Objectives

- To define addiction
- To identify the signs and symptoms of alcoholism
- To understand how to manage patients experiencing alcohol withdrawal in an acute care setting
- To list the long-term complications of chronic alcohol addiction and misuse
- To identify the signs and symptoms of opioid addiction
- To understand how to manage patients experiencing opioid withdrawal in an acute care setting
- To list the long-term complications of chronic opioid addiction and misuse

Scope of our talk

- What and which drugs?
- Why now?
- Who abuses prescription drugs?
- What can we do?
DSM 4 Criteria for Drug Abuse

- Significant impairment or distress resulting from use
- Failure to fulfill roles at work, home, or school
- Persistent use in physically hazardous situations
- Recurrent legal problems related to use
- Continued use despite interpersonal problems

DSM 4 Criteria for Drug Dependence

- ≥3 of the following occurring in the same 12-month period
  - Desire or unsuccessful efforts to cut down on use
  - Large amount of time spent obtaining drugs, using drugs or recovering from drug effects
  - Social, occupational, or recreational activities reduced because of drug use
  - Drug use continued despite knowledge that a physical or psychological problem is being caused or exacerbated by use
  - Use of drug in larger amounts or for longer periods of time than originally anticipated

Tolerance

- Need for an increasing amount of drug to achieve desired effect OR
- Diminished effect with continued use of the same amount of drug

Withdrawal

- Withdrawal manifests with cessation of use, reduction of use, or use of an antagonist.

- Drugs or related substances relieve or avoid withdrawal symptoms.
How does someone become addicted?

Addiction pathways continued

Drugs of Abuse: Not Just Opioids

- Opioids and other pain killers
- Stimulants
- Anti-anxiety medications
- Sedatives/hypnotics
- Antidepressants
- Steroids
- Psychedelics

Epidemiology

- Prescription drug abuse is increasing at an alarming rate.
- 2010: 7.0 million persons in the US were considered users of prescription drugs.
  - Pain relievers – 5.1 million
  - Tranquilizers – 2.2 million
  - Stimulants – 1.1 million
  - Sedatives – 0.4 million
- 1 in 12 high school seniors report nonmedical use of Vicodin™
- 1 in 20 high school seniors report abuse of OxyContin™
Epidemiology

After Cannabis, Nonmedical use of Prescription and Over-the-Counter Medications Account for Most of the Commonly Abused Drugs in 12th Graders (in the past year)

Commonly Abused Opioids

<table>
<thead>
<tr>
<th>Hydromorphone</th>
<th>Dilaudid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine</td>
<td>Demerol</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Loratad, Viodin, Norco</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>OxyContin, Percodan, Percocet, Tylox</td>
</tr>
<tr>
<td>Diacetylmorphine</td>
<td>Heroin</td>
</tr>
</tbody>
</table>

Oxycodone and Oxycodone CR

- Oxycodone: OxyIR, Roxycodone
  - Acute pain
  - Duration of action: 4-6 hours
  - Available as tablets, capsules, and liquid
- Oxycodone CR: OxyContin
  - Chronic pain, opioid tolerant patients
  - Duration of action: 12 hours
  - Not for “as needed” use
  - Available in tablets only
Rates of emergency department (ED) visits for nonmedical use of opioid analgesics by type – US 2004-2008

Opioid Effects

- Desirability
  - Euphoria
  - Prolonged sense of contentment
- Undesirable
  - N/V
  - Respiratory depression
  - Constipation
  - Pupillary constriction
Opiate Withdrawal

- Major withdrawal symptoms peak 48-72 hours after the last dose
- Duration and intensity dependent on quantity and type of opiate used
  - Heroin withdrawal subsides after a week
  - Methadone withdrawal can last weeks

Symptoms of withdrawal

Opiate Overdose Treatment

- Respiratory depression, CNS depression, myosis, signs of drug abuse history
- R/O hypoglycemia, acidemia, fluid and electrolyte abnormalities
- Provide airway, ventilation, and cardiac function support
- Naloxone HCl 0.4-0.8 mg initially, repeat as needed

Treatment of Opiate Dependence

- Multi-modal comprehensive treatment gives best chance of lasting remission.
  - Opiate replacement or pharmacologic support of withdrawal symptoms
  - Cognitive behavior treatment: counseling, 12-step work
**Group Question**
Which of the following is NOT a symptom of opiate withdrawal?
A. Sweating
B. Anxiety
C. Tachycardia
D. Urge to sleep
E. None of the above

**Effects of Common Opiates at Mu Receptor**

<table>
<thead>
<tr>
<th></th>
<th>Full agonist</th>
<th>Morphone like effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin, morphine, methadone</td>
<td>Partial agonist</td>
<td>Weak morphine-like effects with strong receptor affinity</td>
</tr>
<tr>
<td>Buprenorphine, tramadol</td>
<td>Partial agonist</td>
<td></td>
</tr>
<tr>
<td>Naltrexone, Nalmefene, Naloxone</td>
<td>Antagonist</td>
<td>Partial agonist</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antagonists</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“dummy key”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No-effect in absence of an opiate or opiate dependence</td>
</tr>
</tbody>
</table>

**Alcohol Abuse**

**Current perspectives about alcohol abuse**

- “Alcohol is the number one drug of choice among our nation’s youth. Yet the seriousness of this issue does not register with the general public or policymakers.”

Enoch Gordis, MD Director, National Institute on Alcohol Abuse and Alcoholism
Epidemiology

- 7.4% of adult population in the US are alcoholic
- 185 billion dollars
  - Cost of alcohol abuse in the US
- 100,000 annual deaths related to alcohol
- 1.2 billion dollars spent on wine, beer, and liquor advertisements in the US

Fetal Alcohol Syndrome (FAS)

- Most common preventable cause of adverse CNS development
- 4,000 – 12,000 infants in the US per year
- Characteristics:
  - Growth retardation
  - Facial malformations
  - Small head
  - Greatly reduced intelligence
- Milder form of FAS
  - 7,000 – 36,000 infants per year in the US
  - Characteristics:
    - Growth deficiency
    - Learning dysfunction
    - Nervous systems disabilities

Effects of Prenatal Alcohol

Acute Effects of Alcohol

- CNS depressant
- Depression of inhibitory control
- Vasodilation, warm, flushed, reddish skin
- Emotional outbursts
- Decreased memory and concentration
- Poor judgment
- Decreases reflexes
- Decreased sexual response
Long term adverse effects of alcohol

- Alcoholism, death, cancer (oral cavity, esophagus, liver), fetal effects
- Alcoholism
  - Cirrhosis of the liver, appetite loss, poor judgment
- Indirect effects
  - Lost of productivity, impaired performance, motor impairment, cost to society

Minor withdrawal symptoms

- Insomnia
- Tremulousness
- Mild anxiety
- Gastrointestinal upset
- Headache
- Diaphoresis
- Palpitations
- Anorexia

Minor Withdrawal Symptoms Timeline

- Present within 6 hours of last drink
  - Even if BAL is still elevated
- Resolves in 24-48 hours
Withdrawal Seizures

• Generalized tonic-clonic convulsions
• Occur within 48 hours of last drink
  ▫ May occur as soon as 2 hours from last drink
• 3% of chronic alcoholics have withdrawal-associated seizures
  ▫ 3% of this group may develop status epilepticus

Alcoholic Hallucinosis

• Not synonymous with delirium tremens
• Develop within 12-24 hours of abstinence
• Resolves within 24-48 hours
• Usually visual, may be tactile or auditory

Delirium Tremens

• Occurs in 5% of alcoholics
• Signs and symptoms:
  ▫ Hallucinations, disorientation, tachycardia, hypertension, low grade fever, agitation, and diaphoresis
• Develops 48-96 hours after last drink, lasts 1-5 days

Who develops DT?

• Risk factors:
  ▫ History of prolonged and sustained drinking
  ▫ Previous DT
  ▫ Age > 30 years
  ▫ Number of days since last drink
  ▫ Presence of comorbid conditions
Is DT fatal?

- Mortality rate: ~5%
  - Associated with arrhythmias and pneumonia

DT signs and symptoms

- Clinical manifestations:
  - Hallucinations
  - Disorientation
  - Tachycardia
  - Hypertension
  - Low-grade fever
  - Agitation
  - Diaphoresis
  - Elevated cardiac indices
  - Elevated oxygen delivery and consumption
  - Respiratory alkalosis
  - Hypokalemia and hypomagnesemia

Alcohol Withdrawal Timeline

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Clinical Findings</th>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td>Tremulousness, mild anxiety, headache, diaphoresis, palpitations, anorexia, GI upset</td>
<td>6-36 hours</td>
</tr>
<tr>
<td>Seizure</td>
<td>Generalized, tonic-clonic seizures, status epileptics (rare)</td>
<td>6-48 hours</td>
</tr>
<tr>
<td>Alcoholic hallucinosis</td>
<td>Visual, auditory, and/or tactile hallucinations</td>
<td>12-48 hours</td>
</tr>
<tr>
<td>Delirium tremens</td>
<td>Delirium, tachycardia, hypertension, agitation, fever, diaphoresis</td>
<td>48-96 hours</td>
</tr>
</tbody>
</table>

Treatment of alcohol withdrawal

- Rule out alternative diagnoses
- Control symptoms with supportive care
- Treatment with benzodiazepines
Alternative diagnoses

• LP
• Cranial CT
  ▫ R/O infection, head trauma, metabolic derangements, drug overdose, hepatic failure, and gastrointestinal bleeding
  ▫ Can mimic or co-exist with alcohol withdrawal

Treatment of alcohol withdrawal

• Rule out alternative diagnoses
• Control symptoms with supportive care
• Treatment with benzodiazepines

Supportive care

• Psychomotor agitation, prevention of severe withdrawal
  ▫ Benzodiazepines
• Metabolic abnormalities
  ▫ IV fluids, nutritional supplementation

Treatment of alcohol withdrawal

• Rule out alternative diagnoses
• Control symptoms with supportive care
• Treatment with benzodiazepines
Benzodiazepines

- Treats psychomotor agitation
- Prevents progression of withdrawal symptoms
- CIWA protocol
  - Diazepam (Valium) – 5 to 10 mg IV every 5 to 10 minutes
  - Preferred by some: longer-acting with active metabolites
  - Lorazepam (Ativan) – 2 to 4 mg IV every 15 to 20 minutes
  - Shorter half-life, no active metabolites, prevents oversedation
  - Chlorazepoxide (Librium)
    - Long half-life may lead to oversedation in patients with severe liver disease
- Route
  - IV therapy for initial management
  - Guaranteed absorption, rapid onset
  - Avoid IM – variable absorption

CIWA-Ar

- Total score is sum of each item score (max score is 67)
  - <10: very mild withdrawal
  - 10-15: mild withdrawal
  - 16-20: modest withdrawal
  - >20: severe withdrawal

Group Question

What is the preferred benzodiazepine for alcohol withdrawal?
A. Lorazepam
B. Diazepam
C. Temazepam
D. All of the above
Refractory DT
• Possibly due to low GABA levels or conformational changes to GABA
  ▪ Not clearly defined may be present if > 50 mg of diazepam or 10 mg of lorazepam is required to control symptoms in 1st hour of treatment
• Barbiturates may be an effective alternative

Prophylaxis
• For those with a hx of seizures, DT, or prolonged heavy alcohol consumption
  ▪ In minimally symptomatic and asymptomatic
  ▪ Chlordiazepoxide 50 to 100 mg every 6 hours for day one, 25 to 50 mg every six hours for an additional 2 days

Group Question
Per the CIWA protocol, scheduled dosing is the preferred method of benzodiazepine administration:

  a. True
  b. False

References
• Saitz R, O'Malley SS. ... Alcohol withdrawal syndromes - prediction from detailed medical and drinking histories. Drug Alcohol Depend 1983; 11:177.
References


• Hack JB, Hoffman RS. Thiamine before glucose to prevent Wernicke encephalopathy: examining the conventional wisdom. JAMA 1998; 279:583.


• Group on Pharmacological Management of Alcohol Withdrawal. JAMA 1997; 278:144.