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## Special Points of Interest:

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- Policy and Procedures Update
- Potential Risk of Confusion between Bloxiverz (neostigmine) injection and Vazculep (phenylephrine injection)
- Are Antidepressant Medications Safe to Use in Pregnancy?
- Potential Treatment Options for Ebola: an Area of Investigation
- Meet Our Two New Pharmacists and One Pharmacy Technician

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## P&T Update

### Formulary Addition/Deletion

1. Dexmedetomidine (Precedex®) – line extension  
Dexmedetomidine (Precedex®) 80mcg/20mL – Line extension approved
2. Ganciclovir intravitreal implant (Vitrasert®) – formulary deletion  
Discontinued by the manufacturer – Formulary deletion approved
3. Darunavir 800 mg/cobicistat 150 mg (Prezcobix™) – line extension-Approved
4. Atazanavir 300 mg/cobicistat 150 mg (Evotaz™) – line extension-Approved
5. Rabies vaccine (Rabavert®) – line extension  
Motion to add Rabavert® to the formulary in addition to Imovax® which will remain as the preferred formulation – Approved
6. Pralidoxime (Protopam®) 1g vials were discontinued by the manufacturer are now available. A formulary reinstatement motion was proposed. – Approved
7. Bupropion IR (Wellbutrin®) – line extension, was recommended to be added to formulary. The XL formulation is already formulary. – Formulary addition of bupropion IR tablets approved

### Policies & Procedures/Floor Stock Update

1. 707-600-180 Sentry Data Systems:  
The policy describes the role of Sentry Data Systems in the 340B process at University Hospital. Sentry Data Systems will assist University Hospital in the operation of its 340B program. – Policy revision approved
2. 707-600-180A - 340B Program at University Hospital – new policy  
Pharmacy presented this policy as it covers the 340B program at University Hospital. This policy discusses how University Hospital will maintain compliance with the 340B program. – Policy approved
3. 2015-16 dangerous cautionary medication cards were presented.– Approved
4. 2015-16 class reviews for mood stabilizers, antidepressants and antipsychotics were presented – Approved
5. 2015-16 The pharmacy policy and procedure binder was presented for the annual approval. – Approved
6. 2015-16 High risk/high alert medication list was submitted for review and approval. – Approved
7. 2015-16 Look alike/sound alike medication list was submitted for review and approval. – Approved
8. 2015-16 Standardized IV drip concentration list for adults/pediatrics was presented which is a part of policy on standard infusion concentrations for medications (#707-500-115) – Approved
9. 2015-16 Dangerous abbreviations list was presented for review and approval – Approved

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## Policies & Procedures/Floor Stock Update

(Continued from page 1)

- 10. 2015-16 Drug formulary book was submitted online for review and approval.  
<http://pharmacy.core.umdnj.edu/UHPharmacyFormulary.pdf> – Approved
- 11. Order entry, verification, and provision of restricted anti-infective - policy revision. Significant revisions

include MICU/SICU unrestriction of meropenem for 5 days, removal of colistin/tigecycline unrestriction for MICU for 3 days, allowing single first doses of restricted anti-infectives to be dispensed without ID approval, removal of ID approval requirement for non-formulary antibiotics, and pharmacist work flow changes to optimize therapy with the restricted anti-infectives.  
– Policy revisions approved

## Potential Risk of Confusion between Bloxiverz® (neostigmine) injection and Vazculep® (phenylephrine injection)



On March 23rd 2015, the Institute for Safe Medication Practices or ISMP issued an official National Alert Network warning on the potential

dosing and a maximum daily dose of 5 mg. Whereas Vazculep®, given IV bolus, has a recommended dose of 40-100 mcg indicated for hypotension during anesthesia and 100-500 mcg indicated for hypotension with shock. In the event Vazculep® was used instead of Bloxiverz® and 5 mL of Vazculep® was drawn, we would have an extreme case of Vazculep® overdose. The result of an exponentially elevated level of phenylephrine includes cardiac arrest, extreme hypertension or death.

medication mix-up between neostigmine injection (Bloxiverz®) and phenylephrine injection (Vazculep®). Both products are manufactured by Eclat™ Pharmaceuticals. Bloxiverz® and Vazculep® have packaging similarities with respect to vial size, color, and font. If the wrong medication was given to the wrong patient, serious life-threatening side effects can occur.

To prevent further mix-ups, the ISMP highly suggests the two drugs be stored far apart from each other in both short-term and long-term storage areas, even though the starting letters of the two generic drug names are alphabetically close. Further awareness should be stressed to hospital staff members of the possible mix-up. Implementing barcode scanning of these medications during drug dispensing and administration allows staff to double-check for mistakes. ISMP has notified Eclat™ Pharmaceuticals of the potential risk of mix-ups; a suggestion to revise container design and labeling has been made. Furthermore, FDA is aware of the alert and concerns and appropriate actions are being taken.

Approved by the FDA in 2013, Bloxiverz® is a neostigmine product with parasympathomimetic cholinesterase inhibiting activity. It is indicated for both the symptomatic treatment of myasthenia gravis as well as for the reversal of non-polarizing neuromuscular blockades. Bloxiverz® is available in 2 concentrations, 5mg/10mL vials and 10mg/10ml vials. On the other hand, Vazculep® or phenylephrine is a direct-acting alpha-adrenergic agonist was FDA approved in 2014 for the treatment of hypotension or paroxysmal supraventricular tachycardia. It is available in a standard concentration of 10 mg/mL with the vial sizes of 1 mL, 5 mL, and 10 mL pharmacy bulk packages.

This national alert was discussed at the Pharmacy and Therapeutics Committee meeting. The UH Pharmacy has intermittently ordered these products due to the national backorder on the generic products. The Anesthesia and Surgery Depts. have been informed to be vigilant about this potential mix up.

The ISMP has received 8 reports about the look-alike packaging of Bloxiverz® and Vazculep®. Reports claim Bloxiverz® has often been misplaced for Vazculep® and vice versa. Luckily, all mistakes were caught upon checkup. Bloxiverz®, given IV push, has weight based

### References:

"Warning! Potentially dangerous confusion between neostigmine (Bloxiverz®) injection and phenylephrine (Vazculep®) injection." The Institute of Safe Medication Practices and the American Society of Health-System Pharmacists  
<[http://www.nccmerp.org/sites/default/files/nan\\_alert\\_2015final.pdf](http://www.nccmerp.org/sites/default/files/nan_alert_2015final.pdf)>.

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## Antibiotics as an Alternative to Surgery for the Treatment of Appendicitis

Appendicitis is defined as inflammation of the appendix. The strongest diagnostic predictors of appendicitis include migration of pain to the right lower quadrant of the abdomen and vomiting.<sup>3</sup> It remains the most common reason for emergency abdominal surgery with a lifetime incidence of 7-14%.<sup>3</sup> The usual treatment of appendicitis is appendectomy, which involves laparoscopic removal of the appendix. Appendectomy is usually initiated promptly, as there are concerns of potential perforation.

However, recent studies show that appendectomy may not be the only treatment option for appendicitis. Several small randomized trials have suggested the use of antibiotics in lieu of surgery. Typical protocol is 48 hours of IV antibiotics in the hospital, followed by 7 days of oral antibiotics that target the typical causative organisms of abdominal infections (e.g., ciprofloxacin and metronidazole).<sup>3</sup> The studies concluded that approximately 70% of patients treated with antibiotics did not require surgery. Patients assigned to antibiotic therapy also had lower or similar pain scores, required fewer doses of narcotics, and had a quicker return to work.<sup>3</sup> Additionally, those who received antibiotics were 39% less likely to have developed complications such as perforated appendix, peritonitis, or infection around the appendectomy incision.<sup>2</sup> The use of antibiotics in the treatment of appendicitis was initially considered when antibiotics first became available in the 1940s and 50s. For example, they were administered to American soldiers on nuclear submarines during the Cold War with positive results and no deaths or complications.<sup>1</sup> Although not thoroughly evaluated, antibiotic therapy may also be advantageous in terms of cost. Studies in Turkey and Sweden showed higher total costs of care with prompt appendectomy.<sup>1</sup>

Removing the appendix may also pose a long-term risk to the patient. Historically, the appendix has been regarded as an organ with no significant physiologic role. However, recent theories have emerged which suggest otherwise. Bacteria sequestered in the appendix may be beneficial by repopulating the gut with healthy bacteria after a massive diarrheal disease. For example, recurrence of *Clostridium difficile* infection is significantly more common in patients with a history of appendectomy.<sup>3</sup> Such findings suggest that removal of the appendix may put the patient at risk for future abdominal infections.

Additionally, prompt removal of the appendix may not be as urgent as was once thought. Most often, appendicitis is self-resolving and does not lead to a perforated appendix. A cohort of adult patients undergoing appendectomy showed that the time between evaluation in the emergency department and surgery was not a predictor of the risk of perforation.<sup>3</sup> Also, trials found that those who had surgery after receiving antibiotics first did not have any more complications than those who received emergency surgery. With this evidence, physicians may be able to confidently delay surgery with low concerns of perforation. Antibiotics can be tried first to potentially avoid an otherwise unnecessary surgical procedure.

The biggest concern associated with this alternative treatment is the possibility of reoccurrence. Trials showed that eventual appendectomy after antibiotics occurred in 10-37% of patients, but 13% who underwent later appendectomy did not actually have appendicitis. Also, about 20% of those treated with antibiotics had a return of pain or other symptoms and needed to go back to the hospital.<sup>3</sup> The results may be skewed due to over-diagnosis and uneasiness of patients who did not receive appendectomies. Therefore, the data must be further evaluated to draw conclusions on the rate of reoccurrence in both groups.

Overall, it is unclear at the moment if antibiotics should be recommended as first-line treatment for appendicitis. Researchers from Nottingham University Hospitals in England concluded that administering antibiotics early "merits consideration as the initial treatment option for uncomplicated appendicitis." The World Society of Emergency Surgery states that "this conservative approach features high rate of reoccurrence and is therefore inferior to the traditional appendectomy... non-operative antibiotic treatment may be used as an alternative treatment for specific patients whom surgery is contraindicated." As of now, appendectomy is still considered standard of care for uncomplicated appendicitis, but patients should be informed of their options. In order to confidently implement antibiotics as a mainstay of treatment, larger and more comprehensive trials must be initiated in attempt to answer several important clinical questions.

(Continued on page 4)



## Antibiotics as an Alternative *(Continued from page 3)*

### References:

1. Kolata, Gina. "Antibiotics Resurface as Alternative to Removing Appendix." *The New York Times* 18 May 2015: D1. Web. 20 May 2015.
2. Skerrett, Patrick J. "Antibiotics instead of surgery safe for some with appendicitis." *Harvard Health Publications*. Harvard Health

Blog, 11 Apr. 2012. Web. 20 May 2015.

3. Solomon, Caren G., and David R. Flum. "Acute Appendicitis – Appendectomy or the "Antibiotics First" Strategy." *New England Journal of Medicine* 372.20 (2015): 1937-943. Web. 20 May 2015.

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# Irritable Bowel Syndrome: General Overview and Treatment Options

## Overview

Irritable Bowel Syndrome (IBS) is characterized by alterations in bowel pattern predominantly showing signs and symptoms of abdominal pain, vomiting, nausea and GI discomfort. The pathophysiology is not fully known but it is an autoimmune disease that alters GI motility, visceral hypersensitivity, inflammation, fecal flora and food sensitivity. IBS is one of the costliest disease states in USA currently. Annual costs of IBS are estimated to be between \$1.35 billion, as the direct costs, to \$1.56 billion, including the indirect costs incurred. Irritable bowel syndrome can lead to increased indirect costs due to increased absenteeism from work.

## Diagnosis

Patients must be diagnosed by GI specialists, or gastroenterologists, who can use tools such as the Rome III criteria to diagnose patients with IBS. IBS is based on stool pattern and may be classified as IBS-D (predominant diarrhea), IBS-C (predominant constipation) or IBS-M (mixed subtype). IBS may be diagnosed based on the Rome III criteria as recurrent abdominal pain or discomfort on at least 3 separate days per month in the past 3 months associated with 2 or more of the following: improving symptoms upon defecation, change in stool frequency or change in form of stool.

## Treatment Options

IBS treatment generally is based on symptom management, which includes the use of antispasmodics, antidepressants and probiotics mainly for IBS-D. Antispasmodics, such as dicyclomine or hyoscine, are used for smooth muscle relaxation because spasms in IBS can trigger the symptoms such as abdominal pain and lead to constipation or diarrhea. These agents may be used to treat global symptoms as well as abdominal pain. Antidepressants have dual effects on both brain and gut and therefore they benefit patients with either IBS-C or IBS-D. Since IBS may be precipitated by depression or anxiety, these may be the agents of choice in patients who have

concomitant health matters that require treatment with antidepressants. Tricyclic antidepressants (TCAs) have anticholinergic properties and hence benefit those with IBS-D more because they slow motility. SSRIs are prokinetic agents therefore are more useful for patients with IBS-C. Probiotics may be used to restore the normal flora in the gut for patients with IBS-D. Other agents used for IBS include loperamide or serotonin 5-HT<sub>3</sub> receptor antagonists.

Additional treatment options for IBS-C include fiber and psyllium as OTC supplements. Psyllium resulted in significant improvement in patient's clinical status with a reduction in abdominal pain for at least 2 out of 4 weeks compared to placebo. Adverse events from this type of regimen have included bloating, abdominal distension and pain. Notable adverse events of antidepressants include insomnia, restlessness, constipation or diarrhea, and nausea. Specifically for IBS-C, patients may be able to use osmotic laxatives, chloride channel activators such as lubiprostone, linaclotide and serotonin 5-HT<sub>4</sub> receptor agonists.

## Conclusion

IBS is a complex disease state that requires early management to prevent excess deterioration. It has multiple mechanisms of pathogenesis but it is primarily immune-mediated and involves the dysfunction of multiple bodily systems acting together. Based on whether a patient has IBS-C or IBS-D, treatment consists of either GI motility enhancing agents or GI motility decreasing agents, respectively. Other agents may be added on to control pain symptoms of IBS. Regardless, management of IBS is critical to limit healthcare costs and to optimize the outcomes for patients.

### References:

1. Barboza JL, Talley NJ and Moshiree B. Current and Emerging Pharmacotherapeutic Options for Irritable Bowel Syndrome. *Drugs*. 2014; 74: 1849-1870.
2. Anastasi JK, Capili B and Chang M. Managing Irritable Bowel Syndrome. *AJN*; 2013;113(7): 42-52.

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## Beta-Lactam/Beta-Lactam Inhibitor Combination for the Treatment of Infections Caused by Extended Spectrum $\beta$ -Lactamase Producing Bacteria?

A recent focus in medicine has been finding alternative options for treating multi-drug resistant pathogens such as extended-spectrum beta-lactamase producing *Escherichia coli* (ESBL-EC). *E. coli* is a gram negative bacteria with variable strains. Most concerning strains are pathogenic as well as multi-drug resistant. One such example is ESBL-EC which produces a beta-lactamase enzyme that renders the pathogen more resistant to standard anti-infective therapy. First-line antibiotic options used to treat typical non-resistant *E. coli* strains are trimethoprim/sulfamethoxazole, fluoroquinolones, penicillins, and cephalosporins.

According to the Centers for Disease Control and Prevention and recent studies from around the world, outbreaks of ESBL-EC strains have risen over the past decade in parts of Spain, France, and North America with values ranging from 4.5-30% from 1995-2002. ESBL-EC, if left untreated, has the potential to cause severe and complicated urinary tract infections, bacteremia, as well as gastrointestinal/abdominal infections. The rise in infections due to resistant pathogens reported all over the world is a cause of concern because of the over-utilization of carbapenems which may further exacerbate the issue of resistant pathogens. Such was seen in a recent clinical trial conducted in Seville, Spain approved by the Ethics Committee of the Hospital Universitario Virgen, where an increasing prevalence of *E. coli* strains that produce a carbapenamase enzyme which will inactivate the highly used carbapenems class was found to be an imminent threat. As a result, the study explored a strategy to limit the usage of carbapenems by evaluating the efficacy of beta-lactam/beta-lactamase inhibitors (BLBLI) to combat pathogens producing ESBL, bacteria which carbapenems are often used to treat. This was an observational, nonrandomized, post hoc cohort study that evaluated patients from 6 different prospective cohorts in the treatment of ESBL-EC in different parts of Spain. Patients were non-mutually excluded into categories of empiric therapy versus definitive therapy with either amoxicillin-clavulanate (AMC) or piperacillin-tazobactam (PTZ) being the drugs of choice for BLBLI versus imipenem or meropenem as the drugs of choice for the carbapenem class. Despite the study

demonstrating non-inferiority of BLBLI to carbapenems for the treatment of ESBL-EC, the trial's results had some limitations. These limitations include the nonrandomized bias, inefficient data collection in regards to pathogen strain and susceptibility results (MIC), and discrepant dosing regimens and route of administration (for AMC) compared to US standards.<sup>4</sup> The trial results concluded that to "use AMC or PTZ, at appropriate doses, for definitive therapy of susceptible ESBL-EC strains [(that cause blood stream infections, mainly in the urinary and biliary tract)] to help prevent the over-usage of carbapenem" may be greatly restrictive and minimize the development of carbapenamase resistance.<sup>4</sup>

Although the initiative was taken to address a rising problem in ESBL-EC strains, the study does not fully apply to clinical settings especially in the US. The need to find alternative treatment options for multi-drug resistant gram-negative bacteria is still a concern, which is increasing the demand for more clinical trials that compare other classes of drugs (or even other BLBLI) to carbapenems when treating ESBL-producing organisms.

### References:

1. Collignon, P. (2009, January 1). Resistant *Escherichia coli*— We Are What We Eat. Retrieved from <http://cid.oxfordjournals.org/content/49/2/202.full>
2. Koebler, J. (2013, January 1). Study: 'Dramatic Increase' of Infections Caused by Drug-Resistant *E. coli*. Retrieved from [http://www.usnews.com/news/articles/2013/03/12/study-dramatic-increase-of-infections-caused-by-drug-resistant-e-coli-Martin, K. \(2013, January 1\).](http://www.usnews.com/news/articles/2013/03/12/study-dramatic-increase-of-infections-caused-by-drug-resistant-e-coli-Martin, K. (2013, January 1).)
3. Treatment of ESBL-producing *E. coli* Lower Urinary Tract Infection - See more at: <http://www.pharmacytimes.com/publications/health-system-edition/2013/November2013/Treatment-of-ESBL-producing-E-coli-Lower-Urinary-Tract-Infection#sthash.NzU3EFvt.dpuf>. Retrieved from <http://www.pharmacytimes.com/publications/health-system-edition/2013/November2013/Treatment-of-ESBL-producing-E-coli-Lower-Urinary-Tract-Infection>
4. Emergence of Community-Acquired Extended-Spectrum Beta-Lactamase *Escherichia coli* (ESBLEC) in Honolulu: A Case Series of Three Individuals with Community-Acquired ESBLEC Bacteriuria (Hawaii Medical Journal) Hoshida, Reid, Heath Chung, and Jinichi Tokeshi. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3233400/>
5. Rodríguez-Baño, J. (2012).  $\beta$ -Lactam/ $\beta$ -lactam inhibitor combinations for the treatment of bacteremia due to extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli*: A post hoc analysis of prospective cohorts. US National Library of Medicine National Institutes of Health.

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## Are Antidepressant Medications Safe to Use in Pregnancy?

Depression is a fairly common medical disorder that is often treatable. Depression affects people of all ages, ranging from adolescents to geriatric patients. There are serious risks when prescribing antidepressant medications, especially in special populations like pregnant women. Due to possible negative effects on the fetus, physicians and pharmacists must collaborate and weigh the risks and benefits of using these types of medications in pregnant women.

The classes of antidepressant drugs used during pregnancy include tricyclic antidepressants, selective serotonin re-uptake inhibitors, and serotonin norepinephrine re-uptake inhibitors. Although no physician, scientist, or pharmacist can say with absolute certainty that these medications are completely safe during pregnancy, there is more promising data with the SSRIs.

A study was conducted in Rotterdam, Netherlands where 7,696 pregnant women were examined. From this number, three different groups were obtained. The first group consisted of 7,027 women who had no depressive symptoms. The second group comprised of 570 women who possessed significant depressive symptoms but were not placed on any antidepressants, and the last group comprised of 99 women who were put on selective serotonin re-uptake inhibitors. The study was extensive and each mother was observed during all three trimesters and fetal ultra-sonographies were performed. The mothers who had depression but were not treated had more depressive symptoms than

the 99 mothers who were on medication. Although the study showed benefits of using antidepressants during pregnancy, the babies had a higher likelihood of preterm birth and reduced head growth when their mothers were on SSRIs.<sup>1</sup>

Women who have the highest risk of depression during pregnancy are those who have a medical history of it. Other significant risk factors include bipolar disorder, single motherhood, low socioeconomic standing, nicotine usage, and past history of domestic abuse. Depression ranges from mild to severe, and when untreated, there can be significant issues. The consequences of untreated depression during pregnancy include tobacco and alcohol use, suicide attempts, and poor prenatal care, all of which tend to cause significant harm to the unborn fetus. Depression can begin during the time of pregnancy or it can be the continuation of a previous diagnosis. Discontinuing prescribed medication during the start of pregnancy may be harmful, so clinicians suggest that women with a higher risk of depression during pregnancy should continue their medication usage. For milder cases, it may be beneficial to use non-pharmacological treatment such as psychotherapy.<sup>3</sup>

Depression should be treated differently based on severity. In milder cases of depression, it may be beneficial to avoid pharmacotherapy altogether. Instead, practicing yoga during pregnancy has shown to improve depressive symptoms. Other non-pharmacological treatments include psychotherapy and counseling. In cases where it is not recommended to let depression go untreated, pharmacotherapy should be employed. Of the known antidepressants, selective serotonin re-uptake inhibitors are proven safest. Each case should be evaluated individually, and if pharmacotherapy is recommended, it should be beneficial for both the mother and the baby.

### References:

1. Citrome, Leslie. "To Treat or Not to Treat Depression in Pregnancy: What's Best for the Baby?" Medscape. N.p., 2 Aug. 2012. Web. 19 May 2015.
2. Dolan, Siobhan M. "Medication Exposure During Pregnancy: Antidepressants." Medscape. N.p., 22 Apr. 2005. Web. 20 May 2015.
3. Stewart, Donna E. "Depression during Pregnancy." New England Journal of Medicine N Engl J Med 365.17 (2011): 1605-611. Web.

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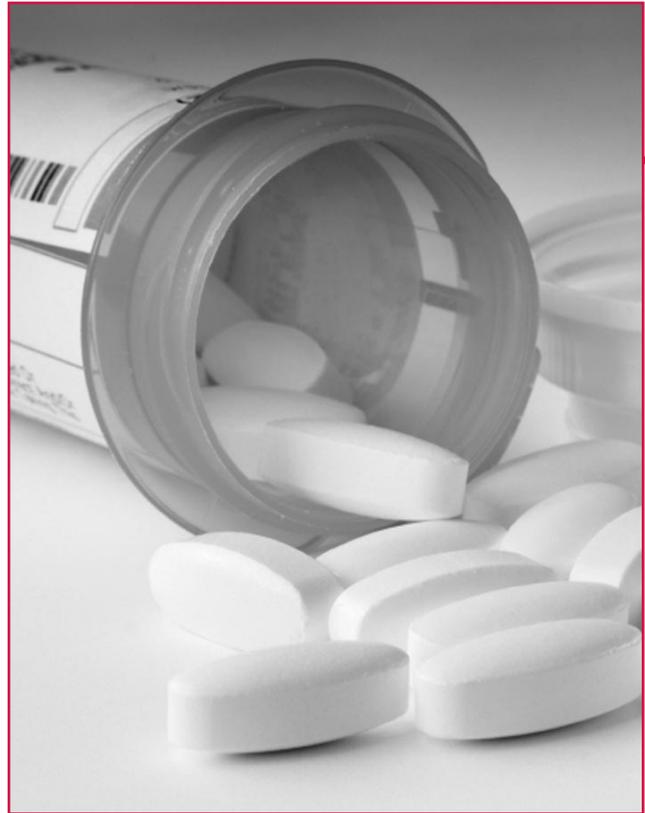
## Adverse Effects of SGLT2 Inhibitors

SGLT2 inhibitors were first introduced in March 2013 for the treatment of diabetes mellitus, when the drug canagliflozin (Invokana®) was approved by the FDA. SGLT2 inhibitors restrict the sodium glucose transporter 2, which reduces plasma glucose by limiting glucose reabsorption in the kidney and increases glucose excretion in the urine.<sup>1</sup> This new class of drugs has better side effects as compared to the older agents such as sulfonylureas, thiazolidinones, incretin therapies and exogenous insulin. The SGLT2 inhibitors decrease glycosylated hemoglobin (A1c) levels, improve pancreatic B-cell function and have a mild osmotic diuresis and weight reduction in patients.<sup>2,4</sup> There are some limitations in using this drug despite its numerous advantages seen in type II diabetic patients.

Canagliflozin (Invokana®) is only approved for type II diabetic adult patients and should be used with caution in those with renal impairment and older patients due to the slight decrease in blood pressure.<sup>1,4</sup> Hypotension is caused by the osmotic diuresis and glucosuria. One major concern has led to an ongoing trial evaluating bladder cancer risk, although no definitive relationship between the risk of bladder cancer and concomitant usage of SGLT2 inhibitors has been found. As concluded by US regulatory authority, a modest dose-dependent increase in bone resorption was seen with canagliflozin.<sup>4</sup>

Since the drug was only recently approved, long term adverse effects are currently being studied. The FDA recently issued a warning that SGLT2 inhibitors may result in serious ketoacidosis. According to the FDA Adverse Event Reporting System (FAERS) database, there have been 20 cases of acidosis reported from March 2013 to June 2013 where hospitalization was required for each case.<sup>3</sup> Some common symptoms of ketoacidosis include difficulty breathing, nausea, vomiting, abdominal pain, confusion, unusual fatigue or sleepiness. Patients can be at risk for ketoacidosis even when blood sugar is not high. All health professionals are encouraged to report any adverse event case to MEDWATCH at 1-800-FDA-0178.

Two independent studies were carried out to observe long term adverse effects. Both reported a paradoxical increase in endogenous glucose production (EGP) along with an overall decrease in fasting plasma glucose in their findings. Two drugs that were studied separately were dapagliflozin and empagliflozin, and both showed the same response in EGP increase. Thus,



this conclusion can be attributed to the SGLT2 inhibition and not to a specific effect of any particular agent. Moreover, it suggests that SGLT2 inhibition with incretin therapies would provide a synergistic response for the treatment of hyperglycemia.<sup>2</sup> Further studies are needed to prove this combination will be effective. SGLT2 inhibitors have many advantages for the treatment of type II diabetic patients but the long term effects are currently still uncertain.

### References:

1. INVOKANA™[package insert] Titusville, NJ : Janssen Pharmaceuticals, Inc ; 2013 Link: <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM346637.pdf>
2. J Clin Invest. 2014;124(2):485–487. doi:10.1172/JCI74297. Link : <http://www.jci.org/articles/view/74297>
3. "U.S. Food and Drug Administration." FDA Drug Safety Communication: FDA Warns That SGLT2 Inhibitors for Diabetes May Result in a Serious Condition of Too Much Acid in the Blood, 15 May 2015. Web. 21 May 2015.Link : <http://www.fda.gov/Drugs/DrugSafety/ucm446845.htm>
4. Hinnen D Short commentary on empagliflozin and its potential clinical impact. Therapeutic Advances in Endocrinology and Metabolism. 2015 Apr;6(2):68-81. Link: [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4406882/pdf/10.1177\\_2042018815578599.pdf](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4406882/pdf/10.1177_2042018815578599.pdf)

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## Potential Treatment Options for Ebola: an Area of Investigation



The most recent media's pandemic of the season is Ebola. Ebola is a viral disease with case fatality rate of up to 90%, Ebola's first documented outbreaks were in 1976 in central Africa.<sup>1,2</sup> The WHO Director General has recently declared an outbreak in 2014 as Public Health Emergency of International Concern.<sup>1</sup>

Ebola is an enveloped RNA virus in the family *Filoviridae*, genus *Ebolavirus*. Five strains have been identified although only four have been shown to infect humans.<sup>1,2,3</sup> Virus entry into human cells is initiated by interaction of viral GP1 with host cell surface T immunoglobulin and mucin domain 1 (TIM-1) receptors. The Ebola virus is then internalized via endocytosis and GP1 is cleaved to allow binding to cholesterol transporter Niemann-Pick C1 (NPC1), essential for viral-host membrane fusion and viral entry. Once within the cell, the Ebola virus suppresses immune response and utilizes the host's translation and transcription for virion reproduction.<sup>3</sup>

The virus is transmitted through direct contact with the bodily fluids of infected and infectious individuals (starting from the onset of symptoms to upwards of 7 weeks after recovery).<sup>1,3</sup> The virus's incubation period varies, from 2 days to 3 weeks, and the initial symptoms tend to be generalized – fever, fatigue, muscle pain, and headache.<sup>1</sup> This can then be followed by vomiting, diarrhea, rash, and the internal and external bleeding that Ebola is so well known for.<sup>1</sup> Laboratory findings of Ebola patients may include leukopenia, thrombocytopenia, and signs of both kidney and liver damage.<sup>1</sup>

Current treatment protocols for Ebola consist primarily of supportive care. However, in response to the severity of this most recent outbreak, a number of new treatments are being developed, though none have yet been approved.<sup>1,2</sup>

### **ZMapp** (Mapp Biopharmaceutical)<sup>4</sup>

A combination of 3 monoclonal antibodies intended to target the Ebola virus. Availability of the medication was low this past year. Currently grown in modified tobacco leaves, other production routes in mammalian cells are being explored. In addition, the few case reports of efficacy are questionable as they were not under controlled settings. Human trials in West Africa are underway and results are expected within the next year.

In addition to the agents under investigation described below, at least two other antiviral agents for the Ebola virus are still in the earliest stages of development. Furthermore, two prospective Ebola vaccines entered large-scale human trials earlier this year.<sup>4</sup>

### **TKM-Ebola** (Tekmira Pharmaceuticals)<sup>5,6</sup>

A small interfering RNA (siRNA) that targets the Zaire Ebola Virus RNA protein polymerase L protein, thereby inhibiting RNA translation and viral spread via the RNAi pathway. Efficacy in prevention after infection exposure was promising in animal models. However, in mid-2014 initial phase I studies were stopped due to unspecified side effects. It has since been approved for partial clinical hold, permitting studies with already infected individuals.

### **Favipiravir; T-705** (Toyama Chemical)<sup>7,8</sup>

Approved in 2014 in Japan for treatment of influenza by acting as a nucleotide analog that selectively inhibits viral RNA- dependant RNA polymerase. It has shown promising efficacy against Ebola virus in mouse models. Trials by French medical research institute INSERM of favipiravir in Ebola positive patients were announced in 2014.

Yet even with all the promising treatments and vaccines in the pipeline, results of studies are not expected until later in the year. The question is then raised regarding exactly what medications may be feasible alternative therapies in the interim. A small amount of existing data exists that suggests the potential for using currently on the market medications as supplemental therapies to decrease the disease's viral load.<sup>3</sup> The therapeutic options suggested are listed below:

### **Convalescent whole blood or plasma serum**<sup>3,9,10</sup>

The concept of utilizing the antibodies present in the blood of recently recovered individuals. The theoretical

*(Continued on page 9)*



## Potential Treatment Options for Ebola: an Area of Investigation *(Continued from page 8)*

basis upon which one of the in-development Ebola medications – Zmapp – is based, the actual efficacy of such treatment is unclear. WHO encourages interest in convalescent therapy for Ebola treatments, yet the currently available data is insufficient to draw firm conclusions. It is unclear whether or not patient survival is due to the convalescent therapy or the supportive care received.

### Chloroquine<sup>3,11</sup>

The antimalarial drug increases endosome pH, theoretically preventing the cleaving of GP1 which is essential for Ebola virus entry into the host cell. However, studies in mouse models have shown the specific proteases targeted (CatB and CatL) are not absolutely required for Ebola replication, as glycoprotein cleavage seems to be mediated by a wider spectrum of proteases.

### Cationic amphiphiles (amiodarone, dronedarone, verapamil, and clomiphene)<sup>3,12</sup>

The efficacy of these medications relies upon the development of NPC1 disease-like phenotype. NPC1 is essential for viral entry and patients with NPC1 disease have been shown to be resistant to the Ebola virus.

### Interferon-Beta<sup>3,13</sup>

Interferon induced transmembrane proteins inhibit viral fusion and release of viral contents into the cytosol, potentially inhibiting Ebola infection early on in the virus cycle. Use of interferon-beta in rhesus macaques infected with lethal doses of Ebola virus has been shown to prolong survival time (though not mortality). However, as early treatment with interferon-beta has shown to be improve mortality in Marburg virus infection, there may be promise in post-exposure therapy with interferon-beta for Ebola.

### Na<sup>+</sup>/K<sup>+</sup> exchangers (amiloride)<sup>3,14</sup>

Through inhibition of less well defined ion exchangers, the medications disrupt the electrolyte balance of magnesium and manganese within the body, blocking the macropinocytic pathway that ebola utilizes to enter the host cell.

### Na<sup>+</sup>/K<sup>+</sup> - ATPase pump inhibitors (digoxin)<sup>3</sup>

ATP is essential in multiple steps of the viral replication process. Na<sup>+</sup>/K<sup>+</sup> - ATPase has specifically been identified as interacting with Ebola viral protein VP24, an important protein in viral budding and egress among other things. The use of Na<sup>+</sup>/K<sup>+</sup> - ATPase pump inhibitors has been shown to inhibit replication of other enveloped viruses such as the influenza virus and the Newcastle disease virus.

### Antioxidants (high-dose NAC)<sup>3</sup>

Accumulation of Ebola glycoproteins GP1 and GP2 leads to endoplasmic reticulum stress, eventually activating subsequent inflammatory response. Ebola mutations with enhanced glycoprotein accumulation have been shown to have increased cytotoxic effect compared to wild type viruses. Antioxidant therapy targets the cytokine dysregulation characteristic of Ebola virus and to which the early endothelial vascular damage patients experience is attributed.

All of described medications are primarily theoretical in their efficacy against Ebola viruses with minimal evidence available in animal studies. However, while no readily accessible approved treatments are currently available, they provide promising agents to investigate.

### References:

1. World Health Organization (2015). Ebola Virus Disease. Retrieved from <http://www.who.int/mediacentre/factsheets/fs103/en/>
2. Centers for Disease Control and Prevention (2015 April). About Ebola Virus Disease. Retrieved from <http://www.cdc.gov/vhf/ebola/about.html>
3. Lai KY, Ng WY, Cheng FF. "Human Ebola virus infection in West Africa: a review of available therapeutic agents that target different steps of the life cycle of Ebola virus." *Infectious Diseases of Poverty*. 2014. 3:43.
4. Baragona, Steve. "New Ebola Drug, Vaccine Trials to Begin Soon." *VOA. Voice of America*, 22 Jan. 2015. Web. 05 Feb 2015.
5. Geisbert TW, Lee, ACH, Robbins M, et al. "Postexposure protection of non-human primates against a lethal Ebola virus challenge with RNA interference: a proof-of-concept study." *Lancet*. 2010. 375: 9729; 1896-1905.
6. Tekmira (2014 Aug). FDA Modifies Tekmira's TKM-Ebola Clinical Hold to Partial Hold. Retrieved from <http://investor.tekmirapharm.com/releasedetail.cfm?ReleaseID=865208>
7. Oestereich L, Ludtke A, Wurr S, et al. "Successful treatment of advanced Ebola virus infection with T-705 (favipiravir) in a small animal model." *Antiviral Research*. 2014 May. 105; 17-21.
8. Doctors Without Borders (2014 Dec). Guinea: Clinical Trial for Potential Ebola Treatment Starts in MSF Clinic in Guinea. Retrieved from <http://allafrica.com/stories/201412260651.html>
9. Mupapa K, Massamba M, Kibadi K, et al. "Treatment of Ebola Hemorrhagic Fever with Blood Transfusions from Convalescent Patients." *J Infect Dis*. (1999) 179 (Supplement 1): S18-S23. Doi: 10.1086/514298
10. World Health Organization (2015). Ebola Virus Disease. Retrieved from <http://www.who.int/mediacentre/news/ebola/26-september2014/en/>
11. Arie, Sophie. "Ebola: an opportunity for a clinical trial?" *BMJ* 2014: g4997. Doi: <http://dx.doi.org/10.1136/bmj.g4997>.
12. Shoemaker CJ, Schornberg KL, Delos SE, et al. "Multiple cationic amphiphiles induce a Niemann-Pick C phenotype and inhibit Ebola virus entry and infection." *PLoS One*. 2013; 8(2): e56265. Doi: 10.1371/journal.pone.0056265. Epub 2013 Feb 18.
13. Smith LM, Hensley LE, Geisbert TW, et al. "Interferon-β therapy prolongs survival in rhesus macaque models of Ebola and Marburg hemorrhagic fever." *J Infect Dis*. 2013 Jul 15; 208(2):310-8. Doi:10.1093/infdis/jis921. Epub 2012 Dec 18.
14. Aleksandrowicz P, Marzi A, Bienenkopf N, et al. "Ebola virus enters host cells by micropinocytosis and clathrin-mediated endocytosis." *J Infect Dis*. 2011 Nov; 204 Suppl 3:S957-67. Doi: 10.1093/infdis/jir326.

Contributed by: Diana Yang, Pharm D Candidate 2015, Rutgers University



## 2015 NJSHP Beverly Wilt Award Recipient: Mr. Andre Emont

On April 24, 2015, New Jersey Society of Health System Pharmacists (NJSHP) board members awarded the Beverly Wilt Service Award to Mr. Andre Emont, Director of University Hospital's Pharmaceutical Care Division.

Mr. Emont was quite stunned when he learned about the board members' selection, knowing that every other nominee for this award is just as deserving. He stated that this award could not have been attained without the inspiration he received from his seniors and colleagues, for whom he has a deep respect. He acknowledged how much they have truly given him the strength to constantly challenge himself and optimize his performance as it relates to the great profession of pharmacy.

He also mentioned, "We must keep NJSHP strong." The pharmacy leader currently assumes a leadership role in the organization and actively participates in other local, state, and national professional organizations. Giving back and being involved are paramount to professional and personal success.

On a closing note, Mr. Emont wanted to thank everyone for helping him reach a point in his career where he can proudly hold up the Beverly Wilt Service Award as a mark of his achievement. He will continue to support the hospital pharmacy profession and the great organization of NJSHP, as long as members allow him to do so.

***Congratulations Mr. Andre Emont!***



***Pictured from Left to Right:***

Aduke Akere, Sheryl Emont, Andre Emont, Victor Pardo, Michael Chu, Polly Jen, Nermin Boles-Attia and Sung Ho Hahn

## 2015 NJSHP Annual Meeting

The New Jersey Society of Health System Pharmacists held their 2015 Annual Meeting at the Ocean Place Resort & Spa in Long Branch, NJ on April 24-25, 2015. Several pharmacists and pharmacy technicians from University Hospital attended the meeting to support the pharmacy profession and to update their knowledge on clinical, regulatory, and administrative aspects of pharmacy practice.

Dr. Polly Jen, the Infectious Diseases Clinical Pharmacy Specialist at University Hospital, was invited as a speaker for the NJSHP Annual Meeting. She provided Continuing Education on recent changes to pneumococcal and influenza immunization recommendations, as well as practices to reduce the risk of vaccine-related errors.

## Welcome to Two New Pharmacists



### **Eunice Wang, Pharm. D. , RPH**

Dr. Wang graduated from Ernest Mario School of Pharmacy, Rutgers University in 2009 and worked in retail pharmacy for 9 years before joining University Hospital in May 2015. She enjoys being a new mom to her 1 year old daughter and enjoys reading, traveling, cooking and being outdoors.

### **Roxinne Templonuevo, PharmD, BCPS**

Dr. Templonuevo earned her Doctor of Pharmacy degree from the Ernest Mario School of Pharmacy at Rutgers University in 2012. She went on to complete a PGY-1 pharmacy practice residency at Pennsylvania Hospital in Philadelphia, PA in 2014. Prior to joining the pharmacy team at University Hospital, Roxinne also worked as a staff pharmacist within the Barnabas Health System. She is a member of the New Jersey Society of Health System Pharmacists (NJSHP) and the American College of Clinical Pharmacy (ACCP).



# Welcome

## Welcome New Pharmacy Technician



### **Anitra Grant, CPht**

Anitra has been working as a Certified Pharmacy Technician since 2013. She started her career working in retail at Walgreens Corporation and after one year began working in the hospital. She enjoys reading, writing and arts. She is the mother of an energetic 7 year old girl and loves every minute of it. She looks forward to a prosperous career in the medical field.