Volume 4 | Issue 5

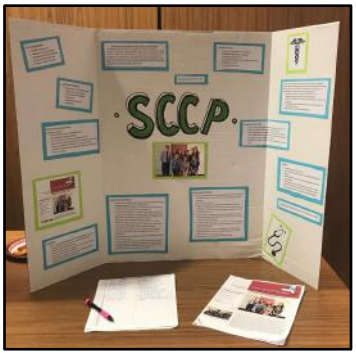
May 2019

NYS-ACCP Insider

D'Youville School of Pharmacy

Special Points of Interest:

Photographed Below: Student members who contributed to the Newsletter



Poster board for P1 orientation

D'Youville School of Pharmacy: ACCP Chapter Synopsis

Over the past academic year, our chapter at D'Youville has focused on upholding ACCP's core values and mission. We have provided our members with information and resources on residencies and careers, research opportunities, and knowledge in order to develop new skills which promotes advancement of pharmacists in healthcare. This year our chapter has continued to support not only clinical research, but also benchtop research and the opportunities to potentially participate in both. We have offered the opportunity to participate in clinical research competitions, invited guest speakers to talk about clinical pharmacy, and collaborated with other organizations within our school.

Student, Shea Bacon working on research projects

Dr. Christine Roth Guest Speaking at D'Youville College School of Pharmacy

Faculty talking to student at the annual research mixer

In November, we held our second annual research mixer. At this event, faculty conducting clinical or benchtop research were invited to attend and showcase their research. This allowed students the opportunity to see what research is currently being done and network with the faculty. The goal of this event was to provide students with an opportunity to meet with professors and see if there may be an interest on both ends for students to become involved in current or future research projects. Many students who attended the event are now collaborating with faculty on different projects highlighting how this event lead to opportunities for both the faculty and student. In the spring, we also sponsored guest speaker Dr. Christine Groth from Strong Memorial Hospital in Rochester, NY, who spoke about research in the clinical setting and all that it entails.

Six of our chapter members attended the NYS ACCP Fall Clinical Meeting on the first weekend in November 2018. During this meeting, the students were paired with clinical pharmacists in their field of interest and able to ask questions to learn about residencies and careers in that field. Of the six members, three competed in the first ever clinical competition, "Pharmacy Quiz Bowl". We promote events and meetings such as this to allow our students to not only network, but also obtain experience before deciding what they would like to do after graduation.

To further encourage the field of clinical pharmacy, we collaborated with the Student Societies of Health System Pharmacy (SSHP) at D'Youville to invite two guest speakers to come and talk about their roles in the field of clinical pharmacy . We had the pleasure of having Dr. Nicole Webb and Dr. Joel Costanzo from Niagara Falls Memorial Hospital come speak to our members about their roles as clinical pharmacists, how they ended up there, the steps they needed to take to get to their positions, and what we could do as students to prepare for a career in clinical pharmacy practice.

Our chapter will continue to work at maintaining and promoting the core values of ACCP at D'Youville College School of Pharmacy. We have many exciting new ideas for the future, including continuing to collaborate with other organizations, hosting a drug spelling bee, inviting new guest speakers, and going on tours of labs at local hospitals. Expanding the knowledge of our student members and encouraging involvement in research and publications will continue to be goals that we uphold. We look forward to seeing what our chapter will accomplish next and the direction in which it is headed here at D'Youville.

2018-2019 E-Board
- *Co-Presidents: Samantha Poblete & Jordan Scott*
- *President Elect: Dupinder Dhaliwal*
- *Vice President: Simona Armenti*
- *Secretary: Brittney Hannot*
- *Treasurer: Preston Palmer*

Student, Chris Ford transferring cells in the lab

Chapter Advisors:
- *Dr. Aubrey Defayette (left)*
- *Dr. Joseph Dunn (right)*

New Approaches to Cocaine Use Disorder

Cocaine is isolated from the Erythroxylum coca plant, found in the Andes Mountain range. Acute administration of cocaine leads to a buildup of dopamine in the nucleus accumbens, where dopamine transporters exist. These transporters normally regulate the amount of dopamine available to interact with receptors. When cocaine is administered, it interferes with this mechanism, and dopamine cannot be retrieved by the transporters, ultimately leading to a euphoric effect.[1] Chronic exposure has been shown to have an effect on transcription factor ΔFosB in the striatum. The accumulation of ΔFosB is thought to influence the development of cocaine use disorder. After chronic administration with consistent use for up to 8 weeks, this factor builds up in several areas of the brain, including the nucleus accumbens, amygdala, and frontal cortex, leading to a long-lasting adaptation.[2]

Currently, there are no FDA approved drugs for the treatment of cocaine use disorder. However, there are drugs that are not FDA approved that display potential mechanisms to assist in the treatment of cocaine use disorder. Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the central nervous system. By inducing GABAergic neurons, dopamine release is decreased.[3] Some medications with this mechanism include baclofen, tiagabine, and topiramate. Baclofen is a $GABA_B$ agonist and is used as a muscle relaxant via reduction of dopamine release.[3] Tiagabine is a selective blocker of GABA reuptake transporter type 1 at the presynaptic and is used for seizures.[3] Topiramate promotes the release of GABA and inhibits the release of glutamate by the AMPA/kinase receptors both leading to a reduction in dopamine.[3]

Disulfiram is another drug that has been used to prevent relapse to cocaine. Disulfiram interrupts the effect of cocaine by inhibiting dopamine β-hydroxylase (DBH), a copper dependent enzyme, which is responsible for converting dopamine to norepinephrine.[4] The primary metabolite of disulfiram is a copper chelator and leads to the inhibiton of DBH.[9] This produces little norepinephrine, which causes decreased activation of the midbrain dopamine neurons.[9] Consequently, the lack of firing will decrease the levels of dopamine contributing to a reduction in euphoria and the effects of cocaine. However, pervious studies have shown varied results with disulfiram and cocaine. One human study concluded decrease in subjective cocaine effects with increase in negative effects such as paranoia and anxiety.[8] Additionally, narcoleptic drugs, such as modafinil, have shown promise in reducing relapse and blocking the euphoric outcomes of cocaine. Modafinil helps with repletion of glutamate levels in the brain which decrease relapse.[3]

A new approach being developed to treat cocaine use disorder is a vaccine. Cocaine is a relatively small molecule that can easily cross the blood brain barrier. The idea behind the vaccine is the ability to inhibit cocaine from crossing the blood brain barrier. The vaccine contains antibodies, relatively ~150,000 daltons, that would target and bind to cocaine molecules to prevent their passage across the blood-brain barrier. This would ultimately decrease the amount of euphoria experienced, leading to an unsatisfied high and limit the chance of relapse. TA-CD anti-cocaine vaccine contains succinyl norcocaine conjugated to cholera toxin B.[5] This vaccine shows promise but the effects were inconsistent among individuals. During a phase IIa, outpatient trial, 18 participants were administered either 4 injections of 100 micrograms or 5 injections of 400 micrograms over a 3-month period. The highest mean antibody was found in the 400-microgram group and levels were found to be 3 times higher than in 100 microgram group. Participants in

This trial was later halted at phase IIb because phase III efficacy was not found. A new vaccine is undergoing phase I trial, dAd5GNE, which uses a third- generation cocaine hapten with a disrupted adenovirus as a carrier. The idea behind changing the hapten and carrier is to increase the potency of immunogencity.[6] This trial will consist of 30 participants who will each be administered either 100 micrograms, 316 micrograms, or 1000 micrograms of vaccine versus placebo at weeks 0,4,8,12,16 and 20. Both male and female participants are eligible if they were between the ages of 21 and 69, diagnosed according to the DSM-V-TR criteria with a cocaine use disorder, had evidence of cocaine use documented in the past 60 days, and a body weight greater than 45 kg. Participants will be excluded if they currently are taking a beta-blocker, have an allergy to soy, significant cardiovascular disease, or history of psychotic disorders. The primary outcome being evaluated is urine cocaine metabolites, and the secondary outcome is cocaine abstinence signs and symptoms. This is an ongoing trial that is suspected to be completed in May of 2019.[7] The results of this trial may lead to a unique approach for treatment of cocaine-dependent individuals.

References

1. Nestler, Eric J. "The neurobiology of cocaine addiction" *Science & practice perspectives* vol. 3,1 (2005): 4-10.
2. Audrey Lafragette, Michael T. Bardo, Virginie Lardeux, Marcello Solinas, Nathalie Thiriet; Reduction of Cocaine-Induced Locomotor Effects by Enriched Environment Is Associated with Cell-Specific Accumulation of ΔFosB in Striatal and Cortical Subregions, *International Journal of Neuropsychopharmacology*, Volume 20, Issue 3, 1 March 2017, Pages 237–246, https://doi.org/10.1093/ijnp/pyw097
3. Kampman, KM. "New medications for the treatment of cocaine dependence" *Psychiatry (Edgmont (Pa: Township))* vol. 2,12 (2005): 44-8.
4. Gaval-Cruz M, Weinshenker D. mechanisms of disulfiram-induced cocaine abstinence: antabuse and cocaine relapse. *Mol Interv*. 2009;9(4):175–187. doi:10.1124/mi.9.4.6
5. Heekin, R. D., Shorter, D., & Kosten, T. R. (2017). *Current status and future prospects for the development of substance abuse vaccines. Expert Review of Vaccines, 16(11), 1067–1077.*
6. Hicks, Martin J et al. "Cocaine analog coupled to disrupted adenovirus: a vaccine strategy to evoke high-titer immunity against addictive drugs." *Molecular therapy : the journal of the American Society of Gene Therapy* vol. 19,3 (2011): 612-9.
7. Clinical trials. URL:https://clinicaltrials.gov/ct2/show/NCT02455479?term=NCT02455479&rank=1 acessed April 1, 2019
8. Haile CN, De La Garza R 2nd, Mahoney JJ 3rd, Nielsen DA, Kosten TR, Newton TF. The impact of disulfiram treatment on the reinforcing effects of cocaine: a randomized clinical trial. *PLoS One*. 2012;7(11):e47702. doi:10.1371/journal.pone.0047702
9. Gaval-Cruz M, Weinshenker D. mechanisms of disulfiram-induced cocaine abstinence: antabuse and cocaine relapse. *Mol Interv*. 2009;9(4):175–187. doi:10.1124/mi.9.4.6

- Brittney Hannot, Pharm D. Candidate of 2020
- Samantha Rowland, Pharm D. Candidate of 2022

Effects of Nicotine in Adolescent Populations

The tobacco industry has found ways to effectively evolve and continue to serve as a hazard to our public health. However, according to the CDC, smoking rates are down from 20.9% in 2005 to just above 14% in 2017. Despite the lower prevalence, this 14% still accounts for over 38 million Americans, with a rise in adolescent prevalence.[1] The CDC also recently reported that 27.1% of adolescent use some form of nicotine. However, only 8.1% frequently use cigarettes.[2] If adolescents are not using cigarettes, how are they satisfying their need for nicotine? The industry has adapted to the latest trends and created electronic nicotine delivery system (ENDS) as a more appealing alternative to the cigarette. Also known as vaping or an electronic cigarette (e-cigarette), this alternative does not offer improved health outcomes for users. The chronic and long term effects of these nicotine products still have significant consequences, including an immediate impact on the brain and overall development. Youth tend to be more vulnerable in developing a dependence on nicotine versus adults. Initial symptoms can be seen within days, and with continued use, a transition to a dependence can present within weeks. Smoking in adolescence, like any habit, is more difficult to break the longer it persists, making cessation as an adult a challenging issue for many.

A publication from the American Academy of Pediatrics written by L. Siqueira reports that nicotine is metabolized primarily by the liver. Only 10% of the nicotine is excreted by the kidneys in it's pure form. Nicotine metabolism involves a two-step process, mediated by cytochrome P450 enzymes, CYP2A6 and CYP2B6. The first step involves the production of the metabolite, cotinine, which is converted to multiple byproducts, 3'-hydroxycotinine being the most abundant. The 3'-hydroxycotinine to cotinine ratio is a reflection of nicotine clearance and is considered the nicotine metabolic rate. This ratio is useful in distinguishing a smoker from a non-smoker.[3] Second hand-exposure to smoke also affects cotinine concentration by 1 ng/mL to 10 ng/mL, whereas in an active smoker the concentration varies from 10 ng/mL to 500 ng/mL. In a study conducted by Ho MK, et al. there are reports that people who carry reduced or null CYP2A6 enzymes are less likely to be smokers and have a decreased risk of progression to nicotine dependence. However, the opposite can be said for individuals with the an enhanced CYP2A6 which leads to a faster metabolism.[4] In a study conducted by Rubinstein, et al., researchers assessed the rate of metabolism in adolescence for nicotine and hypothesized that since a slower metabolism would lead to a lower tendency of frequent smoking, adolescents would experience the same effects. However, this was not the case. The study reported that adolescents who chose to smoke nicotine with slower metabolisms smoked more cigarettes per day and had higher craving scores. The authors hypothesized that since the brains of children are exposed to greater amounts of nicotine for a longer period of time, slower metabolizers would most likely develop dependence in the earlier stages of smoking.[5] Thus, it is difficult to predict the exact role pharmacogenomics will play in nicotine dependency, but a consensus can be reached on the idea that the risk for dependency in adolescents who are still maturing is extremely variable, reinforcing a recommendation to avoid the use of any nicotine products.

An additional concern with adolescent smoking comes from recent studies that show its harm on brain development. One study closely examined nicotine's effects on the adolescent brain and found that continued disruptions of the adolescent brain's cholinergic system via any nicotine products can result in developmental consequences.[6] These consequences may be both structural and neurochemical changes. Structural changes are a result of the fluid state of the brain during adolescence. The specific ratios of white and grey matter in various areas of the brain are still changing as adolescents mature. These changes can be altered by the use of nicotine, causing an imbalanced maturation of areas of the brain, promoting high risk behavior. Furthermore, the neurochemical alterations are a result of the upregulation of the dopaminergic signaling system. This change in dopamine signaling is responsible for noticeable changes in motivation and learning.[6]

Nicotinic acetylcholine receptors (nAChRs) are pentameric, ligand-gated ion channels that are widely distributed in human and rodent brains throughout all development phases. The nAChRs are composed of 2 subunits, both homomeric and heteromeric. These subunits contribute to a diverse receptor pharmacology by regulating agonist affinity/efficacy, ion selectivity, desensitization, and downstream signaling. Each nAChR receptor exhibits distinct patterns of expression and function throughout the central and peripheral nervous system. The most abundant neuronal subtype is the α4β2 nAChR, which has high affinity for nicotine. These receptors are known for desensitizing nicotine at concentrations lower than those required for activation and as a result are mostly desensitized in the brains of smokers. Neuronal nAChRs are central regulators of neurophysiology and signaling in use disorder pathways. nAChR activation in these regions also regulate dopamine, which is heavily involved in drug reinforcement.[6]

Neuronal nAChRs exhibit distinct patterns of expression that parallel key development events within the cholinergic system and are vital when it comes to maturation from prenatal development through adolescence. Scientists have experimented on rodents and found that α4β2 and α7 nAChR expression and binding are higher in many brain regions in adolescents than in adults. nAChRs have higher functional activity in the cortex, hippocampus, striatum, and thalamus during earlier phases of life. Initial exposure to nicotine induces unique effects in adolescence on the ascending serotonin system. More specifically, acute nicotine exposire increases extracellular serotonin overflow in the nucleus accumbens shell while decreasing both dopamine and serotonin in adolescent medial prefrontal cortex in adolescents. Research has shown that nicotine enhances locomotor activity in the adolescent rodents but decreases it in adults. Adolescents also had a greater decrease in anxiety than in adults making it more appealing to younger populations. The more reward associated with nicotine exposure, the more susceptible younger individuals will be to smoking or vaping.[6]

With the continued concern from the Food and Drug Administration (FDA) on the forefront of health care news, it is important to note that this new recreational activity for adolescence can have profound detrimental effects on their health, including cognitive development. The use of ENDS was not intended to increase the availability of nicotine but to provide a potentially less toxic alternative for those struggling with nicotine dependence. About 3.62 million students in America reported using e-cigarettes in 2018, with this number including younger students in middle school. Furthermore, 81% of ENDS users cited that the availably and flavors were primary reasons for use. With the fun and social image associated with ENDS, it is important that all health care providers reinforce this public safety concern moving forward. Pharmacists must back the FDA in discouraging use of these products in our youth to preserve and prolong the growth and prosperity of future generations.[7]

References:

1. Center for Disease Control and Prevention (CDC). https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm. Accessed on May 8, 2019.
2. Center for Disease Control and Prevention (CDC). https://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/index.htm. Accessed on May 8, 2019.
3. Siqueira LM. Nictonine and Tobacco as Substances of Abuse in Children and Adolescents. *Pediatrics,* 2017; 139(1): 391-411.
4. Ho MK, Tyndale RF. Overview of the Pharmacogenomics of Cigarette Smoking. *Pharmacogenomics J,* 2007; 7(2): 81-98.
5. Rubinstein ML, Shiffman S, Moscicki AB, *et al*. Nicotine metabolism and addiction among adolescent smokers. *Addiction,* 2013; 108(2): 406-12.
6. Yuan M, Cross SJ, Loughlin SE, *et al.* Nicotine and the adolescent brain. *Journal of Physiology*, 2015; 593(16): 3397-3412.
7. Food and Drug Administration (FDA). https://www.fda.gov/tobaccoproducts/labeling/productsingredientscomponents/ucm456610.htm. Accessed Feb 25, 2019.

- **Jordan Scott, Pharm D. Candidate of 2021**
- **Asim Ali, Pharm D. Candidate of 2022**

Opioid Use Disorder Treatment

Pain is the response to a stimulus that can produce actual or perceived tissue damage. As the opioid epidemic now plagues this generation, a major concern for healthcare practitioners is how to effectively treat pain in patients receiving medication assisted treatment (AAT). Included below is a chart (Table 1) from the 2017 quarterly report for deaths in Erie County as a result from opioid overdose.[1] Enrollment into MAT programs is increasing as the risks of opioid use are becoming more apparent including abuse, respiratory depression, and death. Additionally, physicians are becoming more hesitant to prescribe opioid analgesia for the treatment of acute pain. [2]

Table 1:

Erie County: Opioid overdoses and crude rates per 100,000 population
(Preliminary data as of November, 2018 - subject to change)

		Apr-Jun, 2017		Jul-Sep, 2017		Oct-Dec, 2017		2017 Total		Jan-Mar, 2018		Apr-Jun, 2018	
Indicator	Location	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Deaths[1]													
All opioid overdoses	Erie	87	9.4	39	4.2	34	3.7	246	26.7	46	5.0	34	3.7
	NYS excl. NYC	604	5.4	533	4.8	430	3.8	2,137	19.1	429	3.8	336	3.0
Heroin overdoses	Erie	18	2.0	14	1.5	11	1.2	70	7.6	12	1.3	9	1.0
	NYS excl. NYC	210	1.9	207	1.8	150	1.3	780	7.0	152	1.4	122	1.1
Overdoses involving opioid pain relievers (incl. illicitly produced opioids such as fentanyl)	Erie	81	8.8	38	4.1	32	3.5	232	25.2	44	4.8	33	3.6
	NYS excl. NYC	526	4.7	466	4.2	389	3.5	1,873	16.7	389	3.5	312	2.8

According to the CDC Guideline for Prescribing Opioids for Chronic Pain, nonpharmacologic therapy and non-opioid pharmacologic therapy are recommended first line for pain management.[2] Opioid therapy should only be considered when benefits for both pain and function are anticipated to outweigh risks to the patient. If opioid therapy is initiated, treatment goals related to pain and function should be established between the clinician and patient.[2]

If a patient presents with mild acute pain, non-pharmacologic and non-opioid analgesic interventions should be initiated first. In moderate to severe acute pain, multimodal analgesia as well as continuation of MAT should be implemented. It is important to prescribe an analgesic as a scheduled medication rather than as needed because letting the pain appear without taking a pain medication will cause unnecessary anxiety and suffering for the patient. Avoid using mixed agonist and antagonist opioids together for the treatment of acute pain. For the management of acute pain, three days or less is an adequate supply. Opioid treatment discontinuation as well as risks and benefits of therapy needs to be discussed. [2]

Further, it is recommended that the clinician prescribe immediate-release versus long-acting opioids, at the lowest effective dose.[2] It has been shown that there is a lower risk of overdose among patients with immediate-release opioids compared to extended-release/long-acting (ER/LA) opioids.[2] Long-term opioid therapy begins with treatment of acute pain. With the recent increase in opioid overdoses, the CDC Guideline for Prescribing Opioids for Chronic Pain encourage the use of the prescription drug monitoring program (PDMP) prior to prescribing to assess a patient's history of controlled substance use. Due to an increased risk of sedation and respiratory depression, patients that are concurrently taking benzodiazepines and experiencing acute pain, should avoid opioids if possible. [2]

Medication assisted treatments, such as methadone and buprenorphine, provide analgesia for many patients. Methadone binds to opioid receptors in the central nervous system, causing inhibition of ascending pain pathways and changes the way pain is perceived. The effects are similar to that of opioid drugs but mainly work to reduce cravings of opioid drugs. In most patients, the low doses of methadone for opioid use disorder treatment do not provide analgesic effects. Alternatively, buprenorphine has high affinity for the mu opioid receptors in the central nervous system and acts as a partial agonist. Buprenorphine is commonly combined with naloxone, an opioid antagonist, to prevent diversion. If taken correctly, the naloxone component is not activated. However, if patients try to parentally administer this drug, naloxone becomes bioavailable and leads to unpleasant withdrawal symptoms.[3]

In patients with a history of substance use, it is believed that the use of opioids may result in relapse; however, there have been few studies that prove this correlation. In fact, patients are more likely to relapse if their pain control is inadequate.[3] The further restriction of opioids without connection to substance use treatment may drive patients to buy illicit drugs on the street which are impure, not monitored by the FDA, and can be altered with additives such as fentanyl. A common challenge that health care practitioners face is "differentiating between *drug-seeking* patients and patients seeking *pain-relief*". These patients are often associated with a stigma and considered "difficult". These misconceptions lead to under dosing and patient dissatisfaction. Pain is most often assessed as a subjective measurement. Health care providers utilize visual analogue scales to help patients rate their pain. Objective assessments can be used as a compliment to the subjective scores to help differentiate between drug seeking and non-drug seeking behaviors. [3]

It is important to understand that patients receiving opioid use disorder treatment with medication assisted treatment do not receive pain relief from it. Analgesic tolerance is another factor that may explain why patients receive little relief from maintenance opioids. Cross-tolerance develops when switching between agents in the same drug class. These patients may require higher doses and frequent dosing of MAT to achieve sufficient pain control. [3]

In a hospital scenario, patients who are taking methadone and experiencing pain may continue to receive their maintenance dose along with short-acting opioid analgesics for acute pain control. If a patient is taking buprenorphine, therapy can be continued and/or titrated via divided doses for acute pain control. Because of buprenorphine's binding affinity, additional opioid therapy may be less helpful. This helps ensure that cravings are curbed and pain is controlled. [3]

Most institutions are implementing a system in which they are reimbursed based on patient satisfaction, making it crucial to properly manage these patients' pain. If a patient's pain is poorly managed, it may lead them to give a lower score. The Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) was the first to release a standardized survey for patient satisfaction.[4] Most hospitals have their own form of survey they distribute to ensure they are up to standard.

There are many factors to consider when faced with a patient on MAT. Utilize objective assessments and maintaining an unbiased and professional approach to these patients will help provide the best care. Moving forward, the end goal is to reduce rates of opioid use disorder. The movement, to eliminate opioid use disorder, is a collective effort by all healthcare providers that actively involve patients.

References:

1. New York State Department of Health. *New York State Opioid Annual Report, October 2018.*
2. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49.
3. Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. Ann Intern Med. 2006;144(2):127-34.
4. HospitalHCAHPS. *CMS.gov Centers for Medicare & Medicaid Services*, 21 Dec. 2017.

- Natalia Dziadosz, Pharm D. Candidate of 2020
- Emily Fayad, Pharm D. Candidate of 2020

Managing the Opioid Crisis: *The Pharmacist Role*

According to the CDC, one out of four patients who receive long-term opioid therapy in a primary care setting struggle with a substance use disorder.[1] This remains a major public health concern in the United States, with approximately 2.5 million Americans suffering from either a prescription opioid or heroin use disorder. In the US, hydrocodone/acetaminophen and oxycodone/acetaminophen remain the 1st and 22nd most dispensed medications.[2] Pharmacists and primary care providers are essential members of the health care team; therefore, they can serve as a critical line of defense against the opioid epidemic by engaging in prevention and treatment of opioid use disorders and overdose.

Multiple national pharmacy organizations have advocated for the pharmacist's role in the opioid crisis, including American Society of Health System Pharmacists (ASHP), who published the following statement: "Pharmacists have the unique knowledge, skills, and responsibilities for assuming an important role in substance abuse prevention, education, and assistance. Pharmacists, as health care providers, should be actively involved in reducing the negative effects that substance abuse has on society, health systems, and the pharmacy profession".[3] Pharmacists have extensive knowledge about the safety, effectiveness, and adverse effects surrounding prescription medications, allowing them to provide care to patients through counseling and monitoring. The American Pharmacists Association (APhA), stated that it "supports recognition of pharmacists as health care providers who must exercise professional judgment in the assessment of a patient's conditions to fulfill corresponding responsibility of the use of controlled substances and other medications with the potential for misuse, abuse, and/or diversion".[4]

Additionally, the National Drug Control Strategy put forward by the U.S. Office of National Drug Control Policy encourages healthcare professionals to screen for and address substance use disorders.[2] Strategies pharmacists can employ to mitigate the misuse of oral drugs include using prescription drug monitoring programs (PDMPs), also known as controlled substance reporting systems, to indicate dispensing behaviors; implementing evidence-based substance abuse screenings or risk assessments, such as the National Drug Control Strategy-promoted screening; and utilizing the brief intervention and referral to treatment (SBIRT) model. Pharmacists can help patients specifically through the dissemination of information specific to available substance use disorder treatment options.[2]

In short, pharmacists can play a vital role in the treatment process for patients with substance use disorders, and while these interventions and advocacy are beneficial, other efforts should be expanded to provide safe and effective treatment for patients with substance use disorder.

Pharmacists can broaden their involvement by incorporating patient-centered opioid screening into existing workflow schedules. Simply asking open-ended questions and actively listening to a patient can alert red flags of opioid misuse.[4] Additionally, PDMPs can be utilized to monitor for diversion of medications as well as substance use disorders. Data in this system allows pharmacists to identify patients who are at increased risk of overdose including those filling multiple prescriptions for different opioids, taking high doses of opioids, or obtaining prescriptions from multiple pharmacies.[1,4] These tools are available for the pharmacist to exercise their professional judgement and duty within their scope of practice.

Also, pharmacists can help counsel patients about the harmful combination of prescription and non-prescription drugs (such as benzodiazepines and recreational drugs), opioid risks, proper storage and disposal of medications, and the harms and illegality of sharing medications with other people.[5] Specifically, the risk of acquiring hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) when sharing needles. Pharmacists can also provide guidance about the use of naloxone, an opioid antagonist and overdose-reversal agent. After administering two surveys simultaneously to community pharmacists in the Ohio area, Riley at al. found that, in addition to these interventions, some other actions can be taken. Pharmacists indicated the importance of referring patients to drug treatment programs within the community, dispensing emergency opioid overdose treatments such as naloxone with opioid prescriptions, and providing naloxone without a prescription.[6]

Despite the variety of tools available for pharmacists, a study by Hagemeier et al. indicated that both pharmacist and practice setting characteristics are associated with the provision of use disorder treatment to patients.[2] Pharmacists who have not had formal training in helping patients with substance misuse or feel awkward and unconfident in their ability to address these issues are less likely to screen patients than pharmacists who are confident or have received such training. Additionally, pharmacists working at independent pharmacies are more likely to discuss prescription misuse with patients relative to pharmacists at chain pharmacies. This may be attributed to a discrepancy in the amount of time or resources available to community pharmacists. This can be addressed by the implementation of written communication to facilitate dialogue, low-cost informational material and accessible tools for both patients and pharmacists, collaboration of pharmacists with local organizations, and continuing education seminars focused on prescription-misuse.[2]

To ensure compliance with proposed strategies and interventions to address prescription opioid misuse, both patients and pharmacists must understand these practices as core components of pharmacy practice.[6] A study by Riley *et al.* found that currently, pharmacists and patients alike view the use of patient counseling and PDMP-based validation of prescriptions acceptable prescription misuse interventions.[6] However, only patients expressed interest in naloxone-based interventions, not pharmacists.[6]

"Considering the high level of access to community pharmacists, legal requirements to counsel patients on their medications, and the trust placed in pharmacists societally, community pharmacists are uniquely positioned to educate patients on multiple aspects of prescription drug abuse and engage patients in prescription drug abuse prevention and treatment efforts".[2] Although the efficacy of the above-mentioned resources is still being studied, they are all valuable tools to potentially help mitigate the misuse of prescription drugs as well as improve pharmacist-patient communication about substance use.

References:

1. CDC: pharmacists on the frontlines – addressing prescription opioid abuse and overdose. https://www.cdc.gov/drugoverdose/pdf/phar macists_brochure-a.pdf. Accessed April 20, 2017. 21.
2. Hagemeier N, Alamian A, Murawski M, Pack R. Factors associated with provision of addition treatment information by community pharmacists. *J Subst Abuse Treat.* 2015;52:67-72
3. Baldwin J, Dole E. ASHP statement on the pharmacist's role in substance abuse prevention, education and assistance. *Am J Health-Syst Pharm.* 2003; 60:1995-8
4. Reynolds V, Causey H, McKee J, Reinstein V, Muzyk A. The Role of Pharmacists in the Opioid Epidemic. *N C Med J.* 2017;78(3):202-205.

References Cont'd:

5. Compton W, Jones C, Stein J, Wargo E. Promising roles for pharmacists in addressing the U.S. opioid crisis. *Res Social Adm Pharm.* 2017 doi: 10.1016/j.sapharm.2017.12.009
6. Riley T, Alemagno S. Pharmacist utilization of prescription opioid misuse interventions: Acceptability among pharmacists and patients. *Res Social Adm Pharm.* 2019 doi: 10.1016/j.sapharm.2019.01.002

- Simona Armenti, Pharm D. Candidate of 2021
- Dupinder Dhaliwal, Pharm D. Candidate of 2021

Lucemyra: For the Management of Opioid Withdrawal

What are the symptoms of opioid withdrawal?

Opioid withdrawal can be categorized as experiencing a number of symptoms after decreasing the amount or stopping the use of opioids.[1] Early symptoms of opioid withdrawal include, agitation, anxiety, muscle aches, increased tearing, insomnia, runny nose, sweating, and yawning. Late symptoms may include abdominal cramping, diarrhea, dilated pupils, goosebumps, nausea, and vomiting. Symptoms usually begin within 12 hours of last opioid usage.

How is opioid withdrawal treated?

Currently, treatment of opioid use disorder and withdrawal symptoms varies on a case by case basis. Those who are being evaluated for an opioid use disorder should undergo an assessment of mental health status.[2] An evaluation should also be performed of past and current use of other substances as concomitant use of alcohol, sedative, hypnotics, or anxiolytics may lead to respiratory depression and require a higher level of care. Current pharmacologic treatment options for opioid use disorder include methadone, buprenorphine, and naltrexone. Methadone can help relieve withdrawal symptoms, help patients with detoxification, and can be used as a long-term maintenance medication for opioid dependence.[1] Buprenorphine is another option to help alleviate symptoms due to opioid withdrawal as well as shorten the length of detox. Like methadone, it may also be used for long-term maintenance. Buprenorphine may be combined with naloxone to help prevent misuse. Naltrexone is also available to help prevent relapse in patients trying to stop using opioids. Other medications such as clonidine are often used to help mitigate symptoms of anxiety and agitation. The choice of which medication to use should be based on clinician, patient, and patient history of treatment, along with treatment setting.[2]

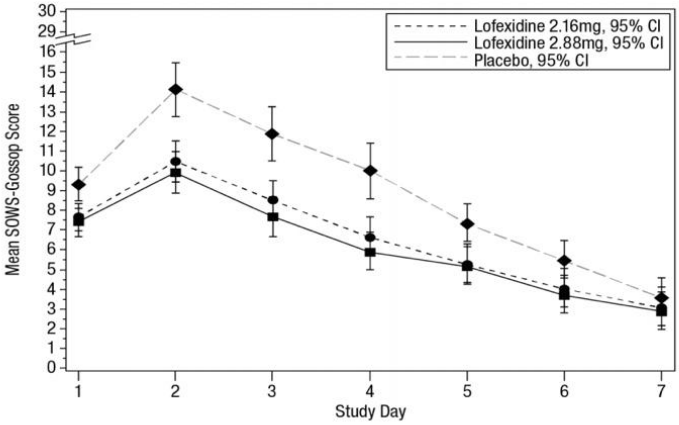
What is lofexidine hydrochloride?

Lofexidine hydrochloride (Lucemyra) is an oral, selective alpha 2-adrenergic receptor agonist that helps manage opioid withdrawal symptoms by reducing the release of norepinephrine[3]. It does so by binding to receptors on adrenergic neurons, reducing the release of norepinephrine in the brain, which is associated with various withdrawal symptoms. It is indicated for short term use in the mitigation of withdrawal symptoms to facilitate abrupt discontinuation of opioids in adults. The dosing regimen consists of three 0.18 mg tablets taken four times a day at 5-6 hour intervals with a gradual reduction over 2-4 days and dosage adjustments for hepatic and/or renal impairment.[4] Lucemyra does not have any current information regarding effectiveness in patients younger than 18 years of age. The most common side effects include hypotension, bradycardia, and syncope. This medication should not be used with alcohol, benzodiazepines, or barbiturates.[5] It is the first FDA-approved non-opioid medication indicated to help patients suffering from opioid use disorder.

What did the clinical trials show?

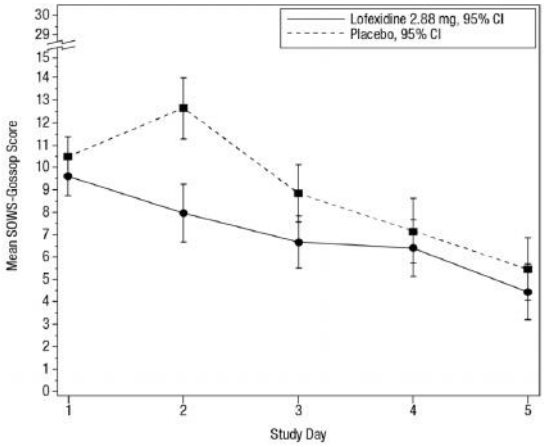
Lofexidine (Lucemyra) was approved by the FDA based on two randomized trials consisting of double-blind and placebo controlled designs. The trials aimed to measure safety, efficacy, and high quality data for the treatment of opioid withdrawal symptoms in adults who suffered from opioid use disorder. Trial 1 included 603 participants who were 18 years or older, had current dependence on any opioid similar to heroin or morphine, were seeking treatment for opioid dependence, and screened positive for opioids but negative for methadone/buprenorphine.[6] This study was a 2-part efficacy, safety, and dose response study, beginning with an inpatient 7-day treatment with either lofexidine 2.16 mg daily dose (0.54 mg 4x a day), lofexidine 2.88 mg daily dose (0.72 mg 4x a day), or an equivalent placebo. These patients also had access to complementary medications, such as antacids, guaifenesin, zolpidem, etc. The second part of the study consisted of days 8-14, when patients who successfully completed part 1 were eligible to receive open label treatment with variable dose lofexidine. The two endpoints supporting efficacy were the Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) and the number of patients that completed the study. This scale consists of 10 items found to provide reliable and valid measures of evaluating signs and symptoms of opioid withdrawal. It evaluates symptoms of: feeling sick, stomach cramps, muscle spasms/twitching, heart pounding, feeling cold, muscular tension, aches & pains, runny eyes, insomnia, and yawning. Participants were asked to scale their symptoms as none, mild, moderate or severe which was then scored on the SOWS-Gossop score from 0 to 30, where a score closer to 30 indicates greater withdrawal symptoms. Differences in overall SWOS-Gossop log-transformed least square means for lofexidine 2.16 mg was -2.3 and lofexidine 2.88 mg was -2.7 with significant p values of 0.02 and 0.003 respectively compared to that of placebo (Figure 1). [6]

Figure 1



In trial 2, participants were treated with lofexidine 2.88 mg (0.72 mg 4x a day) or matching placebo for days 1-5.[7] This trial included 264 participants who consisted of males and females over the age of 18, currently dependent on any opioid with a half-life similar to morphine or heroin, and seeking opioid treatment with a baseline objective opiate withdrawal scale score of 2. Participants had access to other support medications if needed throughout the study. On days 6 and 7, all participants received a placebo and were discharged on day 8. The primary outcomes of this study were to investigate the efficacy of lofexidine hydrochloride on day 3 using the SOWS-Gossop scale during treatment phase and time to drop out. The secondary outcomes included determining lofexidine's efficacy in reduction of withdrawal symptoms, reduction in the need for any concomitant medication, increasing the number of completers during the treatment phase and the safety in the study population. On days 1-5 during the treatment phase, the data was statistically significant with a difference of -1.9 with 95% CI (-3.2,-0.6) (Figure 2). As seen in Figure 2, day 2 shows the peak difference in mean SOWS-Gossop scores with placebo scores remaining higher than lofexidine scores throughout the 5-day treatment course. The lofexidine group had fewer early terminators compared to that of the placebo group along with non-completers of the lofexidine treatment arm remaining longer throughout the study compared to those assigned to the placebo group (p=0.0034). Both trials showed that adverse events included hypotension, dizziness, dry mouth, and bradycardia. Adverse events were classified as mild to moderate with no significant differences between treatment groups in either study. [7]

Figure 2



What does this mean for patients and the opioid epidemic?

Based on these clinical trials, Lucemyra is expected to be available this August 2019 and be supplied in bottle quantities of thirty-six and ninety-six count oral tablets with an associated tapering schedule.[4] The cost of therapy has not yet been published but is expected to be high and not covered under many insurance plans. Although this medication is intended for short term use, the cost effectiveness versus other therapies, such as clonidine or buprenorphine, has not yet been completely established. If Lucemyra were to end up being cost-effective while safe and efficacious in the treatment of opioid withdrawal, it could lead to better treatment outcomes of this disorder. As the current opioid epidemic continues, it is imperative that novel treatments are brought to the forefront in order to combat this disorder and its associated overall death.

References:

1. Opiate and Opioid Withdrawal. US National Library of Medicine. 22 March 2019. https://medlineplus.gov/ency/article/000949.htm Accessed 29 March 2019
2. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *J Addict Med*. 2015;9(5):358-67.
3. Lexicomp Online. Hudson, Ohio: Lexicomp, Inc; March 22, 2019.
4. Lucemyra. US WorldMeds LLC. May 2018. https://www.multivu.com/players/English/8314851-us-world-meds-lucemyra-fda-approval/docs/PrescribingInformat_1526505076265-1171755477.pdf Accessed 18 Feb 2019
5. Center for Drug Evaluation and Research. "Drug Approvals and Databases - Drug Trials Snapshots: LUCEMYRA." *US Food and Drug Administration Home Page*, Center for Drug Evaluation and Research.
6. Fishman M, Tirado C, Alam D, *et al*. Safety and Efficacy of Lofexidine for Medically Managed Opioid Withdrawal: A Randomized Controlled Clinical Trial. *J Addict Med*. 2018 Nov 29. doi: 10.1097/ADM.0000000000000474
7. Gorodetzky C, Walsh S, Martin P, *et al*. A phase III, randomized, multi-center, double blind, placebo controlled study of safety and efficacy of lofexidine for relief of symptoms in individuals undergoing inpatient opioid withdrawal. Drug and Alcohol Dependence 2017;176:79-88.

- Samantha Poblete, Pharm D. Candidate of 2020
- Shea Bacon, Pharm D. Candidate of 2022

Clinical Faculty Spotlight:

Dr. Rachel Gorodetsky, PharmD, DABAT

What made you decide to choose the profession of pharmacy?

Dr. Gorodetsky states that she worked as a pharmacy technician from the time she was in high school and continued through her undergraduate education. She was therefore exposed to the profession of pharmacy for a long time and grew to highly respect the pharmacists that she worked with. When it came time for her to choose a profession, it seemed an obvious choice.

What led you to your clinical pharmacy specialty?

"I was exposed to the practice of Clinical Toxicology during my last APPE Module during my 4th year of Pharmacy School, when I did a rotation at the Upstate NY Poison Center in Syracuse, NY. Prior to that, I did not have any specific area of interest that I thought I might specialize in, but after a few weeks at the Poison Center, I knew Toxicology was for me."

"Don't expect others to hand success to you. Create it."
– Rasheed Ogunlaru

What are your current roles and responsibilities?

"I currently wear many different hats. First and foremost, I am faculty at D'Youville College in the Department of Pharmacy Practice. In addition to a number of other faculty responsibilities, I teach Toxicology in the core curriculum as well as an elective course. I also maintain and host APPE students at my clinical practice site at the University of Rochester Medical Center - Strong Memorial Hospital, where I serve as a Clinical Toxicologist on the bedside toxicology consult service. This service consults on patients with poisonings and drug overdoses as well as those with substance use-related problems. Finally, I am also a Consultant for the Upstate NY Poison Center, which I am the Toxicologist on call for approximately 2 days per month and also participate in various web conferences such as journal clubs and case conferences."

Do you or have you conducted research? If so what does it entail?

"I do conduct research. My research is of a clinical nature and typically involves retrospective chart reviews. My current project, which is near completion, involves looking through the charts of all patients who had received the antidote physostigmine over a 5-year time period and trying to identify adverse effects as well as markers of efficacy. Also, as part of a research group at my practice site, I have been involved in a number of studies related to drug or alcohol use and its impact on suicide."

How to you utilize your specialty to provide service to the community?

"Within my specialty, the major focus for community service are activities focused on poison prevention and activism for harm reduction programs for individuals suffering from addiction."

What do you do outside of your career to stay involved in pharmacy organizations?

"I am very active within the toxicology pharmacy organizations - The American Academy of Clinical Toxicology and the American Board of Applied Toxicology. I am involved in several committees for both and was recently elected to the Board of Directors for the latter."

What are tasks and roles you dislike in the clinical pharmacy setting?

"For the most part, other clinicians are very appreciative of the information we provide and the interventions we suggest. However, there are times when the provider interprets our input as obstructionist, and the relationship becomes an antagonistic one. This situation is the only thing I dislike about being a clinical pharmacist. Thankfully this is uncommon as pharmacists become more and more accepted as contributing members of the team."

What do you enjoy most about clinical pharmacy?

I truly enjoy being able to fill the gap in patient care that a clinical pharmacist is uniquely qualified for. I see on a daily basis the impact clinical pharmacists in every specialty have on patient care. We are the experts on medication therapy, and we are continuously making interventions that benefit the patient, and our knowledge is constantly sought after by the other providers on the treatment team. Having the feeling that you are a valued member of the health care team is what leads to job satisfaction.

Preston Palmer, D'Youville School of Pharmacy

Pharm D. Candidate of 2021

A special thanks to:
D'Youville College School of Pharmacy—Student ACCP Chapter; Dr. Aubrey Defayette and Dr.Joseph Dunn (ACCP Faculty Liaison/Editor); Julia Blak and Chelsea Weselak PharmD Candidates, Class of 2019 (Peer-reviewers)

Questions? Please contact:
Bennett Doughty, PharmD, BCPS, BCPP
NYS-ACCP Secretary/ Treasurer
bdoughty@binghamton.edu