RHO PX CHI POST

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AUGUST 1ST 2012

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A student-operated newsletter by the St. John's University College of Pharmacy and Health Sciences Beta Delta chapter

SINGLE-LINE STORIES

- Welcome back to College of Pharmacy and Health Sciences Fall 2012 Semester!
- Editors of the Rho Chi Post like to extend our welcome to incoming Pharm.D. Candidates
- 6th year Pharm.D. Candidates prepare to Study Abroad during the Fall semester
- International Student Orientation by Multicultural Affairs in Marillac Hall on Aug 22
- College's New Student Convocation on Aug 28 in Marillac Hall

BACTROBAN NASAL® FOR MRSA DECONTAMINATION BY: MOHAMMAD A. RATTU, PHARM.D.

Over the last couple of decades, with the increased prevalence of Methicillin-Resistant Staphylococcus Aureus (MRSA) infections, healthcare institutions are actively seeking methods to contain and possibly eradicate causative bacteria to prevent further infection.[1] Nasal decontamination of bacterial colonies via mupirocin calcium ointment 2% (Bactroban Nasal®, 90% pseudomonic acid A) is a proposed, verified, and FDA-indicated method for decreasing the number of MRSA infections in adults and healthcare workers.[1] Currently, two bacterial strains of Staphylococcus aureus (S. aureus) are resistant to mupirocin: MuL (L = low-level resistance) and MuH (H = high-level resistance).[2] MuL strains are not deemed clinically significant, while MuH strains warrant the use of other medications and/or processes for eradication.[2]

Up to 40% of the normal population carries S. aureus in the anterior aspect of the nostrils.[3] There are greater carriage rates in hospitalized patients and their attendants.[3] Transmission occurs primarily from colonized or infected patients to others via health care personnel's hands.[4] The increasing incidence of MRSA is associated with inpatient outbreaks, which lead to considerable morbidity, mortality, and disruption of hospital workflow.[3] Because of the undesirable outcomes associated with MRSA infections, their preventable nature, and the current "requirement" for treatment with vancomycin (which actually does not eradicate nasal carriage), it is reasonable to invest resources and education into controlling the transmission of MRSA.[4] In addition to hand disinfection, site cleansing with chlorhexidine gluconate, barrier precautions, and segregation of colonized patients, another viable investment is the topical antibiotic called mupirocin.[4]

Mupirocin inhibits bacterial protein synthesis by binding reversibly and specifically to isoleucyl-tRNA synthetase.[5] Systemically, the body rapidly metabolizes mupirocin.[1] Hence, in community pharmacy practice, prescriptions for mupirocin 2% ointment or cream dosage forms are primarily dispensed for treating impetigo or related superficial skin and skin structure infections.[1] The topical agent has excellent *in-vitro* activity against staphylo-

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cocci and most streptococci, but less activity against other gram-positive and most gram-negative bacteria.[1,5] Due to its limited route of administration and unique chemical structure (monoxycarbolic acid), cross-resistance is less likely to occur than with other currently available topical antibacterial agents.[1,5] Even with repeated use of the medication, there is remarkably little development of resistance; and should resistance occur, it is unlikely to be clinically significant.[2,6]

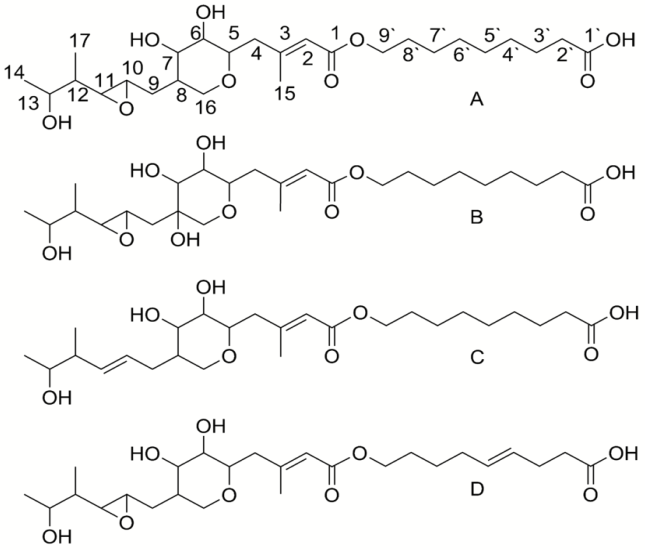

Figure 1. Basic structures of mupirocin (Bactroban®, Bactroban Nasal®), often a mixture of pseudomonic acids A (≥ 90%), B, C, and D.

Image source: http://upload.wikimedia.org/wikipedia/commons/thumb/e/e9/Pseudomonic_acid_A-D.png/845px-Pseudomonic_acid_A-D.png

Intranasal mupirocin calcium ointment 2% is only FDA-indicated for adults and healthcare workers with nasal colonization of MRSA.[3,5,7] When applied topically within the nostrils, local concentrations exceed the minimum inhibitory concentrations (MICs) for staphylococci and remain detectable for up to 72 hours.[3,5] The recommended dosage for intranasal decontamination of MRSA is 500 mg (half of one single-use tube) applied into each nostril twice daily for five days.[5,7] A total of 10 single-use tubes should be dispensed for this frequency and duration.[5,7] After the patient places half of the single-use tube's contents into each nostril, he or she should press the nostrils together and massage the nose for approximately one minute (to ensure an even application of the medication on the inner surfaces of the nostrils).[5,7]

"Mupirocin inhibits bacterial protein synthesis by binding reversibly and specifically to isoleucyl-tRNA synthetase."

As with all medications, counseling for intranasal mupirocin calcium ointment 2% is essential. Anecdotally, when patients did not receive appropriate consultation, they made at least one of the following mistakes:

- failed to blow their nose prior to use (while there may be mucus within the nostrils)
- applied the contents of one single-use tube (1 gram) into a single nostril (an overuse) and subsequently "ran out" of the medication within three days
- applied the medication externally on their nose (and not within their nostrils)

Mupirocin seems to be well-tolerated, but mild to moderate adverse events were reported.[5,7] These include headache (9%), respiratory

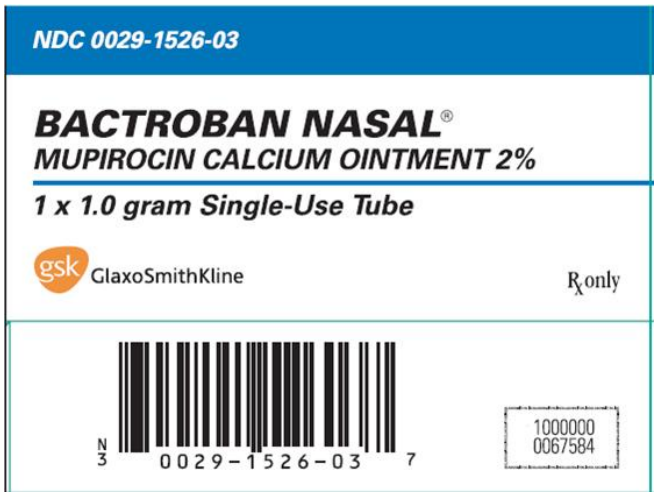

Figure 2. Exterior packaging of commercially available product containing mupirocin calcium ointment 2% (Bactroban Nasal®).

Image source: http://dailymed.nlm.nih.gov/dailymed/image.cfm?id=49239&type=img&name=c95717e7-d977-4453-aa5e-b24795fad4c8-02.jpg

disorders (5%), pharyngitis (4%), taste perversions (3%), cough (2%), and effects confined to the nose, such as rhinitis (6%), erythema, swelling, burning or stinging (2%), pruritus (1%), and dryness.[5,7]

Based on several studies, mupirocin could treat serious site infections (SSIs) caused by S. aureus in up to 90-95% of subjects within a variety of clinical settings.[3,8] These settings include MRSA outbreaks, neonatal nurseries, hemodialysis, cardiothoracic surgery, and familial staphylococcal infections.[3,8] Study results were heterogeneous when nasal mupirocin was used for the prevention of SSIs and/or sepsis in major clean or elective surgery (*e.g.* implant surgery).[9-12] In addition, a recently published high-quality study utilizing mupirocin in cardiosurgical patients actually reported negative outcomes.[12] Therefore, mupirocin ought to be used to prevent SSIs (due to MRSA) before surgeries, but not in elective or cardiosurgical patients.[12]

"...mupirocin could treat serious site infections (SSIs) caused by S. aureus in up to 90-95% of subjects within a variety of clinical settings."

Overall, as one could infer from above, while mupirocin is a great investment for inpatient institutions, it may not be appropriate in certain situations (*e.g.* prevention of surgical site infections).[13] Intranasal application of mupirocin has limited effectiveness in eradicating colonization in patients who carry the organism at multiple body sites (*i.e.* other than the nose).[14] Mupirocin should be avoided in areas with prevalent MuH strains as cost-analysis studies effectively demonstrated that a MRSA screen-and-treat approach is cost-saving, but only as long as the prevalence of mupirocin resistance in S. aureus is low.[2,6,15] Otherwise, if MuH strains one day become a common item, modified and new antibiotics should be synthesized based on the understanding of resistance mechanisms (*e.g.* MuH resistance is conferred via the presence of isoleucyl-tRNA synthetase with similarities to eukaryotic enzymes).[16] In addition, eradicating nasal carriage of MRSA among patients and personnel could be useful during epidemics or outbreaks, but the cost-effectiveness in hospitals with a low prevalence of MRSA is yet to be determined.[13]

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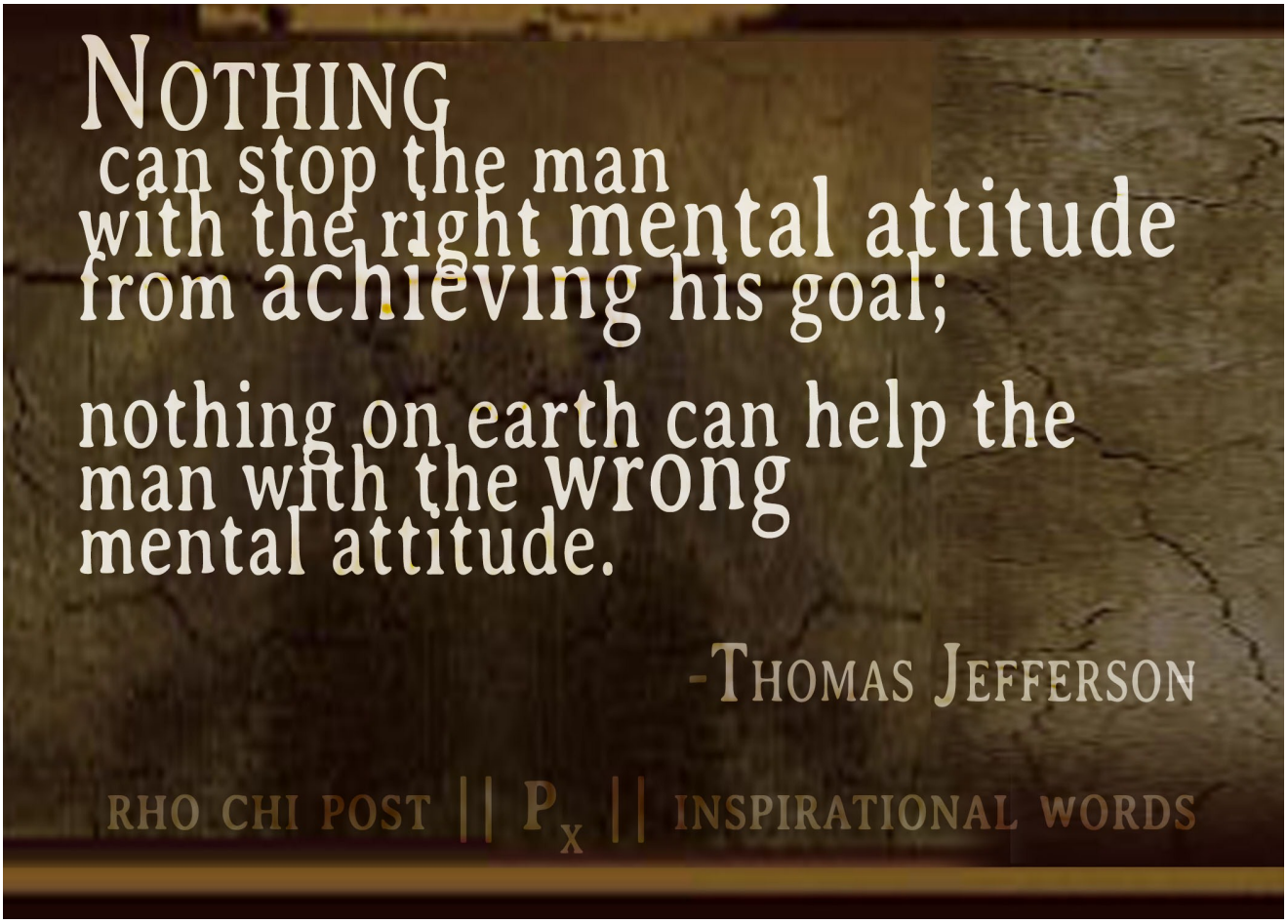
QUOTE OF THE MONTH BY: ALEENA CHERIAN, STUDENT CO-COPY-EDITOR



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ST. JOHN'S STUDENTS COLLABORATE TO INNOVATE IN PHILADELPHIA

BY: MICHAEL CRONIN, PHARM.D. CANDIDATE C/O 2014

The Drug Information Association (DIA) student chapter at St. John's University College of Pharmacy and Health Sciences began in March of 2012 to provide a local forum for cultivating awareness of opportunities within the pharmaceutical industry among doctor of pharmacy and allied health professions candidates. Within two months of its inception, the group grew quickly and was able to host several well-attended meetings and informational sessions. In May, I and ten other students traveled to Philadelphia for the DIA 2012 Annual Meeting to learn about current events within the pharmaceutical industry and network with like-minded students and healthcare professionals. As a global pharmaceutical organization, DIA serves as a neutral forum for drug researchers and developers, government officials, and employees of pharmaceutical and biopharmaceutical companies to meet, debate, and exchange information. This year's conference was aptly entitled "Collaborate to Innovate".

"... DIA serves as a neutral forum for drug researchers and developers, government officials, and employees of pharmaceutical and biopharmaceutical companies to meet, debate, and exchange information."

For first-time students, the DIA annual conference could be intimidating. The sheer size of the meeting, combined with the realization of how many people come from all over the globe to take part in the event, could leave one at a loss for words. The flawless planning and execution of the conference was incredible. The opening plenary session displayed more than just enchanting music from a local orchestra or the inspiring words of Dean Kamen, the brilliant inventor responsible for the Segway®. It displayed the worldwide scale of DIA, as well as what the organization does to improve public health around the globe. Along with my fellow students, at first I felt more than a bit out of place in the new, grand environment.

Image Source: http://www.diahome.org/

Fortunately, it was apparent from the beginning that DIA is also committed to student involvement. Programming was geared directly toward students and first-time attendees: there were student forums and "speed networking," which made us more comfortable during the meeting. Our uneasy feelings soon dissipated. Once I found my voice and footing, as well as learned to keep up with all of the new acronyms, the conference became an opportunity like none other.

"Programming was geared directly toward students and first-time attendees..."

The various sessions and content provided a snapshot of where the pharmaceutical industry is presently and where it is heading in the future. Gaining insight into the ongoing dynamics, as well as the politics between regulatory personnel working for pharmaceutical companies and government officials at Center for Drug Evaluation and Research (CDER) [the branch of the Food and Drug Administration (FDA) in charge of drug approvals], was most beneficial. This dynamic was highlighted at the conference, which took place at a remarkably appropriate time. There was much focus placed on the fact that while the conference proceeded, the Supreme Court was ruling on the constitutionality of President Obama's Affordable Care Act (ACA) and the

Senate was preparing to vote on the Prescription Drug User Fee Act V (PDUFA V).

While monumental decisions were being made in Washington, DC, presenters at the conference spoke about regulatory issues and literally were uncertain of these federal decisions. A prime example of this laid in a discussion on the regulatory framework for the development and approval of biosimilars (the provision for biosimilar development is included within the ACA). Since there was a legitimate chance that, within the next few days, part or all of the ACA would be declared unconstitutional (and subsequently struck down), all informational sessions on biosimilars came with the same basic disclaimer. They stated that, tomorrow, all of this progress may be irrelevant, and the push to bring biosimilars to the market in the United States would have to start from scratch.

The underlying subplot of the conference came to a head at the CDER town hall meeting (on the last day). The Supreme Court made the ruling while individuals asked the CDER panel questions. Midway through the meeting, we learned that the act was upheld. Many in the audience cheered while others let the more staunch supporters of the ACA have their day in the sun. All of those present calculated the implications of the ruling.

The dramatic scene made a fitting conclusion to the entire meeting for me. This was the living and breathing DIA that I was hoping to see when I went to Philadelphia. The experience superseded all of my expectations. It was amazing to have taken part in such a monumental occasion and to have had the opportunity to witness it firsthand. To my fellow students at St. John's University College of Pharmacy and Health Sciences, if you are interested in the pharmaceutical industry, I encourage you to use DIA as an avenue to explore your career aspirations. For more information about programming planned for the upcoming fall semester (or on how to join DIA), please email: diascstj@gmail.com.

"To my fellow students at St. John's University College of Pharmacy and Health Sciences, if you are interested in the pharmaceutical industry, I encourage you to use DIA as an avenue to explore your career aspirations."

Image Source: http://www.diahome.org/en/Flagship-Meetings/~/media/12103-Clinical-Forum/Sliders/12103-MS-Banner1-615x265.ashx?h=265&w=615

MEET THE NEW BETA 3 AGONIST: MIRABEGRON (MYRBETRIQ®) BY: STEVE SOMAN, CO-EDITOR-IN-CHIEF

Mirabegron (Mybetriq®), known also by the brand name Betanis® in Japan, is a new once daily oral drug. First in its class, it is a selective β(3)-adrenoceptor agonist that improves symptoms associated with over active bladder (OAB) such as urinary incontinence, urgency, and urinary frequency by enhancing storage function and relaxing the urinary bladder.[1,2] The medication was approved by the Food and Drug Administration (FDA) on June 28, 2012 and is expected to be available by sometime in October of 2012.[3]

The mechanism of action of mirabegron as a selective beta 3 adrenergic receptor agonist relaxes the detrusor smooth muscle during the storage phase of the urinary bladder fill-void cycle by activating this receptor and thus increasing the bladder capacity.[2] The recommended starting dose is 25 mg once daily and based on efficacy and patient tolerance, may increase to 50mg once daily.[2] The 25mg dose is effective within 8 weeks of initiating therapy. Mirabegron needs to be dose adjusted at 25 mg once daily for severe renal impairment (CrCl of 15 to 29 mL/min) or in moderate hepatic impairment (Child-Pugh Class B).[2] It is not recommended in end stage renal disease or in severe hepatic impairment (Child-Pugh Class C) due to lack of available safety data.[2] The product is available as 25mg and 50mg extended release tablets that may not be crushed, chewed, or cut.

"...mirabegron as a selective beta 3 adrenergic receptor agonist relaxes the detrusor smooth muscle during the storage phase of the urinary bladder fill-void cycle by activating this receptor and thus increasing the bladder capacity."

Precaution should be used when treating patients with uncontrolled hypertension (>180/110 mmHg) as the drug can raise blood pressure.[2] In two randomized placebo controlled studies with healthy volunteers dosed with 50mg, the blood pressure increase was 3.5 mm Hg/1.5 mm Hg greater than placebo.[2] In another clinical trial using patients with OAB, the blood pressure increase was 0.5 mm Hg/1 mm Hg greater than placebo.[2]

Multiple clinical trials evaluating adverse effect were conducted using mostly Caucasian female population with a mean age of 59 years old.[2] The most commonly reported adverse reactions were hypertension, nasopharyngitis, urinary tract infection, and headache. Other important side effects that are not frequent (<1%) but important to note in geriatric patients are constipation, tachycardia, diarrhea, abdominal pain and fatigue.[2,4] The drug may also raise AST/ALT levels from baseline but in the study, these markets returned to baseline while the patients continued taking mirabegron 50mg therapy.[2]

The drug also has the potential for drug interactions through the cytochrome P-450 system, more specifically CYP 2D6. Mirabegron is a CYP 2D6 inhibitor, so drugs using the same pathway should be monitored and dose adjusted to prevent occurrence of adverse reactions or toxicity.[4] There is increased systemic exposure of metoprolol (Toprol XL®, Lopressor®) and desipramine (Norpramin®, Pertofane®) seen when co-administered with mirabegron due to this interaction.[2] Mirabegron also uses the CYP 3A4 pathway (minor) along with dealkylation, glucuronidation, and amide hydrolysis in its metabolism.[2] These pathways allow for more theoretical interactions with medications that use the same metabolic pathway.

"Mirabegron is a CYP 2D6 inhibitor..."

When mirabegron and digoxin (Lanoxin®) are coadministered, there is a noted 27% increase in digoxin AUC and 29% increase in digoxin Cmax, so treating patient with the lowest dose of digoxin and titrating the dose to desired clinical effect while monitoring serum digoxin levels is

recommended.[2,5] Mirabegron lacks safety data in pregnancy and thus is category C and should only be used if the benefits outweigh the risks.

Mirabegron generally reaches maximum plasma concentrations (Cmax) within 3.5 hours.[2] The bioavailability (F) is 29% at 25mg dose and 35% at 50mg dose. The drug reaches steady state within seven days of once daily dosing. A high fat meal can reduce the absorption of mirabegron which is seen in a 45% reduced Cmax and 17% reduced area under the curve (AUC).[2] Mirabegron is 71% bound of plasma proteins with a volume of distribution at steady state (Vss) of 1670L.[2] The half-life of mirabegron is 50 hours. It is eliminated through the urine and feces, 55% and 35% respectively.[2] Approximately 25% of the drug is excreted unchanged renally, and the renal clearance rate is around 13L/hour.[2]

There is limited postmarking data available on this medication since it is newly approved however worldwide post marketing experience from an undefined population demographics (size etc.) without specific information of frequency or role of mirabegron in the side effect reported that patients on the medication experienced urinary retention.[2]

A multi-centered study from UK, Spain, and Dubai concludes that mirabegron may be used as a treatment for OAB in patients intolerant of or who have a suboptimal response to anti-muscarinic agents such as tolterodine SR (Detrol LA®).[6,7] Mirabegron (Mybetriq®) is still a new agent, so more monitoring and safety evaluation is required before its role in therapy can be well defined.

"„„mirabegron may be used as a treatment for OAB in patients intolerant of or who have a suboptimal response to anti-muscarinic agents..."

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QUICK UPDATE: TRIPTAN PHARMACOLOGY BY: NEAL SHAH, CO-EDITOR-IN-CHIEF

Migraines can be "classic" or "common." While all migraines feature unilateral, pulsating headaches, classic migraines feature an "aura" upon onset (whereas common migraines do not). Pharmacologic treatment of migraines generally includes serotonin agonists (triptans).[1]

Triptans are selective agonists of the 5-hydroxytryptamine 1B and 1D ($5HT_{1B/1D}$) subtypes. By activating these receptors, triptans cause vasoconstriction and inhibit the release of vasodilatory mediators. $5HT_{1D}$ is found on neurons, whereas $5HT_{1B}$ is found on cerebral vessels.[2] Cerebral vasodilation causes pressure against nerves and initiates migraines[3], whereas triptans act to relieve this pressure to abort migraines.

Interestingly, a there is an experimental drug called lasmiditan (COL-144) currently in Phase II trials.[4] It differs from current triptans because it is an oral $5HT_{1F}$ agonist devoid of vasoconstrictive activity.[4]

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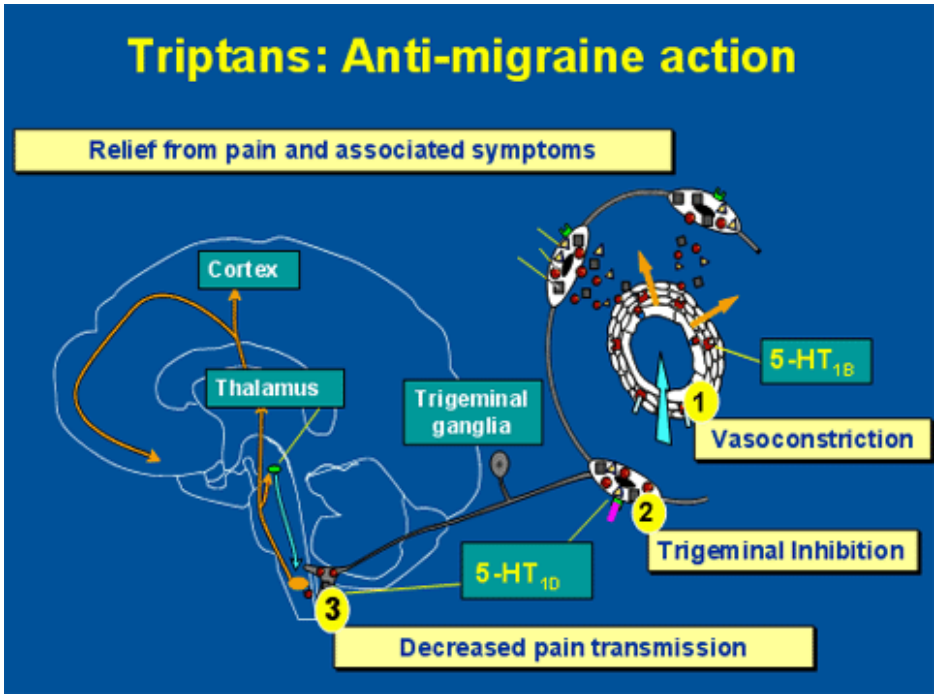


Summary of how Triptans work

Image Source: http://www.epgonline.org/images/migraine/1934_01.gif

RHO CHI EXECUTIVE BOARD MEMBER INSIGHT: ELIZABETH MO

BY: MOHAMMAD A. RATTU, PHARM.D. [PGY-1 RESIDENT AT VA NYHHS]

We sometimes need to step back and look at our foundations for success. Without the support of past and present Rho Chi executive boards, there would be no Rho Chi Post newsletter. From our May to September issues, we will learn about each of our local chapter's board members on a more personal level. Our insight will predominantly include their nicknames, hobbies, favorite quotes, reasons for accepting the Rho Chi invitation, and motivations for becoming part of the executive board.

Our fourth executive board member insight is with Elizabeth Mo, current fourth year student pharmacist and Secretary of Rho Chi at St. John's University's College of Pharmacy and Health Sciences.

Q: We all have nicknames, for one reason or another. What have people called you, either in the past or right now in college?

A: People seem to keep it simple with my nickname: Liz!

Q: Hah, that was short and sweet! So, what are some of the things that you like doing outside of pharmacy?

A: Well, I like trying new foods and baking some on my own. I also enjoy exercising and traveling when given the chance.

Q: I could just imagine how involved you would be during our local restaurant weeks, sampling the varieties and coming up with your own! So, what is your favorite quote?

A: "Darkness cannot drive out darkness; only light can do that. Hate cannot drive out hate; only love can do that." – Martin Luther King, Jr.

Q: That is very interesting! Now, when you received an invitation to join the Rho Chi Academic Honor Society, why did you accept it?

A: Since I heard about the prestigious invitation-only honor society that accepted only the top 20% of each class, I strived to remain academically competitive. Therefore, when the invitation came, I was quite ecstatic that my hard work paid off!

Q: Definitely have been there – learning about opportunities and working toward successes. Finally, what was your impetus for applying to an executive board position?

A: I wanted to become more active as a student pharmacist and not just bury my head in my notes. Additionally, being on the executive board would require me to be a leader and team player. I felt that leadership and teamwork were never my strongest points, but with a desire to improve these skills and become more involved in pharmacy, it seemed natural to run for a position.

We thank Elizabeth for taking the time to provide us with this insight, and look forward to highlighting the other Rho Chi executive board members.

If you have any additional questions for Elizabeth, please email her at: elizabeth.mo08@stjohns.edu

Tell us about your E-Board members at

rhochis@gmail.com and we will feature your article in our next issue!

MATCHING CHALLENGE: OVER THE COUNTER PRODUCTS

BY: MOHAMED DUNGERSI, ASSOCIATE STUDENT EDITOR

Try to match each OTC product with its corresponding fun fact.

Please view the sources and answers on page 25

A. This product has been used to treat liver disease, including hepatitis and cirrhosis. It has also been used as a protective agent after the liver was exposed to alcohol, acetaminophen, and carbon tetrachloride.

B. This product is extracted from a dwarf palm tree and is native to the southeast coastal region of the United States. It has been used to treat benign prostatic hyperplasia (BPH). It is usually dosed at either 160 mg twice daily, or 320 mg once daily.

C. This product is most commonly used to treat insomnia and for the prevention of jet lag in air travelers. It is a hormone produced by the pineal gland; it regulates sleep and circadian rhythms. For insomnia, 0.3 to 5 mg can be taken 30 minutes prior to bedtime.

D. This product is an evergreen bush native to North America. It has been used to prevent and treat urinary tract infections (UTI). It is normally paired with fructose, although unsweetened forms are available.

E. This product is native to Europe and Asia, although it grows in most parts of the world. It is normally used for alleviating insomnia and anxiety. Most clinical trials using this product to treat insomnia used its extracted form in a dosage of 400 to 900 mg, administered 30 to 120 minutes before bedtime. \

F. This product has been used to treat the symptoms of premenstrual syndrome (PMS), dysmenorrheal, menopause, and rheumatoid arthritis. The most commonly used commercial preparation is called Remifemin.

G. This product is normally present in animal cartilage. It is most commonly used as a dietary supplement to treat osteoarthritis and joint health. It serves as building material for cartilage production and inhibits an enzyme responsible for cartilage degradation.

H. This product is native to southeastern Asia. It is considered a performance enhancer because of the stimulant effect from caffeine. When used in large doses, it may antagonize the effects of Warfarin, although brewing destroys most of its vitamin K content.

I. This product is most commonly used to lower cholesterol concentrations. For hyperlipidemia, the dosage is 1.2 to 2.4 grams per day in two divided doses. In the past, certain of these products were declared illegal, because they contained an unauthorized drug. If the product is not fermented correctly, it can contain citrinin, a nephrotoxic compound.

J. This product is most frequently recommended to reduce postprandial glucose elevations and to reduce the severity of cold and upper respiratory infection symptoms. Its active ingredient is considered an adaptogen, a substance that aids the body in returning to normal function and adapting to stress. Its concomitant use with warfarin has been shown to decrease the effect of warfarin. It is therefore recommended to avoid concomitant use.

1. Melatonin
2. Black cohosh
3. Milk thistle
4. American ginseng
5. Red yeast rice
6. Saw palmetto
7. Valerian
8. Chondroitin
9. Cranberry
10. Green tea

MATCHING CHALLENGE: LOOK-ALIKES, SOUND-ALIKES

BY: ADDOLORATA CICCONE, STUDENT COPY EDITOR

The following medications are easily confused.
Try to match each one with its corresponding fun fact.
If you need help, please view the answers on page 25.

1. This antilipemic competitively inhibits 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that catalyzes the rate-limiting step in cholesterol biosynthesis. Among other medications in this class, patients are least likely to experience myopathy or rhabdomyolysis while on this agent.
2. This newest antilipemic HMG-CoA reductase inhibitor (statin) is available as 1 mg, 2 mg, and 4 mg oral tablets. Like the other agents in its class, there are multiple significant drug-drug interactions for this medication that require dosage adjustments. Concomitant use of rifampin, for example, caps the statin dose at 2 mg day.
3. This non steroidal anti-inflammatory drug (NSAID) should be taken with food or milk to reduce GI distress. Labeled indications are only osteoarthritis and rheumatoid arthritis, although it is used off-label for a number of other pain processes. Most recently, a potential neuroprotective effect in cerebral ischemia is being investigated.
4. This serotonin reuptake inhibitor is a widely used antipsychotic. It has the most anticholinergic effects of its class; the sedation is useful for use in insomnia depression and extrapyramidal symptoms.
5. This barbiturate is indicated as a sedative/hypnotic for insomnia and an antiepileptic for refractory status epilepticus. In neurology intensive care units, it is used off-label to treat barbiturate coma in patients with severe brain injury (e.g. hemorrhagic stroke, traumatic brain injury) and increased intracranial pressure.
6. This barbiturate is indicated as a sedative/hypnotic for insomnia and an antiepileptic for managing generalized tonic-clonic (grand mal), status epilepticus, and partial seizures. Off-label indications include sedative/hypnotic withdrawal, neonatal hyperbilirubinemia, chronic cholestasis, and neonatal seizures.
7. This antibiotic inhibits cell wall synthesis in sensitive bacteria. It should be taken on an empty stomach either one hour before or two hours after a meal.
8. This broad-spectrum antibiotic inhibits both cell wall and sputum synthesis in a wide range of gram-positive, gram-negative, and anaerobic bacteria. It is often given in combination with a penicillinase inhibitor to increase its bactericidal efficacy.
9. This glucocorticoid should be used at the lowest possible dose for the shortest possible period of time and tapered down after chronic use to avoid adrenocortical insufficiency. Side effects include hyperglycemia, fluid retention, osteoporosis, infection, and mental changes.
10. In addition to the above, this glucocorticoid is available in an ophthalmic formulation for the treatment of glaucoma.

A. Paroxetine
B. Penicillin V
C. Pentobarbital
D. Phenobarbital
E. Piperacillin
F. Piroxicam
G. Pitavastatin
H. Pravastatin
I. Prednisolone
J. Prednisone

INDICATIONS FOR DIALYSIS: A MNEMONIC AND EXPLANATION

BY: NEAL SHAH, CO-EDITOR-IN-CHIEF

Dialysis is the removal of substances from intravascular circulation by filtration.[1] Typically, dialysis is ordered when kidney function declines to 10–15% of normal function.[2] The National Kidney Foundation's Kidney Disease Outcome Quality Initiative (K/DOQI) recommends that planning for dialysis begin when patients reach chronic kidney disease stage 4, which is when glomerular filtration rate or creatinine clearance reaches below below 30 mL/min.[3] However, this is not the only indication for the initiation dialysis. A subset of acute and chronic renal failure indications are provided below:[4]

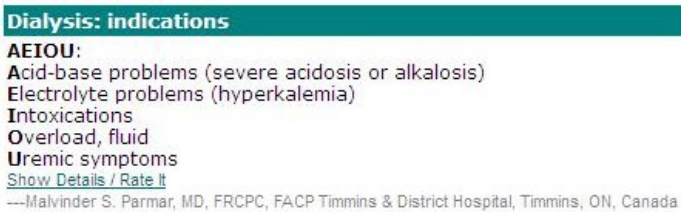
Indications of dialysis in acute renal failure (ARF):

- Severe fluid overload
- Refractory hypertension
- Uncontrollable hyperkalemia
- Nausea, vomiting, poor appetite, gastritis with hemorrhage
- Lethargy, malaise, somnolence, stupor, coma, delirium, asterixis, tremor, seizures,
- Pericarditis (risk of hemorrhage or tamponade)
- bleeding diathesis (epistaxis, gastrointestinal (GI) bleeding and etc.)
- Severe metabolic acidosis
- Blood urea nitrogen (BUN) > 70–100 mg/dl

Indications of dialysis in chronic renal failure (CRF):

- Pericarditis
- Fluid overload or pulmonary edema refractory to diuretics
- Accelerated hypertension poorly responsive to antihypertensives
- Progressive uremic encephalopathy or neuropathy such as confusion, asterixis, myoclonus, wrist or foot drop, seizures
- Bleeding diathesis attributable to uremia

A simple mnemonic is used to remember the indications for dialysis: A-E-I-O-U.[5]



The normal bodily pH averages 7.4. Respiratory centers act to maintain the pH between 7.35 and 7.45 and the kidneys act to remove bicarbonate or ammonium in response to acid-base changes. In severe kidney disease, this homeostatic mechanism is disrupted, and the body can rapidly turn acidotic or alkalotic regardless of compensation from the respiratory centers. This acid-base problem is an indication for dialysis, where these molecules can be removed and normal pH can be restored.[6]

The kidneys normally actively secrete potassium from the distal convoluted tubule and loops of Henle. When kidney failure or injury sets in, hyperkalemia can easily develop. Symptoms of hyperkalemia include fatigue, myalgia, and muscular weakness. Severe hyperkalemia can present as tented T-waves on an EKG and progression to ventricular fibrillation. Dialysis removes excess potassium from the bloodstream and returns the body back down to physiological levels.[6]

Overdose and intoxication of substances that are found in the blood may be an indication for dialysis. These drugs should have a low volume of distribution and shouldn't be highly bound to plasma proteins. Unfortunately, some common overdose or intoxicant drugs like digoxin and tricyclic antidepressants have volumes of distribution in hundreds of liters, and are not readily removed by dialysis.[6] Ethanol is easily removed via dialysis, as are some anti retroviral drugs, aminoglycosides, and antibiotics.[7]

Indications for fluid resuscitation are numerous, ranging from hypovolemia to hypotension.[6] When patients regain clinically acceptable statuses, the fluids administered are then considered to

be fluid overloads, and should be removed to prevent iatrogenic heart failure. Dialysis can be used to remove excess fluids from patients' bodies.

Uremia often develops in chronic kidney failure, brought on by the inability to excrete nitrogenous wastes, parathyroid hormone, proteins and other physiological substances in toxic levels.[8] Since these substances are floating in the bloodstream, dialysis can easily clear the body of these toxins to restore physiological homeostasis.

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THE UNSUNG HEROES BY: STEVE SOMAN, CO-EDITOR-IN-CHIEF

As Americans, we often admire the courage and sacrifice of the men and women serving our country in the armed forces. As members of the pharmacy community, we admire the professionalism and achievements of our colleagues making outstanding accomplishments in their respective practice settings. However, often I think we overlook a special niche for pharmacists, members of both the pharmacy community and the armed forces who sacrifice much more than many and play a critical role on the forefront of disaster relief and medical relief programs yet often do not receive the recognition they deserve.

Thus, it is my pleasure and privilege to depict pharmacists and technicians who work tirelessly in the armed forces of the United States and other nations while representing the core values of a pharmacist in their honesty, integrity, and accountability while delivering quality patient focused care with genuine leadership skills, professional ethics and morals, cultural competency, and substantive commitment to the social needs of the communities they serve.

The following pictures are from the Joint Task Force based in Bravo Soto Cano Airbase in Honduras; the Australian Defense Force medical team who participated in Operation Pakistan Assist and volunteer pharmacists who served with Medical Wings International in Haiti relief programs. These pictures truly expose us to a unique path in pharmacy where few dare to tread but the rewards and potential to change lives are indescribable.

Top: Flight Lieutenant Tim Strickland (right) talks to village leaders at Bailgiran about environmental health issues while Captain Jada Bendall (center) and Corporal Adrian Miller look on.

Left: Sergeant Stephen Davidson draws up a vaccination in the village of Bailgiran in the Neelum Valley in preparation for vaccinating local children.

Image Source:
Australian Government, Department of Defense
Australian Defense Force Medical Team
http://www.defence.gov.au/op/index.htm

Top: Maj. Brian Sydnor, the pharmacist with the Medical Element at Soto Cano Air Base, Honduras, explains the proper use of medications to patients during the medical civic action program here. The pharmacy delivered 1,685 prescriptions throughout the four clinic days.
(U.S. Air Force photo/Tech. Sgt. Benjamin Rojek)

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Lt. Col. Douglas Odegard, Joint Task Force-Bravo Medical Element Ancillary Services officer, fills a prescriptions at a makeshift pharmacy. Colonel Douglas was part of a Medical Readiness and Training Exercise held there to assist the Honduran Ministry of Health in providing basic medical services to residents of the area.
(U.S. Air Force photo/Capt. John T. Stamm)

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Giving a patient a bag of vitamins, Spc. Christopher Black, with the Joint Task Force-Bravo Medical Element, mans the preventative medicine station during the medical civic action program. Team Bravo medical professionals assisted the El Salvador Ministry of Health treat almost 800 patients. (U.S. Air Force photo/Tech. Sgt. Benjamin Rojek)

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Volunteer pharmacists play a vital role in collaborative drug therapy management and pharmaceutical care during disaster relief operation as seen during the aftermath of the 2010 Haiti earthquake. The picture taken above is from September 2010 in Port-au-Prince Haiti, where pharmacists provided wide range of health care services and patient education.

Image Source:
Medical Wings International
http://www.medicalwings.org/pharmaceutical-care/

Top: Lieutenant Tamara Lee, a pharmacist with the Australian Army 1 Health Support Battalion based at Holsworthy Barracks in Sydney, checks pharmaceutical supplies at Camp Bradman, near Dhanni, Kashmir.

Image Source:
Australian Government, Department of Defense
Australian Defense Force Medical Team
http://www.defence.gov.au/op/index.htm

"It is fun to show them that, though we wear camouflage to work, we are still as clinical as any other pharmacist out there."
- Maj. Jeffery Neigh, PharmD, BCPS

Top: Using a classroom as a makeshift pharmacy, Army Sgt. Rachel Mayhill and Air Force Capt. Manuel Silveira set up during MEDRETE in Morolica, Honduras. MEDRETEs offer medical troops a one-of-a-kind opportunity to go through an entire deployment process and treat patients in the field training that is a departure from the typically simulated medical training exercises.
(U.S. Air Force photo by Tech. Sgt. William Farrow)

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Left: Air Force Capt. Manuel Silveira (center), MEDEL pharmacist, explains a prescription in San Diego, El Salvador. JTF-Bravo Medical Element performed a Medical Civil Action Program, or MEDCAP, treating 2,987 people in several different cities affected by the El Salvador mudslides. The MEDEL personnel distributed more than $23,000 in medical supplies during the MEDCAP. The medicines ranged from prescription medicine to common pain-killers
(U.S. Air Force photo/Staff Sgt. Chad Thompson).

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Servicemembers worked side-by-side in the pharmacy delivering more than 2,000 prescriptions to patients seen by the medical civic action program team made up of Soldiers, Airmen, and civilians from Joint Task Force Bravo as well as Nicaraguan Soldiers and Ministry of Health personnel in El Ayote, Nicaragua.
(U.S. Air Force photo by Staff Sgt. Bryan Franks)

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Army 1st Sgt. Jorge Ortiz, of Joint Task Force-Bravo's Army Forces, explains the directions of a medication to a woman seen during the task force's medical readiness exercise here May 14th and 15th 2010.

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Capt. Elizabeth Sewell, a pharmacist from JTF-Bravo's Medical Element, explains a medication to a patient in Burrell Boom, Belize. More than 600 people were seen by U.S. and Belize military medical personnel in two different villages ravaged by flood water.

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

Top: Explaining the proper use of the medication, Staff Sgt. Raquel Martinez, with the Army Forces at Soto Cano Air Base, assists the Medical Element with interpreting during a Medical Readiness Training Exercise. Team Bravo regularly assists the Honduran Ministry of Health and Honduran military with delivering medical care to remote villages around the country.
(U.S. Air Force photo/Tech. Sgt. Benjamin Rojek)

Image Source:
United States Military
Joint Task Force - Bravo, Soto Cano Air Base, Honduras
http://www.jtfb.southcom.mil/photos/index.asp

NUTRITION SUPPORT PHARMACY PRACTICE

BY: JAMES W. SCHURR, PHARM.D. CANDIDATE C/O 2014

Nutrition Support Pharmacy is a specialized practice pertaining to the needs of patients receiving Parenteral (PN) or Enteral Nutrition (EN). Nutrition Support Pharmacists (NSPs) are integral members of the nutritional support team and bring valuable skills and knowledge to the clinical practice setting. The Board of Pharmacy Specialties (BPS) recognizes Nutrition Support Pharmacy as a practice with a certification examination and the designation of Board Certified Nutrition Support Pharmacist (BCNSP). NSPs have active responsibility in direct patient care and promoting the maintenance or restoration of optimal nutrition status as well as designing and modifying treatment regimens according to individualized needs of the patient.[1] Furthermore, the American Society of Health-System Pharmacists (ASHP) recognizes and accredits Postgraduate Year Two (PGY2) pharmacy residencies in Nutrition Support. Three programs are listed in the ASHP residency directory; they include Emory Healthcare (located in Georgia), the University of Arizona Medical Center, and the University of Wisconsin Hospital.[2]

The American Society outlines the standards of practice for Nutrition Support for Parenteral and Enteral Nutrition (ASPEN) and details guidelines for NSPs[3]. ASPEN guidelines list eight key components of practice including nutrition assessment; development and implementation of the nutrition care plan; compounding the feeding formulation; monitoring parameters and management of nutrition support services; advancement of Nutrition Support Pharmacy practice; research; and ethics. A survey of Nutrition Support Pharmacists revealed areas of knowledge most important to their practice.[4]

These Key Knowledge areas of Nutritional Support Pharmacists are:

- Laboratory tests and findings used to assess nutrition status
- Effects of disease states on nutrition status and vice versa
- Pharmaceutical calculations used in compounding feeding formulations
- Guidelines for the parenteral admixture compounding and dispensing
- Effects of medical and surgical therapies on nutrition status
- Indications or contraindications for the use of parenteral nutrition (PN) products and feeding formulations
- Compatibility and stability of PN formulations
- Knowledge of disease states affecting ingestion, digestion, absorption, metabolism, and elimination of nutrients
- Therapeutic considerations for the co-administration of medications and PN formulations
- Knowledge of fluid, electrolyte, and acid-base balances
- Composition of PN products
- Metabolic, nutritional, and clinical responses to specialized nutrition support
- Indications / contraindications for methods of administering PN formulations
- Metabolic complications of specialized nutrition support
- Infectious complications associated with specialized nutrition support
- Methods used to prevent and manage metabolic complications associated with specialized nutrition support
- Methods used to prevent infectious complications associated with specialized nutrition support
- Sources of information regarding compatibility and stability of PN and EN formulations

The NSP's role in nutrition assessment involves collaboration with other healthcare professionals to identify patients who are either malnourished or at risk of becoming malnourished. This identification is accomplished through patient interviews, medical record and history reviews (i.e. therapies, laboratory findings, and physical assessments that may factor into their nutritional

status), biochemical assessment, and record documentation. The assessment of nutrient requirements involves calculations of daily energy and protein requirements as well as caloric distribution between fats, carbohydrates, and proteins. Vitamins, minerals, fluids, and electrolytes should also be assessed in this process. The NSP is ideal to assessing possible drug-nutrient, nutrient-nutrient, or drug-drug interactions that may be detrimental to nutrition support therapy. Pharmacoeconomic considerations are also made during nutrient assessment in efforts to curb costs and determining the appropriateness of certain Nutrition Support therapy paradigms.[2]

The nutrition care plan includes an interdisciplinary and evidence-based approach that addresses the goals, communication considerations, route and formulation selection, and nutritional support access needed for each patient.[5] During the establishment of the nutrition care plan, the recommendations for a patient-specific formulation, pharmacologic adjuncts to nutrition support (i.e. H_2 antagonists, is made by the NSP.[2] The selection of the route of administration involves clinical factors requiring astute judgment by the nutrition support team. The NSP should provide insight into the decision, utilizing pharmaceutical knowledge in conjunction with clinical practice guidelines and algorithms, such as those provided by ASPEN.[5]

Compounding formulations for nutrition support therapy is an area of practice in which the NSP is uniquely qualified to provide both clinical decision-making and physical product preparation. Nutrition support can be provided as either enteral or parenteral formulations, both in which the pharmacist plays an active role. As previously mentioned, the survey of NSPs showed that approximately 95% of compounding activities were related to parenteral formulations and only 5% to enteral formulation.[4] Parenteral nutrition (PN) support preparations are compounded, prepared, and stored according to United States Pharmacopoeia chapter <797>: Pharmaceutical Compounding-Sterile Products.[6] The NSP is also integral in developing policies and procedures for the compounding of PN preparations that include aseptic technique, recommended safe practices, methods for detection and/or prevention of formulation incompatibilities or instabilities, and staff education and training.[3] Moreover, NSPs are involved in preparation of enteral nutrition (EN) formulations in providing proper training to personnel, utilization of aseptic technique, and clinical judgment in modifications to formulation.[5] In addition, automated compounding devices should be monitored by the pharmacist with proper adherence to guidelines. [7]

The NSP participates in monitoring activities for their patients and include nutrient intake, tolerance of therapy, inspection of feeding formulation, laboratory parameters monitoring pertinent to clinical and nutritional status, changes in nutrient requirements, organ function, pharmacotherapy, gastrointestinal tract function, weight and growth rate, and fluid balance. The pharmacist uses these findings to participate in the follow-up plan for the patient's therapy. The efficacy of the nutrition support therapy chosen for the patient must be evaluated throughout the duration of treatment including both parenteral and enteral orders and any complications that arise.[2] Frequency of monitoring depends on severity of illness, level of metabolic stress, and degree of malnutrition.[8]

Management of nutrition support services is yet another administrative function of the NSP. Activities involve the development, documentation, and review of organizational policies, protocols, and procedures. Ensuring continuity of care for patients through all levels of healthcare is an important role of the pharmacist requiring administrative skills and the ability to serve as a liaison between the nutrition support team and other medical teams while maintaining professional relationships in order to facilitate communication and workflow. Development and maintenance of a nutrition support formulary is a key role of the NSP in providing appropriate care for patients that is also cost-effective for the health system.[2]

Pharmacist-to-pharmacist communication is another essential process for the continuity of care in terms of discharges to other care setting.[5]

Advancement and professional progress of nutritional support is achieved through participation in interdisciplinary teams, education of colleagues and students, participating in research activities, professional organization affiliations, and maintenance of ethical code. Evidence based research is a cornerstone of practice for NSPs. Active participation in research in paramount in identifying nutrition related clinical problems and methods of resolution. In addition, participation in research committees, analyzing research for application, developing research based policies and protocols, education of others, and participating in data collection are key aspects of professional growth.[2]

Nutrition Support Pharmacy has been a recognized specialty area of practice by the Board of Pharmaceutical Specialties since 1988. It continues to be an area in which clinical pharmacists provide exceptional patient care. Professional organizations such as ASPEN recognize the important value of the Nutrition Support Pharmacist as a part of the nutrition support team evidenced by pharmacist inclusion into practice guidelines.[2,5] With the advancement of clinical pharmacy practice, NSPs have established themselves as invaluable clinicians in improving outcomes for patients in need of nutrition support therapy.

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THE ROLE OF N-ACETYLCYSTEINE IN CONTRAST INDUCED NEPHROPATHY

BY: NEAL SHAH, CO-EDITOR-IN-CHIEF

Contrast dyes enhance imaging for computer tomography (CT), magnetic resonance (MR), and X-rays.[1] Dyes usually consist of barium, iodine, or gadolinium, depending on the procedure.[2] CT and X-ray scans often use iodine for systemic imaging and barium sulfate for GI imaging, whereas MR imaging primarily uses gadolinium.[2] Gadolinium and iodine contrast dyes have renal elimination, and could lead to contrast-induced nephropathy (CIN), especially in patients with pre-existing renal impairment.[3]

The pathophysiology of CIN involves reduced blood flow to the kidneys (that causes ischemia), which leads to toxicity within tubular epithelial cells.[3] The resulting reactive oxidative species (ROS) damage nephrons within the kidney and induce necrosis.[3] CIN is defined as an abrupt increase in serum creatinine of 0.5 mg/dL or a 25% increase from baseline levels 48 hours after injection of contrast media.[4,5] Current strategies for managing CIN include: removal of nephrotoxic compounds, aggressive hydration, and administration of vasodilatory compounds (*e.g.* theophylline) or anti-oxidant medications (*e.g.* N-acetylcysteine [NAC]).[3-5] NAC seemed a promising agent for mitigating CIN due to its low cost, multiple indications, and ease of use, but perspectives have changed.

NAC is a modified amino acid used traditionally to reverse acetaminophen-induced hepatotoxicity and provide mucolytic activity in bronchial diseases.[6] NAC is a precursor to the free radical scavenger, glutathione (GSH). Normally, free radicals oxidize GSH, which reduces the damage caused by ROS to our cells. GSH is depleted upon major oxidative stress, and administration of NAC replenishes this depleted GSH content.[7] Other uses of NAC include: increased ovulation and fertility in polycystic ovarian syndrome (PCOS) patients,[8] chemoprevention of certain cancers,[9] and oxaliplatin-induced neuropathy.[10]

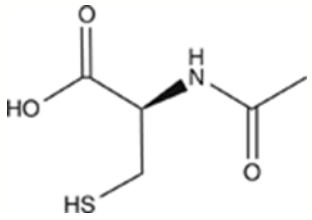

Figure 1. Structure of N-acetylcysteine (NAC).[7]

The efficacy of NAC in CIN is widely debated. Data from 2011 and 2012 demonstrate that NAC is not efficacious in minimizing or preventing CIN. Anderson *et. al.*'s MEDLINE meta-analysis concluded that papers published from 1990—2010 had no conclusive clinical evidence on NAC's safety or efficacy in the prevention of CIN.[11] They found that while NAC improved serum creatinine levels, there was no improvement in overall renal function.[11] A clinical trial in Brazil, published in September 2011, reported that in 2,038 patients with at least one risk factor for CIN, administration of NAC and placebo resulted in similar outcomes of CIN.[12] The paper concluded that there were no significant risk reductions or enhanced outcomes of any kind with the administration of NAC.[12] Tanaka *et. al* reported that the administration of NAC in CIN had no significant differences in morbidity or mortality compared to placebo.[13]

Aligoglu *et. al.* conducted a study measuring renal function with creatinine and cystatin C levels.[14] Upon administration of oral NAC, there was no significant reduction in creatinine or cystatin C in patients with CIN treated with placebo or NAC.[14] Jaffery *et. al.* conducted a study in 398 patients, defining CIN as an increase in creatinine concentration ≥ 25% above the baseline level within 72 hours of the administration of intravenous contrast.[15] They reported that high-dose intravenous NAC failed to reduce the incidence of CIN.[15] Aslanger *et. al.* examined NAC's prophylactic utility in CIN with a study of 312 patients, but found that intrarenal and intravenous NAC had no significant benefit compared to placebo.[16]

The most conclusive evidence against NAC's efficacy in CIN came from a paper by Gurm *et. al.* published in January 2012. A retrospective analysis of NAC use in 10,574 out of 90,578 patients who underwent percutaneous coronary intervention (PCI) demonstrated no statistical significance between NAC treated patients and non-treated patients that developed CIN.[17] The authors concluded that there was no clinical improvement associated with NAC use in CIN.[17]

Overall, while NAC remains efficacious in exerting mucolytic effects in bronchial diseases and assisting in decreasing acetaminophen-induced hepatotoxicity, overwhelming clinical evidence has reported against using NAC in CIN.

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MATCHING CHALLENGE: OVER THE COUNTER PRODUCTS (ANSWERS) BY: MOHAMED DUNGERSI, ASSOCIATE STUDENT EDITOR

1 = C, 2 = F, 3 = A, 4 = J, 5 = I, 6 = B, 7 = E, 8 = G, 9 = D, 10 = H

Go back to page 12?

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"There is no trouble so great or grave that cannot be much diminished by a nice cup of tea."

~ Bernard-Paul Heroux

Image Source: http://mish-mash.ucoz.com/index/green_tea/0-11

MATCHING CHALLENGE: LOOK-ALIKES, SOUND-ALIKES (ANSWERS) BY: ADDOLORATA CICCONE, STUDENT COPY EDITOR

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1 = H, 2 = G, 3 = F, 4 = A, 5 = C, 6 = D, 7 = B, 8 = E, 9 = J, 10 = I

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TREATMENT OPTIONS FOR ESBL PRODUCING ORGANISMS

BY: MOHAMMAD A. RATTU, PHARM.D. [PGY-1 RESIDENT AT VA NYHHS]

While we may have good intentions for utilizing empiric, broad-spectrum antibiotics in serious gram-negative infections, the overuse of select agents has led to considerable resistance rates in many parts of the world.[1]

The risk of developing colonies or active infections with resistant bacteria generally increases with:[1]

- longer stays in the hospital, intensive care unit, and/or long-term care facilities (*e.g.* nursing homes)
- abdominal surgeries and related procedures
- venous, arterial, and/or urinary catheters
- prior antibiotic administrations
- hemodialysis
- disease severity (*e.g.* sepsis > septicemia > bacteremia > superficial skin and skin structure infections)

Initially, there were (and still considerably are) bacteria that simply produced beta lactamase: an enzyme that hydrolyzed the beta lactam ring of penicillins (see Figure 1) and first-generation cephalosporins (*e.g.* cefazolin [Ancef®, Kefzol®]).[1] Over time, particularly with the advent of cefotaxime (Claforan®), a third-generation cephalosporin, certain gram-negative bacteria strains (*e.g.* of Klebsiella pneumoniae) conferred resistance by producing extended-spectrum beta lactamase (ESBL).[1] In other words, cephalosporins with an oxyimino side chain, like cefotaxime, no longer had strong activity against these bacteria (see Figures 2-6).[1]

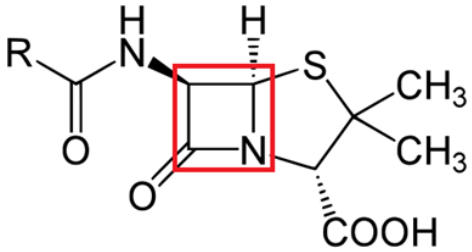

Figure 1. Basic structure of penicillin antibiotics, with the beta-lactam ring highlighted in red.
Source:http://upload.wikimedia.org/wikipedia/commons/thumb/9/99/Penicillin_core.svg/500px-Penicillin_core.svg.png

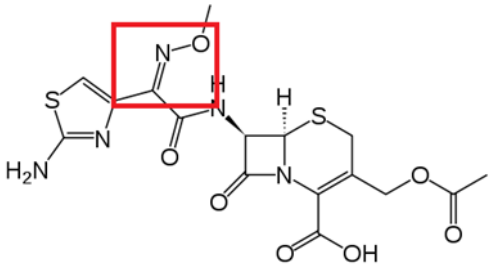

Figure 2. Structure of cefotaxime (Claforan®), a third-generation cephalosporin, with the oxyimino side chain highlighted in red.
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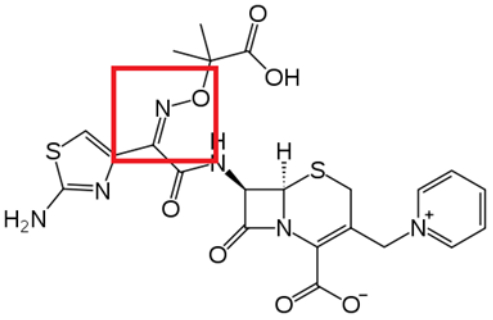

Figure 3. Structure of ceftazidime (Fortaz®, Tazicef®), a third-generation cephalosporin, with the oxyimino side chain highlighted in red.
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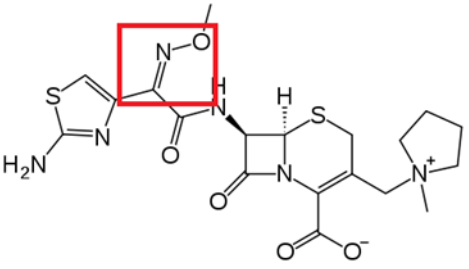

Figure 4. Structure of cefepime (Maxipime®), a fourth-generation cephalosporin, with the oxyimino side chain highlighted in red.
Source: http://upload.wikimedia.org/wikipedia/commons/thumb/e/e4/Cefepime.svg/500px-Cefepime.svg.png

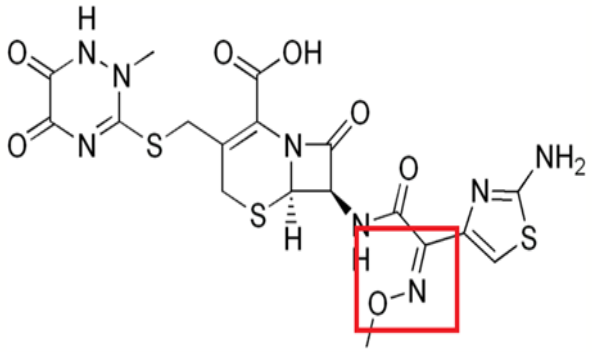

Figure 5. Structure of ceftriaxone (Rocephin®), a third-generation cephalosporin, with the oxyimino side chain highlighted in red.
Source: http://upload.wikimedia.org/wikipedia/commons/thumb/0/0c/Ceftriaxone_structure.png/640px-Ceftriaxone_structure.png

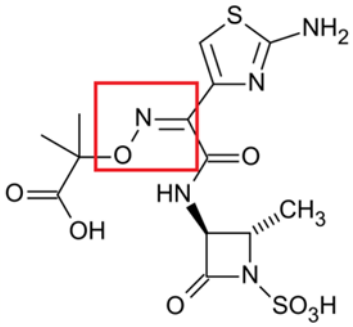

Figure 6. Structure of aztreonam (Azactam®), a monobactam, with the oxyimino side chain highlighted in red.
Source: http://upload.wikimedia.org/wikipedia/commons/thumb/4/4d/Aztreonam_structure.svg/500px-Aztreonam_structure.svg.png

Unfortunately, there are hundreds of ESBL-producing variants, broadly categorized as TEM, SHV, CTX-M, OXA, PER, VEB, GES, BES, SFO, or TLA.[1] *For reading ease, we will not delve into the specifics of these acronyms.* Gram-negative organisms that produce the various ESBLs are primarily Klebsiella pneumoniae, Klebsiella oxytoca, and Escherichia coli, but Acinetobacter, Burkholderia, Citrobacter, Enterobacter, Morganella, Proteus, Pseudomonas, Salmonella, Serratia, and Shigella species may also contain ESBLs.[1] Due to the numerous ESBL organisms and varieties, some laboratories may not be able to identify correct susceptibilities and resistances (but advancements in this area are ongoing).[1]

Nonetheless, treatment options for infections identified with ESBL-producing organisms historically included:[2]

- carbapenems (*e.g.* imipenem-cilastatin [Primaxin®], meropenem [Merrem®], doripenem [Doribax®], ertapenem [Invanz®]) – some preferred over others in the class
- piperacillin-tazobactam (Zosyn®) – not preferred for serious infections
- aminoglycosides (*e.g.* gentamicin, tobramycin, amikacin [Amikin®])
- fluoroquinolones (*e.g.* ciprofloxacin [Cipro®])
- cefepime (Maxipime®)

Carbapenems, particularly imipenem-cilastatin and meropenem, provide the *best* chances for survival and bacteriologic clearance.[1,2] A practitioner ought to select between these two based on certain criteria, such as toxicity profiles – "meropenem is favored in the setting of seizures or pregnancy because of the possible central nervous system toxicity and unknown safety in pregnancy of imipenem. …Meropenem also may be easier to dose in the setting of changing or impaired renal failure."[1] Data for doripenem and ertapenem is increasing, but the latter was involved in cases of resistance and should not utilized in patients with severe sepsis.[1]

Piperacillin-tazobactam is associated with treatment failures.[1] Yet, it may still be effective for ESBL isolates with piperacillin-tazobactam MIC ≤ 16/4 mcg/mL, as well as for urinary tract infections, regardless of susceptibility (due to much higher drug concentrations seen in urine compared to plasma).[1] As with ertapenem, prescribers should avoid piperacillin-tazobactam in patients with severe infections.[1-3]

Positive data regarding aminoglycosides and fluoroquinolones is sparse, and it would also be preferable to avoid these agents for serious infections.[1] For instance, amikacin is an option with low MICs, but, as expected, the clinical success rates decrease drastically with higher MICs.[2] Fluoroquinolones, like ciprofloxacin, may be viable options for simple urinary tract infections, but are generally avoided as first-line treatment due

to very high resistance rates.[2,3]

As cautioned with piperacillin-tazobactam, aminoglycosides, and fluoroquinolones, treatment of severe infections due to ESBL-producing Klebsiella pneumoniae with oxyimino-beta-lactams (*i.e.* cefotaxime, ceftazidime, ceftriaxone, cefepime) is "likely to result in treatment failure, even if the organism demonstrates in vitro susceptibility."[1] Although cefepime is more stable than its third-generation counterparts, there is very limited data with high-doses (2 grams every eight hours instead of 1 gram every 12 hours) so such practice is *not* encouraged.[1] Resistance to cephamycins (*e.g.* cefoxitin [Mefoxin®], cefotetan [Cefotan®], cefmetazole [Zefazone®]) also developed, and it would be preferable to *avoid* utilizing this structurally similar class.[1]

Considering the above recommendations and recent (2011) data on success rates, table 1 may aid clinicians in proper antibiotic selection:[3]

[Table 1 Featured on Next Page]

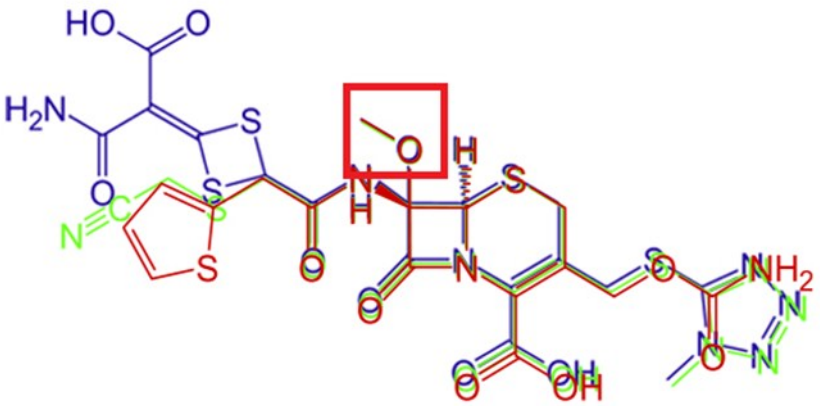

Figure 7. Overlap of three cephamycins: cefoxitin [Mefoxin®] (maroon), cefotetan [Cefotan®] (blue), and cefmetazole [Zefazone®] (green). The methoxy group on the C-7 carbon (highlighted in red) is indicative of cephamycin antibiotics, often classified under a cephalosporin generation.

Sources: http://upload.wikimedia.org/wikipedia/commons/thumb/1/1a/Cefoxitin.svg/500px-Cefoxitin.svg.png, http://upload.wikimedia.org/wikipedia/commons/thumb/4/47/Cefotetan.svg/500px-Cefotetan.svg.png, http://upload.wikimedia.org/wikipedia/commons/thumb/f/f1/Cefmetazole.svg/500px-Cefmetazole.svg.png

If our first-line carbapenems do not provide improvement, particularly with Klebsiella pneumoniae, we may elect to try less-preferred agents and/or consider possible therapy with tigecycline and/or colistin (polymyxin E).[3-5] Caution: "there are no clinical data supporting the use of double antibiotic coverage for treatment of ESBL producing organisms."[1]

We are becoming increasingly limited in our options for treating resistant organisms.[1,4,5] We need to improve the detection, treatment, and containment of infections with ESBL-producing organisms. These bacteria are "associated with higher mortality rates, longer hospital stays, greater hospital expenses, and reduced rates of clinical and microbiologic response compared with similar infections with gram-negative bacteria that do not produce ESBL."[1] Barrier protections and restrictions on third and fourth generation cephalosporins, in addition to reducing aforementioned risk factors, are just some of the methods to decrease the likelihood of ESBL unfections.[1]

Organism	First-line therapy	Second-line therapy
Empirical therapy[b]		
Monomicrobial infection	Carbapenem Tigecycline (not in urinary tract infections) with or without an antipseudomonal agent	Piperacillin-tazobactam (low inoculum) Colistin
Mixed gram-positive and gram-negative infection	Anti-MRSA agent plus a carbapenem Tigecycline (not in urinary tract infections) with or without an antipseudomonal agent	Anti-MRSA agent plus piperacillin-tazobactam (low inoculum) Anti-MRSA agent plus colistin
Directed therapy[c]		
ESBL-producing Enterobacteriaceae	Carbapenems Piperacillin-tazobactam (low inoculum) Fosfomycin (oral formulation for simple urinary tract infections)	Tigecycline (not in urinary tract infections) Fluoroquinolone Colistin
Carbapenemase-producing Enterobacteriaceae	Tigecycline Colistin	Fosfomycin (parenteral formulation)
Multidrug resistant *Pseudomonas aeruginosa*	Antipseudomonal agent (among carbapenems, use doripenem or meropenem)	Colistin Combination therapy

[a] ESBL = extended-spectrum β-lactamase; MRSA = methicillin-resistant *Staphylococcus aureus*.
[b] Local susceptibility patterns should be taken into consideration before deciding on empirical therapy.
[c] Based on available culture and susceptibility results.

Table 1. "Suggested Approach to the Management of Patients With Serious Infections Due to Multidrug-Resistant Gram-Negative Pathogens."[3]

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E S E I D U A U O K S E S

G U D O G F C X N X S G U

R A L R L N I L A N A R A

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TRIVIA: Which one of these brand name medications….does not exist?

ANSWER: BOMIDA®

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@ Neal Shah *(6th Year, STJ)*
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I am in a continuous process of self-definition, and constantly testing the boundaries of this world. I enjoy channeling my inspiration through words and photographs. As a witness to an evolving profession, I look forward to keeping you updated! Who knows where we will be tomorrow?

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I believe it is important for students and everyone else in the profession to stay informed about current pharmacy events. Rho Chi Post is a great way to continue learning information about what is happening on our campus and in the nation.

@ Addolorata Ciccone *(6th Year, STJ)*
I am thrilled to serve as a Co-Copy Editor of Rho Chi Post. Whether you are brand new to the world of pharmacy, a seasoned veteran of this profession, or anywhere in between, I hope you find our work engaging, relatable, and informative. I look forward to reading your comments and feedback.

@ Aleena Cherian *(5th Year, STJ)*
The Rho Chi Post has been a source of current information and great advice to students and professionals in this evolving profession. After years of experience in media and graphics-related work, it is now my privilege to be a part of this endeavor as a Co-Copy Editor. I hope you learn as much from future editions of the newsletter as I have, and I welcome your feedback!

CO-COPY EDITORS

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