Extracorporeal Membrane Oxygenation (ECMO) is a last line for treatment for patients with respiratory or cardiac failure. During ECMO, patients are frequently systemically anticoagulated because of the high risk of circuit related thrombosis. Additionally, venoarterial (VA) ECMO increases the risk of systemic thrombus formation and thromboembolic events due to retrograde blood flow causing low flow states in the lungs, left atrium, and left ventricle. Heparin is the most commonly used anticoagulant in ECMO as it is well known and its anticoagulant effects can be easily reversed. However, during ECMO therapy heparin levels can fluctuate resulting in unstable anticoagulation and heparin carries the risk of heparin-induced thrombocytopenia (HIT) and thrombosis. Heparin resistance can occur due to the consumption of antithrombin III resulting in subtherapeutic anticoagulation despite large doses of heparin. Bivalirudin, a direct thrombin inhibitor, does not increase the risk of HIT and does not require antithrombin III to exert its effect. The use of bivalirudin is recognized by the Extracorporeal Life Support Organization (ELSO) as an alternative to heparin. There are several retrospective studies evaluating the use of heparin and bivalirudin in adults requiring ECMO. A concise review of these trials can be found in Table 1 on page 2.

Recipe: Cinnamon–Swirl Banana Muffins

Ingredients:
- 3 to 4 overripe bananas, mashed
- 1/3 cups unsalted butter, melted
- 3/4 cup granulated sugar
- 1 egg, beaten
- 1 teaspoon vanilla extract
- 1 teaspoon baking soda
- 1/4 teaspoon salt
- One and one-half cup of all purpose flour

Instructions:
1. Mix the following together and set aside: 1/3 cup granulated sugar and 1 tbsp ground cinnamon
2. Preheat oven to 350°F. Spray muffin pan with nonstick cooking spray, set aside.
3. Mix mashed bananas, butter, sugar, egg, and vanilla extract in a large bowl.
4. Combine the flour, baking soda, and salt. Gently mixing into the banana mixture. Do not over mix.
5. Fill the muffin slots halfway with batter. Evenly distribute half of the cinnamon/sugar mixture into muffin slots. Add remaining batter to the top of each muffin slot.
6. Using a butter knife, swirl the batter.
7. Sprinkle each muffin slot with remaining cinnamon/sugar mixture.

Written by Morgan White, PharmD Candidate 2022
Savannah, GA

Written by Haley Peters, PharmD Candidate 2022
Augusta, GA

Edited by Nathan Wayne, PharmD, BCP, BCCP & Ashley Taylor, PharmD, BCCCP
Table 1: Unfractionated Heparin Vs. Bivalirudin in Adult ECMO: Literature Summary

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Intervention</th>
<th>Results and Conclusions</th>
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</table>
| Pieri et al.                 | Retrospective, Case control study | UFH (n=10) vs. Bivalirudin (n=10) VV-ECMO or VA-ECMO | • More frequent aPTT variations >20% of previous value in heparin group compared to bivalirudin group (52 vs 24, \( p \leq 0.001 \)).
  | 4 n=20 2013                  |                      | • Dose corrections occurred more frequently in the heparin group (58 vs 51, \( p = 0.4 \)), although not statistically significant. |
| Berel et al.                 | Retrospective         | UFH (n=28) vs. Bivalirudin (n=44) 91% VA-ECMO & 9% VV-ECMO | Compared to UFH, patients receiving bivalirudin showed similar rates of thrombotic events across three time points
  | 5 n=72 2018                  |                      | • Initial 96 hours of anticoagulation: 17.9% vs 9.1%, \( p = 0.47 \)
  |                              |                      | • Over the course of entire ECMO run: 21.4% vs 11.4%, \( p = 0.41 \)
  |                              |                      | • Anytime during the admission: 25% vs 22.7%, \( p = 1.00 \)
  |                              |                      | • No difference observed for in-hospital (32.1% vs 36.4%, \( p = 0.91 \)) or 30-day mortality (32.1% vs 36.4%, \( p = 0.91 \)) |
|                              |                      |                                                  | Bivalirudin had less frequent aPTT variations than UFH.                                   |
| Kaseer et al.                | Retrospective         | UFH (n=33) vs. Bivalirudin (n=19) VV-ECMO or VA-ECMO | • Bivalirudin had a numerically lower percentage of thrombotic complications per 7-day period as compared to UFH (26.3% vs 33.3%, \( p = 0.6 \)), although not statistically significant. |
| 6 n=52 2020                 |                      |                                                  | Bivalirudin may have reduced thrombotic complications, although this finding was not statistically significant in this study. |
| Rivosecchi et al.            | Retrospective, Observational Cohort Study | UFH (n=162) vs. Bivalirudin (n=133) VV-ECMO | • In-circuit thrombosis UFH vs bivalirudin: 32.7% vs 17.5%, \( p = 0.003 \)
  | 7 n=295 2021                 |                      | • Bivalirudin patients received less PRBC: 992.1mL vs 2617.6mL, \( p < 0.001 \)
  |                              |                      | • Bivalirudin patients received less FFP: 22.6mL vs. 477.6mL, \( p < 0.001 \)
  |                              |                      | • Bivalirudin patients received less PLT infusions: 94.1mL vs. 548mL, \( p < 0.001 \) |
|                              |                      |                                                  | Compared to UFH, bivalirudin was more efficacious due to less thrombotic events, and safer due to the lower amount of blood products needed. |
| Sheridan et al.              | Retrospective, Cohort Study | UFH (n=50) vs. Bivalirudin (n=100) VV-ECMO | • Thrombotic events in bivalirudin vs UFH group: 1 vs 0 events, \( p > 0.05 \)
  | 8 n=150 2021                  |                      | • Percent time in therapeutic range bivalirudin vs UFH: 86% vs 33%, \( p < 0.001 \)
  |                              |                      | • Bivalirudin took less time to therapeutic range: 2 vs 18 hours, \( p < 0.001 \)
  |                              |                      | • No difference in incidence of bleeding: 10% vs 12% |
  |                              |                      |                                                  | Bivalirudin has a favorable pharmacokinetic profile in achieving and maintaining therapeutic range. There were no differences in the bleeding rates and one thromboembolic event occurred in the Bivalirudin group. |

Abbreviations: UFH-Unfractionated Heparin; VV-ECMO- Veno venous Extracorporeal Membrane Oxygenation; VA-ECMO- Veno Arterial Extracorporeal Membrane Oxygenation; PRBC- packed red blood cells; FFP- fresh frozen plasma; PLT- platelets

Conclusions:
Prospective, multicenter, randomized trials are needed to evaluate the optimal approach to anticoagulation in adult ECMO patients. Based on the available literature, bivalirudin appears to be a safe alternative that may provide more consistent anticoagulation with similar efficacy to heparin for adult patients receiving ECMO.

References:
Off Block Adventures!

Fourth year students taking time off after working hard during a year’s worth of rotations. Here are a few of the incredible places our P4s have visited this year!

Hannah Henderson
Disney World
Orlando, FL
Savannah Campus

Kellie Hauck
Universal Studios
Orlando, FL
Savannah Campus

Chloe Baskowitz & Blake Terrell
Bright Angel Trailhead
Grand Canyon Village, AZ
Savannah Campus

Amy Phillips
Savannah, GA
Savannah Campus

David Perez
New York City, NY
Savannah Campus

Haley Peters
Emerald Outback Trails
Beech Mountain, NC
Augusta Campus
Living with Sickle Cell Disease in an Opioid Epidemic

The opioid epidemic began in the United States during the 1990s with the first wave in 1999. In 1999, there were many prescriptions related to opioid overdose deaths. In 2010, the second wave occurred with a rise in heroin overdose deaths. The third wave began in 2013 with the rise in synthetic opioid overdose deaths. About 841,000 people have died since 1999 from a drug overdose, and over 70% involved an opioid. Just in 2019, at least 49,700 have died from opioid overdose. Opioids are drugs, whether legal or illegal, that act on the opioid receptors for pain relief. They are highly addictive substances, which lead to drug dependency and drug withdrawal. Symptoms of withdrawal can be as bad agitation, anxiety, insomnia, tremors, etc. These symptoms of withdrawal make it difficult for everyday living, and relief is often found through intake of more opioids. An example of an illegal opioid is heroin, and legal opioids include oxycodone, hydrocodone, codeine, morphine, and fentanyl.

Sickle Cell Disease (SCD) is a red blood cell disorder that changes the shape of the red blood cells. Instead of the round shape, it is C-shaped, hence the name “sickle”. These sickle cells are hard and sticky, which causes the blood to get stuck and clog in the blood vessels. This obstruction causes ischemic injury to the organ and results in pain. Stressors of any kind, ranging from physical stress to psychological stress, can trigger onsets of painful episodes. Failure to treat acute pain may lead to intractable chronic pain syndrome, where the cause of the pain is unknown. Per the American Society of Hematology, opioids are most often used as treatment for patients with acute sickle cell disease. Due to the opioid epidemic and patients with SCD needing opioid treatment, patients with SCD face barriers to treatment and care.

African Americans are more likely to be suspected of opioid abuse compared to other races, and in the US, SCD mostly affects African Americans. This leads to barriers to management of the patient’s pain with Sickle Cell Disease. In a qualitative study by Sinha et al, 15 adults were interviewed. 10 of the 15 interviewed patients said they had to sign a treatment agreement with their physician about the purpose of opioids, opioid dependency, and reductions in opioid prescriptions. They did not discuss alternative therapies, and the reduction in opioid prescription prevents the patient from increasing medication dosage at an onset of pain crisis. Some of the interviewers talked about their experience at the emergency department, and they were forced to negotiate with the ED physician for their usual dose of opioids. The physicians in the emergency department would wait for blood work to confirm acute sickle cell crisis rather than assess the patient’s physical presentation. The decrease in access to opioids, increased stigmatization towards African Americans, and the lack of proper delivery of care leads to a decrease in guidance or support in the management of patients with Sickle Cell Disease.

There are ways to improve delivery of care for all patients with Sickle Cell Disease. Treatment should be considered as benefits in both pain and function for the patient. Opioids should be used in combination with nonpharmacologic methods and non-opioid therapies, such as NSAIDs. Patients should not have to rely only on opioids, and physicians should offer other treatment options to supplement their opioid therapy. Healthcare professionals should engage in more conversations about goals for pain relief for each patient, and it should be individualized to meet that certain patient’s needs rather than the general population. Healthcare professionals must take into consideration that each patient is different in pain tolerance, and their treatment should be catered to what they can handle. Lastly, healthcare professionals must act regardless of race. Racial discrimination can influence the treatment of care, and regardless of race, we must treat all patients equally.

Written by Jillian Calderon, PharmD Candidate 2022  
Savannah, GA  
Edited by Misha Watts, PharmD

References:


### Where are the P4’s going next?!

**Congratulations, Class of 2022!**

<table>
<thead>
<tr>
<th>Aliya Abdulla, PGY-1 Methodist Hospital</th>
<th>Kendall Huntt, PGY-1 University of Kentucky Healthcare</th>
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<tbody>
<tr>
<td>Amanda Sweat, PGY-1 University of South Alabama Health University Hospital</td>
<td>Kendall Huntt, PGY-1 University of Kentucky Healthcare</td>
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<tr>
<td>Amber Adams, PGY-1 Piedmont Athens Regional</td>
<td>Kosha Patel, PGY-1 WellStar Cobb</td>
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<td>Anna Beth Bowles, PGY-1 Grady Memorial Hospital</td>
<td>Kristine Nguyen, PGY-1/PGY-2 Pharmacotherapy University North Carolina Medical Center</td>
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<tr>
<td>Austin Burnette, Adena Regional Medical Center</td>
<td>Latia Jones, PGY-1 Bonheur Children’s Hospital</td>
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<td>Austin Dykes, PGY-1 Erlanger Health System</td>
<td>Laura Beth Nalley, St. Joseph’s/Candler Hospital</td>
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<td>Bayleigh Carver, PGY-1 New York Presbyterian</td>
<td>Logan Bradley, PGY-1 St. Joseph’s/Candler Hospital</td>
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<td>Becca Powell, PGY-1 University of Colorado Health</td>
<td>Logan Johnson, PGY-1 University of Florida Health</td>
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<td>Blake Harrington, Publix Pharmacy</td>
<td>Madeline Shepherd, PGY-1 Piedmont Atlanta Hospital</td>
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<td>Blake Terrell, PGY-1 Piedmont Atlanta</td>
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<td>Brandy Smith, Walmart Pharmacy</td>
<td>Mona Modi, PGY-1 Optum Specialty Pharmacy</td>
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<td>Brianna Beldon, PGY-1 Moses Cone Hospital</td>
<td>Morgan White, PGY-1 Blount Memorial Hospital</td>
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<tr>
<td>Brittany Brooks, Kroger Pharmacy</td>
<td>Natalie Ung, Publix Pharmacy</td>
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<td>Busola Fowowe, PGY-1 Rush University Medical Center</td>
<td>Nathan Adams, Thomaston Prescription Shop</td>
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<tr>
<td>Carly Loudermilk, PGY-1 Augusta University Medical Center</td>
<td>Nick Steese, Kroger Pharmacy</td>
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<td>Carson Brock, S&amp;W Pharmacy</td>
<td>Rachel Shelley, PGY-1 Ambulatory Care Moses Cone Hospital</td>
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<td>Christy Davenport, PGY-1 Atrium Health Navicent</td>
<td>Raymond Patterson, PGY-1 WellStar Kennestone Hospital</td>
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<td>Cynthia Duvall, PGY-1 Redmond Regional/Advent Healthcare</td>
<td>Remi Fagbamiye, PGY-1 WellStar Kennestone</td>
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<tr>
<td>Daniel Padron, PGY-1/PGY-2/MS Health System and Administration in Kansas City, KS</td>
<td>Ryan Bok, PGY-1 West Virginia University Medicine</td>
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<tr>
<td>David Perez, PGY-1/PGY-2 Froedtert &amp; the Medical College of Wisconsin</td>
<td>Sahand Golpayegany, PGY-1 Emory University Hospital</td>
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<tr>
<td>Dustin Bivins, PGY-1 Piedmont Atlanta Hospital</td>
<td>Samar Husain, Brand Manager Abbvie</td>
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<td>Emily Royal, PGY-1 Augusta University Medical Center</td>
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<td>Tram Le, PGY-1 Providence St. Peter Hospital</td>
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<tr>
<td>Haley Peters, PGY-1 Northeast Georgia Health System</td>
<td>Whitney Worth, U-Save-IT Pharmacy</td>
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<tr>
<td>Jillian Calderon, PGY-1 Piedmont Columbus Regional Midtown</td>
<td>Kellie Hauck, Kroger Pharmacy</td>
</tr>
<tr>
<td>Jonathan Schnider, PGY-1 Carl Vinson VA Medical Center</td>
<td>*Includes those students who submitted their plans for next year- not all P4’s are listed</td>
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<tr>
<td>Kellie Hauck, Kroger Pharmacy</td>
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<tr>
<td>Kelsey Bouwman, PGY-1 Vidian Medical Center</td>
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Important Dates!

April 4th
Earliest regalia and commencement ticket pick up date
Athens, GA

April 30th
Request transcripts for licensing

May 3rd-6th
NAPLEX & MPJE Review
UGA COP, Athens, GA

May 5th
Reception at 5:30 p.m.
Georgia Center, Athens, GA

May 7th
Commencement at 3 p.m.
Students to arrive by 1:45 p.m.
Guest seating at 2:15 p.m.
Stegeman Coliseum, Athens, GA

June 11th-15th
APhA Summer Meeting– In person!
Phoenix, AZ

July 8th-10th
GSHP Summer Meeting– In person!
Amelia Island, FL