POMA Substance Use Disorder Education Series

LIVE WEBINAR

Session I

"MAT and the Disease Model of Addiction" – Karen Arscott, DO

"The Management of Withdrawal and Overdose" – Eric Milie, DO

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THE FACTS – ADDICTION IS A DISEASE

*AND HOW CAN WE TREAT THE PATIENTS?

Karen E. Arscott, DO, MSc

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WHAT IS SUBSTANCE USE DISORDER?

DSM V Criteria

PHYSIOLOGIC:
- Taking the substance in larger amounts or for longer than you're meant to.
- Needing more of the substance to get the effect you want (tolerance).
- Development of withdrawal symptoms, which can be relieved by taking more of the substance.

PSYCHOLOGIC:
- Wanting to cut down or stop using the substance but not managing to.
- Cravings and urges to use the substance.
- Not managing to do what you should at work, home, or school because of substance use.

BEHAVIORAL:
- Spending a lot of time getting, using, or recovering from use of the substance.

EXTERNAL:
- Continuing to use, even when it causes problems in relationships.
- Giving up important social, occupational, or recreational activities because of substance use.
- Using substances again and again, even when it puts you in danger.
- Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance.

In the past 12 months:
2-3 = Mild
4-5 = Moderate
6+ = Severe

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DISEASES

- Diabetes Mellitus
- Hypertension
- Hyperlipidemia
- Myocardial Infarction – "heart attack"
- Cerebrovascular Disease – "Stroke"
- Substance Use Disorder

Chronic Progressive and Ultimately Fatal

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TERMINOLOGY

People First Language

Person with a Substance Use Disorder or Person with Alcohol Use Disorder

NOT

"Addict", "Alcoholic", "Junkie", "Abuser", "Drunk", "User", "Dirty", "Clean",…..

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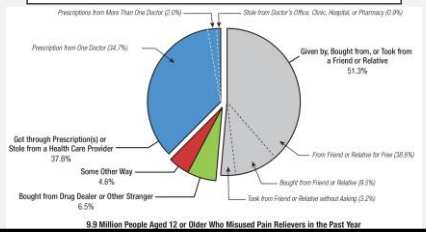
SAMHSA NATIONAL SURVEY ON DRUG USE AND HEALTH, 2018



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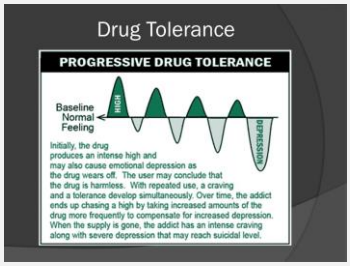

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NEUROANATOMY OF ADDICTION

- Who are the players?
- The Limbic System – responsible for emotional context and the affective response to learned associations
  - Limbic Lobe – Subcallosal Area, Cingulate, and Parahippocampal gyri
  - Amygdala
  - Hippocampus
  - Parts of the Hypothalmus
  - Habenula
  - Olfactory Cortex

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NEUROANATOMY OF ADDICTION – CONT.

- More Players:
- The Basal Ganglia – motor system – divided into:
- Input module is the Striatum – composed of three nuclei: Caudate, Putamen, and Ventral Striatum
- Ventral Striatum contains the Nucleus Accumbens (Nacc) and is considered part of the Limbic System. This is where "motivation is translated into action"

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NEUROANATOMY OF ADDICTION

- More players!!!
- The Prefrontal Cortex (PFC) – the "hub" of executive function in the brain. Divided into 3 regions:
- Orbitofrontal Cortex and the Ventromedial areas (vm-PFC) – processing reward
- Dorsolateral Prefrontal Cortex (dl-PFC) – decision making
- Anterior and Ventral Cingulate Cortex – helps to control whether a particular behavior will be performed and to what intensity.

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HOW DO DRUGS ALTER NEUROCHEMICALS?

- Neurotransmitters – the following are extensive and almost every area of the brain is innervated by one, two, or all 3 of these – and various substances impact these in various ways:
- Dopamine (DA)
- Noradrenaline (NA)
- Seratonin (5-hydroxytryptamine [5-HT])

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PSYCHOSTIMULANTS

- Cocaine binds to DA, NA, and 5-HT transporters – blocks the reuptake of neurotransmitters
- Amphetamine acts additionally as a releasing agent
- Results in Increased concentration!!!

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OPIOIDS

- Opioid receptors are throughout the brain – especially in the limbic and limbic-related structures.
- Three types of receptors:μ, κ, δ
- μ receptors – analgesia, euphoria, respiratory depression, emesis, and antidiuretic effects – most likely abused
- κ receptors (experimental compounds) - analgesia, dysphoria, and diuretic effects
- δ – less know about these receptors

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ALCOHOL

- Enhance release of Dopamine in limbic and cortical circuits that regulate motivated behavior.
  - -The Dopamine neurons with these projections are in midbrain ventral tegmental area
- Stimulants and opioids bind to specific protein receptors – alcohol interacts with a wide variety of targets – lipids and proteins
- Alcohol enhances GABA $_A$ and Glycine function – Stress may alter GABA receptors leading to increased drinking during stressful times
- Glutamate - major excitatory neurotransmitter in brain – processes involving cognition, learning, and memory
- Chronic exposure to alcohol increases density and clustering of NMDA receptors and increased neuronal excitability --> seizures

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WITHDRAWAL

- Different drugs will have different withdrawal symptoms and timelines depending on how they interact with the brain and bodily functions
- Drugs are absorbed and remain active in the body for differing amounts of time
  - This is referred to as the drug's "half life" and relates to the different withdrawal timelines for each substance
- The severity and duration of withdrawal is influenced by the level of dependency on a substance and a few other factors

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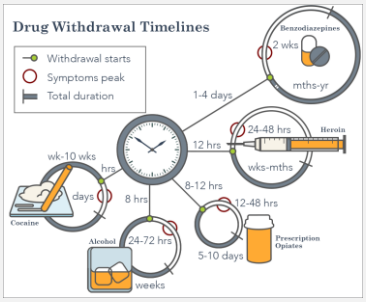

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WITHDRAWAL

- Opiates
  - Physical symptoms mimic the flu
  - Physiological symptoms
    - Early
      - Muscle aches, tearing, runny nose, yawning, insomnia, agitation, anxiety, and sweating
    - Late
      - Nausea, vomiting, chills or goosebumps, diarrhea, abdominal cramps, and dilated pupils

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WITHDRAWAL

- Alcohol
  - Withdrawal symptoms are many
    - Tension, panic attacks, tremors, difficulty concentrating, short term memory loss, anxiety, irritability, disturbed sleep, headaches, heart palpitations, sweating, nausea and vomiting, dizzy, shaky, mood swings, depression, nightmares, loss of appetite, and many more
  - Severe withdrawal include DTs, seizures, severe confusion, agitation, hallucinations, delirium, and death

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WITHDRAWAL

- Benzodiazepines
  - When the brain is dependent, if this drug is suddenly removed, a rebound effect can occur
  - There are heightened levels of anxiety and insomnia in the early stage
    - Tension, panic attacks, tremors, difficulty concentrating, short term memory loss, anxiety, irritability, disturbed sleep, headaches, heart palpitations, sweating, nausea
    - Seizures and death

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STIMULANTS WITHDRAWAL

- Cocaine withdrawal is usually manifested in three main phases
  - Initial crash
    - Nine hours to 4 days, symptoms are opposite the stimulant effects
    - Person may sleep for days, increase appetite, depression, agitation
  - Acute withdrawal
    - 1-3 weeks
    - Irritability, fatigue, depression, insomnia, anxiety, and drug craving
  - Extinction period
    - Cravings for cocaine along with depressed moods and even potentially suicidal thoughts may continue for several months after stopping use of cocaine

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STIMULANTS WITHDRAWAL CONT.

- Methamphetamine/Amphetamine
- Depression: hopelessness, sadness (weeks 1-3)
- Muscle Weakness (week 1-2)
- Decreased Appetite or increased carb cravings (weeks 1 -3)
- Fatigue/sleepiness: Lack of Motivation (week 1)
- Anxiety and Irritability (weeks 1 -5 and further)
- Insomnia despite exhaustion
- Headache from dehydration (week 1)
- Muscle pain – especially in jaw from clenching teeth (week 1)
- Psychosis – hallucinations (week 1)

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DETOX

- Goal of detox is to achieve a safe and comfortable level of physical stability so psychological manifestations of withdrawal can be addressed
- Various medications to provide relief of symptoms of withdrawal: N/V, Diarrhea, Constipation, etc…..
- Specific Medications will be used in detox as a means of achieving the above
  - Benzodiazepines/alcohol: phenobarbital is a long acting barbiturate - Goal is to prevent seizures from occurring
    - If history of seizures may add additional anti-seizure medication
  - Stimulants: Support and Clonidine (Catapress) to help with anxiety
  - Opiates: Clonidine and buprenorphine to help control physical symptoms

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MEDICATION ASSISTED TREATMENT

- MAT can be used in conjunction with other aspects of recovery, including group meetings (e.g. AA, NA), counseling, psychotherapy
- Alcohol: Naltrexone/Vivitrol, Disulfiram, Acamprosate
- Opiates: Naltrexone/Vivitrol, Buprenorphine (oral and long-acting injection), Methadone
- Methamphetamine: Naltrexone/Bupropion; Topiramate

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BUPRENORPHINE

- Buprenorphine: semi-synthetic opioid – derived from thebaine – naturally occurring alkaloid of the opium poppy
  - Analgesic
  - Maintenance therapy for Opioid Use Disorder
  - Partial agonist at opioid μ receptor
  - Clinical affects similar to methadone (less due to partial): analgesia, sedation, euphoria, and respiratory depression
  - Less cardiac toxicity
  - Longer duration of action

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BUPRENORPHINE - CONTINUED

- Why treat OUD?
  - Treatment of a disease
  - In France - patients who discontinued treatment (Bup or Methadone) were ~29 times more likely to die than those on Buprenorphine (Dupouy et al. 2017)
  - Heroin-related overdose deaths in Baltimore 1995 – 2009 decreased significantly as methadone and buprenorphine became available (Schwartz et al. 2013)
  - Reduced illicit opioid-related crime (Sullivan and Fiellin 2005)
  - Decreased transmission of communicable diseases (HCV and HIV). (Volkow et al. 2014)

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BUPRENORPHINE - CONTINUED

- High affinity for the mu-opioid receptor
  - 1.7 times that of hydromorphone
  - 5.4 times that for morphine
  - 6.2 times that of fentanyl
  - 120 times that of oxycodone
- Difficult to displace – blocks subjective and physiological effects of other opioids
- Precipitate withdrawal if given while person with recent opioid use
  - Thus the need for a person to be in withdrawal for induction

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NALTREXONE

- Blocks the μ receptors – it is an opioid antagonist.
- Used for Alcohol – it stops the cravings – not sure of mechanism of action
- One theory is that it prevents the "feel good chemicals" from being released (stops the endorphin rush). With time, the brain disassociates alcohol from feeling good.
- For opiates – it directly blocks the effects of opiates – it is an antagonist

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METHADONE – 50 YEARS

- Long-acting full opioid agonist – Schedule II medication
- Used for both OUD and for pain management
- When taken as prescribed it is safe
- Unintentional overdose is possible
- High rates of retention
- Lower rates of illicit opioid use
- Reduced mortality, criminal behavior, and HIV/HCV disease
- Half-life 8-59 hours – average 24 hours

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METHADONE – PRECAUTIONS/WARNINGS

- No Ceiling effect!
- Increasing doses produces maximum effects – plasma levels reach steady state in 5 days – toxicity can happen even without increasing dose
- Many drug – drug interactions – CYP450
- Respiratory depression
  - COPD or Asthma
  - Concurrent Benzodiazepine or alcohol use
- **QTc Prolongation**
  - Personal or Family history cardiac disease
  - Current use of medications that may increase QTc interval
  - Patient history of cocaine or methamphetamine use
  - Electrolyte assessment

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METHADONE TO BUPRENORPHINE

- Challenging
- Patient must wean down Methadone
- Must be in withdrawal for buprenorphine induction

- More ease in dosing with possible transition to monthly long-acting injection of buprenorphine from daily observed dosing of methadone

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PREGNANCY AND MAT

- **Withdrawal will kill the baby!**

- Transition to either Buprenorphine or Methadone can be challenging
- Mothers with substance use disorder are really stuck – most want to stop all substances but are not allowed due to the risk of withdrawal and miscarriage
- **Neonatal abstinence Syndrome** (NAS) is less with buprenorphine

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POST-ACUTE WITHDRAWAL SYNDROME (PAWS)

- There are 2 stages of withdrawal
  - Acute: usually lasts a few weeks
  - May experience physical symptoms
  - Post-Acute Withdrawal: fewer physical symptoms but more emotional and psychological withdrawal symptoms
- PAWS
  - Occurs because your brain chemistry is gradually returning to normal
  - As your brain improves the levels of your brain chemicals fluctuate as they approach the new equilibrium

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Thank you!

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