Pharmacy News

UNIVERSITY HOSPITAL
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Special Points of Interest:

P&T Update

Formulary Additions

- **Lidocaine 4% Patch Formulary Addition.**
  Formulary addition with additional automatic substitution of Lidocaine 5% to Lidocaine 4% patch orders by pharmacy department – Approved

- **Intravenous (IV) Immune Globulin (IG) (Gammagard®) liquid backorder**–
  - IVIG has multiple indications. Subtle differences exist among the various IVIG brands. UH preferred brand is Gammagard®. A national backorder of Gammagard® had depleted available inventory to less than 200 grams. This prompted pharmacy to work with the division chief of Neurology, Peds Neurology and Allergy/Immunology to allow automatic substitution to Privigen® brand during the period of shortage and stock out.

  - Temporary Formulary addition of Privigen® brand & automatic substitution during IVIG Gammagard® stock out

Formulary Deletions

- All formulary deletion requests were approved for deletion (see below).
  - Cyclosporine non-modified 25mg, 100mg caps, 5000mg/50mL oral liquid
  - Levothyroxine 125mcg, 150mcg, 175mcg tablets
  - Mupirocin cream
  - Spironolactone-Hydrochlorothiazide (HCTZ) 25mg-25mg tablet
  - Calcium gluconate 500mg tablet

Line of Extension - approved

- Prismasol & Phoxillum Solutions Line Extensions
  - Formulary line extensions with restriction to Nephrology and Surgical Intensive Care Service – Approved
- Generic cyclosporine modified formulation of 25mg, 100mg caps, 5000mg/50mL oral liquid
- Fluorescein strip
  - It was recommended to procure fluorescein/proparacaine eye drop as automatic substitution anytime there is fluorescein strip stock out.
  - Temporary Formulary addition & automatic substitution during fluorescein strip stock out

Policies & Procedure/Floor stocks

- **707-500-110 High Risk/ High Alert (HRHA) Medications and Look Alike/ Sound Alike (LASA) Medications - Revised**

  The updates include:
  - Subcutaneous Heparin and heparin flushes administration does not require an RN double-check prior to administration
  - Continuous IV infusion and titration of Heparin is a High Risk/High Alert process that requires medications to be independently checked by another RN for accuracy of drug and dosage/rate.
  - Subcutaneous Insulin administration does not require an RN double check prior to administration.

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P&T Updates
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- Continuous IV infusion and titration of Insulin is a High Risk/High Alert process that requires medications to be independently checked by another RN for accuracy of drug and dosage/rate.
- Also for epidural/intrathecal medications, dual RN signatures on the MAR are required in accordance with the Epidural analgesia policy 601-100-0935

- **707-500-115 Standard Concentrations for Intravenous (IV) Infusion Medications (Adult and Pediatrics)- Revised**
  The updates include:
  - Addition of PENTObarbital Standard Mix: 2500 mg/500 mL and Concentration: 5 mg/mL
  - Addition of Vasopressin Standard Mix: 20 unit/50 mL and Concentration: 0.4 units/mL
  - These additions apply to both Adult, Neonatal & Pediatric Standardized Continuous Infusion Drug Concentrations.

- **Safe Prescribing, Dispensing and Administration of Oral Methotrexate – Approved**
  - The purpose of this policy is to provide guidelines to ensure the safe prescribing, administration, dispensing and monitoring of patients receiving oral methotrexate

- **UH Anti-Infective Dosing Adjustment Guideline – Approved**
  - The purpose of this guideline to optimize anti-infective dosing based on indication for use and renal function. This is meant as an aide to clinical decision providers and pharmacists when entering/verifying anti-infective agents for patients.

- **707-400-102 Drug Recall P&P revision – Revised**
  - The update includes that only for Class I recalls, there will be notification from the pharmacy management to patients and the healthcare personnel. Class II and III recalls will be communicated monthly to the P&T Committee.

- **707-500-122 Automatic Therapeutic Exchange Policy (ATEP) revision – Approved**
  Policy revision to reflect :
  - IVIG substitution allowed from Gammagard® to Privigen® during national shortages
  - Magnesium IV replacements of 1G and 2G interchangeable by pharmacy to premix, pharmacy batch in 50mL or 100mL or any base solution for magnesium replacement runs

- **Dose Rounding of Chemotherapeutic and Biologic Agents – New P&P – Approved**
  The purpose of this policy is to provide guidelines allowing automatic dose rounding of chemotherapeutic to less than 5% & biologics to less than 10% of ordered does to the nearest vial size.

Management of Epidermal Necrolysis with Cyclosporine

Epidermal Necrolysis is a potentially fatal skin reaction involving the loss of the cutaneous and mucosal membranes. It includes Steven Johnson Syndrome (SJS) which involves less than 10% of body surface area (BSA) and Tumor Epidermal Necrosis (TEN) which is skin detachment greater than 30% of body surface area (BSA). Epidermal necrosis is caused by specific gene polymorphisms and over two hundred medications but the major offending drugs are sulfonamides, anticonvulsants, beta lactams, nevirapine, and acetaminophen.

Symptoms include sore throat, fever, conjunctivitis, skin lesions and blisters. Its complications comprise of dehydration, shock, and thromboembolism; thus, management often involves general supportive care measures such as fluid administration, cessation of the offending drug, and heparin.

Currently there are no set guidelines for the management of SJS/ TEN, but some clinicians prescribe short term use of high dose systemic corticosteroids to help with treatment. However, this is controversial because corticosteroids may impair wound healing and has also not shown any benefit in later course of the illness. On the other hand, cyclosporine, which is an immunosuppressive agent, has been tested in numerous studies and meta-analysis and has shown benefits in reducing mortality by 60%. One study conducted by Gonzales-Herrada, et al. at a Burn Unit in Madrid found that majority of patients with epidermal necrolysis admitted there reached a BSA stabilization within the first 3 days of treatment and a complete re-epithelialization within the first 12 days when given cyclosporine oral dose of 3 mg/kg/day. Though the exact mechanism of action is unknown, it is speculated

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that cyclosporine's benefit in EN stems from its ability to arrest the disease progression.

Through numerous meta-analysis, retrospective studies and systemic reviews, cyclosporine has shown to reduce mortality in epidermal necrolysis with little side effects. It is well tolerated and efficacious both as a monotherapy and as dual therapy with medium-/high-dose intravenous corticosteroids (50–250mg/day). Common dosing regimen used in majority of the studies is 3–6 mg/kg body weight/day of a cyclosporine formulation with good bioavailability as initial dosage divided in two daily doses. Blood levels need to be monitored with a plasma concentration aim of 150 to 200 ng/ml, measured before morning drug administration. Though cyclosporine seems promising in epidermal necrosis, it should be noted that the drug is contraindicated in patients with severe renal disease, severe infections, or internal malignancy and additional large studies are needed to further support the current evidence.

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The Smart Pill: A Technological Approach to Ensuring Medication Adherence

Background:

Medication adherence is the extent to which patients take their medication as prescribed by their doctor. This is important to ensure the patient gets the optimal therapeutic outcome from their medication. Some factors that impact adherence include forgetfulness, disorganized behavior, cognitive impairments, and having a poor understanding of the reasons for taking a certain medication. As the duration of therapy and the number of medications a patient has to take increases, nonadherence also increases.

As many as 50% of patients fail to adhere to, or comply with physician prescribed treatment regimens. It is estimated that the problem costs about $290 billion in emergency-room visits and other avoidable medical expenses in the United States. Studies have shown that non-compliance causes 125,000 deaths annually in the US, leads to 10 to 25 percent of hospital and nursing home admissions, and is becoming an international epidemic. In an effort to increase compliance with medications, technology is starting to play a big part, especially sensors.

How it Works:

The ingestible sensor is a device that allows patients, families, and physicians to measure when the medication is ingested and adherence patterns in real time, relate pharmaceutical compliance to important physiologic metrics, and take appropriate action in response. The device can be incorporated into a tablet during tablet compression, placed inside a hard gelatin capsule during capsule filling, or attached to the surface of a tablet or capsule using an edible adhesive layer.

In 2012, the FDA has approved the world's first electronic "Smart Pill" called Ability MyCite (aripiprazole tablets with sensor). Abilify MyCite, used for bipolar disorder and schizophrenia, has an ingestible sensor about the size of a grain of sand, embedded in the pill that records that the medication was taken. The sensor is activated when it comes into contact with stomach acid and sends a message to a wearable patch the patient wears on their rib cage. The patch transmits the information to a mobile app via Bluetooth so that patients can track the medication on their smartphone. The sensor is able

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to track when the pill was taken and the dosage as well as other things such as sleep patterns, heart rate and blood pressure. Patients can permit their caregivers and physician to access the information through a web-based portal.

Impact:

With a sensor that allows for the detection of these important patient-specific metrics, it will provide healthcare professionals to get a more comprehensive picture of what is happening, granting a more accurate and beneficial intervention. The continuous measurement and rapid sharing of data between patients and caregivers offers opportunities for diagnosing disease, tailoring treatment and responding to new information quickly. In the future, this technology has the ability to be integrated into more medications, using them for other chronic disease states such as diabetes and hypertension. However, other methods to ensure compliance should be used alongside the sensor. This could be anything from follow up telephone calls, medication reconciliation and using a personalized, up-to-date medication list for patients to keep with them at all times. Patient adherence can substantially decrease unnecessary costs and improve patient outcomes, so it is very important that patients are compliant.

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Artificial Pancreas Device System

The Artificial pancreas device system is a group of systems which does the function of regulating the blood glucose. The device system uses a continuous glucose monitoring (CGM) system and insulin blend drive. The CGM is calibrated by a blood sugar tool such as a sugar meter. CGM and insulin mixture pump are connected to a computer–controlled algorithm. A closed-loop system, autonomous system, or automated insulin delivery are other names used to refer to the artificial pancreas device system. Other than monitoring the blood glucose levels, artificial pancreas device system also adjusts insulin delivery automatically to lower high levels of glucose and reduce cases of low blood glucose, with little to no patient input. The blood sugar levels are regulated twenty-four hours a day. It is effective for people who live with Type I Diabetes (Trevitt & Wood, 2016). There are no competitors for the artificial pancreas device system. This is the first glucose controlling device which has been approved by the FDA. Data from the device was evaluated by the FDA from a clinical trial which had 123 participants with Type I Diabetes. It is the first kind of technology that has offered patients with Type I Diabetes the freedom to monitor the levels of blood sugars consistently and manually. However, the device has not yet been fully automated as an artificial pancreas. The patients with Type I Diabetes will still need to figure out the number of carbohydrates in their food and enter that information in the system. The system will only be for people at least 14 years of age and over. The device is currently undergoing trials for the young patients who are 14 years or younger (Cobelli & Kovatchev, 2011). The artificial pancreas system device monitors the glucose levels continuously. A computer algorithm finds out if the blood sugar levels are too high or too low. If the levels are too high, the device gives the right insulin dose that will help in lowering the level of blood sugar. A small catheter inserted underneath the skin and fixed to the insulin pump helps the device in controlling sugar levels. After approximately three days, the insulin delivery site needs to be changed. If the levels of blood sugar are too low, the insulin delivery is automatically shut down. The artificial pancreas measures the levels of glucose every five minutes and administers or withholds insulin automatically. Some of the risks associated with the system include hyperglycemia, hypoglycemia, and redness or irritation of the skin on the place where the device has been infused (Doyle, et al 2014).

The system enhances the current process. Type I Diabetes patients inject themselves with insulin and glucagon after vigilantly testing blood glucose with a glucose meter, calculate insulin doses and administer the right levels of insulin. The system has helped people to continuously monitor their glucose levels because this

device is automatic and shows the levels of insulin needed promptly. This device however, does not work for those with type II diabetes. Also, it is not a cure for diabetes but improves the quality of life for the people who have this condition (Thabit & Hovorka, 2016).

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The Effect of Electronic Health Records

Electronic health records (EHR) have emerged as fundamental technology in the healthcare sector. However, there is mixed reception to their adoption in hospital settings. While the new technology includes merits such as enhanced efficiency and improved record keeping, there are concerns about the safety of information stored in such systems. Following increased incidents of cyber attacks and breaches to private information systems, there are concerns that patient information may be leaked to third parties, a prospect that might compromise the privacy of the patients (Entzeridou, Markopoulou & Mollaki, 2018). Studies have since been conducted to outline the scope of EHR and the preparedness of various facilities to adopt the new technology. Moreover, the views of both patients and physicians on the ideality of the EHR have been intensely reviewed in different studies.

According to Entzeridou, Markopoulou and Mollaki (2018), there is a generally positive reception of the EHR. The study which is based on a convenient sample of physicians and patients indicates that the new technology has drastically improved the work environment within the hospitals. Furthermore, the study highlights the views of the respondents that the adoption of EHR has significantly enhanced decision making.

According to the respondents, the time spent reviewing patient files and records has been shortened significantly. As such, the physicians are able to make informed decisions faster.

On the other hand, Entzeridou, Markopoulou and Mollaki (2018) point out that the coordination between different healthcare professionals has improved drastically following the adoption of the EHR. According to the study, interdisciplinary teams are more efficient and information sharing between the various factions is faster. Nurses have more direct contact with the doctors, a prospect that the study associated with improved treatment outcomes. Also, it is possible to share information between the various stakeholders involved in the treatment process in real-time (Entzeridou, Markopoulou & Mollaki, 2018). In addition, the study suggests that the EHR has enhanced the culture of consultation between physicians since they can easily share data remotely.

The study by Rezaeibagha, Win and Susilo (2015), however, indicates that the suggested negative implications of the EHR include the economic burden that they would impose on the facilities. The initial cost of installation of the system as well as the management of the system is relatively costlier compared to the paper-based system according to the submissions by the physicians involved in the project. Also, the study notes that physicians were skeptical about the time that will be needed to train them on the new systems (Rezaeibagha, Win & Susilo, 2015). Failure to roll out such essential training would prevent effectiveness and efficiency of the EHR. Therefore, physicians argue that the workflow in the facilities adopting the EHR might be affected significantly.

On a different note, Rezaeibagha, Win and Susilo (2015) suggest that the electronic model will create new loopholes that could be exploited to compromise patient data. According to Entzeridou, Markopoulou and Mollaki (2018), however, the storage of patient information on the electronic systems could be a liability, especially in instances of downtime. It could be difficult to access the stored information in cases of power outages and when the systems break down. Therefore, it is necessary to have a hybrid information system that includes both paper and electronic records. Campanella et al. (2015) suggest that the degree of contact between the healthcare professionals

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The Effect of Electronic Health Records

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and the patient could be significantly reduced when the electronic health records are adopted. According to the study, most nurses would spend more time on their computers and electronic devices, a significant deviation from the conventional approach of direct contact between the patients and the nurses. Therefore, the delivery of patient-centered care could be compromised.

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Medication Reconciliation

Healthcare is known to be a collaborative effort, and it is essential that proper communication is maintained throughout the continuity of care. This includes obtaining the patient's medication history, which can be done through a process called medication reconciliation. According to The Joint Commission, "Medication reconciliation is intended to identify and resolve discrepancies – it is a process of comparing the medications an individual is taking (and should be taking) with newly ordered medications. The comparison addresses duplications, omissions, and interactions, and the need to continue current medications.3" This process is an approach towards one of TJC's national patient safety goals of improvement in safe medication use.

One setting where medication reconciliation is especially useful is in the emergency room, where the patient's self-management at home is transitioned to acute care by providers in the emergency department, and then possibly to an additional stay in the inpatient ward. Upon arrival, the patient's history is taken and they are triaged according to their initial assessment. Although the obvious priority is to treat the acute condition leading to the visit, management of the patient's overall health needs to be addressed. This includes all of the medications that the patient is taking at home, which may be for the maintenance of their other health conditions. Knowledge of this information also reduces the potential for medication errors, making viable a more inclusive means of screening for duplications and interactions.1 Development of a more structured method of obtaining medication histories led by pharmacists, can lead to improved accuracy, and allows proper recommendations to be made when discrepancies are present.2

Complete medication reconciliation includes an interview with the patient or caregiver, and cross referencing medication bottles they may have, medical records from previous admissions, and reaching out to outpatient pharmacies or other providers for clarification.1 The latter may be more accurate sources of what was prescribed to the patient, but communication with the patient is necessary because we also want to assess how the patient is taking their medications. This helps bring forth any issues pertaining to adherence, which is pertinent information in instance such as asthma exacerbations, uncontrolled seizures, and several other reasons for ER visits.

Medication reconciliation has always been a part of obtaining a patient's medical history, but it is still very young as its own entity. Especially with the ongoing advancements in technology, there exists endless opportunities to fine tune this aspect in patient care.

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Stop the Bleed – Andexanet Alfa for Anticoagulation Reversal of Major Life Threatening Bleeding

Direct factor Xa inhibitors are a class of anticoagulants widely used for the treatment and prophylaxis of VTE and prophylaxis for stroke in patients with atrial fibrillation. These agents work within the clotting cascade to inhibit factor Xa-mediated conversion of prothrombin to thrombin and include the following agents: rivaroxaban (Xarelto), apixaban (Eliquis) and edoxaban (Savaysa). When compared to warfarin, these agents are non-inferior with regards to efficacy but have a slightly better safety profile when it comes to bleeding events, particularly intracranial hemorrhage which can have devastating consequences.

The current guidelines for anticoagulant reversal developed by the Neurocritical Care Society and Society of Critical Care Medicine recommend that in the setting of intracranial hemorrhage, 4-factor prothrombin complex concentrate (4-FPCC) or activated PCC (aPCC) be used for reversal of anticoagulation if within 3-5 half lives of drug exposure or liver failure. These agents provide coagulation factors II, VII, IX and X and are considered to be the antidote for vitamin K antagonists like warfarin. While anticoagulant reversal has not been shown to directly improve clinical outcomes, administration of 4-FPCC or aPCC has been shown to prevent hematoma expansion. Additionally, the American College of Cardiology also recommends the use of 4-FPCC for anticoagulation reversal in the setting of major bleeding. At University Hospital, we use the aPCC product FEIBA for all major bleeds. However, this will be replaced with 4-FPCC product Kcentra as soon as the medication is released from shortage.

In May 2018, the FDA approved a new agent for anticoagulant reversal aimed specifically at direct and indirect factor Xa inhibitors. Andexanet alfa (Andexxa) is a recombinant modified factor Xa protein that acts as a decoy and binds to factor Xa inhibitors, preventing the inhibitors from binding to endogenous factor Xa, and thereby neutralizing the anticoagulant effect. Currently, andexanet carries an FDA approval for use in patients treated with apixaban or rivaroxaban requiring anticoagulant reversal in the setting of life-threatening or uncontrolled bleeding. The dosing scheme is as follows:

Andexanet alfa Dose Based on Apixaban or Rivaroxaban Dose			
FXa inhibitor	FXa inhibitor last dose	Timing of FXa Inhibitor Last Dose Before Andexanet alfa Initiation	
		<8 Hours or Unknown	*≥8 Hours*
Apixaban	≤5 mg	Low dose[¥]	Low dose[¥]
	>5 mg/unknown	High dose[*]	
Rivaroxaban	≤10 mg	Low dose[¥]	
	>10 mg/unknown	High dose[*]	

[¥] Low dose: 400 mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 4 mg/minute IV infusion for up to 120 minutes

[*] High dose: 800 mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 8 mg/minute IV infusion for up to 120 minutes

Evidence supporting the efficacy and safety of this reversal agent is summarized as follows:

Trial name	Study population	Intervention	Endpoints	
			Efficacy	*Safety*
ANNEXA-A (Phase III)	Healthy older volunteers, aged 50-75 Given apixaban 2.5 mg BID for 3.5 days	Andexanet low dose[¥]	↓ Factor Xa activity vs. placebo ≥ 80% anti-factor Xa activity reversed	N/A
ANNEXA-R (Phase III)	Healthy older volunteers, aged 50-75 Given rivaroxaban 20 mg daily for 4 days	Andexanet high dose[*]		
ANNEXA-4 (Phase IIIb/IV)	Patients ≥ 18 y/o with major bleed who received last dose of apixaban or rivaroxaban ≤ 18 hours of andexanet administration Mean age – 77 years old (n = 227) Bleed type – 61% intracranial; 27% GI Mean time to andexanet tx – 4.7 hours	Andexanet low[¥] or high[*] dose depending on agent, dose and timing	↓ Factor Xa activity Excellent or good hemostasis at 12 hours – 83% of patients	30 day thrombotic event– 18% (n =12) Death – 15% (n = 15)

[¥] Low dose: 400 mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 4 mg/minute IV infusion for up to 120 minutes

[*] High dose: 800 mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 8 mg/minute IV infusion for up to 120 minutes

While the evidence is limited and the safety data is alarming with regards to the incidence of thrombotic events, andexanet will likely become standard of care for reversal of life threatening bleeding secondary to anticoagulation with apixaban or rivaroxaban. However, there are currently several trials being conducted globally to further determine the efficacy and safety of andexanet alfa as a reversal agent for direct and indirect factor Xa inhibitors. When making the decision to reverse anticoagulation, all patient factors including thrombotic risk should be considered and weighted against any potential benefit. Additionally, goals of care should also be discussed with the patient and family, when feasible since life threatening bleeds are often detrimental and reversal agents have not been shown to directly improve outcomes.

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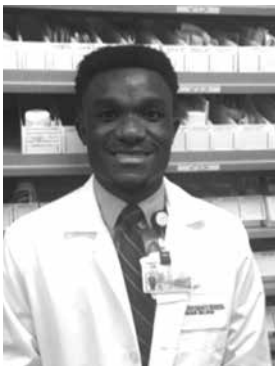
Welcome to Two New Pharmacists

Park Hwee, Pharm. D.

Dr. Hwee graduated from Ernest Mario School of Pharmacy at Rutgers University and worked for St. Mary's Hospital in Passaic before joining University Hospital. She is very excited to be part of the great team at UH and is eager to learn the new system. Outside of work, she enjoys watching hockey games and NASCAR races. She is a big fan of March Madness, loves ice cream, and believes in "better late than never." I like to challenge and expand my horizon.



Ernest Pianim, Pharm. D.

Dr. Pianim received his Pharm D. from Regis University in Denver, Co in 2017. As a Newark kid and a graduate of Science Park High School, it has always been a dream to work in the city of Newark and be part of the University Hospital team. On his time out of work, he enjoy traveling to experience new cultures and systems around the world.

Welcome to Pharmacy Technicians

Denise Tom, CPhT

Denise Tom graduated with a Bachelors of Arts in Psychology at Kean University. She worked at CVS pharmacy for 8 years as a Lead Pharmacy Technician and Inventory Specialist and is Nationally Certified by PTCB. She transitioned to hospital pharmacy and worked at Jersey City Medical Center for over 4 years and over 1 year at Hackensack University Hospital at Westwood. She also worked at the Hudson County Jail for 1 year. Her hobbies are traveling, reading and working out.

Christian Salinas, CPhT

Residing in Jersey City for a majority of his life, Christian had the advantage of getting to know a multitude of different people. Becoming a pharmacy technician back in 2014 was like second nature; his people skills, dedication and can-do attitude helped him become the technician he is today. Starting at Walgreens in 2014, Christian's skills were put to the test while also learning new things along the way. 2 years later he became PTCB certified and also was given the title of Senior Certified Pharmacy Tech that same day, something he holds to the highest regard. Christian prides himself in being an asset and a valiant member of the team, and he hopes to do just that here at University Hospital.