

Substance Related Disorders

Laura Ferguson MD
Sonali Kothari MD

Substance Disorders

- Substance Intoxication
- Substance Withdrawal
- Substance Induced Psychotic Disorder
- Substance Induced Mood Disorder
- Substance Induced Anxiety Disorder
- Substance Induced Sleep Disorder
- Substance Induced Delirium
- Substance Induced Persisting Dementia
- Substance Induced Persisting Amnesic Disorder
- Substance Induced Sexual Dysfunction

Epidemiology: Prevalence

- Alcohol Abuse: 20% for males, 10% for female
- Alcohol Dependence: 10% for males, 5% for females
- 20% lifetime prevalence of illicit substance abuse
- 40% of people use one or more illicit substances in their lifetime
- 15% of people used in the past year

The financial cost of addiction in the US

- For ETOH alone the US spends \$300 billion dollars/year
- 13 million Americans require treatment for alcohol abuse
- 5.5 million Americans (27% of the population >12 years of age) require treatment for drug use

Other costs of addiction

- . 40% of hospital admission have drug/ETOH as a factor
- . 25% of all deaths!
- . 100,000 deaths/year from drug/ETOH
- . Intoxication is associated with 50% of all MVAs, 50% of all DV cases and 50% of all murders

Phenomenology:intoxication

- Intoxication: a specific syndrome of maladaptive behavioral or psychological changes due to the recent ingestion of or exposure to a substance that acts of the CNS

Substances inducing intoxication identified in the DSM IV

- Alcohol
- Amphetamines
- Caffeine
- Cannabis
- Cocaine
- Hallucinogens
- Inhalants
- Opiates
- Phencyclidine
- Sedatives/hypnotics/7 anxiolytics
- Residual category (steroids, nitrous oxide)

Clinical picture of intoxication depends on:

- Substance
- Dose
- Duration/chronicity
- Individual degree of tolerance
- Time since last dose
- Person's expectations as to the substances effect
- Contextual variables

Neuroadaptation:

- Refers to the underlying CNS changes that occur following repeated use of a drug such that the person develops tolerance and/or withdrawal

Tolerance

- The need to use a greatly increase amount of a substance in order to achieve the desired effect **OR**
- A markedly diminished effect being associated with continued use of the same amount of the substance
- The degree to which tolerance develops varied greatly between drugs

Withdrawal

- Maladaptive behavioral change with physiological & cognitive effect that occurs
- when concentration of a substance declines in the body

Substance Abuse

- a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one or more of the following
1. Failure to fulfill role obligations or poor work performance.
 2. Use on hazardous situations
 3. Substance related legal problems
 4. Persistent or recurrent social or interpersonal problems
- And never met criteria for dependence

Substance Dependence

- A maladaptive pattern of substance use leading to clinically significant impairment or distress, manifested by 3 or more of the following occurring at any time within the same 12 month period:
- Tolerance
 - need for more to achieve the same effect
 - decreased effect with same amount
- Withdrawal
 - Characteristic withdrawal syndrome
 - Using substance to avoid withdrawal Sx

Substance Dependence cont.

- Substance taken in larger amt or for longer time than intended
- Persistent unsuccessful attempts to cut down or control use
- Great deal of time spent obtaining, using, or recovering from use
- Important social, occupational, recreational activities given up or reduced
- Use is continued despite knowledge that has persistent or recurrent physical or psychological problems that were caused or exacerbated by use

Substance Dependence Course Specifiers

- Early remission- no criteria met for > 1 month and <12 months
- Sustained remission - no criteria met for > 12 months
- Partial remission- occasional criteria met
- Full remission- no criteria met

Learning and Physiological Basis for Dependence

- Reinforcing behaviors / Pleasure Circuit/ reward circuit/ hippocampal and limbic memory circuit
- acute increases of levels of neurotransmitters in the brain
- Ex. Increased Dopamine (DA) in the limbic areas (ventral tegmental DA neurons synapsing on the nucleus accumbens neurons is very rewarding.
- Some drugs also increase serotonin and/or norepinephrine.

Learning and Physiological Basis for Dependence

- After using drugs or when stop – leads to a depleted state resulting in dysphoria and/or cravings to use, reinforcing the use of more drug.
- Response of brain cells is to downregulate receptors and/or decrease production of neurotransmitters that are in excess of normal levels.

Typical Presentation and Course:

- pts present in acute intoxication, acute / chronic withdrawal or substance induced mood, cognitive disorder or medical complications
- Abstinence depends on several factors including: environmental, social, internal factors (presence of other comorbid psychiatric illnesses)
- Remission and relapses are the rule (just like any other chronic medical illness)
- Frequency, intensity and duration of treatment predicts outcome
- 70 % of pts are eventually able to abstain or decrease use to not meet criteria

TREATMENT OF SUBSTANCE RELATED DISORDERS

1. Address the Behavior (motivational interviewing)
 - Explore desire to stop drinking/using vs perceived benefits of ongoing use
 - Gentle confrontation with education (risks to health) / therapeutic alliance
 - Involve family and friends for support
 - Educate pt regarding substance dep & need for rehabilitation plan

2. Treat the Medical Complications
 - Detoxification- oupt, "social detoxification" program, inpt with close medical care
 - Address associated medical complications: dehydration, malnutrition, DT's, seizures, pneumonia, cardiomyopathy, etc

Options for where to treat

- Hospitalization-
 - Due to drug OD, risk of severe withdrawal, medical comorbidities, requires restricted access to drugs, psychiatric illness with suicidal ideation
- Residential treatment unit
 - Do not require intensive medical / psychiatric monitoring
 - Require a restricted environment
 - Partial hospitalization
 - Step down unit
- Oupt Program -No risk of med/ psych morbidity/ highly motivated pt

3. Address Comorbid Psychiatric Conditions
 - 50% pf people with SRD have another mental disorder
4. Address Internal & External Reinforcers
 - Group, individual, family therapy/ educations counseling, AA

5. Treatment in the Ambulatory Setting & Relapse Prevention
 - Modify persistent/ habitual behaviors
 - Intensity of therapy is important
 - Cognitive Behavioral Therapy
 - Relapse prevention model- education and dev. of skills
 - Motivation enhancement therapy
 - "Client centered"- focus on benefits of stopping vs benefits of ongoing use

- Group therapy
 - Gain support from others with similar difficulties
 - Improve communication skills
- Family therapy
 - Family support/ address "enabling behaviors"
- Self Help Groups
 - 12 step approach/AA/ Rational recovery

SPECIFIC SYNDROMES: ALCOHOL- CNS depressant

Intoxication- clinical s/s

- BAL (blood alcohol level) 0.08 or 1.0 g/dl- legal definition
- Mood lability, impaired judgment, ataxia. At higher doses see nystagmus, slurred speech, decreased concentration, anterograde memory loss "blackouts".

Alcohol Withdrawal

- Early on sx of anxiety, irritability, tremor, decreased con, insomnia, N/V etc
- As withdrawal continues, increased risk of delirium tremens (confusion, alternating level of consciousness, hallucinations, HTN, tachycardia, diaphoresis, vascular collapse) and seizures. DTs usually appear within 72 hours after stopping.
- Seizures within 48-72 hrs

Alcohol Withdrawal cont.

- CIWA (Clinical Institute Withdrawal Assessment for Alcohol)
- Assigns numerical values to things such as orientation, N/V, tremor, sweating, anxiety, agitation, tactile/ auditory/ visual disturbances and HA. VS checked but not recorded. Total score of > 10 give meds and re check in 1 hour. (Checks but does not score VS)

Alcohol Withdrawal cont.

- Benzodiazepines agonist of GABA and cross tolerant with alcohol reduce risk of SZ and provide comfort/ sedation
- Anticonvulsants reduce risk of SZ, may reduce kindling, helpful for protracted withdrawal. Carbamazepine 200mg po tid or Valproic acid 250mg po tid or bid > 65 yr for at least 3 weeks

Alcohol treatment

- Outpatient CD treatment- support, education, skills training, psychiatric and psychological tx, AA
- Medications including Disulfiram, Naltrexone and Acamprosate

Medications to treat ETOH dep

- Disulfiram (antabuse) 250mg – 500mg po qd
- Inhibits aldehyde dehydrogenase and dopamine beta hydroxylase
- Aversive reaction when alcohol ingested- vasodilatation, flushing, N/V, hypotension/ HTN, coma / death
- Hepatotoxicity check LFT's and h/o hep C
- Neurologic with polyneuropathy / paresthesias that slowly increase over time and increased risk with higher doses
- Psychiatric side effects with psychosis, depression, confusion, anxiety
- Dermatologic rashes and itching
- Watch out for disguised forms of alcohol- cologne, sauces, mouth wash, OTC cough meds, Nyquil, alcohol based hand sanitizers, etc

Medications to treat ETOH dep cont.

Naltrexone 50mg po qd

- Opioid antagonist thought to block mu receptors reducing intoxication euphoria and cravings
 - Hepatotoxicity at high doses so check LFT's
- Acamprosate(Campral) 666mg po tid
- -Unknown mech of action but thought to stabilize neuron excitation and inhibition, may interact with GABA and Glu receptor, cleared renally

Benzodiazepine(BZD)/ Barbiturates

Intoxication similar to alcohol but less cognitive / motor impairment

- variable rate of absorption into the CNS (lipophilic), onset of action and duration
- the more lipophilic and shorter the duration of action , the more " addiction " they can be
- all can be addicting

Benzodiazepine Withdrawal

- Similar to alcohol with anxiety, irritability, insomnia, fatigue, HA, tremor, sweating, poor concentration- time frame depends on half life
- Common detox mistake is tapering too fast; symptoms worse at end of taper
- Convert short elimination BZD to longer elimination half life drug and then slowly taper
- Outp taper- decrease dose every 1-2 weeks and not more than 5 mg Diazepam dose equiv.
- May consider carbamazepine or valproic acid especially if doing rapid taper

Benzodiazepines

- Alprazolam (Xanax) t1/2 6-20 hrs
 - *Oxazepam (Serax) t1/2 8-12 hrs
 - *Temazepam(Restoril) t ½ 8-20 hrs
 - Clonazepam (klonopin) t1/2 18-50 hrs
 - *Lorazepam(Ativan) t1/2 10-20 hrs
 - Chlordiazepoxide (Librium) t1/2 30-100 hrs (less lipophilic)
 - Diazepam(Valium) t ½ 30-100 hrs (more lipophilic)
- *Oxazepam, Temazepam & Lorazepam- metabolized through only glucuronidation in liver and not affected by age/ hepatic insufficiency.

OPIOIDS

Drugs that bind to the mu receptors in the CNS to modulate pain

- **Intoxication-** pinpoint pupils, sedation, constipation, bradycardia, hypotension and decreased respiratory rate
- **Withdrawal-** not life threatening unless severe medical illness, but extremely uncomfortable. s/s dilated pupils lacrimation, goosebumps, n/v, diarrhea, myalgias, arthralgias, dysphoria or agitation
- **Rx-** symptomatically with antiemetic, antacid, antidiarrheal, muscle relaxant such as methocarbamol, NSAIDS, clonidine and maybe BZD
- **Neuroadaptation:** increased DA and decreased NE

Treatment for Opiate dependence

CD tx including support, education, skills building, NA , opiate substitution

Medications

- Naltrexone 50mg po qd
 - Opiate blocker, mu antagonist
 - Methadone for opiate substitution therapy
 - Mu agonist
 - Start at 20-40mg and titrate up until not craving or using illicit opioids
 - Average dose 80-100mg qd
 - Pt needs to be enrolled in a certified opiate substitution program

Treatment for Opiate dependence cont.

- Buprenorphine
 - Partial mu agonist/ antagonist; low doses act as an agonist with pain control; at higher doses no increased effect (less risk of OD) and may behave like an antagonist (can trigger withdrawal)
 - Any physician can rx after taking certified ASAM course
 - Helpful for highly motivated people who do not need high doses

STIMULANTS

- **Intoxication(acute)**- psychological and physical signs-
 - Euphoria, enhanced vigor, gregariousness, hyperactivity, restlessness, interpersonal sensitivity, anxiety, tension, anger, impaired judgment, paranoia
 - Tachycardia, papillary dilation, HTN, diaphoresis, chills, N/V, wt loss, chest pain, cardiac arrhythmias, confusion, seizures, coma

STIMULANTS cont.

- **Chronic intoxication**- affective blunting, fatigue, sadness, social withdrawal, hypotension, bradycardia, muscle weakness
- **Withdrawal** is not severe but have exhaustion with sleep (crash). Treat with rest and support

Cocaine

- Route nasal, IV or smoked
- Has vasoconstrictive effects that may outlast use and increase risk for CVA and MI (obtain EKG)
- Can get rhabdomyolysis with compartment syndrome from hypermetabolic state
- Can see psychosis associated with intoxication that resolves
- **Neuroadaptation**: cocaine mainly prevents reuptake of DA

Treatment of Cocaine Dependence

- CD treatment including support, education, skills CA
- Disulfiram (Antabuse) 250mg po qd may be helpful for cravings by inhibiting dopamine-beta-hydroxylase, increasing CNS dopamine levels

Amphetamines (dexadrine, amphetamine, methamphetamine, crystal, ice)

- Similar intoxication syndrome to cocaine but usually longer
- Route- oral, IV, nasally, smoked
- No vasoconstrictive effect
- Chronic use results in neurotoxicity possibly from glutamate and axonal degeneration
- Can see permanent amphetamine psychosis with continued use
- Treatment similar as for cocaine but no known substances to reduce cravings
- **Neuroadaptation**: Amphetamines inhibit the reuptake of DA, NE, SE and greatest effect by increased release of DA

Treatment of Amphetamine Dependence

- CD treatment including support, education, skills CA
- No specific medications have been found helpful in treatment although some early promising research using atypical antipsychotics (methamphetamine)

NICOTINE

- Most important preventable cause of death / disease in USA
- 25%- current smokers, 25% ex smokers
- 20% of all US deaths
- 45% of smokers die of tobacco induced disorder
- Second hand smoke causes death / morbidity
- Psychiatric pts at risk for Nicotine dependence- 75%-90 % of Schizophrenia pts smoke

NICOTINE cont.

- **Nicotine intoxication**- abd pain, dizziness, HA, N/V, palpitations; self limited
- **Neuroadaptation**: nicotine acetylcholine receptors on DA neurons in ventral tegmental area release DA in nucleus accumbens
- Biphasic effect
- **Tolerance** Rapid
- **Withdrawal**- dysphoria, irritability, anxiety, decreased concentration, insomnia, increased appetite/ wt gain, cravings

Treatment for Nicotine

- Cognitive Behavioral therapy
- Agonist substitution therapy- nicotine gum, transdermal patch, nasal spray
- Medication: bupropion(Zyban) 150mg po bid

HALLUCINOGENS

- Naturally occurring- Peyote cactus(mescaline)/ Magic Mushroom(Psilocybin)
- Synthetic agents - LSD, lysergic acid diethylamide- oral
- DMT, dimethyltryptamine- smoked, snuffed, IV
- STP, 2,5-dimethoxy 4-methylamphetamine –oral
- MDMA , 3,4-methylenedioxymethamphetamine, ecstasy (XTC)-oral

MDMA (XTC or Ecstasy)

- Designer club drug
- Enhanced empathy, personal insight, euphoria, increased energy, 3-6 hr duration
- Parkinsons ds in animals, hyperthermia, dehydration, seizures, CV, renal failure, coma, death
- **Intoxication**- illusions, hyperacusis, sensitivity of touch, taste/ smell altered, synesthesia, "oneness with the world", tearfulness, euphoria, panic, paranoia, impairment judgment
- Tolerance develops quickly and unpleasant side effects with continued use (teeth grinding) so dependence less likely

MDMA (XTC or Ecstasy) cont.

- **Neuroadaptation-** affects serotonin (5HT), DA, NE, but predominantly 5HT2 receptor agonists
- Debate about chronic hallucinogen causing / contributing to chronic psych illness
- **Withdrawal** – unclear syndrome (maybe similar to mild stimulants-sleepiness and depression due to 5HT depletion)

CANNABIS

- Most commonly used illicit drug in America
- THC levels reach peak 10-30 min, lipid soluble; long half life of 50 hours
- **Intoxication-** subtle/ appetite and thirst increase
 - Colors/ sounds/ tastes are clearer
 - Increased confidence and euphoria
 - Relaxation
 - Increased libido
 - Transient depression, anxiety, paranoia
 - Tachycardia, dry mouth, conjunctival injection
 - Slowed reaction time/ motor speed
 - Impaired cognition
 - Psychosis

CANNABIS cont.

- **Neuroadaptation-** CB1, CB2 cannabinoid receptors in brain/ body
- Coupled with G proteins and adenylate cyclase to CA channel inhibiting calcium influx
- Neuromodulator effect; decrease uptake of GABA and DA
- **Cannabis withdrawal** not listed in DSM but can occur with insomnia, irritability, anxiety, poor appetite, etc

CANNABIS cont.

- **Cannabis dependence** can lead to "amotivational syndrome"
- **Treatment**
 - Detox and rehab
 - Behavioral model
 - No pharmacological treatment but may treat other psychiatric symptoms

PHENACYCLIDINE (PCP) "Angel Dust"

- Dissociative anesthetic
- Similar to Ketamine, used in Anesthesia exp with children
- **Intoxication:** severe dissociative reactions – paranoid delusions, hallucinations, and can become very agitated/ violent with decreased awareness of pain. Do not try to "talk down"- needs quiet and low stimulation.
- Cerebellar sym- ataxia, dysarthria, nystagmus (vertical and horizontal)
- With severe OD see mute, catatonic, muscle rigidity, hyperthermia, rhabdomyolysis, seizures, coma and death

PCP cont.

- **Treatment:** antipsychotic drugs or BZD if required
- Acidify the urine with IV Ammonium Chloride if severe toxicity/coma
- **Neuroadaptation**
- Opiate receptor effects
- Allosteric modulator of the glutamate NMDA receptor
- **No tolerance of withdrawal**