

**Chronic Disease Assignment:**

**Opioid Dependency and Abuse**

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## Introduction

Opioid Dependency is a neurobiological disease characterized by the body's reliance on opioid drugs to maintain homeostasis. If an afflicted individual does not consume opioids, they suffer intense pain caused by the overproduction of the neurotransmitter noradrenaline (Kosten, 2002). If they consume too much, they suffer respiratory failure and death. However, as the disease progresses, drug tolerance develops and drives the person to consume ever increasing amounts making overdose more likely (Blanco, 2019). Understanding the pathophysiology of the disease may help reduce social stigma and support preventative measures.

Risk factors of the disease are difficult to ascertain, as anyone can develop Opioid Dependency, though it is believed that histories of sexual abuse, physical abuse, social isolation, and stigma may place an individual at greater risk of addiction (Maté, 2008; Hser, 2015; Silva, 1990; Waldinger, 2015). In 2021, Canadian males between the age of 30 to 39 accounted for 76% of opioid overdoses with rates 5.6 times higher among First Nations individuals as opposed to non-indigenous (Hatt, 2022).

With the marketing and over-prescription of opioids between 1999 and 2008, North America has lost more lives to the Opioid Epidemic than to HIV/AIDS (Dyer, 2021; Theisen, 2018). The Center for Disease Control in the United States reported 70,237 drug related overdose deaths in 2017, 67.8% of which involved an opioid, and in Canada the rate of deaths rose from 11 per day to 20 per day between 2017 and 2022 (Health Canada, 2019; Public Health Agency of Canada, 2022; Scholl, 2019).

## Pathophysiology

Mu-opioid receptors are located postsynaptically in the dorsal horns of the spinal cord and in the periaqueductal gray area of the brain- a region responsible for autonomic nerve function including heart rate, respiratory rate, and pain sensation. Under normal conditions, sensory neurons in the peripheral nervous system detect stimuli and send action potentials (signals) through nerve tracts to the central nervous system where they are processed. Signals are sent back out to the somatic nervous system (voluntary action) and the autonomic nervous system (involuntary) where effector tissues carry out the command on muscles and organs. K<sup>+</sup> ions are concentrated inside of nerve cells, and Na<sup>+</sup> ions are concentrated outside causing polarization. Sodium-potassium pumps in their cell membranes use adenosine triphosphate (ATP) to maintain a resting concentration gradient but can open to allow the flow of ions and send an electrical signal down a nerve tract. Between neurons within the tract, junctions called synapses allow for the transmission of different signals over a small gap, called a synaptic cleft, using neurotransmitters. The presynaptic cell releases these chemicals into the cleft which are then picked up by receptors on the postsynaptic cell. If there are more neurotransmitters than there are receptors, the excess can be recycled by reuptake, removed by enzymes, or they simply diffused away. Under normal conditions, the transmission of signals to and from the central nervous system happens unimpeded (Cohen, 2019).

When opioids enter the bloodstream from the consumption of drugs- inhaled, injected, or consumed- and reach the nervous system, they bind to mu-opioid receptors more strongly than natural neurotransmitters, inhibiting K<sup>+</sup> conductance and preventing action potential signals between neurons. In the dorsal root ganglion of the spinal cord, this stops the transmission of pain information to the brain. At the same time, opioids bind strongly to mu-opioid receptors in the brain, which signal the Ventral Tegmental Area to release dopamine into the Nucleus Accumbens causing immense pleasure. This triggers the Mesolimbic Reward System that is usually activated by food, sex, and other life functions, until the drug wears off and creates memories of pleasure. These memories induce cravings in the individual when they encounter similar environments again. Normally, the Prefrontal Cortex helps override the desire to seek pleasure at the expense of self-harm, but this feedback appears to be compromised in individuals struggling with dependence. The tolerance to opioids develops with repeated use and the consumer must increase their dosage to achieve desired effects. The mechanisms for drug tolerance involve slower opioid receptor-G protein uncoupling, decreased receptor recycling, and the body's reduction of opioid receptors in response to overstimulation (Kosten, 2002).

At the same time, opioids repress the release of Noradrenaline (NA)- a neurotransmitter that stimulates wakefulness, breathing, and blood pressure. Large concentrations of opioids induce a state of drowsiness, slower respiration, and low blood pressure. This is called opioid intoxication. To compensate and return to normal functioning, the Locus Ceruleus produces higher levels of NA, but when intoxication wears off production levels do not return to normal. NA then surges through the body causing hyper-alertness, anxiety, muscle cramps, and diarrhea. This is known as Opioid Withdrawal Syndrome. Afflicted individuals are simultaneously pulled by the compulsive desire to seek pleasure and pushed by the pain of withdrawals to consume again, only to further increase their own tolerance- a positive feedback loop with dire consequences (Kosten, 2002).

The greatest risk of death is after a patient has sought help for their condition. After detoxifying their body of opioids and persevering through withdrawals, an individual may lose their physical dependence and tolerance to opioids, yet the mechanism for addiction remains. If not properly cared for, the person is likely to consume opioids again but at their pre-treatment dosage levels leading to fatal hypoxia. Even with careful planning of dosage, street drugs are the only opioids a patient can likely afford at this point, many of which are cut with fentanyl- a synthetic opioid 100 to 10,000 times more potent than morphine (Bergh, 2021), **Figure 1**. A single grain of fentanyl, equivalent in size to a grain of sand, is enough for an average person to fatally overdose. As such, 64% of all opioid overdoses test positive for fentanyl, and 91% of fatal overdoses occur in hotels, motels, or private rooms where a patient unknowingly consumes fentanyl without supervision (Somerville, 2017).



*Figure 1: Pharmaceutical Hydrocodone/Acetaminophen Tablet vs. Counterfeit Tablet laced with Fentanyl. (Sutter, 2017)*

## **Symptoms and Progression**

Contraction of the disease often begins with the repeated consumption of opioids, or the single consumption of a large dose. Most frequently, a patient will enter a hospital for an unrelated trauma and require analgesics. They may be inappropriately prescribed opioids for their treatment and develop dependence before their recovery is finished (Theisen, 2018).

Alternatively, an individual may be exposed to recreational opioid abuse through their social groups. Either way, the first symptoms of withdrawal set in due to the over-production of NA and include the following: muscle aches, stomach pain, fever, vomiting, anxiety, diarrhea, vulnerability to stress, and opioid cravings.

As tolerance develops, the strength of withdrawals increases, and higher doses are needed to keep the body functioning in an awakened state- too much will lead to opioid intoxication or overdose, and too little will cause immense pain. Other ongoing effects may include depression due to damaged synapses, and obsessive thoughts to obtain and use opioids. The compulsion to consume despite environmental hazards, and self-harm, may lead to physical abrasions, dehydration, weight loss, increased risk of HIV, hepatitis B, and hepatitis C (due to sharing of intravenous needles), and impaired neurological function. Other consequences may include the

loss of employment, housing, financial savings, and social connections which contribute to depression and compel the individual to seek further relief through opioids (Kosten, 2002; Sutter, 2017).

During a state of overdose, noradrenaline (NA) is suppressed causing hypotension, hypoxia, eye miosis (constricted pupils), and unconsciousness. As low oxygen levels endure, cellular function is inhibited and the heart stops. A first-responder's top priority is to restore oxygenation to the brain and body before irreversible cell damage is sustained. Working safely in pairs, one paramedic will administer cardiopulmonary resuscitation (CPR) while the other prepares an automated external defibrillator (AED). Once regular heart rhythms return, they stop any major bleeds and administer naloxone if they believe there are signs of opioid use. Naloxone is a competitive mu-opioid receptor antagonist; it has a higher binding affinity than most opioids and does not activate receptors or inhibit the autonomic nervous system. The effects are temporary, 30 to 90 minutes, and if the overdose is severe, multiple doses may not be enough to resuscitate the patient. Long-term symptoms of a recovered and rehabilitated patient may include impaired neurological function, psychiatric disorders, shortened life expectancy, and persistent opioid cravings (Kosten, 2002; Sutter, 2017).

### **Assessment and Treatment**

Standard opioid testing is done through immunoassay urine drug testing. A sample of urine is mixed with a chemical solution containing antibodies specific to the target opioid. If opioids are present, they bind to the antibodies and form a larger, detectable complex. Fentanyl is a fully synthetic opioid; it is not picked up by regular tests and needs its own targeted urine test (Bergh, 2021; Sutter, 2017). Verbal assessments may also be effective as patients may seek help voluntarily or at the request of family members (Katz, 2002). The Diagnostic and Statistical Manual of Mental Disorders (DSM5) uses an 11-question assessment to determine severity of the disorder, with questions ranging from dosage and frequency to behaviours and cravings (American Psychiatric Association, 2013).

Methadone is commonly prescribed as a long-term treatment option for Opioid Dependence but is, in fact, an opioid. Dependence will still develop, but the advantage is that methadone produces minimal opioid tolerance in the central nervous system due to a steadier influence on mu-opioid receptors. This allows patients to maintain a consistent dosage for years until rehabilitation is possible. However, methadone can be expensive, must be prescribed by a physician, only stays in the body a few days, and does not induce euphoria which may complicate treatment for cravings. Patients who continue with methadone for 2 or more years are far less likely to experience relapse (Kosten, 2002).

Longer Acting Derivative of Methadone (LAAM) works similarly to Methadone but acts on the body for longer. Doses may be given 2 to 3 times per week and can normalize cortisol and stress levels for the patient. Concerns about heart rhythm complications have limited LAAM's popularity as a method of treatment (Kosten, 2002).

Naltrexone, like naloxone, is a competitive mu-opioid receptor antagonist and blocks the effects of opioids on the brain. It may be administered twice weekly and binds to receptors 100 times stronger than opioids do. It does not produce feelings of pleasure, however, and patients may struggle with cravings. It is important that patients are fully detoxified from opioid use before beginning naltrexone treatment or they may experience severe withdrawal effects. Due to the lack of euphoria, naltrexone has poor compliance ratios amongst heroin consumers at only 15% (Kosten, 2002).

Clonidine is an alpha-adrenergic agonist that suppresses NA production and may be used in conjunction with naltrexone to rapidly detoxify a patient while minimizing the effects of withdrawal (Kosten, 2002).

Buprenorphine is a partial opioid agonist that acts on mu-opioid receptors with two possible responses: (1) in low doses it produces effects like methadone, and (2) in high doses it behaves like naltrexone. It binds to receptors and gives euphoria but has milder effects than other opioids. This helps with cravings, but then automatically prevents overdose if abused. Buprenorphine is sometimes mixed with naltrexone within tablets to prevent illicit use (Kosten, 2002).

Long-term studies on successful treatment are mostly associated with methadone, though the effectiveness of naltrexone and buprenorphine have yet to be assessed. Opioid Dependence appears to be a chronic disorder; successful abstinence from opioid use is around 30% after 10-30 years. Some people have overcome Opioid Dependence and gone on to live successful lives, though many struggle with lifelong cravings. The likelihood of future stable abstinence increases significantly after 5 years of sobriety (Hser, 2015).

### **Patient and their Environment**

As mentioned in the introduction, certain socio-economic factors place some individuals at higher risk than others. Persons who become dependent often consume their first dose in a social setting where they are looking for acceptance, respect, and to combat loneliness. Groups may form around the consumption of the drug, and cravings to repeat pleasurable feelings set in. Once dependency matures, all waking thoughts become fixated on procuring more of the drug. People will ruin themselves financially, steal from friends and family, and commit crimes to avoid the pains of withdrawal and feel normal again. The loss of their social connections, financial stability, and health drives them further into desperation and loneliness. Street dealers will pretend to be a new customer's friend and are prepared to resell stolen property so that clients may buy more. Dehydration, malnutrition, compulsive behaviour, and severe weight loss start to alter an afflicted person's appearance. To save resources, similarly dependant individuals will share intravenous needles and risk contracting HIV, hepatitis, and other blood-borne diseases.

Eventually, criminal activity leads a patient to incarceration where they suffer withdrawals: methadone and other treatments are not provided in prisons. "Your intestines and your bones

[feel] like they are on fire one minute, then being frozen the next. You [get] horrible sweats, you're... sick, you get diarrhea, you [can't] keep still, you [get] twitches, your mind [won't] switch off, you can't sleep... and, because you're not [properly treated before you come out], within an hour [you're] taking heroin again" (LADbible TV, 2020). When patients are released from Canadian prisons without proper treatment, they are at severe risk of death due to overdose and violent crime.

No person is immune to the effects of Opioid Dependence. Family members that enter hospitals for physical trauma may be inappropriately prescribed opioids, develop dependence, and follow a downward trajectory as they struggle to maintain jobs and relationships (Dyer, 2021). It is important for loved ones to know that recovery is possible and directly depends on the social support of friends and family (Maté, 2008; Hser, 2015; Silva, 1990; Waldinger, 2015). Knowledge of the pathophysiological origins of Opioid Dependence may help relatives understand that it is not a choice, it is a real disease, and no one is immune.

The physical half of the disorder may be treated medically, but the other half must be treated socially for recovery to be successful. The resolution of the Canadian Opioid Epidemic must come from a multi-pronged approach:

- Pharmaceutical legislation:
  - Stronger restrictions on opioid prescriptions (Dyer, 2021)
  - The elimination of over-the-counter opioids (Frei, 2010)
  - The promotion of non-opioid, medically proven pain killers (Nicol, 2017)
- Federal legislation:
  - The establishment of a national drug insurance plan under the Canada Health Act (Morgan, 2016)
  - The full decriminalization of illegal substances (Greenwald, 2009)
  - Access to rehabilitation and employment programs for Canadian prison inmates (Giersten, 2012; Skardhamar, 2012)
- A cultural shift in perspective:
  - The promotion social skills from a young age (Silva, 1990)
  - More frequent connections with loved ones (Waldinger, 2015)
  - Empathetic recovery support from friends and family if they are able.

The opioid epidemic should belong to a new class of disease: one afflicts the social fabric of our culture and may only be prevented by the slow stitching and repairing of our relationships. Forgive family members and friends for transgressions, call and ask how they've been, and make plans to see each other in person (Silva, 1990; Waldinger, 2015), because "the opposite of addiction is not sobriety, [it is] connection" (Mate, 2008).

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