

Pharmacy Updates from the ASHP Midyear Clinical Meeting

Orlando is more than just Disney World and Universal Studios

The 2017 ASHP Midyear Clinical Meeting took place this past December in Orlando, Florida. This meeting is one of the largest gatherings of pharmacists in the world and is attended by more than 20,000 pharmacy professionals from 86 different countries. It provides health system pharmacy practitioners a venue for updating their knowledge, networking with colleagues, enhancing their skills, and learning about the latest products and technologies.

This year, at the 52nd annual ASHP Midyear Clinical Meeting, a large number of participants from RWJBarnabas Health presented posters and educational sessions. Our residency programs were also able to recruit future residents for the next residency year at the showcase. The Midyear Clinical Meeting is just one of the many ways that we are able to advocate for all of the great things that pharmacy does at RWJBarnabas Health.

There are hundreds of educational activities at the Midyear Clinical Meeting intended to develop, maintain, and enhance the knowledge, skills, and abilities of pharmacists and associated personnel in health systems. For those unable to attend this year, the RWJBH pharmacy residents attended some of the educational sessions and have written summaries on the updates and clinical pearls presented at the meeting.

Review Articles Table of Contents

Stop the Benzodiazepines: Identifying High-Risk Patient Populations to Successfully Taper These Medications.....	2
Clinical Application and FDA Guidance on Biosimilars: An Expert Panel Presentation	3
Novel Approaches in the Management of Severe Alcohol Withdrawal.....	4
This is Going to Hurt! Current Debates in Pain Management	5
Creating and Sustaining Ambulatory Care Practices for the Medically Underserved	6
Emergency Medicine Pearls 2017.....	7
Guidelines-Based Management of Heart Failure and Arrhythmic Complications	8
When the Unexpected Happens: Pharmacy’s Role in Disasters	9
Inside the VA: Multifaceted Approach to Combating the Opioid Crisis	10
Are You Really Allergic to Penicillin? Effectively Managing Self-Reported Cases	11
When Good Hormones Go Bad: Acute Management of Endocrine Emergencies	12
Multimedia Analgesia from ERAS to the Critically Ill: Strategies for the Clinical Pharmacist	13
Evidence-Based Updates: Current Topics in Pediatrics.....	14
Addiction in the Genes: How Pharmacogenetics Plays a Role in Opioid Addiction	15
View from the Top: The Impact of The Joint Commission’s Standards on Pain Management.....	16
Go with the Flow: Pharmacotherapy in ECMO.....	17
Focus on Naloxone: Lifesaver or Addicts’ Rescue?.....	18
Seeing Through the Smoke: Clinical Management of Medical Cannabis.....	19
Narcotics in the Emergency Room: Helpful or Harmful for Headaches?.....	20

STOP THE BENZODIAZEPINES:

IDENTIFYING HIGH-RISK PATIENT POPULATIONS TO SUCCESSFULLY TAPER THESE MEDICATIONS

Courtney Tomaselli, PharmD
PGY-1 Pharmacy Resident
Saint Barnabas Medical Center

Benzodiazepines are a class of medications that are commonly used for the treatment of anxiety, insomnia, and mood disorders. While these drugs are traditionally recommended for short-term use, long-term use has become increasingly more common. Although these agents can be extremely effective, there are significant risks associated with long-term use, with a major risk being accidental overdose when combined with sedatives and opioids. Other negative sequelae include depressed mood, falls, development of tolerance, and traffic accidents. While these agents are certainly appropriate to use in certain clinical situations, it is important as practitioners to be able to identify patients that are more prone to the risks of benzodiazepines. In these situations, we must be able to weigh the benefit of rapid symptom relief against the risks of side effects, overdose, tolerance, and withdrawal.

Although tapering off of benzodiazepines seems like a daunting task for many patients and practitioners, previous studies have demonstrated successful discontinuation rates of up to 60-80%. In order to have success in tapering patients off of benzodiazepines, it is crucial to be able to create an individualized plan to ensure the success of your patients. Below are educational strategies that have been utilized to assist patients with tapering off of benzodiazepines.

High-risk patient groups

Chronic respiratory disease
Co-administered opioids
Dementia
Elderly (≥ 65 years)
Substance use disorder (SUD)
Post-traumatic stress disorder (PTSD)

Brief Educational Intervention

- Medication review
- Explanation of risks and benefits
- Assessment of patient readiness
- Provision of a withdrawal schedule

Direct-to-Consumer Education

- Booklet with explanation of risks of benzodiazepine use
- Peer success stories
- Alternative treatment options
- Encouragement to discuss tapering with prescriber

Augmentation

- Psychotherapy
- Pharmacotherapy

When designing a tapering regimen for patients, it is important to plan for a slow, gradual tapering schedule over 3-6 months to minimize withdrawal symptoms. In order to ensure successful discontinuation, practitioners must be flexible with regard to allowing for extra doses and a slower taper. Other treatments may be added on to assist with tapering, such as cognitive behavioral therapy or pharmacologic options such as carbamazepine, controlled-release melatonin, or pregabalin. Ultimately, not all patients will succeed in their attempt to taper off of benzodiazepines. However, pharmacists are in a unique position to empower patients to either taper off completely or decrease the dose they are using to minimize their long-term risk.



Clinical Application and FDA Guidance on Interchangeability Biosimilars: An Expert Panel Presentation

Jigisha Patel, PharmD
PGY-1 Pharmacy Resident
Saint Barnabas Medical Center

Biologics are a rapidly growing area in current medical practice, accounting for approximately 50% of US prescription drug expenditures. Converting to biosimilars has a projected cost savings of \$40 to \$250 billion over the next 10 years.

Biosimilars are not generic medications of their bio-originator. When compared to a generic medication, biosimilars are larger and more complex in structure. They are prone to instability and are associated with an increased risk of immunogenicity.

Currently, interchangeability of biosimilars is based upon individual state laws. The Food and Drug Administration (FDA) is in process of formulating interchangeability laws.

The FDA has approved interchangeable biosimilars for Infliximab (Remicade®), Adalimumab (Humira®), Etanercept (Enbrel®), Filgrastim (Neupogen®) and Bevacizumab (Avastin®).

Choosing the best treatment option is a multifactorial approach based on each patient, tolerability and product safety and cost.

Rheumatology and gastroenterology are two areas of practice where biosimilars are often used. Treating patients with rheumatic diseases continues to be a shared-decision making process of efficacy, safety and costs between the patient and healthcare professional. Switching patients from a bio-originator to biosimilar may not always be the best option. Approved biosimilars can be used to treat patients in the same manner as their bio-origimators, however patients must be aware of all changes in their treatment and entered into registries. Biosimilars must significantly lower cost of treatment (about 15-30%) and increase optimal therapy for patients.

As the number of new diagnoses in diabetes continues to climb

yearly, confusion continues to exist about biosimilars and bioequivalence amongst insulins.

When speaking about insulin, it is referred to as “follow-on” insulin, as it has the same amino acid sequence and demonstrated similar safety and efficacy to the originator. Currently, Insulin Glargine (Basaglar®), is the only approved “follow-on” insulin and cannot be interchanged with others. The increasing yearly diagnoses of diabetes, along with increased research and marketing of biologics and biosimilars makes this area of pharmacy one that is deserving of more practitioner education.

As the future of medicine trends towards biologics and biosimilars, education of its use in practice should be provided to all healthcare professionals. It is not to forget that patient safety and efficacy must remain at the forefront of all treatment options.

NOVEL APPROACHES IN THE MANAGEMENT OF SEVERE ALCOHOL WITHDRAWAL

BARNABAS HEALTH BEHAVIORAL HEALTH CENTER
TOMS RIVER, NJ

Alcohol withdrawal in the ICU can present in a variety of ways, and assessment can be challenging due to a patient's inability to communicate or other comorbidities such as delirium and pain. A myriad of questions must be answered before an ideal treatment plan can be initiated. Is the patient still intoxicated? Is this an acute case of intoxication not precipitated by a long standing history of alcohol abuse? If this is determined to be a case of withdrawal, is it a mild or severe withdrawal? A thorough assessment is therefore the first step.

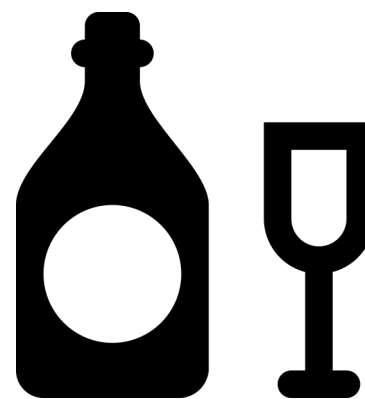
It is important to note, that if a patient is still intoxicated when they present to the hospital, no treatment for withdrawal is indicated. This may be evidenced by lateral nystagmus, slurred speech, and unsteady gait. These patients can be treated symptomatically until the effects of the alcohol safely wear off. Treating with benzodiazepines can further compromise respiratory function so caution is advised. Also, just because a patient is withdrawing from alcohol while admitted to the ICU does not mean the withdrawal is severe. Therefore, severity of the withdrawal must also be assessed.

To screen for a patient's risk for withdrawal, there are several tools that can be utilized. The Clinical Institute Withdrawal Assessment for Alcohol (CIWA) is a 10 item assessment used to objectify the severity of alcohol withdrawal, however it not validated in ICU patients, delirious patients or those with a history of alcohol withdrawal seizures, or in non-communicative patients. The Minnesota Detoxification Scale (MINDS) is an alcohol withdrawal scoring tool specifically for ICU patients, but it has limited published data and is

not validated. The Cut down, Annoyed, Guilty, and Eye opener questionnaire (CAGE) focuses on signs of use and dependence despite consequences, but does not differentiate between current and past alcohol abuse. The Alcohol Use Disorders Identification Test (AUDIT) is a 10-question survey about both frequency of current drinking and drinking history. The AUDIT-Condensed (AUDIT-C) is a shortened version of the AUDIT survey and uses the first three AUDIT questions. The Prediction of Alcohol Withdrawal Severity Scale (PAWSS) is a potentially useful tool that is based on 10 yes/no questions. A limitation to these scales is that patient interaction is required, since biomarker predictors of withdrawal are lacking. In general, a high risk patient is one who is in active withdrawal, delirious, or has a history of alcohol withdrawal, seizures or delirium tremens (DT). Low risk patients are typically those that have no symptoms, are communicative, and have no history of seizures or withdrawal.

'Typical' alcohol withdrawal is usually treated with GABA receptor agonists targeting CNS excitation (benzodiazepines, barbiturates), medications that target adrenergic hyperactivity (clonidine, dexmedetomidine), and medications to treat the delirium or hallucinations (antipsychotic agents, most commonly haloperidol). Benzodiazepines are the foundation of therapy in most ICU literature. Thiamine is administered due to the fact that thiamine deficiency is often present in alcoholics and can result in severe CNS deficits. This multi-modal approach to therapy

most frequently uses a GABA agonist as the backbone, adding the symptom triggered medications as needed. Barbiturates, specifically phenobarbital, may have a role in "benzodiazepine-resistant" alcohol withdrawal. Patients with refractory withdrawal may benefit from alternative treatment options, such as dexmedetomidine, propofol, and ketamine. Dexmedetomidine has been shown to have use as a benzodiazepine sparing agent, but more studies are required in this area. Propofol is reserved for severe and intubated patients only. Ketamine, as well as a few other adjunctive agents including baclofen, valproate and gabapentin, do not have sufficient data at the time.



TAKE AWAY POINTS:

- *Exercise caution when considering treatment in a currently intoxicated patient*
- *Proper risk assessment and symptom monitoring is critical to properly managing alcohol withdrawal in the ICU*
- *Symptom-orientated therapy should be implemented to avoid excessive GABA agent administration*

This Is Going to Hurt!

Current Debates in Pain Management

Review Article by: Rebecca Chow, PharmD
PGY-1 Pharmacy Practice Resident
Robert Wood Johnson University Hospital Somerset

Between the safety risks of NSAIDs, the clinical use of cannabis, and the CDC's guidelines on opioid prescribing, management of chronic pain is an area of continued controversy and development. For treatment of a condition as subjective as pain, clinical judgment comprises of a careful balance of the application of practice guidelines, the review of the current literature, and weighing the risks versus the benefits.

Safety and Appropriateness of COX-2 Inhibitors for Chronic Pain

With the need for alternatives to opioid therapy, there has been an increase in use of NSAIDs for chronic pain. COX-2 inhibitors are a common choice for chronic pain due to the reduced risk of gastrointestinal toxicities compared to other NSAIDs. However, COX-2 inhibitors also carry a greater risk of cardiovascular disease. Supporters of COX-2 inhibitors cite the PRECISION trial which showed that celecoxib was non-inferior to ibuprofen and naproxen in terms of cardiovascular risk. However, critics will claim a major limitation of the trial was its use of lower than recommended doses of celecoxib. The appropriate use of COX-2 inhibitors is dependent on weighing the patient's risks versus benefits and depends on strong communication with the patient about these risks.

Medicinal Cannabis: What is the Evidence in an Era of Expanded Legalization?

With the DEA's hard stance on marijuana serving "no currently accepted medical use" conflicting with the National Academy of Science's claim of cannabis' "substantial evidence ... [as] effective treatment for chronic pain", the debate for medicinal marijuana is polarizing. With literature supporting its effectiveness in chronic pain and more states legalizing medical marijuana, an increase use of cannabis will lead to a decrease in opioid use. However, its increasing use for pain leads to questions about identifying the best types of cannabinoids for individual indications and the management of long-term consequences. Regulatory issues also come to light, such as safe administration and dispensing as well as driving under the influence. Ultimately, marijuana may have its place in pain management but stronger regulations are needed to ensure best safety practices for its use.

CDC Guidelines for Opioid Prescribing for Chronic Pain

The CDC released guidelines for opioid prescribing targeted towards primary care clinicians in an effort to address the opioid epidemic. However, several recommendations were met with question, such as the preference of immediate-release (IR) over extended-release (ER) opioids and the use of the lowest dose possible. There is a lack of evidence suggesting that ER opioids are more dangerous; ER opioids have a lower peak than IR opioids and, thus, are arguably a safer choice. Though higher opioid doses are associated with higher mortality, the lowest dose of an opioid may not be appropriate for all patients depending on body weight and pharmacogenetic differences. Overall, these recommendations are targeted to change prescribing practices to tame the opioid epidemic, but should not replace clinical judgment for effective pain management.

Creating and Sustaining Ambulatory Care Practices for the Medically Underserved

Jaklin Hanna, Pharm.D

PGY-1 Pharmacy Resident

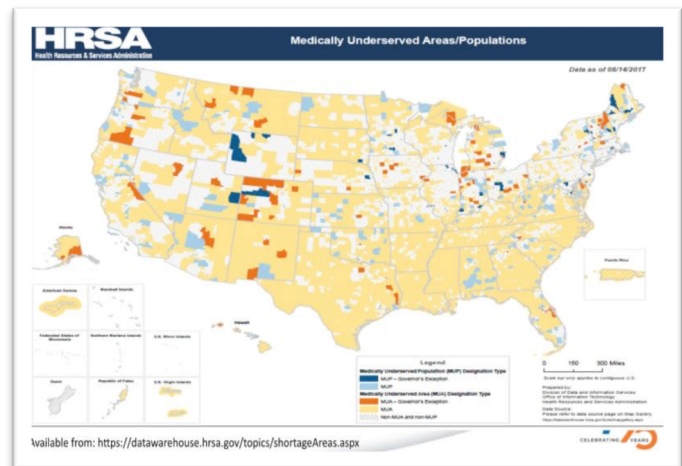
Robert Wood Johnson University Hospital – New

Who are the underserved?

Medically underserved populations are defined as subgroups of people living within a geographic area with a shortage of primary care health services. The medically underserved populations face economic, cultural, or linguistic barriers to healthcare. According to recent statistics, approximately 80% of the geographic U.S. is considered medically underserved. Examples of underserved populations include the uninsured patients, Medicaid/Medicare eligible populations, minorities and immigrants, families of low income, and homeless patients.

How can targeting the underserved benefit the overall health-system?

Low income, low standard of education and unemployment are powerful determinants of adverse health outcomes and are consistent predictors of medical morbidity and premature mortality. As new health-care delivery and reimbursement models demonstrate a significant impact on cost reductions, fewer ED visits, fewer hospital visits and readmissions, and improvements in population health; targeting the underserved can decrease cost and increase quality of care.



What is the role of pharmacists in serving the medically underserved?

Pharmacists can provide unique and vital services such as working with physicians to optimize drug therapy, improve team education, improve patient medication adherence, streamline medication reconciliation and refills, and provide effective, higher quality team-based care. Ways to integrate pharmacist into practice include: embedding them into the care team, utilizing telehealth or telephone to provide pharmacist consults, or using contracted networks such as independent pharmacists to provide services to employers and health plan.

What are some challenges to provide services to the medically underserved?

Barriers providers caring for the underserved may face include lack of awareness, illiteracy and innumeracy, and unintentional provider cultural insensitivity or patient disrespect. It is important for providers to establish effective relations with patients, understand the cultural and socioeconomic considerations, express empathy and embrace motivational interviewing skills to educate and empower patients to create team-based and patient-centered primary care.

EMERGENCY MEDICINE PEARLS 2017



By: Jeffrey Tagle, PharmD
PGY-1 Pharmacy Resident
Saint Barnabas Medical Center

In a world where medicine is constantly evolving, it is essential to stay up to date with the latest evidence and guideline recommendations. Robert Pugliese, PharmD, BCPS, moderated an educational session comprised of 14 speakers each sharing a 5-minute clinical pearl relevant to emergency medicine. The clinical pearls encompassed various topics, including the use of procainamide in atrial fibrillation and ventricular tachycardia, the use of tPA in frostbite refractory to initial rewarming, and the use of sodium acetate in toxicologic emergencies in the wake of the sodium bicarbonate shortage. For the purposes of this article, I summarized 3 of the 14 pearls presented at this session.

Fixed Dose KCentra® (Presented by Michelle Maguire, PharmD)

Four-Factor Prothrombin Complex Concentrate (KCentra®), or 4F-PCC, is indicated for the reversal of vitamin K antagonists in patients with acute major bleeding or need for invasive surgery and is commonly used off-label for the reversal of clinically significant bleeding for patients taking a direct oral anticoagulant. The dose is based off the patient's INR and the patient's weight. In an ideal clinical situation, this information is known and the correct dose can be calculated. Oftentimes, in emergent settings, this information is not readily available and may delay the administration of 4F-PCC. Klein, et al. found that in 39 patients with an initial median INR of 3.3, a fixed dose of 1500 IU led to successful INR reversal to a median INR of 1.4 ($P < 0.01$) and no thrombotic adverse events in 7 days. Varga, et al. also found that in 103 patients requiring reversal of warfarin therapy, a fixed dose of 1000 IU led to a final INR ≤ 1.5 in 50 patients (48.5%), a final INR of 1.6-2.0 in 45 patients (43.7%), and an excellent clinical response with control of bleeding in 86 patients (83.5%). Utilizing fixed doses of 4F-PCC may lead to a reduced time to therapy and a cost savings compared to traditional weight-based and INR-based dosing, but prospective randomized trials should be conducted to confirm the clinical benefit.



Hypertonic Saline for TCA Overdose (Presented by Kim Friend, PharmD)



In the wake of a sodium bicarbonate shortage, hypertonic saline (3% HTS) is a possible option for the reversal of hypotension and arrhythmia during a tricyclic antidepressant (TCA) overdose. Normal dosing of sodium bicarbonate is 1-2 mEq/kg bolus that may be repeated in 5 minutes. In terms of equivalent dosing, 2 ampules of sodium bicarbonate and 200mL of 3% NS have 100 mEq of sodium. During a study in domestic swine that developed a prolonged QRS interval >120 ms and SBP ≤ 50 mmHg, 3% HTS reduced the mean QRS interval to 80 ± 14 ms and increased mean SBP to 134 ± 21 mmHg, whereas sodium bicarbonate reduced the mean QRS interval to 105 ± 38 ms and mean SBP to 85 ± 19 mmHg. There are no prospective, randomized clinical trials comparing sodium bicarbonate to hypertonic saline and only case reports have been published on the use of hypertonic saline in TCA overdose in humans.

Tranexamic Acid in aSAH (Presented by Blake Porter, PharmD)

Aneurysmal subarachnoid hemorrhage (aSAH) requires surgical intervention through clipping or coiling of the aneurysm. If surgery is delayed, the patient is at risk for rebleeding, which may increase mortality to about 60%. Tranexamic acid (TXA) is an antifibrinolytic agent that may reduce the risk of rebleeding after an aneurysmal subarachnoid hemorrhage. The recommended dose is 1000mg IV q 6-8 hours for up to 72 hours or until surgical management. A 2013 Cochrane Review included 10 randomized trials (9 in TXA) that demonstrated a decrease in risk of rebleeding (RR 0.65; 95% CI 0.44-0.97), but did not demonstrate a difference in relative risk for poor outcomes (RR 1.02; 95% CI 0.91-1.15) and death from all causes (RR 1.00; 95% CI 0.85-1.18). In addition, an increased risk of cerebral ischemia was noted (RR 1.41; 95% CI 1.04-1.91). A multicenter, prospective, randomized, open-label trial is currently underway to investigate if ultra-early and short-term administration of TXA will lead to better functional outcomes. Based on this systematic review, early administration of tranexamic acid may be considered to reduce the risk of rebleeding if a delay in surgical management is suspected.





Guideline-Based Management of Heart Failure and Arrhythmic Complications

Jo E. Rodgers, PharmD, BCPS, FCCP, FNAP, FHFSA, FAHA, Clinical Associate Professor at UNC Eshelman School of Pharmacy

James E. Tisdale, PharmD, BCPS, FCCP, FAPhA, FNAP, FAHA, Professor at Purdue University College of Pharmacy

Summary: **Briana Botros**, PharmD, PGY1 Pharmacy Resident at Saint Barnabas Medical Center

Heart Failure Management

It is important to gain a solid understanding of the guideline-directed therapy (GDT) of heart failure (HF) management due to the continuous rise in prevalence and cost in the US. The projected number of patients diagnosed with heart failure in the US will increase by 46% and is estimated to reach 8 million in 2030, which translates to 1 in every 33 people. The projected cost is estimated to double from \$31 billion in 2013 to \$70 billion in 2030, 80% of which is directly related to the patients hospitalization.

PERTINANT TRIALS:

- ◆ GUIDE-IT Trial
- ◆ PARADIGM-HF Trial
- ◆ SHIFT Trial
- ◆ TOPCAT Trial
- ◆ SPRINT Trial

The GUIDE-IT trial showed practitioners that biomarker-guided therapy (goal NT-proBNP level < 1000 pg/ml vs. usual care) made no difference in terms of managing high risk HF patients. While we may obtain BNP or NT-proBNP initially for portraying the degree of fluid overload the patient has, it should not be used to guide the amount of diuretics required.

The PARADIGM-HF trial is a landmark study that introduced a new class into HF management. This double-blind, randomized-control trial compared sacubitril/valsartan to enalapril and found that sacubitril/valsartan had less risk of cardiovascular death and HF hospitalization. This is a great option for patients with class 2-4 HF, frequent hospitalizations, and a stable blood pressure and potassium level.

The SHIFT trial also introduced a new class into HF management, known as ivabradine, a selective If (funny) channel inhibitor. Ivabradine works to decrease heart rate (HR), thereby, reducing the workload on the heart. The guidelines state it can be beneficial to reduce HF hospitalizations for patients with NYHA class 2-4, stable, chronic HFrHF (EF<35%), who are receiving GDT, including a beta-blocker at maximum tolerated doses, in normal sinus rhythm with a resting HR > 70 BPM.

The TOPCAT trial spironolactone may be considered to reduce hospitalizations in select patients with HFpEF, in addition to the benefits shown for HFrEF (EF≤35).

The SPRINT trial showed benefits using intensive GDT to attain SBP < 130 mmHg in HFrEF and HFpEF.

"The projected number of patients diagnosed with heart failure in the US will rise to 8 million in 2030, which translates to 1 in every 33 people."

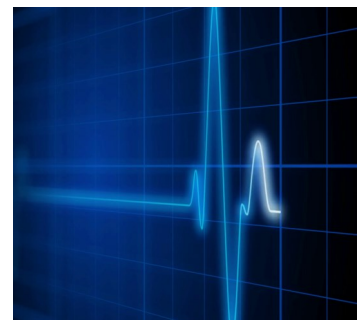
Arrhythmia Management

There have been no major changes in terms of managing arrhythmias, however, it is important to review to ensure management with solely arrhythmias or concomitantly with HF are managed properly to reduced mortality and hospitalizations.

Atrial fibrillation (AF) is common in patients with HF and is associated with increase in mortality. Management of normal sinus rhythm maintenance in patients with AF and HF includes amiodarone, dofetilide, and catheter ablation. Other agents are contraindicated in HF and creatinine clearance (CrCl) must be taken into consideration as well, as dofetilide can't be used if CrCl is < 20 ml/min.

Also, certain antiarrhythmic drugs should be avoided in HFrEF due to the negative inotropic activity, increased risk of drug-induced arrhythmias, and/or increased mortality. These agents include non-dihydropyridine calcium channel blockers, dronedarone, flecainide, propafenone, and sotalol.

Lastly, ventricular arrhythmias are the most dangerous types of arrhythmias we try to prevent. In patients who present with hemodynamically stable ventricular tachycardia with HFrEF, amiodarone IV is the drug of choice. In addition, many patients with HF may require an AICD to reduce the risk of sudden cardiac death.



Pharmacy's Role in Disasters

Eleanor Lee, PharmD
PGY1-Pharmacy Resident at Clara Maass Medical Center



Preparedness Cycle

A disaster is defined as a calamitous event that brings great damage, loss, or destruction, which exceeds the ability of a community to cope using its own resources—essentially creating a situation where need exceeds demand. What is recommended by the DHS/FEMA for these disasters, is preparedness, described by a 4-step-cycle (Figure 1). These four steps include: Plan, Organize/Train/Equip, Exercise, and Evaluate.

PLAN

In the setting of these situations, Homeland Security uses a National Incident Management System (NIMS) that includes an Incident Command System (ICS), or a chain of command that includes Finance, that accounts for and recovers costs, Logistics, that provides support, Operations, that direct tactical actions, and Planning, which creates the Incident Action Plan (IAP). The IAP will define roles and responsibilities and define the objectives, strategies, and resources to be utilized in the disaster.



Figure 1. The Preparedness Cycle is recommended by the DHS/FEMA in anticipation of disasters.

ABCDE

During an actual disaster, things happen fast and steps will have to be simple, like ABCs. ABCDE is a quick approach to tackle a disaster: Assess, Basic Triage, Communicate, Do, and Evaluate.

- **Assess:** Gather incident (type of injuries, such as blunt force, burn, chemical, drowning, etc., expected number of admits to ER, OR, ICU, etc.) and resource information (bed availability, current utilization, who can be discharged, how many must stay).
- **Basic Triage:** IDMED tags may facilitate the triage process:
 - Immediate/critically ill (red)
 - Delayed/seriously-injured (yellow)
 - Minimal/minor injuries (green)
 - Expectant/non-survivable injuries (gray)
 - Dead (black)
- **Communicate:** Incident, resource, and proposed IAP information should be communicated to all involved staff
- **Do:** Execute plan.
- **Evaluate:** Evaluate resources and steps to be improved.

In summary, the disaster tackling process includes a preparation step (Plan and Organize), a response (ABCDE) step (Exercise), and improvement step (Evaluation).

Pharmacy

Given the drug expertise, pharmacy should play an active role in disaster preparedness planning and execution. Proper assessment of an incident and anticipation of types of injuries may allow time and preparation for resource and staff management.

Pharmacy's Role:

- Deploy trained pharmacists and other staff to ED and alternate, needed units
- Procure, prepare, dispense, and restock medications
- Supply allocation: RSI medications, IV fluids, vasopressors, hemostatic agents, IV or PO analgesics, antibiotics, tetanus and other pertinent vaccinations
- Patient monitoring and prioritization of medical problems
- Drug information consults
- Drug administration

Finally, the three S's (Staff, Supply, and Space) should be continuously monitored and provided for as needed. Pharmacies can also reach out to the Disaster Medical Assistance Teams (DMAT), which are a group of volunteer professionals that travel with supplies and medications sufficient for 72 hours and often collaborate with local hospital pharmacies.



Inside the VA: Multifaceted Approach to Combating the Opioid Crisis

Authors: C. Bernie Good, M.D., M.P.H. and Thomas Emmendorfer, Pharm.D.
Prepared by: Ahmed Selevany , PharmD, Newark Beth Israel Medical Center

The United States (which consists of only 4.6% of the world’s population) consumes 81% and close to 100% of the oxycodone and hydrocodone respectively worldwide. The number of patients prescribed an opioid more than doubled from 1999 to 2010, where it peaked at approximately 81 opioid prescriptions/100 elderly patients. This can partly be attributed to the American Pain Society where, in 1996, published that pain should be addressed as the “5th vital sign”. In 2016, VA opioid prescriptions totaled more than 7 million prescribed by > 30,000 prescribers!

The VA endorses 4 main strategies to address the opioid epidemic : education, pain management, risk mitigation, and addition treatment. Since 2007, they have introduced initiatives, take back programs, and issued guidelines to help mitigate the opioid crisis. In 2016, Congress passed the Comprehensive Addiction and Recovery Act (CARA) based largely on the VA’s pain management, opioid safety, and integrative health initiatives. One-on-one provider education is also offered and conducted by specially trained VA pharmacists.

So what are these Initiatives and what have they shown??

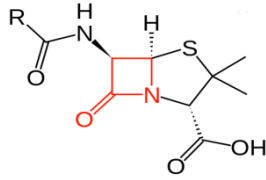
Timeline	Initiative	Results
2007	Medication Assisted Treatment (MAT)	<ul style="list-style-type: none"> ◆ Veterans with opioid use disorder (OUD) must be offered medication assisted treatment ◆ Started in 2007, in 2015 31% of OUD patients were offered MAT and the VA now has 63 residential rehab treatment programs (> 1600 total beds)
2013	Opioid Overdose Educations and Naloxone Distribution Program (OEND)	<ul style="list-style-type: none"> ◆ Supplied naloxone kits to VA facilities (102,000 naloxone kits have been distributed to veterans since the start of the program) ◆ 172 documented opioid reversals occurred over the span of 2 years
2013	Opioid Safety Initiative (OSI)	<ul style="list-style-type: none"> ◆ Was developed to trend opioid dispensing patterns ◆ From 2012-2017, a 35% reduction was seen in veterans that were dispensed opioids. 41 % reduction in veterans on long term opioid therapy.
2014	Medication take back program	<ul style="list-style-type: none"> ◆ Free service to veterans (mail back envelopes and 100+ on site receptacles). ◆ 45 tons have been collected thus far!
2016	Integrative Health Programs	<ul style="list-style-type: none"> ◆ > 1,000 VA providers trained in acupuncture ◆ Tai Chi, Mindfulness, Yoga also provided for assistance in management of chronic pain
2016	VA Provider Opioid Education	<ul style="list-style-type: none"> ◆ VA developed mandatory training programs ◆ 96% of staff had documented meeting training requirements.

Are You Really Allergic to Penicillin? - Effectively Managing Self-reported Cases

Hamza ElHaouati, PharmD

PGY1 Pharmacy Practice Resident

Community Medical Center, Toms River, NJ



Penicillin (PCN) is a group of antibiotics characterized by specific structural feature known as the β -lactam ring. Together, β -lactam compounds represent the most widely used group of antibiotics with established indications such as: surgical prophylaxis, Methicillin-susceptible *Staphylococcus aureus* (MSSA), Group A streptococcal infections, and several sexually transmitted infections. However, penicillin allergy is one of the most frequently reported hypersensitivity. According to the Center for Disease Control and Prevention, approximately 10% of the population reports a penicillin allergy. Over 90% of the patients reporting hypersensitivity do not have a true penicillin allergy leading to suboptimal antibiotic usage.

Penicillin allergy carries considerable implications including: increased adverse effects, increased hospital stays, development of multidrug resistant infections, increased usage of broad-spectrum antibiotics and increased costs. The mean antibiotic cost for patients allergic to penicillin is 63% higher than those not allergic to penicillin due to cost of the alternatives, additional lab work, management of side effects, and increased length of stays. Establishing Penicillin Skin Testing (PST) has the potential to optimize antibiotic usage, decrease usage of more expensive alternatives, and avoid the usage of broad-spectrum antimicrobials.

Allergy Assessment First:

- Detailed patient/family interview
- Previous hospital stay medication history
- Utilizing local pharmacies for more information

The Antimicrobial Stewardship now has guideline recommendations for Penicillin Skin Testing: “in patients with a history of β -lactam allergy, we suggest that antimicrobial stewardship programs promote allergy assessment and PCN skin testing when appropriate”. There are important considerations to address prior to initiating a PST program such as: ownership of the program and its structure, personnel training, and who qualifies for testing. Current models in practice now include: pharmacist-managed (State law dependent), pharmacist-nurse, pharmacist-Infectious disease, outpatient/peri-operative referrals. Financially, PST testing can be bundled into the Diagnosis Related Group (no direct reimbursement), performed as procedure by physicians (allergists or infectious disease), billed outpatient Product, or billed as outpatient Office Visit.

Skin Testing Procedures at St. Joseph’s/Candler Health System

- Restricted to infectious disease physicians or stewardship pharmacist recommendation
- Required a physician order to complete under a P&T approved protocol
- Protocol contained reaction medications in case of allergic reaction
- Performed by nursing staff under the direction of clinical pharmacists
- Post-procedure follow-up
 - o Patients monitored for signs of allergic reaction
 - o Results called to prescribing physician
 - o New orders for antimicrobial written (if applicable)
 - o Allergies updates in the electronic medical record

Steps:

I. Puncture Test

- a. Histamine
- b. Saline
- c. Penicillin G
- d. Benzylpenicilloyl Polylysine

II. Intradermal Test

- a. Saline
- b. Penicillin G
- c. Benzylpenicilloyl Polylysine

III. Oral Challenge (optional)

- a. Amoxicillin 250mg PO x 1

When Good Hormones Go Bad: Acute Management of Endocrine Emergencies

Presented by Kyle Weant

Summarized by Brandon Chen, PGY1 Clara Maass Medical Center

Endocrine emergencies make up only about 1.5% of emergency department visits, but prompt diagnosis and treatment are essential to successful patient recovery. Such low incidence can cause insufficient exposure for individual pharmacists. Individuals may not be as confident in their management of these cases, which can lead to delays in identification of proper treatment and acquisition of medications from the inpatient pharmacies.

Adrenal Insufficiency/Crisis

The acute presentation of adrenal insufficiency includes hypotension, fever, myalgia, nausea, and confusion. Diagnosis can be made through measures of serum cortisol and ACTH and ACTH and CRH stimulation tests. Treatment consists of fluid resuscitation, electrolyte optimization, identification of precipitating cause, and stress-dose steroid administration. Steroid options include hydrocortisone or dexamethasone.

Pheochromocytoma

Pheochromocytoma is a neuroendocrine tumor of the adrenal glands that secretes excess catecholamines. The three cardinal symptoms, headache, palpitations, and hypertension, may appear in spells. Suspicion of pheochromocytoma should be highest in symptomatic young patients without other comorbidities. The only curative measure is surgical excision of the tumor. Bridging to surgery includes acute blood pressure management with alpha and beta blockade. Beta-blockers should not be started before alpha antagonists.

Hypothyroidism

Symptoms are often vague or minimal. Upon physical exam, the patient may have pale, cool skin, edema, and bradycardia. Treatment includes supportive care with fluid resuscitation, mechanical ventilation, thyroid hormone replacement, and glucocorticoid supplementation.

Hyperthyroidism

Patients typically present with heat intolerance, palpitations, chest pain, shortness of breath, nervousness, weight loss, and hair loss. Treatment includes supportive care, antithyroid medications (methimazole and propylthiouracil), radioactive iodine, lithium carbonate, beta-blockers, and thyroidectomy.

Conclusion

Endocrine emergencies, while rare, require immediate medical attention. High clinical suspicion, quick diagnosis, and accurate treatment are key to decreasing patient mortality. Pharmacist involvement in choice of drug and dosing can be effective in optimizing patient outcomes and minimizing risk of medication errors.

Multimodal Analgesia from Enhanced Recovery After Surgery to the Critically Ill: Strategies for the Clinical Pharmacist

Review Article Written By: Divita Singh, PharmD
Monmouth Medical Center

Acute pain is a very common problem, with almost all patients experiencing pain after a surgery, procedure or injury. Opioids have historically been the foundation of acute pain management but due to related adverse events such as GI disturbances, rash, itching, hives, and hypoxia, a multimodal analgesic approach to treating acute pain is highly recommended. Multimodal analgesia combines two or more analgesic agents or techniques that act by different mechanisms to provide analgesia resulting in a decrease in opioid use. Decreasing the use of opioids post operatively has shown to decrease lengths of stay by up to 29% and result in a decrease in patient reported pain scores.

Key Concepts of Enhanced Recovery Protocols for Multimodal Analgesia

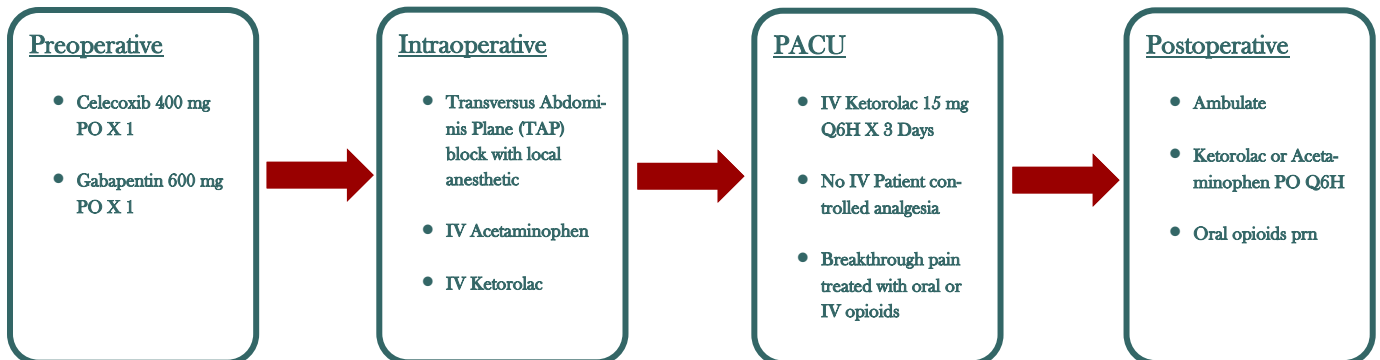
- Regular administration of acetaminophen and NSAID's unless contraindicated
- Use of small dose opioids for breakthrough pain
- Oral opioids preferred
- Use adjunct medications such gabapentin, local anesthetics, ketamine, alvimopam, and dexamethasone



Pharmacologic Multimodal Pain Treatment Options

Modality	Side Effects
Opiates	Respiratory depression and decreased motility
Acetaminophen	Hepatotoxicity, nausea, and vomiting
NSAIDs	GI toxicity, renal failure, and bleeding
Alpha-2 Agonists	Hypotension, bradycardia, and tachycardia
NMDA Antagonists	Hallucinations, tachycardia, and hemodynamic changes
Anticonvulsants	Hallucinations, withdrawal, and seizures

Example of an Enhanced Recovery Protocol for Multimodal Analgesia



Evidence-Based Updates:

Current Topics in Pediatrics

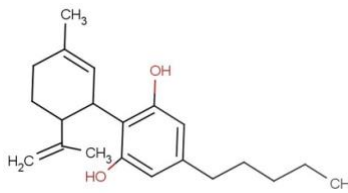


Delirium in Pediatric Patients

Delirium is a change in cognition that is typically acute in onset and fluctuant in its course. The last several years have seen an explosion of research on adult delirium, as well as an increased focus on pediatric delirium- which occurs in up to 25% of PICU patients. Studies show substantially increased costs in pediatric patients who experience delirium, as well as increased length of stay and in-hospital mortality. Recommended tools for delirium assessment include the CAPD and p/psCAM-ICU, although the latter is not used in patients < 6 months old and has not been validated in developmental delay. Daily assessment using these tools is essential to early detection. In the management of any delirium: less is more. Prioritize assessing potential patient-specific causes. Pharmacologic options for treatment include haloperidol, risperidone, quetiapine, olanzapine and ziprasidone. Non-pharmacologic approaches can go a long way to managing this disease state.

Cannabidiol Use in Pediatric Epilepsy

Medical marijuana is defined as the use of cannabis or derivatives to treat disease or alleviate symptoms. It is currently classified by the DEA as a C-I substance, and is often avoided as a treatment option due to euphoric effects and habit-forming potential. Cannabinoids, however, may represent a new class of antiepileptic medication. The cannabidiol molecule lacks the euphoric effect of THC, and also demonstrates anticonvulsant properties with Class I level of evidence for treatment of Lennox Gastaut (LGS) and Dravet Syndromes. The most common side effects include sedation, diarrhea, decreased appetite, nausea and vomiting – although some may be related to the drug vehicle. The interaction between cannabidiol (CBD) and other antiepileptic medications, especially clobazam, must be considered, as CBD has been shown to inhibit CYP3A4 and CYP2C9/19. Having demonstrated high rates of efficacy in LGS and Dravet syndrome, cannabidiol may represent an alternative treatment option for reducing seizure activity in these patients.



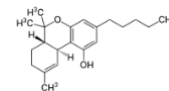
CBD

Allison Pezick

PGY-1 Pharmacy Practice Resident
Monmouth Medical Center

Patent Ductus Arteriosus

The ductus arteriosus (DA) is an essential structure during fetal circulation that diverts blood from the pulmonary artery, allowing blood to bypass the lungs in utero. Patent Ductus Arteriosus (PDA) occurs when the DA fails to close spontaneously. PDA correlates inversely with gestational age, and increases the risk of serious birth complications and mortality. Current treatment options include watch/wait, pharmacologic closure with COX₂ inhibitors or prostaglandin synthesis inhibitors, or surgical ligation. However, treatment may not always be necessary, and the above options for closure come with other side effects and risks. Spontaneous closure of the DA occurs in 30-35% of extremely low birth weight (ELBW) infants (<1000g) and 70% of very low birth weight (VLBW) infants (<1500g) by 1 week of life. Therefore, treatment should be reserved for those with hemodynamically unstable PDA's, and decisions should be made on a case-by-case basis. While indomethacin and ibuprofen remain first-line therapy, studies have shown acetaminophen is equally effective with a preferable safety profile. Acetaminophen may be a treatment option for PDA closure in infants with contraindications to NSAIDs.



THC

Addiction Is in the Genes: How Pharmacogenetics Plays a Role in Opioid Addiction

By Aya Abukwaik, PGY-1 at Robert Wood Johnson Hospital in New Brunswick, NJ

Public health officials call the national opioid epidemic the worst drug crisis in American history. Sales of prescription opioids have quadrupled from 1999 to 2014 without a change in the overall pain that Americans report. In 2015, 52,404 people died as a result of drug overdoses with 63% of deaths involving opioids.¹ Half of the opioid related deaths involved a prescription opioid. Although doctors are writing for less opioid prescriptions every year since 2010, the number of patients receiving prescription opioids is still too high according to the CDC's Morbidity and Mortality Weekly Report.²

A study by Tsuang et al. collected data on drug use from 3,372 pairs of twins from the Vietnam Era Twin Registry comprised of male twin pairs that served in the US military between 1975 and 1975. Drug use disorder was defined as having a diagnosis of drug abuse or met the criteria for drug dependence on the Diagnostic and Statistical Manual, Third Edition Revised, (DSM-III-R). The significant difference between concordance rates for monozygotic (26.2%) vs. dizygotic (16.5%) twins indicates that developing a drug use disorder may be influenced by genetic factors.³

In another study by van den Bree et al., male and female twins were recruited through an alcohol and drug treatment program to assess for genetic influence in drug use and dependence. Evidence of genetic influences on drug abuse and/or dependence in males was found for all drug classes including sedatives, opiates, cocaine, stimulants and cannabis. For females, evidence of genetic influences was found for cocaine, stimulants and cannabis abuse and/or dependence. No heritable component was found for drug abuse and/or dependence of sedatives and opiates.⁴

Genetics can influence the way opioids are metabolized. Opioid metabolism takes place mainly in the liver and undergoes phase 1 and phase 2 metabolism resulting in the production of both active and inactive metabolites. The metabolite may be more potent than the parent compound. CYP2D6 enzyme is a part of Phase 1 metabolism and its activity may be influenced by genetic factors. Hydrocodone, codeine and dihydrocodeine are all metabolized by

CYP2D6 to their active metabolites. There are four phenotypes for the CYP2D6 enzyme including poor, intermediate, extensive and ultra-rapid. Poor metabolizers have a lower risk of becoming dependent on opioids. Patients who are rapid opioid metabolizers may experience increased opioid effects with an average dose of codeine because their rapid metabolism produces a higher concentration of morphine.⁵

The catechol-O-methyltransferase is an enzyme involved in the degradation of catecholamine including dopamine, norepinephrine, and epinephrine. Individuals with the G-variant of the COMT gene are 'Warriors': they have higher enzymatic activity, lower dopamine levels, higher pain threshold, better stress resiliency and ultimately a lower risk for addiction. Those with the A-variant are 'Worriers': they have lower enzymatic activity, higher dopamine levels, lower pain threshold, enhanced vulnerability to stress, and an increased risk for addiction.¹

Genetic testing of various enzymes, transporters, and receptors are available to provide more information in predicting a patient's response to opioids offering a personalized approach to medicine. Some of these pain panels will include a list of drugs and how best to approach them in terms of drug selection, dose, and frequency based on the patients' results.¹

It is important to recognize that genetics is only one contributing factor amongst many potential contributing factors in opioids addiction. Structured programs are effective in getting high risk patients to manage medications similarly to low risk patients. Furthermore, careful prescribing and monitoring has been shown to reduce the rate of misuse behavior by fifty percent.¹

References:

1. Farrell C., Goodbar N. Addiction is in the Genes: How Pharmacogenetics Plays a Role in Drug Addiction. ASHP Midyear 2017. December 5, 2017
2. Rudd R, Aleshire N, Zibbell J, Gladden M. Increases in Drug and Opioid Overdoses deaths. *Morbidity and Mortality Weekly Reports*. Retrieved from: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm>
3. Tsuang MT, Lyons MJ, Eisen SA et al. Genetic influences on DSM-III R drug abuse and dependence: a study of 3,372 twin pairs. *Am J Med Genet*. 1996 Sep 20;67(5):473-7
4. van den Bree MB, Johnson EO, Neale MC, Pickens RW. Genetic and environmental influences on drug use and abuse/dependence in male and female twins. *Drug Alcohol Depend*. 1998 Nov 1;52(3):231-41.
5. Smith HS. Opioid Metabolism. *Mayo Clinic Proceedings*. 2009;84(7):613-624.
6. Jovey RD. Opioids, pain and addiction – practical strategies. *British Journal of Pain*. 2012;6(1):36-42.

View from the Top: The Impact of The Joint Commission's Standards on Pain Management

Travis Tsang PharmD
PGY1- Pharmacy Resident at Newark Beth Israel Medical Center

Pain has always been a problem in today's society. Changes in opioid prescriptions have been steadily increasing since the 90's. There is a need for clarification and a standard of care throughout hospitals to help with pain management. Various examples the Joint Commission attributes this problem to is the fact that there is minimal assessment for history of opioid use or addiction, the use of opioid when not necessary for pain control, and patients not being educated about addictive potential, side effects and proper methods of disposal.

The Joint Commission is trying to figure out ways to set up an organizing framework for new standards. One such way is implementing opioid stewardship.

Essential Elements of Opioid Stewardship

Leadership	Provider Education
Accountability	Tracking/Reporting use
Patient Education	Drug Disposal

What the Joint Commission is trying to do is to obtain greater involvement of patients in their own pain management in the hospital. They suggest doing this by:

- **Developing realistic expectations and measurable goals** that are understood by the patient for the degree, duration and reduction of pain
- **Discussing the objectives used to evaluate treatment progress** (for example, relief of pain and improved physical and psychosocial function)
- **Providing education** on pain management, treatment options and safe use of opioids when prescribed



*"Divine is the task to relieve pain."
-Hippocrates*



Key Standards Related to Pain Assessment and Management ¹ Effective January 1st 2018

Standard LD.04.03.13

Pain assessment and pain management, including safe opioid prescribing, is identified as an organizational priority for the hospital.

Elements of Performance for LD.04.03.13

1. The hospital has a leader or leadership team that is responsible for pain management and safe opioid prescribing and develops and monitors performance improvement activities
2. The hospital provides nonpharmacologic pain treatment modalities.
3. The hospital provides staff and licensed independent practitioners with educational resources and programs to improve pain assessment, pain management, and the safe use of opioid medications based on the identified needs of its patient population.
4. The hospital provides information to staff and licensed independent practitioners on available services for consultation and referral of patients with complex pain management needs.
5. The hospital identifies opioid treatment programs that can be used for patient referrals.
6. The hospital facilitates practitioner and pharmacist access to the Prescription Drug Monitoring Program Databases
7. Hospital leadership works with its clinical staff to identify and acquire the equipment needed to monitor patients who are at high risk for adverse outcomes from opioid treatment.

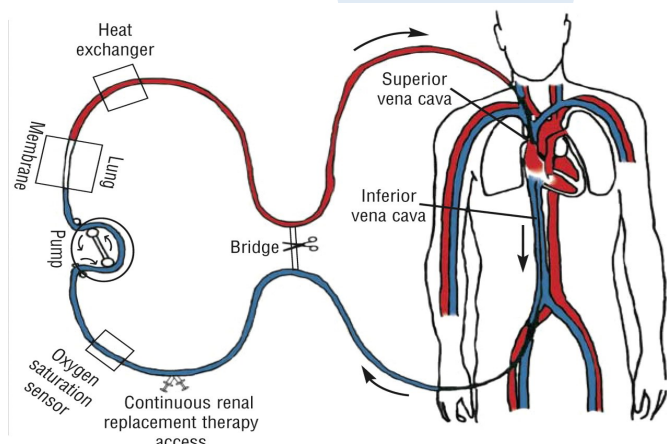
Reference:

1. Joint Commission Enhances Pain Assessment and Management Requirements for Accredited Hospitals. *The Official Newsletter of The Joint Commission*. 2017;37(7):1-4.

Go with the Flow

Pharmacotherapy in ECMO

Written by Nicole Leonida, PharmD
PGY-I Pharmacy Resident, Jersey City Medical Center



Depiction of ECMO. Bibro C, et al. *Crit Care Nurse*. 2011;31(5):e8-e24.

Extracorporeal membrane oxygenation (ECMO) is an external method of gas exchange for the human body. It utilizes a high-flow technique with a drainage and return cannula, along with a large oxygenator, to exchange gas in the blood while allowing the lungs and heart to rest. ECMO is a modality used as a last resort in critically ill patients with hypoxic or hypercapnic respiratory failure, cardiac arrest, and cardiogenic shock. It is also used when bridging patients who are to undergo organ transplant.

During ECMO, a patient is at increased risk of coagulopathy. The exposure of cellular components to the ECMO system produces an inflammatory response, which interacts with the activated coagulation system.² The body attempts to mediate its procoagulant state with anticoagulant counterparts; this can cause increased consumption and activation, which can result in clotting factor deficiencies, thrombocytopenia, and fibrinolysis.² Because of this, patients require continuous parenteral anticoagulation while on ECMO; the table below lists the recommended agents.²

Recommended Anticoagulants for ECMO

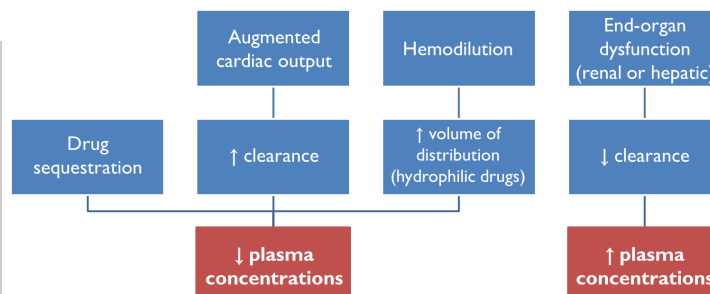
	Heparin	Bivalirudin	Argatroban
Dosing	Loading dose: 40-80 units/kg Maintenance infusion: 10-30 units/kg	Initial rate: 0.08-0.2 mg/kg/h Maintenance: change of rate between 0-0.03 mg/kg/h	Initial rate: 0.25 mcg/kg/h to 2 mcg/kg/min Maintenance: change of rate between 0-0.6 mcg/kg/h
Monitoring	Draw aPTT 2-6 h after original dose Goal aPTT: 40-120 sec	Draw aPTT every 2-4 h post-initiation until 3 values are within 40-120 sec, then draw every 6-12 h	
Half-Life	1-2 h	25 min to 3.5 h	39-51 min

Patients on ECMO also require analgesia and sedation to decrease oxygen consumption, synchronize breathing between the patient and the ventilator, and prevent removal of the device by the patient.³ But similar to the critically ill, patients on ECMO have altered pharmacokinetics due to both the ECMO circuit and drug characteristics.³ Polyvinyl chloride tubing within the ECMO circuit is one important factor that can lead to potential drug loss, while lipophilicity and protein binding are the most vital drug factors that influence pharmacokinetics in this population.³ To date, there are no set dosing recommendations for analgesics and sedatives for patients on ECMO, but data from previous studies suggest that this population requires higher than normal doses, especially for lipophilic drugs that go through significant loss in the ECMO circuit (e.g. fentanyl, midazolam).³

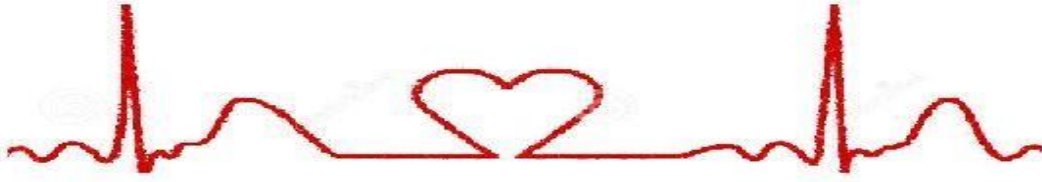
For patients on ECMO, it is equally important to prevent coagulopathy and maintain analgesia and sedation while keeping the body oxygenated. These patients require regular monitoring to ensure enough medication is being delivered and maintained.

References

1. Bibro C, Lasich C, Rickman F, et al. Critically ill patients with H1N1 influenza A undergoing extracorporeal membrane oxygenation. *Crit Care Nurse*. 2011;31(5):e8-e24.
2. Oliver WC. Anticoagulation and coagulation management for ECMO. *Semin Cardiothorac Vasc Anesth*. 2009;13:154-75.
3. Dzierba AL, Abrams D, Brodie D. Medicating patients during extracorporeal membrane oxygenation: the evidence is building. *Crit Care*. 2017;21(66):1-7.



Changes in pharmacokinetics with ECMO. Dzierba AL, et al. *Crit Care*. 2017;21(66):1-7.



'What a QT'ie!' What We Know About Drug-induced QT Prolongation in Children

Review Article Written By: Gary Burdge, PharmD
 PGY1 Pharmacy Resident
 RWJBarnabas Health Behavioral Health Center

QT prolongation is a widely discussed topic in medicine and for pharmacists particularly. On an electrocardiogram (ECG), the QT interval represents the total duration of ventricular activation and recovery. The QT interval is corrected for heart rate using several different formulas: Bazett, Fridericia, Framingham and Hodges formula. The prolongation of the QT interval is associated with an increased risk of deadly ventricular arrhythmias such as Torsades de Pointe (TdP). The normal ranges for the QTc interval are listed below in table 1. A QTc interval > 500 msec is considered a higher risk for developing an arrhythmia.

	1-15 years	Adult males	Adults Females
Normal	<440 msec	<430 msec	<450 msec
Borderline	440-460 msec	430-450 msec	450-470 msec
Prolonged	>460 msec	>450 msec	>470 msec

Table 1. Normal ranges for QTc interval

There are several factors that play into QT prolongation. Some of the key factors are : gender, genetics, cardiac structural abnormalities, electrolyte abnormalities and medications. Genetic polymorphisms of potassium channels especially the KCNH2/HERG gene is thought to contribute to QT prolongation. Many medications affect the QT interval, sometimes intentionally ie. Class III antiarrhythmics but most of the time unintentionally. This is the reason why pharmacists must be vigilant in monitoring patients who are taking medication that can prolong the QT interval. Combining several QT-prolonging medications may lead to additive effects on the QT interval and pharmacokinetic interactions may increase the plasma levels of QT prolonging medications. Crediblemeds.org is a website that compiles data on QT prolonging medication and is a good resource for evaluating a patient's medication from a cardiac standpoint. Table 2 shows some of the medication classes known to affect the QT interval.

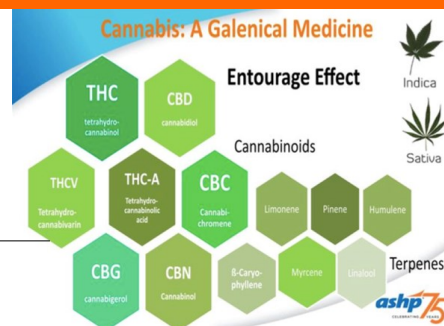
Medication classes that affect the QT	Antidepressants, Antipsychotics, antibiotics, antifungals, ADHD medication, Anti-emetics, Prokinetics, Antiarrhythmics, Anesthetics, Misc (methadone, doxapram)
----------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Table 2. medication classes that affect the QT interval

When it comes to children and the QT interval, there is not a large amount of primary literature. QT-prolonging medications in adults have been shown to have the same effect in children based on case reports, observational studies, and retrospective chart reviews. By utilizing crediblemeds.org, pharmacists and other healthcare providers can evaluate the QT prolongation risk of a patient's medication regimen and obtain an ECG if there is a risk, whether it be pediatrics or adults.

Seeing through the Smoke

Written by: Shadwa Salem, PharmD



Cannabinoids have historically been used for spiritual practices and pain management in ancient civilizations, documented in China, Egypt, India and the Middle East.¹ The endocannabinoid system is an ancient, evolutionarily, conserved lipid signaling system implicated in a number of physiological and pathological processes.² This article will describe the *Cannabis sativa* plant's contents, effects, therapeutic uses, formulations, and drug interactions.

As a brief background review, the endogenous cannabinoid system consists of 2 receptors, cannabinoid 1 and 2 (CB₁ and CB₂). Endogenous agonists include anandamide and arachidonylglycerol (2-AG). They bind to pre-synaptic neurons and inhibit excitatory and inhibitory neurotransmitter release: glutamate, norepinephrine, GABA, dopamine, and acetylcholine. The CB₁ receptor is found in the central and peripheral nervous system. It's located in the cerebral cortex, hippocampus, amygdala, adipocytes, hepatocytes, spleen, heart and lung. CB₂ is most commonly found in tis-

plant strain, soil, climate, and cultivation technique. For drug manufacturing purposes, the plant needs to be reliably grown and handled, ideally following good manufacturing practices. The plant needs to be assayed, labeled, and dated for cannabinoids and terpene content. It also should be void of contaminants.³

Cannabinol, a product of Δ9-THC oxidation, has only 10% of the activity of the parent compound. Nine- tetrahydrocannabinol is a partial agonist at both CB receptors and causes euphoria, relaxation, anxiety, and memory impairment. CBD is a negative allosteric modifier that inhibits THC binding to CB₁. It decreases some of the psycho-toxic effects of THC as anxiety and memory effects.¹ Terpenes have a variety of effects: sedation, analgesia, anxiolysis, anti-inflammation, and anti-convulsive among others. The psychoactive property of the preparation depends on the amount of CBD or THC content. The more THC dominant the more psychoactive a compound is, while the more CBD dominant the less psychoactive it is.³

Concurrent cannabinoid administration with other drugs results in numerous drug interactions. Cannabinoids interact with CYP enzymes 2C19, 2C9, and 3A4, resulting in drug interactions with a number of medications.³ Taking cannabinoids along with alcohol, narcotics, and benzodiazepines results in excessive CNS depression. The efficacy of protease inhibitors and theophylline is decreased when taken with cannabinoids because of their increased clearance.⁴ Although documentation of interactions may be limited, more studies are needed to assess safety and efficacy concerns.⁴

As laws and regulations change to accommodate an increase in the therapeutic use of cannabis. Pharmacists are encouraged to keep up to date with regulations and indications. Cannabis has multiple pharmacologically active components. The components differ based on growth patterns. When using cannabis, consideration must be given to the formulation, route, and potential interaction that may result.

Route	Onset	Duration
Inhalation	0-5 min	2-6 hours
Oral Ingestion	30-120 min	4-8 hours
Sublingual	15-60 min	2-13 hours
Topical	15-120 min	1-8 hours

sues and cells of the immune system, bone, liver and nerve cells.¹ Marijuana is the commonly known *Cannabis sativa* plant. The *Cannabis* plant contains at least 489 distinct compounds among 18 different chemical classes. Of these, the compounds with the most effect are Δ9- tetrahydrocannabinol (THC), cannabinol, and cannabidiol (CBD).¹ Individual plant's compound contents vary based on

Cannabinoids have a multitude of therapeutic uses. Certain states permit its use for serious chronic indications, such as severe nausea and vomiting associated with cancer and chemotherapy, weight loss related to a debilitating illnesses (HIV, cancer), spasticity secondary to neurologic disease, pain syndromes, and glaucoma.⁴ The onset and duration of formulations differ based on the mode of administration. Refer to table for more information. Cannabis may be delivered via a variety of medical formulations locally as lotions and systemically as capsules and patches.³



References:

1. Aggarwal SK. Cannabinergic Pain Medicine: A Concise Clinical Primer and Survey of Randomized-controlled Trial Results. Clin J Pain. 2013; 29(2):162-71
2. Information for Health Care Professionals: Cannabis (marijuana, marijuana) and the cannabinoids [Prepared by Health Canada February 2013]
3. Roussel C, Morgan JJ, Bersten M. Seeing through the smoke: clinical management of medical cannabis. 3 December 2017, Orange County Convention Center, Orlando, Florida.
4. Seamon MJ, Fass JA, Maniscalco-Feichtl M et al. Medical marijuana and the developing role of the pharmacist. Am J Health Syst Pharm.



Narcotics in the Emergency Room: Helpful or Harmful for Headaches?

By Priya Shah, PharmD
PGY-1 Pharmacy Resident
RWJ Somerset

*Originally presented by Richard
Wenzel, PharmD, CPPS*



Why narcotics?

This is a question that comes up often when discussing pain management. The answer is usually patient satisfaction scores and/or prescriber miskonwledge. With current data on opioid abuse rates, as clinical practitioners we should strive to effectively control the patient's pain level yet use the least potent medication with the fewest adverse effects that will diminish the pain.

What constitutes a "headache?"

"Headache" is a term used colloquially to represent pain or pressure felt in the head near the forehead area. A migraine is a headache persisting for 4-72 hours concurrently with symptoms such as photophobia, phonophobia, and nausea/vomiting. Many patients who present to the ER are experiencing a migraine rather than a headache and nearly 49% of these patients are treated with a narcotic. A majority of these patients have used acetaminophen or ibuprofen at home with little relief. Therefore, clinicians resort to opioids as the next line treatment. However following ER discharge, 64% of migraine sufferers experience a recurrent headache within 24 hours.

Assessing the severity of a migraine

The use of validated headache scales help determine migraine severity and if treatment is warranted. Scales include the MIDAS score criteria, which measures headache related debilitation and Migraine ACT, which can help ER practitioners adjust the patient's migraine medications based on medication effectiveness. Treatment goals include restoring a patient's ability to function and avoiding recurrence.

First line agents for migraine

The ideal agent that can provide quick relief for a migraine is an agent with a fast onset of action that targets the pain severity. The triptans, particularly sumatriptan 6 mg as a subcutaneous injection, should be the first line agent as triptans have proven to show restoration in function and are FDA approved for acute migraine. Intravenous metoclopramide 10-20 mg and prochlorperazine 10 mg are great options in patients who experience nausea or vomiting secondary to their migraine.

Adjunct agents for migraine

Adjunct agents that can be used for treatment of migraine are ketamine for analgesia, magnesium, ketorolac, and nonpharmacologic modalities. Intravenous corticosteroids may help reduce the incidence of migraine recurrence. There are numerous effective non-narcotic drugs for migraine sufferers but the initial step is always to assess the severity of pain and provide appropriate coverage.

When should narcotics be used?

Opioids have proven to increase the risk of episodic headaches becoming chronic and heighten sensitivity to pain. The prescribing of opioids has increased by nearly 70% since 2001 while the prescribing of triptans has decreased by 30%. If a patient has failed triptan and adjunctive therapy, consider low potency opioids after evaluating the risk of sedation and abuse. The American Headache Society recommends the use of narcotics for acute migraine in the following circumstances: intolerance to triptans, migraine lasting greater than four hours, minimal risk of abuse and sedation, and previous response to opioid therapy. By treating migraines with opioids as initial therapy, we are doing a great disservice to our patients who require more appropriate pharmacotherapy to resolve the episode and prevent future migraine attacks.

If anyone would like more information from the presentations we attended or has any questions about the articles that we wrote, please feel free to contact us at the email addresses listed below.

Thank you for reading!

PGY-1 Pharmacy Practice Residents

Courtney Tomaselli
Saint Barnabas Medical Center
Email: Courtney.Tomaselli@rwjbh.org

Brandon Chen
Clara Maas Medical Center
Email: Brandon.Chen@rwjbh.org

Jigisha Patel
Saint Barnabas Medical Center
Email: Jigisha.Patel@rwjbh.org

Divita Singh
Monmouth Medical Center
Email: Divita.Singh@rwjbh.org

Nicole Daniel
Barnabas Health Behavioral Health Center
Email: Nicole.Daniel@rwjbh.org

Allison Pezick
Monmouth Medical Center
Email: Allison.Pezick@rwjbh.org

Rebecca Chow
Robert Wood Johnson Somerset
Email: Rebecca.Chow@rwjbh.org

Aya Abukwaik
Robert Wood Johnson New Brunswick
Email: Aya.Abukwaik@rwjbh.org

Jaklin Hanna
Robert Wood Johnson New Brunswick
Email: Jaklin.Hanna@rwjbh.org

Travis Tsang
Newark Beth Israel Medical Center
Email: Travis.Tsang@rwjbh.org

Jeffrey Tagle
Saint Barnabas Medical Center
Email: Jeffrey.Tagle@rwjbh.org

Gary Burdge
Barnabas Health Behavioral Health Center
Email: Gary.Burdge@rwjbh.org

Briana Botros
Saint Barnabas Medical Center
Email: Briana.Botros@rwjbh.org

Priya Shah
Robert Wood Johnson Somerset
Email: Priya.Shah@rwjbh.org

Eleanor Lee
Clara Maas Medical Center
Email: Eleanor.Lee@rwjbh.org

Nicole Leonida
Jersey City Medical Center
Email: Nicole.Leonida@rwjbh.org

Ahmed Selevany
Newark Beth Israel Medical Center
Email: Ahmed.Selevany@rwjbh.org

Shadwa Salem
Jersey City Medical Center
Email: Shadwa.Salem@rwjbh.org

Hazma Elhaouati
Community Medical Center
Email: Hazma.Elhaouati@rwjbh.org

RWJBarnabas
HEALTH