P&T Update

Formulary Additions
1. Desflurane (Suprane®) inhalation vapor – formulary addition request – Approved for anesthesia use only
   Desflurane is an inhaled anesthetic used for the induction and maintenance of anesthesia. The request for the formulary addition of desflurane was submitted by the Anesthesiology Dept. UH currently has isoflurane and sevoflurane on formulary. At the last meeting the P&T committee had requested indications and/or criteria for desflurane use from the anesthesia dept. The anesthesia dept. submitted the following indications for desflurane use: bradycardia, severely or morbidly obese patients, patients with operations of very short duration, low flow anesthesia. It must not be used in patients with laryngeal mask airway. Approved for anesthesia use only. Restricted to the following indications: bradycardia, severely or morbidly obese patients, patients with operations of very short duration, low flow anesthesia

2. IdaruCIZUmb (Praxbind®) – Formulary Addition and MiniFMEA – Approved
   IdaruCIZUmb is a novel drug for the treatment of patients who require emergent reversal of dabigatran-induced anticoagulation. IdaruCIZUmb is a monoclonal antibody that binds and neutralizes the anticoagulant effect of dabigatran selectively. In the clinical studies, the coagulation tests were normalized following a single dose of IdruCIZUmb with the effect lasting up to 24 hours. The medication has been recommended by the Safe Anticoagulation committee to be added to the formulary. It was discussed that the medication would be used by services such as trauma, neurosurgery, neurology, cardiology, intensivists, ED and hematology/oncology. The P&T committee unanimously approved the formulary addition of IdruCIZUmb.

3. Sugammadex (Bridion®) – Formulary Addition and MiniFMEA – Approved
   Sugammadex is a selective relaxant binding agent that binds with the neuromuscular-blocking agents rocuronium or vecuronium, resulting in the reversal of neuromuscular blockade induced by rocuronium or vecuronium. The formulary addition request was submitted by anesthesia dept. In the clinical trials, sugammadex depicted faster and more complete reversal of neuromuscular blockade compared cholinergic agents. The pricing is comparable to neostigmine/glycopyrrolate combination at low doses (2mg/kg). The committee voted to approve sugammadex formulary addition.

4. Filgrastim-sndz (Zarxio®) – Formulary addition – Approved
   Filgrastim-sndz (Zarxio®) is a biosimilar of the recombinant human G-CSF (filgrastim- Neupogen®). Zarxio is significantly cheaper than Neupogen® and has been approved for almost similar indications. The committee voted to approve Filgrastim-sndz (Zarxio®) formulary addition. It was noted that Zárxió® and Neupogen® are not automatically interchangeable, and it was decided to keep Neupogen on formulary at present.

(Continued on page 2)
Formulary Addition/Deletion
(Continued from page 1)

5. Regadenoson (Lexiscan®) – Line extension for expanded indications – Approved
The nuclear medicine services requested an expansion of the restriction criteria for regadenoson to include the following: Submaximal exercise stress testing to convert to a vasodilator stress test, patient’s weight (>300lbs) and referring physician request. The current restriction criteria are: Reactive Airway Disease, History of tachyarrhythmias. The P&T committee voted to approve the expanded criteria for regadenoson use by the nuclear stress testing lab.

Expanded restriction criteria for regadenoson (Lexiscan®) – approved
- Reactive Airway Disease
- History of tachyarrhythmias
- Submaximal exercise stress testing to convert to a vasodilator stress test
- Patient’s weight (>300lbs)
- Referring physician request

6. Prothrombin Complex Concentrate, PCC-4 (Kcentra®) addition request – Approved with restriction
Kcentra® is a Prothrombin Complex Concentrate, PCC-4. It provides increase level of coagulation factors II, VII, IX, X and protein C & S. Kcentra® contains heparin so use in patients with heparin induced thrombocytopenia is contraindicated. A box warning exists on its arterial and venous thromboembolic complication risk. It is FDA approved for use in urgent reversal of acquired coagulation factor deficiency induced by vitamin K antagonist, VKA (warfarin) therapy in patients with acute major bleeding or need for an urgent surgery/invasive procedure. Weight based Dosing for reversal of major bleed is based on presenting INR. Published literature used decrease INR as surrogate marker for efficacy and FDA approval. Compare to FFP, INR decrease quicker with PCC-4 and there is lower risk for fluid overload. Kcentra costs $1.54/ unit, cost per dose for an 80kg patient can range from $1,537 – $6,150/dose. Pros and cons were discussed, Kcentra® was motioned for UH Formulary addition and approved by members. Additional discussion to restrict approval for use ensued. After extensive discussion, PCC-4 will be restricted to the following services: trauma, intensivist, hematology/oncology, ED and neurosurgery. Close monitoring is recommended to identify appropriate use and also to identify additional services who should also be allowed approving the use of the high risk, high cost therapy.

PCC-4, Kcentra® is approved for Formulary addition with restriction to trauma, intensivist, hematology/oncology, ED and neurosurgery approval.

7. Immune globulin GammaGard® liquid – Approved
Ideal body weight to be used for weight based dosing. Purchasing group negotiated better pricing for GammaGard® liquid, proposed brand change approved by both adult & pediatric Allergy, Immunology & Rheumatology/ Infectious disease and Chief of Neurology. Weight based dose to use ideal body weight was also approved.

Formulary Deletions
1. Pentamidine isethionate (Nebupent®) powder for nebulization deletion-approved
The committee reviewed the request to delete pentamidine isethionate (Nebupent®) powder for nebulization from the formulary, as the institution does not stock the Respirgard® II nebulizer required for the administration. The injection form will remain on the formulary.

2. Gamma hexachlorocyclohexane (Lindane®) 1% lotion Formulary deletion – Approved
Lindane 1% lotion is manufacturer discontinued, the shampoo remains available.

3. Isovue multipack 370 deletion – Approved
This multidose contrast media is not used/stocked by radiology. The radiology dept. concurs with removing it from the formulary.

4. Amoxicillin/ clavulanate 600mg-42.9mg/5mL oral suspension – line extension – Approved
DELETIONS: 125mg-31.5mg/5mL, 200mg-28.5mg/5mL, 250mg-62.5mg/5mL

Policies & Procedures/Floor Stock Update
707-600-180, 707-600-180A & B 340b program policy and procedure – Approved
707-600-180 and 707-600-180A are Policy and Procedure for 340b program using Sentry system to track was revised
707-600-180B was developed defining contracted 340b pharmacy program

Miscellaneous
2015 UH antibiogram & anti-infective dosing card approved.

Heparin drip nomogram orderset reviewed and approved. Orderset reviewed no changes.
Introduction
In May 2016, the FDA issued a drug safety warning specifically advising the restriction of fluoroquinolone (FQ) use in uncomplicated infections. Fluoroquinolone use has more risk than benefit for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections (UTIs) who have other treatment options. These three illnesses are the cause for one-third of outpatient fluoroquinolone prescriptions and therefore it is important to educate healthcare professionals on proper usage of this antibiotic class. The FDA has also issued other safety alerts regarding the risk for possibly permanent nerve damage and tendon rupture. Since 2008, there has been a black box warning for tendonitis/tendon rupture on all quinolones. Antibiotic resistance to quinolones can develop quickly; therefore, judicious use of quinolones is important in preserving their spectrum of action. Overuse of unnecessary antibiotics leads to resistance, adverse effects, and avoidable cost.

Basics of Quinolone Use
Fluoroquinolones are commonly used broad spectrum antibiotics because they can be given intravenously or orally to treat a variety of serious infections in outpatient and inpatient settings. The bioavailability for oral formulations ranges from 70-100% and patients being discharged from the hospital setting can easily be transitioned to an oral regimen. Fluoroquinolones work by inhibiting DNA gyrase and topoisomerase, two enzymes necessary for bacterial DNA replication. Quinolones are bactericidal, concentration dependent antibiotics and exhibit a postantibiotic effect following bacterial exposure to inhibitory concentrations. Second generation quinolones such as Norfloxacin (Noroxin®) and Ciprofloxacin (Cipro®) have poor gram-positive and anaerobic coverage, but good gram-negative coverage, specifically against Pseudomonas aeruginosa. Common uses are complicated UTIs (pyelonephritis), prostatitis, bacterial gastroenteritis, intra-abdominal infections, pneumonia, and osteomyelitis. Several third and fourth generation FQ have been withdrawn due to safety concerns such as hepatotoxicity, cardiovascular complications, and glycemic alterations. Currently available 3rd/4th generation options are Gemicloxacin (Factive®), Levofloxacin (Levaquin®), and Moxifloxacin (Avelox®). These respiratory FQs are generally good for treating infections due to Streptococcus pneumoniae and atypical pathogens (Legionella, Mycoplasma, and Chlamydia), especially when drug resistance is suspected. Levofloxacin is commonly used for intra-abdominal, community-acquired and hospital-acquired pneumonia, and P. aeruginosa infections from other sources. Moxifloxacin is usually used for community-acquired pneumonia and some diabetic foot ulcers because of its anaerobic coverage. Moxifloxacin is eliminated primarily in bile and does not reach urine concentrations high enough to adequately treat UTIs and should not be used for this indication. Levofloxacin has better gram-negative coverage when compared to moxifloxacin; however moxifloxacin has better anaerobic coverage (except C. difficile). In general, the advanced generation FQs have expanded gram-positive coverage (penicillin-resistant S. pneumoniae) and expanded activity against atypical pathogens. For treatment of UTIs, quinolones are most appropriate in settings where there is resistance or kidney involvement.

Safety Considerations & Adverse Effects
There are several significant adverse effects that healthcare professionals should be aware of. Common adverse effects include diarrhea, CNS effects (headache, dizziness), photosensitivity, and rash. More significant adverse effects include glycemic control abnormalities, QTc prolongation, and peripheral neuropathy. It is important to recognize other common QTc prolonging agents such as azole antifungals,

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Recent Updates to Fluoroquinolone Safety
(Continued from page 3)

metoclopramide, methadone, macrolide antibiotics, and tricyclic antidepressants in a patient’s regimen. Administration with multivalent cations (aluminum, magnesium, calcium), commonly found in antacids, dairy, and dietary supplements, can result in formation of complexes that are poorly absorbed and administration should be separated by 2-3 hours. Cartilage and bone deformities or arthralgias can occur while using quinolones and thus they are not recommended in children younger than 12 years old or pregnant women. In addition, there is a black box warning for tendon rupture/tendonitis. The risk factors that put patients at risk for tendon rupture are age greater than 65 years, concomitant steroid therapy, and kidney, heart, or lung transplantation. Advise patients to stop taking the fluoroquinolone at the first sign of tendon pain, swelling, or inflammation and to avoid use of the affected area. Tendon rupture, specifically of the Achilles tendon, is possible even with a short duration of therapy. Overuse of quinolones can lead to a variety of side effects and result in resistance to gram-negative and gram-positive pathogens. This can be through alterations in the quinolone targets (DNA gyrase), decreased outer membrane permeability, or the development of efflux pumps. The FDA has warned healthcare professionals several times about the use of quinolones due to their safety concerns; however quinolones have an important role in antimicrobial therapy and can safely be used in hospital acquired infections and cases of resistance. References:


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Role of Fecal Microbiota Transplant in Recurrent Clostridium difficile Infections

Clostridium difficile infections (CDI) are the most common causes of infectious diarrhea in the healthcare setting; accounting for 20-30% of antibiotic-associated diarrhea. The main means by which the organism is spread is through the presence of C. difficile spores on the hands of healthcare workers. These spores are transmitted from person to person through the fecal-oral route. The treatment guidelines for an initial episode of CDI are fairly straightforward in terms of recommendations and strength of evidence. However, recurrent CDI is a growing problem in which there are treatment options and recommendations available, but these treatment modalities may not be effective in patients with multiple recurrences.

A history of treatment with antibiotics or antineoplastics agents within the previous 8 weeks is present in a majority of patients with CDI. The antimicrobial activity of these agents suppresses the normal gastrointestinal flora and thus provides an environment for C. difficile to flourish. Both longer exposure and use of multiple antimicrobials lead to an increase in risk for CDI. The diagnosis of CDI includes the presence of diarrhea (≥3 unformed stools in 24 or fewer consecutive hours) and a stool test positive for the presence of toxigenic C. difficile, its toxins, or findings demonstrating pseudomembranous colitis. The same criteria are used to diagnose recurrent CDI as well.

Treatment of initial mild, moderate, or severe CDI includes a two week regimen of metronidazole or vancomycin. However, data has shown that 6-25% of these patients treated for an initial CDI have experienced at least 1 additional recurrence. These recurrences can either be due to a relapse of the original strain or re-infection of susceptible patients exposed to a new strain. The treatment of a first recurrence of CDI is with the same treatment as for the initial episode; while treatment of a second recurrence...
is with a tapering regimen of oral vancomycin in which a substantial proportion of patients will be cured. Managing patients who do not respond to this regimen for a second recurrence provides a major challenge. There have been recent uncontrolled case studies of patients successfully treated with oral rifaximin, nitazoxanide, intravenous immunoglobulins, and probiotics but there is no compelling evidence to support them.2

Fecal microbiota transplant (FMT) from a healthy donor has been used with a high degree of success in several uncontrolled case series. FMT is a procedure in which fecal matter collected from an appropriately screened healthy donor is mixed usually with a saline solution, strained, and placed in the receiving patient through colonoscopy, endoscopy, enema, or capsules.3 One case series involved a retrospective review of 18 subjects who had received donor stool for recurrent CDI by nasogastric tube. During the 90 days after receipt of FMT, 2 patients died of unrelated illnesses, 1 of the 16 survivors experienced a single recurrence of CDI, and the remaining 15 were cured as their bowel habits returned to their normal functional pattern that had preceded their first episode of CDI.4 There are over 200 case reports that have estimated over 90% success rate with FMT in recurrent CDI.3

In late spring of 2013, the US Food and Drug Administration (FDA) classified human stool as both an investigation new drug (IND) and a biological agent in which only a physician with an approved IND application would be allowed to continue performing FMT. However, due to overwhelming opposition from both physicians and patients, the FDA reversed their position on June 17, 2013 and announced that qualified physicians may continue to perform FMT for recurrent CDI only. The use of FMT for research or to treat any condition other than recurrent CDI still requires an IND permit.3

In March 2016, the FDA released a draft document clarifying the IND requirements for use of FMT in recurrent CDI. The guidance document has not been finalized by the FDA and is intended for comment purposes only as of July 2016. The draft guidance defines the criteria that allows for FMT as a treatment option for recurrent CDI without the need for an IND application. The licensed healthcare provider must obtain adequate consent from the patient (consent should include at a minimum that FMT is investigational), the FMT product cannot be obtained from a stool bank (an establishment that prepares FMT products solely under the direction of licensed health care providers for the purpose of treating their patients [e.g. hospital laboratory] is not considered a stool bank), and the stool donor and stool must be qualified by screening and testing.5

Although FMT has been shown to have positive results in the treatment of CDI, there are also important risks associated with the treatment. Stool donors are carefully screened for transmissible pathogens, but there is always a risk that the tests may fail to detect these organisms. Potential candidates should also check with their insurance company regarding coverage of FMT therapy because it is still considered an experimental treatment. In conclusion, FMT offers a low risk and highly effective treatment for recurrent CDI. Hopefully, future controlled clinical trials will provide robust evidence supporting FMT that will place it into current treatment guidelines.

References:

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Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are well known and understood, but they are still some of the most common hospital-acquired infections that contribute to high morbidity and mortality. HAP is estimated to occur in about 5-10 patients in every 1,000 hospital admissions with a 6-20 fold higher incidence in mechanically ventilated patients. According to data from a randomly selected national sample, approximately 10% of ventilated patients were diagnosed with VAP every year over the past decade.

Approximately 50% of patients with HAP suffer from serious complications such as respiratory failure, septic shock, pleural effusions, and renal failure, especially in the intensive care unit (ICU). VAP is considered to be even more severe than HAP. Two recent studies have shown that VAP extends hospitalization by 11-13 days and prolongs the length of mechanical ventilation by 8-11 days compared to patients without VAP. In addition, VAP increased hospital care cost by approximately $40,000 per patient associated with VAP.

The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) HAP/VAP guidelines define HAP as a pneumonia occurring 48 hours or more after admission that does not involve intubation at the time of admission, while a pneumonia that occurs 48 to 72 hours after endotracheal intubation is defined as a VAP. The etiology of HAP and VAP may be bacterial, viral or fungal, but bacteria are the most commonly implicated pathogen. Common bacteria that are responsible for HAP and VAP include aerobic gram-negative bacilli such as Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli and Acinetobacter species and gram-positive bacteria such as Staphylococcus aureus, which is often methicillin-resistant (MRSA). Early-onset HAP/VAP (occurring within the first four days of hospitalization) is more likely to be caused by antibiotic sensitive bacteria, while late-onset HAP/VAP (occurring on or after day five of hospitalization) is more likely to be caused by multidrug resistant (MDR) bacteria and is therefore associated with a worse prognosis. Patients who had a prior hospitalization or received antibiotics within the past 90 days of the hospitalization are also at higher risk of MDR bacteria and should be considered to have late-onset HAP/VAP.

The IDSA and the ATS recently updated the guidelines for the management of non-immunocompromised adults with hospital-acquired and ventilator-associated pneumonia for the first time in 11 years since the last update in 2005. This update contains new studies that give additional insight into the changes by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE), an evidence-based guideline methodology.

In the 2016 guidelines, recommendations for Healthcare-Associated Pneumonia (HCAP) were removed due to new evidence. HCAP patients were previously thought to be at higher risk for MDR organisms because of a greater interaction with the healthcare system. However, increasing evidence shows that underlying patient characteristics are also an important independent risk factor for MDR and that contact with healthcare system does not necessarily increase the risk of patients contracting MDR pathogens. Therefore, the panel decided that HCAP recommendations should be made in the next CAP guidelines.

Also, it is now recommended that all hospitals generate and distribute a local antibiogram, and to tailor it to the ICU population if possible. Empiric antibiotic regimens should be based on the local distribution of pathogens associated with HAP/VAP to ensure targeted therapy, minimizing unnecessary antibiotic use and reducing antibiotic resistance. If a hospital does not have its local microbial epidemiology, its clinicians can refer to large national and international surveys of organisms and their resistance patterns. Empiric treatment for HAP/VAP depends on the suspected bacterium, risk factors for MDR, high mortality, etc. A common risk factor for MDR in HAP is prior intravenous antibiotic use within 90 days and some risk factors for MDR in VAP include septic shock at time of VAP and acute renal replacement therapy prior to VAP onset (includes prior intravenous antibiotic use within 90 days). Empiric treatment of HAP/VAP should always include vancomycin or linezolid to cover MRSA.
Piperacillin/tazobactam, cefepime, levofloxacin, imipenem and meropenem are recommended for MSSA and antipseudomonal coverage.3

Another change is the recommendation of a 7-day course of antimicrobial therapy for HAP/VAP patients for all antibiotics whereas the older guidelines had different treatment length depending on the bacterium causing the disease.2,3 A short, 7-8 day course of antibiotics was shown to increase the 28-day antibiotic free days and decrease recurrent VAP caused by MDR pathogens with no difference in mortality, recurrent pneumonia, treatment failure, hospital length of stay, or duration of mechanical ventilation when compared to a longer 10-15 day antibiotic treatment course.3 Although the general recommendations for treatment stay the same, there are several new updates in the 2016 guidelines that are important for pharmacists to be aware of that can prevent unnecessary antibiotic use and reduce healthcare cost.

Taking the “pain” out of opioid conversion

“If we know that pain and suffering can be alleviated, and do nothing about it, then we ourselves, become the tormentors.”
Primo Levi – Italian-Jewish writer, chemist & Holocaust survivor.

According to the International Association for the Study of Pain, pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”1 It is estimated that over 120 million adults in the United States have experienced some kind of pain within the past 3 months, 11.2% suffer from chronic pain and 10.3% have reported a lot of pain.2 In 2010 the total annual cost of pain ranged from $560 to $635 million, exceeding the annual costs associated with heart disease, cancer and diabetes.3

Pain can be classified as acute or chronic. Acute pain is often nociceptive (protective and physiological in nature) and maybe due to trauma, surgery, labor, acute illness or medical procedures.4 Chronic pain tends to be more neuropathic (pathophysiological and harmful in nature) and has a cancer or noncancer etiology (fibromyalgia, diabetic neuropathy, post herpetic neuralgia, etc.).4 Neuropathic pain stems from a change in nerve function and transmission which provokes a dysregulation in neuronal signaling.5 Pain is among the most common reasons why a patient may seek medical care. It’s often considered the sixth vital sign and a core measure on how well the patient is being managed. Its very subjective nature and uniqueness to the sufferer make it difficult to differentiate between two individual’s pains. For this reason it is important to tailor treatment to each patient’s circumstances.

Around the early 19th century German pharmacist Friedrich Wilhelm Adam Sertürner isolated morphine from opium revolutionizing pain management. This segued the development of different opiates and opioids, which are now the gold standard for moderate to severe acute pain and chronic cancer pain.4 Opiates (morphine, codeine, and heroine) are naturally derived compounds from opium, while opioids (hydrocodone, hydromorphone, oxycodone, oxymorphone, levorphanol, meperidine, fentanyl, methadone) are synthetic compounds.4 At times it may be necessary to convert between these agents and/or routes of administration due to lack of efficacy, development of intolerable side effects, change in patient status or practical considerations such as cost or availability.

Gammaitoni et al introduced a 5 step guide for converting from one opioid to another.3 This approach includes a global assessment of the patient, utilizing open ended questions and PQRSTU pneumonic (precipitating factor, quality, radiation, severity, timing and you) to help determine the etiology of the pain.5

(Continued on page 8)

References:

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Taking the “pain” out of opioid conversion
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Step 1: Obtain an overall assessment on the patient’s pain
Step 2: Add the total daily opioid usage including all long acting and short acting agents to morphine equivalents
Step 3: The choice of the new opioid is made with patient considerations in mind
  - previous opioid experiences determine potential efficacy and tolerability
  - route of administration
  - drug-drug or drug-interaction
  - cost and availability
Step 4: Using the morphine equivalents, a dose range is determined from the equianalgesic table and breakthrough pain medication doses are assessed

The lack of complete cross-tolerance among opioids should be taken into consideration and the chosen agent’s dose should be reduced by approximately 33%. Rescue and breakthrough doses can be calculated as 10-20% of the total daily opioid dose or 25-30% of the single standing dose.

The following table lists some of the opioids and their corresponding parenteral and oral (PO) doses in morphine equivalents:

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Parenteral</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>—</td>
<td>20-30</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>—</td>
<td>30</td>
</tr>
<tr>
<td>Fentanyl*</td>
<td>0.1</td>
<td>—</td>
</tr>
<tr>
<td>Meperidine†</td>
<td>75</td>
<td>300</td>
</tr>
<tr>
<td>Methadone‡</td>
<td>10</td>
<td>3-5</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Codeine</td>
<td>130</td>
<td>200</td>
</tr>
</tbody>
</table>

*The dose of transdermal fentanyl in μg/hr is approximately 1/2 the 24-hour dose of oral morphine. (eg. 100 μg/hr transdermal fentanyl = 200 mg/day po morphine).

†Metabolite, normeperidine, has a long half-life (12—16 hrs), which can lead to accumulation resulting in CNS toxicities (ie. agitation, seizures). Should not be used to manage chronic pain.

‡Recent data has shown that methadone may be much more potemt than originally believed, particularly when patients have been receiving other opioids for long periods of time and at high doses. Researchers believe this may be due to the partial NMDA antagonist properties of methadone. Estimates put the equianalgesic ratio of po morphine to po methadone at 4-14:1. 24

Step 5: Efficacy and tolerability should be continually reassessed and patient should be followed closely for the first 7-14 days after change

Switching of opioids should be a multifaceted approach considering patient specific factors and not just a simple mathematical calculation. In 2003 the Joint Commission on Accreditation of Healthcare Organizations (now The Joint Commission) listed opioid conversion charts as an intervention for improving quality of pain management. 6 Most conversion ratios present in literature are based on older and single dose studies that do not correctly portray long term dosing or relative agent potency. Several authors have conducted systematic reviews of opioid switching data with the consensus that further trials would be needed in order to obtain a more clinically applicable opioid conversion ratio. 5, 7, 8, 9 This lack of data has led the authors to conclude that a more individualized approach is needed and current ratios should be taken as ballpark estimates and not definitive guidelines. 5, 7, 8, 9 Gamaitoni et al states “in the face of what at best is an inexact science, a blend of empirical reasoning, and disciplined application of clinical principles, all coupled with artful practice and close follow-up, is requisite”. 5

References:

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Stress Ulcer Prophylaxis

**Stress-related mucosal injury** is a term used to describe erosions in the gastric mucosa that occur in most patients with acute and/or life-threatening illnesses. The damage appears as multiple, small erosions confined to the mucosa or it may be deeper and extend into the submucosa. The mucosal lining of the gastrointestinal tract normally sheds and replaces every 2 to 3 days. However, during stress-related mucosal injury, this process is extended due to inadequate blood flow to support replacement process which leads to superficial erosions and the surfaces of the bowel to become denuded.

Stress-related mucosal injury occurs in approximately 70-90% of critically ill patients within 24 hours of ICU admission. Oftentimes, these damages appear to be clinically silent; however, they can promote bleeding and microbial translocation. In about 5% of ICU patients, these damages can cause: clinically significant bleeding within 24 hours; a spontaneous drop in blood pressure > 20 mmHg; increase in pulse > 20 beats per minute; and/or drop in hemoglobin > 2 g/dL. The risk factors for stress ulcers are mechanical ventilation > 48 hours, coagulopathy (platelets < 50,000, INR > 1.5, aPTT > 2x control), circulatory shock, severe sepsis, multisystem trauma, severe head injury, burns involving > 30% of the body surface area, renal or hepatic failure, and steroid therapy.

A prospective study by Cook et al. evaluated the incidence of bleeding in ICU patients and identified a 48.5% mortality rate for patients with clinically significant bleeds compared with 9.1% for other patients (p < 0.001). In addition to an increased mortality rate, stress-related mucosal bleeding has prolonged hospital stay causing an impact on hospital costs. The goal of prophylaxis for stress ulcers is to prevent clinically significant bleeding from stress ulcers. Without prophylaxis, clinically apparent gastrointestinal bleeding occurs in as many as 25% of ICU patients.

The methods of prophylaxis are either to block the production of gastric acids or the use of cytoprotective agents that protect the damaged areas of the gastric mucosa without altering gastric acidity. Histamine type-2 receptors antagonists (H-2 blockers) and proton-pump inhibitors (PPIs) are two drug classes that are commonly used to block the production of gastric acids. The two H-2 blockers of choice are Famotidine IV 20 mg every 12 hours and Ranitidine IV 50 mg every 8 hours. Accumulation in renally impaired patients (CrCl < 50 mL/min) can lead to neurotoxicity (confusion, agitation, seizures). The PPIs of choice are Lansoprazole 30 mg via nasogastric tube (NGT) daily, Omeprazole 30mg NGT daily, and Pantoprazole 40mg IV daily. The advantages that PPIs have over H-2 blockers are a greater reduction in gastric acidity, once daily dosing (i.e. longer duration of action), and no tolerance with prolonged use. The PPIs require no dose adjustments in renal failure, however it is hepatically metabolized. Compared to H-2 blockers, PPI have been speculated to have higher incidences of *Clostridium difficile* and pneumonia. Another viable option is Sucralfate 1 gram every 6 hours. This drug is a protectant, but it has no effect on gastric production. Instead, it promotes the healing of gastric and duodenal ulcers through forming a viscous covering that shields the denuded surface.

References:

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Healthcare facilities have been designated as a safe haven for those who are very sick and cannot improve on their own, but not all that glitters is gold. In fact, healthcare facilities run the risk of nosocomial infections, which are defined as infections obtained in service within 48 hours of admission. Those who are most likely to obtain an infection are those who are already sick and immunocompromised, such as cancer patients, HIV patients, newborns, the elderly, and those in the critical care unit. Bacteria is everywhere, and if conditions are right, fungal species and viruses can survive. A hospital is no exception to that statement. The amount of pathogens usually depends on amount of traffic, moisture, number of people in the environment, and whether the material of the surface is conducive to growth. While the cleaning staff does provide a good effort against bacteria and other pathogens; it is important that other members of the health care team (Physicians, Pharmacist, Nurses, etc.) contribute as well towards a cleaner hospital and work environment. Although the cleaning staff puts in a good effort and a fair fight against bacteria, fungal, and viral pathogens, the patient care team, consisting of doctors, nurses, pharmacists, and physical therapists, radiologists, secretaries, cafeteria workers, and all those who help run the hospital must also contribute to the fight against nosocomial infections.

Most common carriers of bacteria are people themselves. The bacteria reside on skin, hair, clothes, jewelry, underneath nails, and everywhere else. Bacteria becomes more pathogenic and dangerous when someone becomes immunocompromised or is exposed to certain conditions where bacteria can thrive. Recently, there was an abstract presented at the IDWeek convention this past October that highlighted a study performed at Duke University Hospital. Investigators tested the nurses’ scrubs, and the results found that troublesome bacteria, such as MRSA and Pseudomonas, were found on the scrubs, specifically on the arms, pockets, and midriffs. Nurses have the most contact with patients, so these results are not at all shocking. Another study was performed on medical students’ white coats, and the results showed that despite no visible soilage on the white coats, bacterial loads were found on the sleeves and the pockets. However, there has not been any study that can prove nosocomial infections occur because of “unclean” scrubs and white coats, but it certainly does not hurt to take extra steps to decrease the risk.

Even if we are clean ourselves, we cannot forget about the tools that we use daily to go about patient care. There have been studies conducted in which investigators have found that the mobile phones, pens, and stethoscopes that healthcare workers use can also act as reservoir for bacteria. One study investigating phones and keyboards in the ICU and another study investigating stethoscopes in the same setting found that all three tools harbored nosocomial bacteria, such as A cinetobacter and MRSA. Another study focusing on pens have found Staphylococcus and Enterococcus on pens that were not wiped down between patient visits. This can be especially troublesome with the high volume of traffic in and out of patient rooms with said phones, pens, stethoscopes, and keyboards even in non-ICU units.

Despite the seemingly impending doom of nosocomial infections with all the bacteria
surrounding patients and healthcare workers, they can be prevented with the appropriate precautions. Listed below are some general steps that healthcare workers can do themselves:1,2,6,7,8,9

• Observe good hand-washing hygiene i.e. use antibacterial sanitizer scrub before entering and leaving patient rooms, wash hands thoroughly with antibacterial soap before and after patient contact
• Keep nails short and clean, no fake nails
• Wear gloves when handling with patients as well as plants if they are around
• Wear appropriate clothing i.e. scrubs, clean clothes every day, shoes that are easy to clean
• Have shoes designated for the hospital and shoes designated for travel in order to minimize the spread of bacteria outside of the hospital.
• Have scrubs and white coats washed by hospital laundry facility; if not available, hospital must offer instructions on how to launder garments to its workers
• If necessary, remove all jewelry i.e. working in clean rooms, working in the sterilization facility
• Follow precautions on patient rooms if necessary i.e. contact and droplet precautions call for gowns, gloves, and masks
• Perform daily cleaning of touchscreen devices using isopropyl alcohol swabs
• Wipe down pens and stethoscopes in between each patient with isopropyl alcohol swabs
• Practice cleaning workstations with isopropyl alcohol at the start of each shift (i.e. wipe down keyboards, screens, mouses, phones, etc.)

It is no secret that bacteria exists in a hospital, which is something to be concerned about especially when dealing with extremely sick patients. However, it is within our own individual duty as health care professionals to take the necessary steps to reduce the amount of bacteria within the hospital.

References:
1. Guidelines for Environmental Infection Control in Health-Care Facilities Available at: http://www.cdc.gov/hicpac/pdf/guidelines/eic_in_HCF_03.pdf
The Centers for Medicare & Medicaid Services (CMS) continues to develop new standards that are designed to improve the quality of healthcare. In 2010, the Institute of Safe Medication Practices conducted a large survey involving almost 18,000 nurses concerning the requirements in the CMS Conditions of Participation Interpretive Guidelines on administering medications within 30 minutes before or after the scheduled time.\(^1\,\,^3\)

The survey was clear in showing the complexity behind satisfying the CMS’s “30-minute rule”.\(^2\) Nurses are expected to adapt to the constantly changing methods of drug delivery, increasing number of prescribed medications per patient, and rising number of patients assigned. These factors collectively contribute to an increase in pressure on the nursing staff and would sometimes mislead them to consider shortcuts and workarounds, which have the potential to cause medication errors.\(^3\)

Timely administration is extremely important for certain time-sensitive medications, which makes the CMS “30-minute rule” appropriate.\(^1\) This rule however does not apply to other medications where timely administration does not critically affect the outcomes. Although the CMS acknowledges the improvements that can be made to this rule, hospitals are still held accountable according to the Interpretive Guidelines.

According to the ISMP, developing a clear policy with exact definitions is critical for the satisfaction of this standard. At University Hospital the following definitions have been prepared:

<table>
<thead>
<tr>
<th>Medications Not Eligible for Scheduled Dosing Times</th>
<th>One time doses specifically timed for procedures (On Call Doses) Drugs prescribed on an as needed basis (PRN)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medications Eligible for Scheduled Dosing Times</strong>&lt;br&gt;Time Critical scheduled medications</td>
<td>Medications with an early or late administration of &gt; 30 minutes might cause harm or have significant negative impact on the intended therapeutic effect. These medications must be administered within 30 minutes before or after their scheduled dosing time for a total window of 1 hour&lt;br&gt;Antibiotics- Vancomycin, Aminoglycosides&lt;br&gt;Anticoagulants- Enoxaparin (Lovenox) Doses &gt;40 mg&lt;br&gt;Insulin- Aspart (Novolog), Lispro (Humalog)&lt;br&gt;Immunosuppressive agents- Tacrolimus (Prograf), Mycophenolate (CellCept), Cyclosporine (Neoral, Sandimmune)&lt;br&gt;Pain Medications- Oxycodone (OxyContin), Morphine (MS Contin) Medications scheduled more frequently than 4 hours</td>
</tr>
<tr>
<td><strong>Non-time-critical scheduled medications</strong></td>
<td>Medications for which a longer or shorter time interval to administer is allowed since the prior dose does not significantly change the medication’s therapeutic effect or otherwise cause harm&lt;br&gt;Medications prescribed for daily, weekly, or monthly administration may be administered within 2 hours before or after the scheduled dosing time, for a total window of 4 hours&lt;br&gt;Medications prescribed more frequently than daily but no more frequently than every 4 hours may be administered within 1 hour before or after the scheduled dosing time, for a total window that does not exceed 2 hours</td>
</tr>
<tr>
<td><strong>Missed or late administration of medications</strong></td>
<td>When the scheduled medications eligible for scheduled dosing times are not administered within their permitted window of time, Patient Care Services (PCS) will use EPIC tools such as “In Basket Message” to communicate issues requiring immediate action. All of the communications are received in the pharmacy department and need response in a timely manner.</td>
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The ISMP has issued a supportive guideline composed of recommendations to assist institutions in achieving satisfactory reports with regards to the timely administration of scheduled medications.

<table>
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<tr>
<th>TOPIC</th>
<th>DESCRIPTION</th>
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<tr>
<td>Adequate staffing</td>
<td>The institution should maintain appropriate staffing levels both in the pharmacy department and patient care units in order to facilitate the medication utilization process.</td>
</tr>
<tr>
<td>Justification of early or late administrations</td>
<td>Staff should identify acceptable reasons for early, late, or omitted administration or scheduled medications.</td>
</tr>
<tr>
<td>Improve MAR documentation standards</td>
<td>Require staff responsible for the administration of medications to document the exact time the drugs are administered, rather than just initiating the MAR entry.</td>
</tr>
<tr>
<td>Develop a procedure to follow if medication administration is early or delayed</td>
<td>Institutions should establish a clear procedure for the clinical staff to follow if administration of a scheduled medication has been delayed or administered early.</td>
</tr>
<tr>
<td>Event reporting</td>
<td>Establish a process for reporting of untimely administration of all time-critical scheduled medications even if the reason of the untimeliness was documented.</td>
</tr>
<tr>
<td>Data analysis</td>
<td>Continuously analyze data in order to identify patterns leading to timely and untimely administrations of scheduled medications. Data should be collected in order to improve the satisfaction of this quality standard and the overall quality of care.</td>
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Timely administration of scheduled medications is a standard originally designed to assist institutions in improving the overall quality of care. There are multiple studies conducted to evaluate the clinical impact of timely administration of scheduled medications. Although the value behind timeliness of administration of scheduled medications is clear, multiple challenges in the workflow exist thus limiting its feasibility. Institutions should consistently develop ways to monitor the administration of medications and processes to improve the timeliness of medication administration.

References:
3. Updated Guidance on Medication Administration, Hospital Appendix A of the State Operations Manual (SOM) Centers for Medicare and Medicaid Services (CMS) ref: S&G12-05 Hospital Rev 12.02.11 MM.05.01.11

Contributed by: Hamza ElHouati, 2017 PharmD Candidate Fairleigh Dickinson University-School of Pharmacy and Health Sciences
Change in Strains for the Flu Vaccine of 2016-2017 Season

The flu (influenza) vaccine is recommended for the flu season, which takes place from October through April within the Northern Hemisphere. The common flu shot contains an inactivated viral vaccine that is annually updated due to the constant changing nature of the influenza virus. The frequent antigenic shifts of this virus force government agencies such as the Center of Disease Control (CDC) and the World Health Organization (WHO) to constantly update new strands of the flu vaccine.¹ Vaccines are changed for most seasons in anticipation of the new viruses that are predicted to circulate for the following year. Clinical trials have shown how defense from antigenically similar viruses of vaccines runs for at least 6 to 8 months.²

For the 2016-2017 flu season, there has been a change in the strains composed in the vaccine. The three main strains are A/California/7/2009 (H1N1)pdm09-like virus, A/Hong Kong/4801/2014 (H3N2)-like virus and a B/Brisbane/60/2008-like virus (B/Victoria lineage). The four component vaccine will contain the additional strain of B/Phuket/3073/2013-like virus (B/Yamagata lineage), which is different from the previous year’s flu vaccine.²

Each year, flu vaccine recommendations are made by the Advisory Committee on Immunization Practices (ACIP), a division of the CDC, which base there decisions on the recommendations from the World Health Organization. The Food and Drug Administration (FDA) ultimately regulates the flu vaccines in the United States and decides which strains to concoct in the flu vaccines.²

In order to examine the flu vaccine, there needs to be a reevaluation of Influenza A and B, which cause the disease in humans. After examining various cases of the Influenza A (H1N1)pdm09 virus that were collected from September 2015 to January 2016, WHO had found that the virus “A/California/7/2009”, was antigenically similar to the A(H1N1)pdm09 virus. Since October 2015, WHO has found that there is an emerging number of cases with the sub-clades of 6B.1 of the A(H1N1)pdm09. The A/Hong Kong/4801/2014 strain has been shown to be effective against the A(H3N2) sub-clade 3C.2a and inhibited viruses better in egg propogation experiments. It is important to look at the egg propogation experiment because it could initiate changes that could affect the antigenicity.³

In many countries, Influenza B viruses of the B/Victoria/2/87 and B/Yamagata/16/88 lines have been shown to circulate. B/Brisbane/60/2008 or B/Texas/2/2013 viruses has been found to well inhibit against the recent influenza B viruses and are recommended for the 2016 southern hemisphere flu season. B/ Phuket/3073/2013 was shown to do well against the cell cultured and egg-propogated Influenza B viruses, and thus WHO recommended them in quadrivalent vaccines for the 2016 southern hemisphere flu season.³

Additional recommendations made by the ACIP, along with the changes in the strains of the flu vaccine were made. The ACIP does not recommend the use of Live Attenuated Influenza Virus (LAIV) due to the low effectiveness against A(H1N1)pdm09 within the past 3 years. Also the recommendations for vaccines for patients with egg allergies were modified as well. Healthcare providers are now recommended to observe patients with egg allergy for 15 minutes rather than 30 minutes for any anaphylactic related reactions. Any patients with a history of severe egg allergy are recommended to receive their vaccinations within an in-patient or out-patient medical setting, so that a provider could intervene quickly when necessary.²

References:

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Welcome New Pharmacist

Dr. Arun Mattappallil earned his Doctor of Pharmacy degree from the College of Pharmacy and Health Sciences at St. John’s University in New York in 2011. After graduation, he completed his postgraduate year 1 (PGY-1) Pharmacy residency at the Veterans Affairs Hospital in Buffalo, New York. During this time, he developed strong interest in infectious diseases and he went on to complete his PGY-2 infectious diseases pharmacy residency at the same Veterans Affairs Hospital. Dr. Mattappallil has an adjunct faculty appointments with the Rutgers Ernest Mario School of Pharmacy and the Rutgers School of Health Professions, where he precepts pharmacy students and teaches physician assistant students. He is a member of the American College of Clinical Pharmacy (ACCP), the American Society of Health-System Pharmacists (ASHP), and the Society of Infectious Diseases Pharmacists (SIDP).