OPIOID USE DISORDER - PHARMACOLOGY

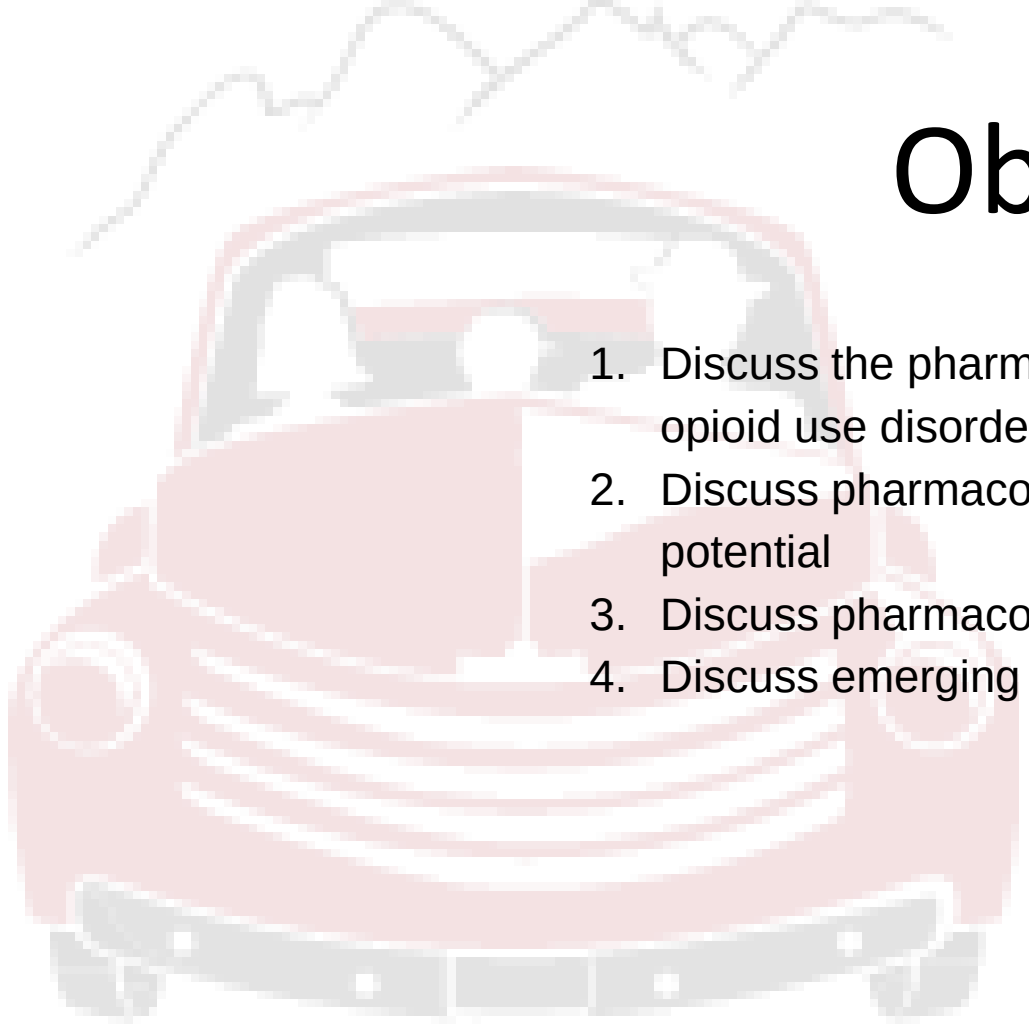
Dr. Patrick Green MD

BONNEVILLE
FAMILY PRACTICE

Patrick Green MD

- My professional career as a medical doctor has focused on providing preventive care, acute and chronic disease management and the treatment of adults with substance use disorders.
- Board certified Family Physician
- Bonneville Family Practice opened 2011 in Tooele Utah
- 15 years treating opiate use disorder in a primary care setting with integrated mental health services
- Methadone treatment added August 2023

Objectives



1. Discuss the pharmacology of specific substances related to opioid use disorder and its treatment
2. Discuss pharmacologic characteristics related to addictive potential
3. Discuss pharmacologic characteristics of treatment options
4. Discuss emerging treatments

Pharmacology

Pharmacodynamics - Effect of a substance in human body

- Mechanism of action
- Effect & side effects

Pharmacokinetics - Behavior of a substance in the human body

- Absorption, Bioavailability
- Onset of action
- Duration of action
- Metabolism & excretion

Opioid Mechanism of Action

- Primary action: Stimulate μ opioid receptor (MOPr)
    - Effect:
        - Euphoria
        - Reduced anxiety
        - Analgesia
    - Side effect:
        - Respiratory depression, Constipation, Nausea, Hypotension, Endocrine abnormalities
- Other actions: Stimulate δ (DOPr) and κ (KOPr) receptors
    - Analgesia
    - Dysphoria, Diuresis, Constipation

Morphine

- **Full** mu receptor **agonist**
- **Moderate** IV availability, low oral bioavailability (25%)
- **Slow** acting, time to peak: 1 hr oral, 10 min parenteral
- ½ life 2 hr
- Metabolized by the liver and excreted by kidneys

Oxycodone

- **Full** mu receptor **agonist**
- **High** bioavailability oral 70%
- **Slow** acting: time to peak 1 hr (oral)
- ½ life 3 hr
- Metabolized by the liver and excreted by kidneys
- Oxycodone:morphine equivalency 1.5:1

Heroin

- **Full** mu receptor **agonist**
- **High** IV, moderate Inhalation, poor oral availability
- 68% of IV reaches CNS
- **Rapid** acting: Time to peak 1 min IV
- Short duration: ½ life 22min
- Metabolized by the liver and excreted by kidneys

Fentanyl

- **Full mu receptor agonist**
- **100x** more **potent** than heroin and morphine
- Relatively good inhalation absorption, poor oral
- **Rapid** acting: Time to peak 2 min INH
- ½ life 2.5 hr for elimination, but redistribution limits duration of action to 1-2 hr
- Metabolized by the liver and excreted by kidneys

Methadone

- **Full** mu receptor **agonist**
- Oral absorption 80%
- 68% of IV reaches CNS vs. 5% of IV morphine
- **Slow** acting, time to peak 2.5 hr
- **Long** duration: ½ life 36 hr
- Metabolized by the liver and excreted by GI & kidneys
- Methadone:morphine equivalency 10:1

Buprenorphine

Subutex, Suboxone, Sublocade, Zubsolv

- **Partial** mu receptor **agonist** with **high affinity** and **low activity**
  - Reduces withdrawal related symptoms
  - Reduces cravings
  - Counteracts reinforcing effects of full agonists (euphoria, analgesia)
  - Little if any euphoric effects
  - Reduced respiratory depression - ceiling effect
- Low oral bioavailability, but sublingual absorption is adequate
- **Slow** acting, time to peak 1 hr (sublingual)
- **Long** lasting, ½ life 36 hr
- Metabolized by the liver and excreted primarily by GI tract

Naltrexone

- mu receptor **antagonist**
- **Oral** absorption 100%
- Time to peak 1 hr
- ½ life 8 hr
- Metabolized by the liver

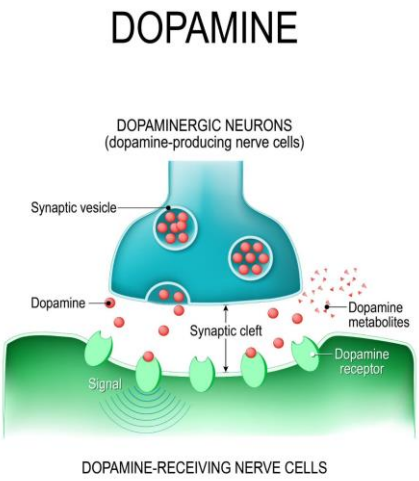
Characteristics favoring substance misuse

- **High** bioavailability - IV
- Rapid CNS entry - INH/smoking
- **Rapid** absorption
- **Short** half-life

Characteristics favoring treatment

- **Good** oral bioavailability = easy to administer
- **Long** half = less frequent dosing, reduced w/d onset
- Agonist **interference** = reduced OUD reinforcement
- Favorable side effect profile
- Safe

Stimulant Mechanism of Action



- Primary action: Increase dopamine (and serotonin, norepi) through varying pathways
    - Effect:
        - Euphoria
        - Energetic
        - Alert and focused
    - Side effect:
        - Tachycardia, agitation, paranoia

Methamphetamine

- Presynaptic dopamine, serotonin and norepinephrine release
- 70% availability INH/Smoked
- **Rapid** acting, time to peak 18 min
- **Moderate** duration: ½ life 12 hr
- Excreted by kidneys

Cocaine

- Synaptic dopamine reuptake inhibition
- **High** availability, 90% smoked, 80% nasal
- **Rapid** acting, time to peak 15 min
- **Short** duration: ½ life 1 hr
- Metabolized by plasma proteins and liver