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<tr>
<th>Signs and Symptoms</th>
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</tr>
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<tbody>
<tr>
<td>Acute users:</td>
<td>Psychological</td>
</tr>
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</table>

Hallucinogen Persisting Perception Disorder (Flashbacks)
- The re-experiencing, following cessation of hallucinogen use, of perceptual symptoms experienced while intoxicated previously (geometric hallucinations, false perceptions of movement in peripheral visual fields, flashes of color, trails of images of moving objects, halos, macropsia, micropsia)
- Cause distress or impairment in social/occupational functioning
- Not due to general medical condition

Question: An 18 y/o male is brought to the ER with extreme agitation. He needs to be held down by 4 security officers. He has prominent drool which is getting on everyone. When he is subdued you note the presence of vertical nystagmus and tachycardia. Which substance is this patient most likely intoxicated with?

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D. Pts intoxicated with PCP are at risk for acidosis and rhabdomyolysis

Question: The lifetime use of inhalants is highest in which of the following age groups?

A. Young adults aged 18 to 25 years
B. Adults aged 26 to 34 years
C. Youth aged 8 to 17 years
D. Adults 40 to 65 years old
E. Adults over the age of 65

Question: Adverse effects on the brain that have been associated with long-term inhalant use include all the following except:

A. Rhabdomyolysis
B. Brain atrophy
C. Decreased intelligence quotient (IQ)
D. Electroencephalographic (EEG) changes
E. Decreased cerebral blood flow
Inhalants
- Often common household products that contain volatile solvents or aerosols
- Rapid high resembling alcohol intoxication (anesthesia, a loss of sensation & unconsciousness at higher doses)
- Among the first drugs that young kids use
- NIDA's 2005 MTF study:
  - 17.1% of 8th graders, 13.1% of 10th graders, and 11.4% of 12th graders said they had abused inhalants at least once

Source: NIDA Infodfacts: High School and Youth Trends

How can inhalant abuse be recognized?
Early identification and intervention are the best ways to stop inhalant abuse before it causes serious health consequences. Parents, educators, family physicians, and other health care practitioners should be alert to the following signs of a serious inhalant abuse problem:
- Chemical odors on breath or clothing
- Paint on or other stains on face, hands, or clothes
- Hidden empty spray paint or solvent containers and chemical-soaked rags or clothing
- Drunk or disoriented appearance
- Slurred speech
- Nausea or loss of appetite
- Inattentiveness, lack of coordination, irritability, and depression

Inhalants of Abuse
- **Arnyl Nitrite, Butyl Nitrite**
  - ("poppers" or “video head cleaner")
  - Sudden sniffing death syndrome, suppressed immunologic function, injury to red blood cells (interfering with oxygen supply to vital tissues)

- **Benzene**
  - (Found in gasoline)
  - Bone marrow injury, impaired immunologic function, increased risk of leukemia, reproductive system toxicity.

Inhalants of Abuse cont.
- **Butane, Propane**
  - (found in lighter fluid, hair and paint sprays)
  - Sudden sniffing death syndrome via cardiac effects, serious burn injuries (because of flammability)

- **Freon**
  - (used as a refrigerant and aerosol propellant)
  - Sudden sniffing death syndrome, respiratory obstruction and death (from sudden cooling/cold injury to airways), liver damage.

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Inhalants of Abuse cont.

- **Methylene Chloride**
  - (found in paint thinner and removers, degreasers)
  - Reduction of oxygen-carrying capacity of blood, changes to the heart muscle and heartbeat.

- **Nitrous Oxide Hexane**
  - “Laughing gas”
  - Death from lack of oxygen to the brain, altered perception and motor coordination, loss of sensation, limb spasms, blackouts caused by blood pressure changes, depression of heart muscle functioning.

- **Inhalants of Abuse cont.**
  - **Toluene**
    - (found in gasoline, paint thinners and removers, correction fluid)
    - Brain damage (loss of brain tissue mass, impaired cognition, gall disturbance, loss of coordination, loss of equilibrium, limb spasms, hearing and vision loss), liver and kidney damage

- **Trichloroethylene**
  - (found in spot removers, degreasers)
  - Sudden sniffing death syndrome, airhosts of the liver, reproductive complications, hearing and vision damage.

Brain atrophy in a toluene abuser  
Demyelination in an inhalant abuser

**Inhalant Intoxication**

A. Recent use of inhalants
B. Maladaptive behavior/psychological changes (belligerence, assaultiveness, apathy, impaired judgment)
C. Two or more of the following:
   1. Dizziness
   2. Nystagmus
   3. Incoordination
   4. Slurred speech
   5. Unsteady gait
   6. Lethargy
   7. Depressed reflexes
   8. Psychomotor retardation
   9. Tremor
   10. Generalized muscle weakness
   11. Blurred vision or diplopia
   12. Stupor or coma
   13. Euphoria
### Inhalant Intoxication

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute:</strong> Euphoria, disorientation, sedation, acute toxicity to CNS, liver, kidneys, sudden hypoxemia, hypotension</td>
<td>Symptomatic medical treatments</td>
</tr>
<tr>
<td><strong>Chronic:</strong> Perpetual nerve, CNS, liver, and kidney damage, plumbism (if leaded gasoline)</td>
<td>Discontinuation of use, supportive therapies (plumbism – chelation therapy)</td>
</tr>
<tr>
<td><strong>Intoxication:</strong> Cardiac arrhythmia and arrest</td>
<td>Resuscitation, hospitalization</td>
</tr>
</tbody>
</table>

### Inhalant Withdrawal

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td><strong>Acute users:</strong> Psychological</td>
<td>Reassurance, support</td>
</tr>
<tr>
<td><strong>Chronic:</strong></td>
<td></td>
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### Question:
The lifetime use of inhalants is highest in which of the following age groups?

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B. Brain atrophy  
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Question: Which of the following is true about MDMA ("Ecstasy"):

A. Produces selective, long lasting damage to serotonergic nerve terminals in animals
B. Produces sympathomimetic effects of tachycardia, palpitations, increased blood pressure, sweating, and bruxism
C. Can cause psychotic reactions
D. Produces feelings of increased self-confidence, sensory sensitivity, peacefulness, and decreased appetite
E. All of the above
Reported Undesirable Effects
(up to 1 week post-MDMA, or longer)

- Anxiety
- Restlessness
- Irritability
- Sadness
- Impulsiveness
- Aggression
- Sleep disturbances
- Lack of appetite
- Thirst
- Reduced interest in
  and pleasure from sex
- Significant reduction
  in mental abilities
Potential Adverse Health Effects

- Nausea
- Chills
- Sweating
- Involuntary jaw clenching and teeth grinding
- Muscle cramping
- Blurred vision
- Marked rise in body temperature (hyperthermia)
- Dehydration
- High blood pressure
- Heart failure
- Kidney failure
- Arrhythmia

Symptoms of MDMA Overdose

- High blood pressure
- Faintness
- Panic attacks
- Loss of consciousness
- Seizures

Long Term Effects of Ecstasy: Animal Studies Indicate Neurotoxicity

Brain chemistry changes
- serotonin reduced
- serotonin metabolites reduced

Brain structure changes
- serotonin transporters reduced
- serotonin terminals degenerate

Serotonin Present in Cerebral Cortex Neurons

Control  2 weeks after Ecstasy  7 years after Ecstasy
Question: Which of the following is true about MDMA (“Ecstasy”):

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