

## 24TH ANNUAL MEETING ABSTRACTS

**EVALUATION OF A PHARMACIST ON-CALL PROGRAM IN A GENERAL PEDIATRIC CLINIC**

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**Background:** As the responsibility of a pediatric pharmacist expands into ambulatory care, demand for access to the unique knowledge base of pharmacists also grows. One way to increase access to pharmacists in this setting is the use of a pharmacist on-call service. While this service is well established for an inpatient pediatric pharmacist, no comparable service has been described in the outpatient pediatric setting.

**Methods:** The University of Oklahoma (OU) Physicians Pediatric Clinic has access to 3 clinical pediatric pharmacists who are employed by the department of pediatrics to an equivalent of one full-time employee (FTE) with responsibilities in outpatient, inpatient, and medical education. Outpatient responsibilities include a presence in the clinic four to seven half-days a week. Providers at the clinic were given various means by which to contact the newly developed pharmacist on-call program when a pharmacist was not present. A central phone number was disseminated, which was answered by one of three pediatric pharmacists. Additionally, providers were able to reach the on-call service through the electronic medical record (EMR) system on a dedicated electronic desktop, and email. A retrospective review was performed to describe the activities completed by the pharmacist on-call. Data collection included: provider type, method of contacting the pharmacist, type of question asked (e.g. drug information question, dosing question, medication appropriateness), time to answer the question, and whether or not the provider took the pharmacist's recommendation. Specific aims were to: 1) compile the number of questions received by the on-call pharmacist; 2) specify the types of questions that were asked of the on-call pharmacist; 3) calculate the time the pharmacist spent answering questions; and 4), describe the percentage of times that the provider used the recommendation for the patient.

**Results:** A total of 228 requests (0.6/day) were made through the on-call program between May of 2013 to June 2014, with the average time for each request taking 17.75 minutes (1-120 min). Of the 228 calls, faculty physicians were the primary callers (52%, n=118), followed by physician assistants (16%, n=38), and nurse practitioners (15%, n=36). Of the 15 categories of queries received, drug information

questions/medication recommendations (29%) were the largest group. Other services provided were dose recommendations (21%), medication error resolution (20%), and insurance formulary/prior authorization assistance (18%). The majority of queries made to the on-call pharmacists were through phone calls (39%) and the EMR (38%), either through direct messaging or through use of a central desktop. The recommendations made by the pharmacist were accepted 89% (n=204) of the time, indicating a benefit of the service.

**Conclusion:** With the expansion of pediatric pharmacist responsibilities into ambulatory care, on-call programs can provide valuable access to pharmacists to positively impact patient care through the provision of information and services.

**IMPROVING THE SAFETY OF PROBIOTIC THERAPY IN THE PICU: DEVELOPMENT OF A CLINICAL ALGORITHM AND SAFE HANDLING GUIDELINE**

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**Background:** Probiotic therapy has been suggested as a treatment for antibiotic-associated diarrhea (AAD), but supportive efficacy data for this indication is variable. Although probiotics are generally considered safe, potentially serious safety concerns exist in critically ill and immunosuppressed patients. These safety concerns are centered on the fact that probiotics contain live microorganisms. Thus, any breach in proper handling and administration of this product in children with central venous catheters may lead to transfer of probiotic microorganisms into the bloodstream. An additional concern is the possible translocation of ingested microorganisms across a poorly intact gastrointestinal epithelium leading to infection and/or transfer of antibiotic resistance to other microorganisms. Published reports of these safety concerns led to a moratorium on probiotic therapy in the pediatric intensive care unit (PICU) at CHCO. Recently, however, CHCO has reconsidered probiotic use in select PICU patients – but only after sufficient review of the literature, formation of a treatment algorithm, and completion of nursing education on safe handling and administration practices.

**Methods:** A multidisciplinary team of clinical pharmacists and dietitians critically reviewed literature on probiotic therapy. A PubMed literature search was performed using the following search terms: “probiotics” OR “lactobacillus” AND “critically ill,” and additional titles referenced in clinical review articles were

obtained. Risk factors for probiotic-associated bloodstream infections and evidence-based indications for probiotic therapy in critically ill children were identified. This information was used to create a PICU-specific algorithm to aid in clinical decision-making. A nursing guideline for “safe handling and administration of probiotics” and detailed administration instructions for probiotic medication files were also developed. **Results/Conclusions:** One-hundred forty-three citations were initially identified for review. Citations were excluded if they did not pertain to AAD in children (n=130), leaving 16 citations for evaluation. Data from these citations were pooled and a treatment algorithm was created. The algorithm identifies acceptable candidates for probiotic therapy using a risk-stratification process, absolute contraindications and suggested dosing strategies. A best-practice guideline was crafted for proper handling and administration of probiotics – with an emphasis on minimizing environmental and patient contamination. The treatment algorithm and administration guideline will be presented to the PICU quality, safety and practice council. After approval, publication of these tools will be disseminated throughout the PICU, added to CHCO formulary and shared with other inpatient units. The impact of this quality improvement initiative will be assessed via annual retrospective reviews of probiotic use in the PICU. Algorithm compliance and probiotic effectiveness will be monitored via chart review, and probiotic-associated bloodstream infections will be monitored via CHCO microbiology results.

### MARIJUANA IS LEGAL! NOW WHAT?

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**Background:** Legalization of medicinal and recreational marijuana on the individual state level has become an intensely debated topic. While the use of medicinal marijuana has been legal in Colorado since the year 2000, Colorado voters made history by becoming one of the first states in the nation to legalize recreational use of marijuana in 2012. Novel strains of marijuana featuring high cannabidiol (CBD) content and low tetrahydrocannabinol (THC) content have also gained national attention and popularity as a potential therapeutic alternative for pediatric patients suffering from debilitating medical conditions. With recent changes in legislation, easier accessibility, and increased interest as a therapeutic option, Children's Hospital Colorado (CHCO) has seen a significant upswing in the volume of patients using cannabinoids in recent months. Due to increasing prevalence in our patient population, the potential for therapeutic benefit, and the possibility for important drug interactions, CHCO felt it necessary to recognize the use of cannabinoid products, specifically the use of CBD

oil for the treatment of seizures and edible products for appetite stimulation. The use of cannabinoids in pediatric patients in a hospital setting is largely without precedent. In addition, there is not definitive guidance on the management of medicinal marijuana in the healthcare setting from a regulatory standpoint. **Methods:** In an effort to provide a stance and standardize an approach as an institution, an interdisciplinary team was tasked with the development of a formal policy and procedure to provide criteria and procedures for the use of cannabinoids while patients are treated at CHCO. Defining a procedure for addressing the use of these products proved to be multi-faceted, and many legal, ethical, and social implications were considered during its development. We would like to share how we embarked upon this challenge in our institution by describing our experience and solutions. Considerations that were addressed include but are not limited to: Parental compliance with Colorado State Statute and registering with the Medical Marijuana Registry, creation of a release and waiver of liability form for CHCO patients, defining the medical, nursing and pharmacist role in the process, addressing the stigma associated with the use of marijuana, and the safe storage of the product. **Results/Conclusion:** It can be safe to assume that the use of medicinal marijuana in the pediatric population will continue to expand based on the overwhelming response in the media and testament of patients and caregivers. In the year 2014 alone, 10 additional states passed legislation making provisions for the use of medicinal marijuana, specifically strains with high CBD:THC content. The increasing prevalence of medical marijuana necessitates a proactive approach to the use of medicinal marijuana within a healthcare system to help avoid the pitfalls and challenges that can arise.

### IMPLEMENTATION OF A NEONATAL STATUS EPILEPTICUS TREATMENT ALGORITHM

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**Background:** Neonatal seizures are common in many high-risk populations, but identification can be challenging and treatment is often variable. Higher seizure burden is associated with increased risk of childhood epilepsy and impaired neurodevelopmental outcomes. To reduce practice variation and time to treatment, an evidence-based treatment algorithm was designed and implemented by a multidisciplinary team specifically for neonates in status epilepticus, defined as a summed

duration of seizures of at least 50% of any one-hour period. Measures included number of neonates diagnosed with status epilepticus and treated with the algorithm, adherence to the algorithm, maximum concentrations and cumulative doses of anti-seizure medications pre- and post-implementation, and length of stay pre- and post-implementation. Future measures will include improvement in seizures vs death, cerebral palsy, and poor neurodevelopmental outcome and epilepsy at 6, 9, 12, 18, and 36 month compared to 2011-2012.

**Methods:** The neonatal intensive care unit (NICU) is a level four, referral only facility with 20% of yearly admissions monitored for suspected seizures/status epilepticus through the use of 24-hour neuro-telemetry. To construct the algorithm, existing guidelines from other institutions were reviewed and an extensive literature search performed. After review, intravenous simulations with Alaris smart pumps were conducted to address the time required for each anti-seizure medication to be completely delivered to the patient. A treatment algorithm was then designed with a specific order of medications, dose, infusion length, time period prior to reassessment, time period to escalation of treatment, and time period to de-escalation of treatment. Specific medications included phenobarbital, pyridoxine, levetiracetam, and midazolam. At all points throughout the algorithm, a neurologist provided real-time feedback regarding results of neuro-telemetry.

**Results/Conclusions:** In the 12 months prior to algorithm implementation in July 2014, 1.1 patients per month were diagnosed with status epilepticus. Since implementation, eight patients were diagnosed with status epilepticus and qualified for the algorithm. The maximum phenobarbital concentration was 66.6 mg/L (average 39.3 mg/L) compared to 74.8 mg/L (average 56.8 mg/L) in the pre-implementation group. Maximum phenobarbital loading dose post-implementation was 45 mg/kg, maximum levetiracetam loading dose was 70 mg/kg, and maximum rate of continuous infusion midazolam was 0.4 mg/kg/hr. While 100% adherence to the algorithm occurred in only one patient, length of stay decreased from 25.7 days to 12.2 days (47%). Reasons for non-adherence to the algorithm included implementation during new resident orientation, variation in medication sequence and timing, and delayed communication with neurology staff. Interpretation of results to this point is challenging due to the small number of patients pre- and post-algorithm implementation.

#### THE ESTABLISHMENT OF A PHARMACOGENOMICS CLINIC TO FACILITATE SAFER AND MORE EFFECTIVE PERSONALIZED PRESCRIBING

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**Background:** Increasing utilization and understanding of pharmacogenomics in the prevention of adverse drug events and achievement of rapid treatment success holds promise for improved patient care. This potential, however, is contingent upon clinicians' willingness to incorporate these principles into practice. In an effort to educate practitioners and guide patients with a history of medication-related adverse events or non-response, Boston Children's Hospital (BCH) established a collaborative outpatient Pharmacogenomics Clinic between the Division of Genetics & Genomics and the Department of Pharmacy. The clinic opened in August 2014 for referrals from both BCH and neighboring healthcare facilities without a pharmacogenomics service, accepting adult and pediatric patients. Co-managed by a pharmacist and geneticist, it also provides a practice site for a pharmacogenomics fellow. Initially operating one afternoon per month, a scalable design is in place for increased demand and frequency.

**Methods:** A BCH Pharmacogenomics Clinic referral generally consists of a testing and subsequent result return visit. During the testing visit, the goals are to: discuss the general science behind pharmacogenomics; document patient concerns and past medical history, focusing on unexpected drug responses; ensure no additive or synergistic comorbidities with pharmacologic implications are present; evaluate risks, benefits and limitations of pharmacogenomic testing, including available results and incidental findings; discuss insurance coverage and self-pay options; and obtain a signed Informed Consent should the patient and/or family choose the testing option. During the result return visit, past events are addressed in the context of results, and variant-specific recommendations for future therapies are discussed, including medications/medication classes to avoid or possibly dose adjustment. The results are provided to the patient/family, the primary care provider and the referring practitioner. Patients are advised to return for periodic reassessment, as pharmacogenomic evidence continuously evolves. When actionable variants are found, testing of first degree relatives is suggested. The Electronic Health Record (EHR) is updated with notes for all visits and select variants with clinical evidence are entered into the patient's problem list, facilitating clinical decision support alerts within the EHR.

**Results:** Logistic challenges have become apparent as the clinic grows. At present, the geneticist serves as the provider of record for billing; however, an effort is underway to implement a Collaborative Drug Therapy Management (CDTM) policy designating the pharmacist as a provider and increasing scheduling flexibility. Additionally, the ability to bill for visits conducted via telemedicine is actively being pursued and would provide patients with a potentially attractive option.

**Conclusions:** The Pharmacogenomics Clinic at BCH focuses on supporting safer therapies and more effective prescribing, with overarching aims of improved outcomes, increased patient satisfaction, decreased costs, and increased pharmacogenomics awareness within healthcare. The dedicated time and space for these efforts have provided a novel realm for the necessary implementation of pharmacogenomic guidelines into practice.

#### DEVELOPMENT AND IMPLEMENTATION OF A PAIN AND AGITATION CONTINUOUS INFUSION TITRATION DELEGATION PROTOCOL FOR MECHANICALLY VENTILATED PATIENTS IN A PEDIATRIC INTENSIVE CARE UNIT

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**Background:** In mechanically ventilated pediatric patients, inadequate sedation may lead to increased exposure to narcotics and benzodiazepines, increased risk of tolerance and withdrawal and has an unknown impact on neurological development, especially in younger infants and children. Current practice permits medication orders for continuous infusion opioid and sedative agents to be written as a range which allows for nurse dose titration within our pediatric intensive care unit (PICU). Our current electronic medical record (EMR) does not require parameters to be entered for dose titration during provider order entry, leading to ambiguous directions as well as potential for over or under sedation. The omission of these parameters results in nurses having to make clinical decisions regarding medication dose titration, which is outside of their scope of practice. This protocol was developed to appropriately delegate clinical decision making responsibility from attending physicians to PICU registered nurses to titrate continuous opioid and/or sedative infusions to achieve analgesia and target sedation goals. **Methods:** An extensive medical literature review was performed by a team of pharmacists and presented to a multidisciplinary team of physicians, pharmacists, nursing leadership, and medical fellows. An institution-specific protocol was then developed by this team to provide the nursing staff with guidance for dose titration of fentanyl, morphine, dexmedetomidine and midazolam. A four-day pilot trial of the protocol was employed following nursing, pharmacist, and practitioner education. After pilot completion, care team feedback was collected and revisions of the protocol were made. **Results:** After final review and approval by P&T Committee and hospital medical board, PICU staff will be provided with further education and updated delegation protocol will be implemented

in full. Pre-and post-intervention data will be collected to evaluate patient time to extubation, FLACC and SBS scores, pain and sedation optimization based on defined goal scores, cumulative opioid and benzodiazepine dose requirements, number of unplanned extubations and PICU length of stay. **Conclusions/Future Directions:** Standardization of analgesia and sedation titration in mechanically ventilated pediatric patients using this protocol may improve sedation and analgesia treatment, prevent unintended extubation, decrease exposure to opioids and sedatives, and reduce intubation duration and PICU length of stay at our institution. Once full implementation is established, measurable outcomes data will be collected to determine true impact of protocol implementation.

#### DISCHARGE PRESCRIPTION INTERVENTIONS BY PHARMACISTS IN THE CHILDREN'S HOSPITAL COLORADO NETWORK OF CARE

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**Introduction:** Pharmacy services have expanded significantly over the past decade as institutions seek solutions to eliminate preventable harm. An area of recent growth in pharmacy services is discharge prescription review. Cesarz and colleagues (2013) reported significant pharmacist impact in piloting a program of prescription review for patients discharged from the Emergency Department. A similar opportunity was identified within the Children's Hospital Colorado Network of Care (NOC) Urgent Cares and Inpatient units. **Methods:** Two NOC sites initiated a pilot program of pharmacist review of outpatient prescriptions for patients discharged from the Urgent Cares and Inpatient units. All discharge prescriptions were entered by providers using CPOE in Epic and reviewed by pharmacists either real-time (during hours of pharmacy operation, 0600-0000) or at the start of the next shift. Prescriptions were reviewed for appropriateness of indication, dose, frequency, duration, route, formulation, drug interactions and allergy cross-reactivity. Providers were contacted if a prescription was determined to have a potential medication error (i.e. incorrect dose, frequency or duration) or if there was an opportunity for therapy optimization (i.e. palatability, rounding to measurable volumes). If a change was determined to be necessary, either the provider or the pharmacist contacted the filling pharmacy and/or the patient's family. In some cases, following clarification, the prescription was deemed appropriate and further information was documented in the medical record. To track this data, interventions were entered into the chart. **Results:** Data was collected from August 4th through December 31st, 2014. During that time, a total of 8,871 prescriptions (approximately 60 per day) were written.



Of all prescriptions reviewed, 124 (1.4%) were identified as either containing a potential medication error or containing an opportunity for therapy optimization. The most common medication classes requiring intervention were antimicrobials (57%), antiemetics (15%), and corticosteroids (9%). The most common reasons for intervention were decreasing the dose (37%), clarification (i.e. incorrect indication documented, confusing instructions, 21%), increasing the dose (14%), and changing the formulation (10%). Interventions were made on numerous high-alert medications including opioid narcotics and oral chemotherapy. Prescriptions requiring pharmacist intervention were written by both midlevel providers (48%) and physicians (52%). **Conclusions:** Our data demonstrated a lower rate of interventions than has been seen with other emergency department prescription review. We suspect this is partially due to treatment recommendations within institution-specific Clinical Care Guidelines, as well as having the majority of prescriptions written by pediatric providers. During the data collection process, medications with frequent prescription errors were identified, and provider education was conducted to address perceived knowledge deficits or misunderstandings. The education is ongoing and the impact has not yet been evaluated. Based on the success of the program, expansion to other NOC sites is anticipated for 2015.

#### IMPLEMENTATION AND INITIAL EVALUATION OF THE WITHDRAWAL EVALUATION OF ANALGESIA FOR NEONATES (WEAN) PROTOCOL

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**Introduction:** Opiate withdrawal occurs when patients are on high doses and long duration of treatment, with patients having a 50% risk of withdrawal when duration of treatment is 5 days or longer. Recently, a neonatal opiate weaning protocol was developed and implemented at our institution by a multidisciplinary team to standardize and reduce the risk of withdrawal. The purpose of this study was to evaluate the WEAN protocol as compared to previous prescribing habits. **Methods:** This was a retrospective chart review of infants in the intensive care nursery at University of California, San Francisco (UCSF) Benioff Children's Hospital whom required multiple days of opiate use between March 2014 and March 2015. Patients were excluded if they received opiates for more than 30 days, had prenatal opiate exposure, renal insufficiency, or did not commence weaning. Outcomes were evaluated by opiate wean length (in days) and total amount of morphine equivalent opiates used (in mg/kg). This

data was compared to patients on the WEAN protocol. **Results:** Between March 2014 and March 2015, there were a total of 15 patients on non-WEAN tapers. Nine patients received opiates between 5-6 days, with an average wean length of 8.95 days and used an average of 2.13 mg/kg of morphine equivalent opiates. Three patients received opiates between 7-14 days, with an average wean length of 8.5 days and used an average of 3.49 mg/kg of morphine equivalent opiates. Three patients received opioids between 15-30 days, with an average wean length of 18.8 days and used an average of 5.30 mg/kg of morphine equivalent opiates. There were a total of 5 patients on the WEAN protocol. Two patients on the protocol received opiates between 5-6 days, with an average wean of 4.65 days and used an average of 1.73 mg/kg of morphine equivalent opiates. Three patients on the protocol received opiates between 7-14 days, with an average wean length of 7.43 days and used an average of 1.99 mg/kg of morphine equivalent opiates. **Conclusions:** Preliminary results from WEAN protocol show taper durations are shorter in length and use less opiates when compared with physician-only managed opioid tapers.

#### PHARMACIST IMPACT ON MEDICATION RECONCILIATION IN A FREESTANDING PEDIATRIC CARE FACILITY

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**Objective:** Medication reconciliation continues to be a prioritized patient safety goal. Pharmacists play a valuable role as medication experts to ensure medication reconciliation is performed with the highest accuracy. Kosair Children's Hospital sought to implement a pharmacist-led medication reconciliation consult service, as well as pharmacist-taught medication reconciliation education for prescribers, in an attempt to improve medication reconciliation services at this institution. **Methods:** Between March 1, 2014 and September 31, 2014, the pharmacy department was consulted to perform medication reconciliation on patients admitted with greater than 10 medications. A pharmacist documented medications added, removed, and revised after interviewing the patient's caregiver, reviewing prescription bottles, or calling outpatient pharmacies. The pharmacist's impact on medication reconciliation was quantitated by the number of medications reviewed, number of interventions made, and time spent completing the task. Beginning in July of 2014, medication reconciliation education was provided by pharmacists for prescribers that included strategies for performing thorough medication reconciliations, as well as instruction on entering this information in an electronic medical record. The pharmacist's impact on prescriber education was quantitated by a knowledge

assessment survey taken by the prescriber before and after completing medication reconciliation education.

**Results:** Of the 801 medications reviewed during the study period, 64% required a pharmacist intervention. For any given patient encounter, an average of 3 medications were added, 3 medications were removed, and 4 medications were revised. The most common revisions included under dosing, incorrect route, and incorrect frequency of administration. The average amount of time spent on medication reconciliation was 43 min, with the total time spent being 37.5 hrs. Fifteen prescribers were provided medication reconciliation education and asked to answer a 9-question knowledge assessment survey. The number of “uncertain” responses before and after medication reconciliation education was 18 and 4, respectively. Prescribers’ scores increased by 8.4% after medication reconciliation education was completed.

**Conclusion:** Pharmacist-led medication reconciliation and pharmacist-taught medication reconciliation education have a significant impact on patient care in a freestanding pediatric care facility.

#### DESIGN AND EVALUATION OF A STUDENT-CREATED ORAL EXAM FORMAT IN A PEDIATRIC ELECTIVE

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**Background:** Flipping the classroom is one way to address students’ tendency to passively learn in the pharmacy curriculum, a habit which could lead to decreased readiness for the experiential fourth year. As flipped classrooms become more common, novel student assessment methods are needed. Student-created exam questions have been reported in the literature, as have student-presented patient cases. Though mock patient counseling has been used frequently in pharmacy education, and creation and enactment of employment-related scenarios has been reported in business education, student-created patient cases have not been described as a method of assessment.

**Innovation:** In our pediatric pharmacotherapy elective for third-year pharmacy students at Butler University, we utilized student-created oral case presentations for assessments in place of written examinations. Though case presentations have been utilized as part of the pharmacy curriculum within the Therapeutics course series, these cases are provided to the student, at which time the student evaluates the case and provides his or her recommendations. In our course, the student was responsible for creating the patient case (including baseline patient information and inclusion of drug- or disease-based problems). The students built their cases into web-based action maze

using the free software Quandary. Students then individually presented their patient case with potential treatment options to peers and faculty, asking the audience to make decisions and justifying their primary treatment selection with supporting literature and logic. Presentations were evaluated using a rubric created specifically for the assignment with three main categories: case pharmacotherapy, the Quandary build, and presentation and communication skills.

**Results & Conclusion:** Rubric inter-rater reliability as measured by intra-class coefficient (ICC) indicated a strong rubric. The overall ICC was 0.918 (0.765-0.973). Evaluation of the case pharmacotherapy showed the highest ICC (0.876) while the evaluation of the actual quandary build demonstrated some room for improvement with the lowest ICC (0.641). As the students created their own case parameters, the responsibility for truly understanding and engaging with the pediatric material was flipped to the learner. Creation of a patient case for presentation requires in-depth knowledge of the disease state, characteristics of affected patients, age-specific pharmacokinetic changes, and evidence-based treatment options. As instructors, this required a totally different mode of student support and preparation for assessment or “exams”. Instead of spending time writing exam questions, which is a time consuming but comfortable practice for faculty, time was spent creating the rubrics and providing support and feedback to our students as they developed their cases. Instructors learned to provide support to the students earlier and provide examples to facilitate the students in this activity, outside of their comfort zones. Overall student performance and response was both impressive and encouraging.

#### IMPACT ON STUDENT KNOWLEDGE OF PEDIATRIC PHARMACOTHERAPY FOLLOWING IMPLEMENTATION OF A CORE CURRICULUM DURING A GENERALIST APPE

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**Objective:** At our institution, the pharmacy practice model includes both clinical specialist and generalist pharmacists. While P4 students may elect to take an APPE with a pediatric clinical specialist, all students are required to complete a 5 week rotation with a generalist pharmacist, distinct from the institutional (i.e., hospital pharmacy) experience. Thirty-six students were assigned to complete a pediatric-specific generalist rotation in 2013-2014, a unique opportunity for students at our institution. During this APPE, students completed a core pediatric curriculum, which included

five topics: 1) general pediatrics review, 2) palatability and medication dosing and administration, 3) pediatric emergencies, 4) pharmacokinetics, and 5) parenteral nutrition. The objective of this study was to assess the impact of the core curriculum on student performance in areas of pediatric pharmacotherapy. **Methods/design:** For the 2013-2014 academic-year, a competency exam was developed to assess student knowledge of the five topics in the core curriculum. All students completing the pediatric generalist APPE took the exam during the first three days of the rotation (pre-test). The five core topics were then covered through a series of lectures and topic discussions, which were reinforced through hands on practical experience throughout the rotation. Students repeated the exam during the last three days of the rotation (post-test). A comparison of student performance on the pre- and post-test was evaluated using Student's t-test, with significance level set at  $p < 0.05$ . **Results:** Students performed significantly better on the post-test than the pre-test ( $p < 0.0001$ ), with a mean improvement of 13.6%. The mean improvement did not significantly differ between rotation blocks. Student performance improved in four of five core topics. The most dramatic improvements were seen in pharmacokinetics and parenteral nutrition. Ten students had prior pediatric experience (completion of a previous pediatric IPPE/APPE or the pediatrics elective, and/or or pediatric related work experience). Pre-test scores for those students with prior pediatric experience were significantly higher compared to those without prior experience, (mean difference of 8.4%,  $p < 0.0046$ ). Students with prior experience had significant improvements in the areas of pharmacokinetics, pediatric emergencies, and nutrition; while students without previous experience improved in all areas. Post-test scores were not significantly different between those with or without prior pediatrics experience. **Conclusions:** The core curriculum within the pediatric generalist APPE is a unique learning opportunity for our students that significantly improved student performance in areas of pediatric pharmacotherapy. Students' prior knowledge of general pediatrics was revealed by high pre- and post-test scores, which reflects previous exposure to this topic during the PharmD curriculum. The highly significant improvements seen in pharmacokinetics and parenteral nutrition may be due to minimal previous exposure to these topics, an emphasis on these initiatives within our hospital's pharmacy department, as well as the core curriculum.

#### THE DESIGN AND EVALUATION OF A PEDIATRIC SPECIALIZATION AT A SCHOOL OF PHARMACY

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**Objectives:** The pediatric specialization within the Doctor of Pharmacy degree at the Southern Illinois University Edwardsville School of Pharmacy was created to prepare students to pursue a career in pediatric pharmacy and to enhance student's competitiveness for pediatric pharmacy practice residency. The objectives of this study are to describe the pediatric specialization and to evaluate students on knowledge, skills and attitudes for treating the pediatric population. **Methods:** The pediatric specialization requirements are: 1) Completion of the pediatric pharmacotherapy elective (3 credit hours) and 2) a 1-credit hour independent study elective in the area of pediatric pharmacy practice during the third professional year; 3) Completion of two Advanced Pharmacy Practice Experience (APPE) electives (6 credit hours each) related to pediatric pharmacotherapy during the fourth professional year. The first elective is a pediatric APPE approved by the course coordinators and the Experiential Education Director and the second, more rigorous APPE is a pediatric elective only provided by faculty. A survey instrument evaluating student knowledge, skills and attitude towards numerous pediatric topics was administered to fourth year professional students ( $n=76$ ) at the start of APPE's for this initial cohort. The same survey will be repeated at the end of the fourth professional year for further evaluation. **Results:** During the first year of implementation, 17 students (22.1%) in their third professional year enrolled in the pediatric pharmacotherapy elective course. Of those students in the didactic course, 6 (35.3%) were accepted to continue in the specialization. Students with additional didactic pediatric coursework, consistently rated their perceived knowledge, skills and attitude at a higher measure of central tendency than their counterparts. All students in the pediatric specialization were interested in pursuing careers in pediatric pharmacy and 4 (66.7%) have committed to pediatric postgraduate training. **Conclusions:** Pharmacy students enrolled in a pediatric specialization are more likely to consider careers in pediatrics and demonstrate greater retention of knowledge and skills related to pediatric pharmacy.

#### PEDIATRIC MEDICATION SAFETY: AN ELECTIVE COURSE TO ADVANCE SAFE AND EFFECTIVE MEDICATION USE IN CHILDREN

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**Background:** Pharmacists play an important role in pediatric patient safety and medication error preven-

tion. To help pharmacy students gain knowledge and confidence in pediatric medication safety, a course was created to teach them to identify prescribing errors in children along with methods of error resolution and communication. The elective course began as an evolution of a clinical practice initiative in a university-based pediatric outpatient clinic. It was found that less than 5% of dosing errors identified from the general pediatric clinic were intercepted at the community pharmacy. This highlighted the need to incorporate pediatric dosing and education into the Doctor of Pharmacy curriculum. Real-time prescription reviews involving pharmacy students started as an independent study elective in 2007. Student interest in the experience, as well as increased pediatric faculty support, led to the creation of the Pediatric Medication Safety elective course in 2010.

**Course Structure:** The elective is offered as a 2-credit hour course to 2nd and 3rd professional year pharmacy students in both the fall and spring semesters. Students are enrolled from 2 campuses and class meetings take place using distance technology. In this course, students check prescriptions written by providers in a general pediatric clinic. Each student or student group is assigned a day of the week for prescription review. After their review, students are required to submit a summary of prescription errors to a faculty mentor and post one de-identified error to an online discussion board, including recommended communication of the error to the prescriber. Feedback is provided to the students each week. In-class discussions focus on medication errors observed, error prevention strategies, approaches for resolution, and tactics for successful communication. Students are also required to answer at least one drug information question from the clinic over the course of the semester.

**Results:** To date, 36 second and 38 third year professional pharmacy students have completed the course. Each student has reviewed an average of 570 prescriptions. The prescription error detection rate improved from 40% on pre-assessments to 93% during the course of the semester. When students were placed in pairs, the error detection rate increased from 82% as individuals to 95% as pairs. Student evaluations note that the ability to work on real world scenarios is appreciated and that their approach to pediatric prescriptions has changed as a result of completing the course. They also voice their improved confidence to work with the pediatric population as well as mechanisms for successful communication with prescribers.

**Conclusions:** The Pediatric Medication Safety elective provides students with opportunities to practice their skills as future pharmacists. This experience provides a strong foundation and awareness for causes of medication errors in children and the pharmacist's role in helping prevent and resolve those errors.

## POLYETHYLENE GLYCOL 3350 AND LACTULOSE USE IN CHILDREN FOR CONSTIPATION

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**Background:** Polyethylene glycol 3350 (PEG 3350) and lactulose are common pharmacologic agents used to treat children with chronic constipation; however there is no information available on long term stability or the mixing of PEG 3350 or lactulose with liquids other than water. According to one parental survey, children have difficulty adhering to constipation treatment, with an average adherence rate of <40%. Therefore, it is important to gain knowledge about ways to increase adherence to constipation pharmacotherapy. One way to do so is by mixing PEG 3350 or lactulose with liquids that a child may be more likely to drink. The purpose of this survey study is to assess the common liquids that are being used to mix PEG 3350, as well as identify prescribing practices related to PEG 3350 and lactulose. Our hypothesis is that clinicians will report that parents mix PEG 3350 with multiple liquids other than water and that prescribers prefer the use of PEG 3350 over lactulose.

**Methods:** This study was granted an exemption from the Institutional Review Board. A 7-item survey on the use and preparation of PEG 3350 and lactulose was administered electronically to pediatric providers in March 2015. The survey consisted of questions regarding patients seen with constipation and liquids used to mix medications. Participants were recruited using emails to the pediatrics department and pediatric gastroenterology department at a children's hospital in a tertiary care medical center. The primary objective was to determine the most common liquids that are used to mix PEG 3350. Descriptive statistics were used to analyze results.

**Results:** There were 13 responses to the survey, which is a response rate of 72%. Pediatricians were the majority of responders (9/13). There were 3 pediatric gastroenterologists and 1 nurse practitioner practicing in a pediatric clinic. 61.5% of responders see more than 5 patients per week with functional constipation. 46% of responders see more than 5 patients per week who are on PEG 3350. The three most common liquids used to mix PEG 3350 were water, apple juice, and other juice (not specified). However, providers report parents using milk, orange juice, formula, soda, and ice tea. Lactulose was prescribed for less than 5 patients per week by 85% of providers, and 92% prescribed lactulose oral solution instead of the lactulose oral packet.

**Conclusions:** PEG 3350 is most commonly mixed in water and juice, but a variety of liquids were reported by practitioners. These liquids should be further tested for stability after mixing with PEG 3350.



# ASSOCIATION BETWEEN ASTHMA PREVALENCE AND ENVIRONMENTAL TOBACCO SMOKE EXPOSURE IN SCHOOLCHILDREN FROM THE PITTSBURGH REGION

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**Background:** Environmental tobacco smoke (ETS) is a known risk factor for pediatric asthma. Despite access to healthcare and effective treatments, asthma prevalence remains high among Pittsburgh inner-city children. The purpose of the study was to evaluate the association between ETS and asthma prevalence among Pittsburgh schoolchildren. **Methods:** This study was approved by the institutional review board of Allegheny Health Network and informed consent/assent was obtained from all subjects prior to participation. Fifth graders from six Pittsburgh elementary schools were enrolled. Demographic information was collected through a self-reported survey. Prior diagnosis of asthma and risk of newly diagnosed asthma were assessed using an abbreviated, validated survey. Salivary cotinine levels were assayed by commercially available Enzyme-Linked Immunosorbent Assay (ELISA). Results were compared using a t-test. **Results:** A total of 146 subjects were enrolled (49.3% female, 50.7% male, 64.4% Caucasian, 31.5% African American, 78% public insurance). Saliva was available for cotinine analysis in 129 (88%) subjects. Of those, 29 (22%) had confirmed ETS exposure. The overall asthma prevalence among ETS and non-ETS exposed subjects was 62% and 32%, respectively ( $p < 0.05$ ). The prevalence of newly diagnosed asthma among ETS and non-ETS exposed subjects was 21% and 8%, respectively ( $p < 0.05$ ). **Conclusion:** These results demonstrate a significantly higher prevalence of asthma among schoolchildren from the Pittsburgh region with documented ETS exposure as compared to those without ETS exposure. Future efforts to improve asthma outcomes in the Pittsburgh region must incorporate smoking cessation strategies.

# PRESCRIBING PRACTICES FOR MANAGEMENT OF SPASTICITY IN PEDIATRICS POST-TRAUMATIC BRAIN AND SPINAL CORD INJURIES

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**Introduction:** Traumatic brain (TBI) and spinal cord (SCI) injuries can result in long term complications and significant impairments can result. One of the most frequent complications is spasticity. Despite lack of evidence to support the various pharmacological agents used in children, there is wide acceptance and utilization by clinicians. Additionally, evidence-based treatment guidelines for spasticity post-traumatic injuries do not appear to exist. The primary objective of this study was to identify the prescribing practices used for treatment of spasticity following trauma at a pediatric specialty rehabilitation hospital. **Methods:** This was a retrospective review of medical records from The Children's Institute (TCI) of Pittsburgh. The study was approved by the Institutional Review Boards at Duquesne University and TCI. Patients were included if they were admitted between January 2012 and December 2014, between the ages of 2 to 18 years, and diagnosed with spasticity secondary to TBI or SCI. Data collection included information on patient demographics, medical history, antispasticity therapy prior to admission and antispasticity therapy initiated during admission. Adverse drug reactions (ADR) and changes in spasticity severity based on Modified Ashworth Scale (MAS) and The Functional Independence Measure for Children (WeeFIM) were also reviewed. Data was analyzed using descriptive statistics. **Results:** A total of 72 subject records were reviewed based on age, date of admission, and ICD-10 codes. Fifty five were excluded (13 for diagnoses other than traumatic injuries and 42 for not having spasticity). Seventeen (28.8%; 76.4% male, 82.4% Caucasian) subjects met inclusion criteria. The median age was 14 (range 2-18) years. Eleven (64.7%) patients were prescribed antispasticity therapy prior to admission and were continued the same therapy throughout admission. Three patients were started newly on antispasticity medication during their stay. Twelve (85.7%) patients received oral baclofen alone or in combination with other antispasticity drugs [diazepam ( $n=4$ ), dantrolene ( $n=1$ ), diazepam and dantrolene ( $n=1$ ), and botulinum toxin ( $n=1$ )]. Two patients were on single therapy with botulinum toxin and diazepam, respectively. In addition to drug therapy, all patients had on-going occupational and physical therapies. Baseline MAS was done in 11 (65%) patients with median score 2.5 (range 1-4). All patients had WeeFIM assessment on admission and discharge. Six (35.3%) patients showed an improvement in their WeeFIM scores from admission (self-care mean score  $1.18 \pm 0.52$  and mobility mean score  $1.24 \pm 0.66$ ) to discharge (self-care mean score  $1.86 \pm 1.59$  and mobility mean score  $2.1 \pm 0.1.73$ ). There were no documented ADR. **Conclusion:** The majority of patients in this study received oral baclofen as part of their initial therapy.

Other drugs used included diazepam, dantrolene, and botulinum toxin. Although there were no documented ADR, it is difficult to conclude with certainty that none occurred. Future studies are needed to develop evidence-based protocols for managing spasticity in pediatric TBI and SCI.

#### RETROSPECTIVE REVIEW OF THE MANAGEMENT OF TRACHEITIS IN HOSPITALIZED PEDIATRIC PATIENTS WITH TRACHEOSTOMIES

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**Introduction:** Patients with artificial airways are at increased risk for developing bacterial infections in the trachea. These often require multiple rounds of antimicrobial therapy during hospitalization. Due to the increasing number of multiple drug resistant organisms, antimicrobial stewardship promotion is imperative, especially in patients who may receive numerous courses of antibiotics. The objectives for this review included: evaluation of documentation, practices of diagnosis and treatment of bacterial tracheitis in patients with tracheostomies, and identification of the most common pathogens cultured to guide potential changes in institutional empiric antimicrobial therapy. **Methods:** Study was an IRB-approved retrospective chart review from March 20, 2010-October 31, 2013. Inclusion criteria included the following: <18 years age, admitted to the Pediatric Intermediate Unit or Pediatric Intensive Care Unit, tracheostomy present with initiation of antimicrobial agent, antibiotic initiated for presumed bacterial tracheitis, and greater than one antibiotic administration documented. Patients were excluded if there were other infections, an infiltrate noted on chest radiograph or if antibiotic was used for prophylaxis as documented in the medical record. Patients were identified by running a usage report of all antibiotics used at institution via electronic medical record and cross referenced to a list of patients with a tracheostomy who are followed by the outpatient Home Ventilation Clinic. Primary analysis evaluated for basic diagnostic tools including C-reactive protein, procalcitonin, sputum culture, sputum gram stain, complete blood count, viral respiratory pathogen array, and chest radiograph. Secondary analysis assessed appropriateness of antimicrobial therapy based upon agent, dosing and frequency, duration of therapy, and time to optimization of therapy based upon sputum culture results. **Results:** A total of 1,104 antibiotic orders were evaluated, with 206 orders included in analysis. Twenty eight patients were identified, with a total of

81 separate treatment encounters analyzed. Results from the primary analysis regarding diagnostic tests showed the following incidences: procalcitonin-14/81 (17.3%), C-reactive protein-9/81 (11.1%), sputum culture-81/81 (100%), sputum gram stain-77/81 (95%), complete blood count-63/81 (77.8%), respiratory viral pathogen array-15/81 (18.5%), and chest radiograph-65/81 (80.2%). Secondary analysis revealed that the most common pathogen was a *Pseudomonas* species, which resulted in 18 of the patients (64.3%). Nine of the twenty eight patients had *Staphylococcus aureus* grow on culture with 6 patients (21.4%) having at least one culture with methicillin resistant strain and 3 (10.7%) with a methicillin sensitive strain. Multi-drug resistant organisms were cultured in 12 of the treatment encounters (14.8%). **Conclusion:** Based upon results, education will be given to providers to improve documentation, along with education regarding antimicrobial stewardship to aid in more appropriate selection of empiric antimicrobial therapy for presumed bacterial tracheitis. Possible development of an order set or treatment guideline to facilitate appropriate evaluation for tracheitis will be considered.

#### EVALUATION OF PROCALCITONIN LEVELS IN A PEDIATRIC CRITICAL CARE UNIT

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**Objective:** Procalcitonin may be a useful biomarker for bacterial infections, but its role in the diagnostic workup of presumed infections in children is not completely understood. Measuring procalcitonin levels could lead to a reduction in unnecessary antibiotic use. The objective of this study was to determine if procalcitonin levels are positively associated with bacterial infections in pediatric critically ill patients. **Methods:** This retrospective study included initial procalcitonin levels collected for a discrete rule-out infection time-period in pediatric patients who were admitted to the pediatric intensive care unit. Patient demographics including admit diagnosis, signs/symptoms of infection within 24 hours of procalcitonin level (serum white blood cell count (WBC) with differential, C-reactive protein (CRP), lactic acid, maximum body temperature), initial procalcitonin level, microbiological data (bacterial, viral, and fungal cultures), initiation of antibiotics, and number of antibiotic days for each discrete rule-out infection time-period were collected. Patients were stratified into two groups according to presence or absence of confirmed bacterial infection, defined as positive culture and/or positive chest radiograph in the presence of clinical signs/symptoms suggestive of infection. Nonparametric tests were employed to compare base-

line characteristics and procalcitonin levels between groups. All analyses were considered significant with  $p$  values  $\leq 0.05$ . A receiver operating characteristic curve (ROCC) was constructed to determine the usefulness of procalcitonin for predicting bacterial infection.

**Results:** Weight was greater in patients with bacterial infection compared to patients without bacterial infection (14.75 kg [8-29.18] vs. 10.7 kg [7.3-16.4], respectively;  $p=0.034$ ), as was height (87.5 cm [66.75-132.25] vs. 74 cm [61-99.5], respectively;  $p=0.046$ ). A greater number of patients with bacterial infection had an admit diagnosis of infection ( $p<0.01$ ). Values for WBC, bands, CRP, lactic acid, maximum temperature, and percentage of patients initiated on antibiotics were not different between groups ( $p=NS$ ). Neutrophil count was statistically greater in patients with bacterial infection compared to patients without bacterial infection (72.75% [55.1-82.7] vs. 64.6% [52.05-77.6], respectively;  $p=0.042$ ). Number of antibiotic days also was statistically greater in patients with bacterial infection compared to patients without bacterial infection (11 days [5.75-15] vs. 3 days [1.5-5], respectively;  $p=0.000$ ). Fifty-four (40%) of 135 procalcitonin levels were associated with a bacterial infection. Procalcitonin levels in patients with bacterial infection were significantly greater than levels in patients without bacterial infection (0.95 ng/mL [0.18-4.64] vs. 0.26 ng/mL [0.06-1.62], respectively;  $p=0.002$ ). Procalcitonin levels did not differ according to type of bacterial infection ( $p=NS$ ). Area under the ROCC was 0.654 ( $p=0.002$ ; CI 0.561-0.748). A procalcitonin cut-off level of 0.75 ng/mL yielded a sensitivity of 0.63 and a specificity of 0.64 for predicting bacterial infection. Higher procalcitonin levels were more specific but less sensitive.

**Conclusions:** Procalcitonin levels  $>0.75$  ng/mL were predictive of bacterial infection in pediatric critically ill patients; however, procalcitonin levels had no impact on antibiotic usage for these patients.

#### ACUTE KIDNEY INJURY WITH CONCOMITANT VANCOMYCIN AND PIPERACILLIN-TAZOBACTAM IN A CRITICALLY-ILL CHILD

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**Case Report:** Vancomycin and piperacillin/tazobactam (pip/tazo) are used as monotherapy or concomitantly in critically-ill children. Recent reports have described increased acute kidney injury (AKI) in adults receiving this combination compared to vancomycin alone, but no reports exist in children. This report describes a child who developed AKI with concomitant

vancomycin and pip/tazo. An 8 year-old girl with past medical history including cerebral palsy and tracheal stenosis was transferred from a long-term care (LTC) facility with respiratory distress and pneumonia. On hospital day (HD) 1, she was admitted to the PICU and began ceftriaxone and vancomycin 18 mg/kg IV every 8 hr (goal trough 15-20 mg/L). On HD 2, ceftriaxone was replaced by pip/tazo 100 mg/kg IV every 8 hr due to worsening clinical status, and vancomycin changed to q 6 hr after a trough of  $<5$  mg/L. On HD 3, pip/tazo was optimized to every 6 hr, and vancomycin unchanged with a trough of 17 mg/L. On HD 4, urine output (UOP) declined and serum creatinine (SrCr) increased to 1.16 mg/dL (374% above baseline), corresponding to a 73% decrease in estimated glomerular filtration rate. This was classified as AKI based on the pediatric-modified RIFLE criteria. A vancomycin trough was 37 mcg/mL, and antibiotics were changed to azithromycin and ceftriaxone. No additional nephrotoxins were noted. Furosemide and 25% albumin were initiated to augment UOP. By HD 5, she had a cumulative 18% positive fluid balance (5.5 L positive) and was switched to a furosemide continuous infusion. By HD 17, AKI had resolved and SrCr returned to baseline. From HD 27-31, she received pip/tazo for multi-drug resistant tracheitis with no evidence of AKI. On HD 31, she was discharged to a LTC facility. A child with respiratory distress developed AKI and fluid overload after concomitant vancomycin and pip/tazo, which resolved after discontinuation of these agents. This event was identified as a probable adverse drug reaction (ADR) using the Naranjo probability scale. Providers utilizing this combination should carefully monitor vancomycin troughs and renal function.

#### USE OF NALOXONE DRIPS IN PEDIATRIC PATIENTS: A RETROSPECTIVE MEDICATION USE EVALUATION

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**Introduction:** Naloxone has been the standard of care for full reversal of opioid overdose in the United States since the 1970s. More recently, newly available literature has led many hospitals to develop protocols to allow the use of naloxone drips to reduce the severity of common opioid side effects including pruritus, nausea and vomiting. The purpose of this study was to evaluate the use of naloxone drips in pediatric patients stabilized on opioids. In addition, patient's further opioid requirements were reviewed to establish possible effects of naloxone drips in partial reversal of analgesia effects. **Methods:** This study was approved by the institutional review board at Children's Healthcare of Atlanta. It is

a retrospective medication use evaluation reviewing all patients who received naloxone drips, in combination with an opioid via a PCA, at the Hughes Spalding campus of Children's Healthcare of Atlanta between January 1st, 2014 and July 31st, 2014. The review's primary outcome was increased opioid demand while the patient was on a naloxone drip and the secondary outcomes included naloxone indication, dose and duration of use. Individual patient charts were reviewed for information about primary disease state, naloxone dose, duration, indication, and patient demographics. Information was also collected about any increase in patient opioid requirements or the need for therapy for emergent pain. Thirty-one patients were reviewed. All collected data was analyzed to establish hospital trends and determine hospital-wide plan of action concerning future use of naloxone drips.

**Results:** Data was pulled for 31 patients who received naloxone drips at Hughes Spalding in the first 6 months of 2014. Patients' ages ranged from 6 yrs to 17 yrs of age. All patients were dosed with weight-based doses ranging from 0.88 mcg/kg/hr to 3 mcg/kg/hr. The majority of patients received either 1 mcg/kg/hr (n=14) or 2 mcg/kg/hr (n=9). Out of the 24 patients with documented indications the majority received the drip for pruritus (n=12), sedation (n=5) or both (n=5). Seven of the patients reviewed had no documented indication for use of naloxone drip. Twelve patients reviewed required increased opioids to control pain after the initiation of naloxone drip.

**Conclusions:** At Hughes Spalding 31 patients were observed who received naloxone drips with traditional opioid therapy. Though the use of naloxone for opioid side effect minimization has been studied in adult populations, data is limited in pediatrics. Doses accepted in adult medicine were associated with potential opioid reversal in these patients. In addition, 6 patients were prescribed naloxone for mild to moderate sedation though little data exists to support this indication. This data has encouraged Hughes Spalding to develop protocols to ensure the appropriate dose, indication and observation of naloxone drips in our population of patients.

#### EVALUATION OF ANTITHROMBIN III DOSES IN CRITICALLY ILL PEDIATRIC PATIENTS

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**Introduction:** Children have decreased levels of Antithrombin III (AT III) compared to adults and these levels may be further decreased during acute illness or thrombosis. Administration of exogenous AT III to patients with AT III deficiency can result in higher AT III levels, increased efficacy of heparin, and lower heparin infusion rates to achieve

therapeutic partial thromboplastin time (PTT) or activated clotting time (ACT). Additionally, higher AT III levels can result in more effective low molecular weight heparin dosing. The objective of this study was to evaluate the safety and efficacy of AT III doses rounded to available vial sizes versus partial vials in critically ill pediatric patients.

**Methods:** A retrospective review was performed to evaluate a cohort of pediatric patients, ages 0-18 years admitted to a 24-bed medical/surgical pediatric intensive care unit between June 1, 2012 and December 31, 2014 who received one or more doses of plasma derived AT III (Thrombate III, Grifols). The review consisted of patients receiving unfractionated heparin continuous infusions, subcutaneous low molecular weight heparin, or no anticoagulation. This review included patients receiving extracorporeal membrane oxygenation and continuous renal replacement. Data collected from medical records included AT III dose; AT III vial size; and AT III assay, PTT, ACT, hemoglobin, and unfractionated heparin infusion rate before and after the AT III dose was administered. Additionally, the medical record was reviewed for documentation of bleeding before and after AT III doses were given. The Mann-Whitney U test was used to compare the non-parametric data (SPSS Statistics version 17.0).

**Results:** During the study period, 80 doses of AT III were administered to 24 patients as doses rounded to full vial sizes (38 doses) or partial vials (42 doses). The ATIII assay recorded after the dose was administered was greater than 80% for 26 of the full vial doses (70.3%) and 16 of the partial vial doses (41.0%); four doses did not have a follow up ATIII assay recorded (1 full vial dose and 4 partial vial doses). For patients who received multiple doses of AT III, the average time between doses was 63 hours following full vial doses, and 40 hours following partial vial doses (p=0.011). Some patients had documentation of hemorrhagic events; however, these events were not solely attributed to AT III administration.

**Conclusions:** Patients who received AT III doses rounded to full vial sizes were more likely to have an AT III assay greater than 80% after the dose was given (usual goal 80-120%). Additionally, when multiple doses were needed, patients who received doses rounded to full vial sizes had a statistically significant longer interval between administrations. No bleeding events were identified which were solely attributed to AT III administration.

#### A RETROSPECTIVE ANALYSIS OF MEDICATION USAGE AND FACTORS ASSOCIATED WITH POLYPHARMACY AMONG PEDIATRIC PATIENTS IN AN OUTPATIENT SETTING

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**Introduction:** Our study aims to identify the pattern of drug usage among children in the outpatient setting to evaluate the prevalence of polypharmacy and identify factors associated with increased medication use.

**Methods:** The study population consists of all pediatric patients age 0-18 years old seen in the outpatient clinic, specialty clinic and Day Treatment Block of the Prince of Wales Hospital (PWH) who received prescriptions from the PWH Outpatient Pharmacy from January 1st 2013 to December 31, 2013. Outcomes measured include number of medications used per patient, prevalence of polypharmacy (use of  $\geq 5$  medications), class of medications used by patients and predictors of polypharmacy as indicated by odds ratio. Difference in prevalence of polypharmacy was determined using Chi-square test. Separate analysis of prevalence of polypharmacy was done-the first including all medications used and the second excluding medications with no active ingredient and/or limited absorption. Logistic regression analysis was used to identify factors associated with polypharmacy.

**Results:** A total of 4167 patients were included in the study. Average number of medications taken per month for all patients was found to be  $2.68 \pm 0.079$ . Among these patients,  $14.9 \pm 1.34\%$  of the population had at least one episode of polypharmacy during the study period and had an average of  $6.07 \pm 0.316$  medications per month. The second analysis showed a more conservative number with  $6.9 \pm 1.33\%$  of the patients with polypharmacy after exclusion of certain medications. For all age groups, dermatological and respiratory medications were the most commonly used medications. The three most commonly used medication by outpatient paediatric patients include Salbutamol ( $n=1300$ , 31.2%), Chlorpheniramine ( $n=1046$ , 25.1%) and Aqueous cream ( $n=979$ , 23.5%). Infants were less likely to be exposed to polypharmacy, with prevalence rate of 4%, followed by children (14.8%) and adolescents (16.9%). Gender did not contribute to prevalence of polypharmacy. The odds ratio for polypharmacy exposure was higher for individuals using Hydroxychloroquine (OR: 174.03,  $p<0.05$ ) dermatological medications (OR: 22.63,  $p<0.05$ ), medications for sensory organs (OR: 8.92,  $p<0.05$ ) and respiratory medications (OR: 8.67,  $p<0.05$ ). **Conclusion:** Our study suggests the average number of chronic medications used among the local pediatric population to be 2.68 medications per month. Although 6.9 to 14.9% of these patients may be on  $>5$  medications per month, individual assessment of each patient's regimen would provide insight to the appropriateness of multiple drug use. Patients with atopic disease states requiring dermatological, respiratory or sensory medications as well as patients with rheumatological disorders are at higher risk of polypharmacy. These patients may benefit from close monitoring for any drug related problems and negative outcomes as-

sociated with multiple drug use. Future investigation could be extended to negative outcomes associated with polypharmacy in children.

#### RITUXIMAB FOR NEUROMYELITIS OPTICA POSITIVE TRANSVERSE MYELITIS

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**Case Report:** There is limited data regarding the use of rituximab in pediatric patients for the use of neuromyelitis optica (NMO) positive transverse myelitis. We report the successful use of rituximab in a 12 year old diagnosed with NMO positive transverse myelitis after presenting with fever, headache, blurred vision, urinary retention, and sudden onset lower extremity weakness and pain. We also review the available literature supporting the use of rituximab for NMO positive transverse myelitis. The patient had received multiple doses of high dose steroids with negligible improvement. Due to persistent symptoms, rituximab was administered at a dose of 375 mg/m<sup>2</sup> intravenously once weekly for 4 wks for 2 cycles of treatment. Over the 6 mo course, patient did experience intermittent relapse on maintenance therapy of mycophenolate 250 mg twice daily and prednisone 10 mg daily that required additional treatment with high dose steroids and plasmapheresis. Although the patient experienced disease progression to the brain stem, clinical response to rituximab therapy is evident based upon reports of no dizziness, headache, eye discomfort, numbness, weakness or joint pain, as well as by the patient now being able to ambulate with minimal assistance at conclusion of cycle 2 of rituximab. Based upon this evidence, rituximab may be considered as an option for treatment of NMO positive transverse myelitis in pediatric patients.

#### BIVALIRUDIN ANTICOAGULATION DURING VA ECMO: A PATIENT CASE

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**Introduction:** To maintain patency of the extracorporeal membrane oxygenation (ECMO) circuit, precise and effective anticoagulation is required. Unfractionated heparin (UFH) is the predominant anticoagulant used at Children's Hospital Colorado (CHCO) due, in part, to its low cost and reversibility. UFH, however, has limitations including variability in dosing. This variability is due to altered binding of UFH to plasma proteins (platelet factor 4, fibrinogen, factor VIII and histidine rich glycoprotein) and the availability of antithrombin III (ATIII, heparin

co-factor). Children less than one year of age are particularly vulnerable to heparin resistance due to physiologically low concentrations of ATIII. We report a case of heparin resistance in an infant on VA ECMO, successfully managed with bivalirudin.

**Case Summary:** A 47 day old female (6.03 kg) was cannulated to VA ECMO secondary to respiratory failure and cardiovascular collapse from severe sepsis. UFH was initiated per CHCO protocol. After six days and multiple attempts to achieve a therapeutic heparin assay, the decision to transition to bivalirudin was made. Therapy was initiated with a 0.1 mg/kg bolus followed by 0.12 mg/kg/hr continuous infusion. The goal aPTT was 2.5 times baseline and was achieved within 24 hours. One day after initiation of bivalirudin, however, frank blood from the endotracheal tube was observed, so the aPTT goal was lowered to 2 times baseline. The patient remained on bivalirudin for an additional 10 days and no other adverse effects were noted. Bivalirudin was discontinued when the patient was de-cannulated. The patient was eventually extubated, improved and discharged.

**Discussion:** This case illustrates the ability of bivalirudin to quickly achieve therapeutic anticoagulation in a previously UFH resistant patient on VA ECMO. Bivalirudin, a direct thrombin inhibitor, is typically reserved for anticoagulation in patients with heparin induced thrombocytopenia (HIT). Although not FDA approved in children, it has been studied in cases of both HIT and heparin resistance. The dose of bivalirudin during ECMO, however, has not been established and published reports suggest a wide range of 0.028-0.5 mg/kg/hr. We elected to initiate therapy, using an intermediate dose, and follow aPTTs to aid in dose adjustments.

**Conclusion:** Bivalirudin represents an alternative method of anticoagulation in children requiring VA ECMO in which conventional UFH is unsuccessful. More research is needed to support the use of bivalirudin in critically ill children.

#### IMPLEMENTATION OF A VTE RISK ASSESSMENT TOOL AT A PEDIATRIC HOSPITAL

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**Introduction:** The rate of hospital-acquired venous thromboembolism (VTE) in pediatric patients is estimated to be 0.2%-0.6% of all hospitalizations with higher rates occurring in patients with central-venous catheters or trauma. Efficacy of risk-factor screening tools at identifying pediatric patients at highest risk of developing VTE has been established in the literature. In the present study, we describe the implementation of

a VTE risk assessment tool aimed at identifying those patients at highest risk for hospital-acquired VTE.

**Methods:** A VTE risk assessment tool was developed for the purpose of categorizing patients as low, moderate or high risk for development on VTE based on the presence or absences of known risk factors. In June 2013, this tool became a required portion of the nursing admissions process for all patients >12 years of age admitted to our pediatric intensive care unit. After tool completion, clinicians are directed to prescribe appropriate VTE prophylaxis based on risk stratification (serial compression devices (SCDs) or SCDs plus pharmacologic prophylaxis for moderate and high risk patients, respectively). Contraindications to prophylaxis are also reviewed as part of the assessment tool. Nurses and clinicians were educated regarding VTE and tool use.

**Results:** To assess tool implementation, chart reviews were conducted to assess VTE screen completion and accuracy as well as the appropriateness of prescribed prophylaxis. Based on review of 100 charts, screenings were completed on 86% of admissions and appropriate prophylaxis was ordered 68% of the time. Risk assessments were scored accurately on 66% of admissions. Reasons for inaccurate risk assessments included inappropriate risk assignment due to nursing misinterpretation of the tool.

**Conclusions:** After implementation of a VTE risk assessment tool, compliance with documentation requirements was not maintained at 100%. Accuracy of risk assessment and appropriateness of prophylaxis ordered did not improve over time, and further education is required to continue to improve these outcomes with a goal of reducing overall rates of VTE.

#### VANCOMYCIN DOSING AND SERUM TROUGH CONCENTRATIONS IN CYSTIC FIBROSIS PATIENTS: IS THE RELATIONSHIP PREDICTABLE?

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**Introduction:** Cystic fibrosis (CF) patients are known to have altered pharmacokinetic properties compared to otherwise healthy pediatric patients. Vancomycin is commonly used for the management of CF exacerbations, although optimal dosing has not been established. Most clinicians agree that vancomycin trough concentrations of 15-20 mg/L are desired for the treatment of CF exacerbations due to increasing antimicrobial resistance and decreased lung penetration. The objective of our study was to examine vancomycin dosing and associated troughs in CF patients and explore their association. **Methods:** We conducted a retrospective chart review of pediatric patients with CF who received vancomycin

at our institution between 2006-2012. Admission-level data were collected, including patient age and sex, vancomycin dosing regimens prescribed, and corresponding serum trough levels, where available. Descriptive statistics were used to characterize the sample. Chi square, Student's t tests, ANOVA, and Pearson correlation coefficients were used to test for associations between dose and trough level.

**Results:** A total of 31 patients received vancomycin during the study period, representing 41 distinct hospital admissions. Troughs were obtained in 40 of the admissions. Patient age ranged from <1 to 17 yrs, with an average age of  $12 \pm 5$  yrs. Initial vancomycin doses ranged between 45 and 100 mg/kg/day (mean =  $62.9 \pm 14.5$  mg/kg/day). The mean trough level was  $9.7 \pm 5.1$  mg/L, with 23 (57.5%) troughs <10 mg/L (mean dose =  $59.5 \pm 12.9$  mg/kg/day), 11 (27.5%) between 10-14.9 mg/L (mean dose =  $62.1 \pm 11.5$  mg/kg/day), 5 (12.5%) between 15-20 mg/L (mean dose =  $79.6 \pm 18.3$  mg/kg/day), and one (2.5%) >20 mg/L (dose = 50 mg/kg/day). Patients received an average of  $1.5 \pm 1.1$  dosage adjustments. Assessing final dosage regimens for each admission, doses ranged between 50 and 120 mg/kg/day (mean =  $78.8 \pm 16.0$  mg/kg/day). The mean trough level was  $13.6 \pm 4.4$  mg/L, with 9 (22.5%) troughs <10 mg/L (mean dose =  $83.2 \pm 25.2$  mg/kg/day), 18 (45%) between 10-14.9 mg/L (mean dose =  $75.8 \pm 10.8$  mg/kg/day), 9 (22.5%) between 15-20 mg/L (mean dose =  $81.2 \pm 13.0$  mg/kg/day), and 4 (10%) >20 mg/L (mean dose =  $77 \pm 20.1$  mg/kg/day). There was no significant correlation between first dose and corresponding trough level ( $r=0.272$ ,  $p=0.09$ ) or between last dose and corresponding trough level ( $r=-0.024$ ,  $p=0.882$ ). Despite the wide range of doses utilized, we were unable to ascertain a strong correlation between dosing and trough concentrations, and most patients never attained a trough of 15-20 mg/L.

**Conclusions:** In CF patients, vancomycin pharmacokinetics are erratic and unpredictable. Even very high doses (>100 mg/kg/day) did not always result in increased trough concentrations, and some patients achieved troughs of 15-20 mg/L with lower doses. This raises concerns of the utility of monitoring vancomycin troughs in these patients. Further studies should be conducted in the CF population to determine correlations between vancomycin dosing and trough concentrations and if higher troughs result in improved patient outcomes.

#### DOSING SCHEMES USED IN PRESCRIBING ADD/ADHD MEDICATIONS IN CHILDREN

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**Introduction:** Several medication treatment recom-

mendations have been developed to treat Attention Deficit Disorder and Attention Deficit/Hyperactivity Disorder (ADD/ADHD) in children and adolescents. Recommendations are generally based on age and/or weight. Further, there is available guidance for switching from one ADD/ADHD medication to another.

**Objectives:** To evaluate the ADD/ADHD medication dosing methods of children and adolescents in a family practice. Secondary objectives are to assess for prescribing trends between attending physicians and residents, and between medication classes.

**Methods:** A retrospective chart review was performed at a family practice from November to December of 2013 on ADD and ADHD patients who were less than 18 years old, diagnosed within the past five years, and prescribed at least one medication within that timeframe. Each medication was analyzed for appropriateness of dose and frequency, and prescribing trends were assessed based on the type of provider as well as the medication class.

**Results:** Of the 86 patients included, there were 84 ADD/ADHD medications initially started and 110 medication switches with a total of 135 physician encounters and 50 resident encounters. There were no statistical differences observed between physicians and residents for appropriate versus inappropriate dosing regimens ( $p=0.23$ ). Further, there were no significant differences between the dosing appropriateness of initial versus switched medications ( $p=0.60$ ) or the method of dosing used (standard, weight-based, or prescriber experience-based;  $p=0.54$ ). However, there were significantly more inappropriate doses (under dosed and over dosed) prescribed for methylphenidate products versus amphetamines ( $p=0.04$ ).

**Conclusions:** Dosing guidelines can be better utilized for prescribing ADD/ADHD medications in order to ensure proper dosing for pediatric patients especially for methylphenidate prescriptions.

#### A MODERN APPROACH TO TREATING INFANTILE HEMANGIOMAS IN PRETERM AND TERM INFANTS: A CASE REPORT

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**Case Report:** Infantile Hemangioma (IH) is a benign, vascular tumor in infancy and estimated to occur in 4% of infants. It has been noted in literature that low birth weight is the most significant risk factor, increasing to 30% incidence in preterm infants weighing < 1.5 kg at birth. Infantile hemangioma growth begins within the first several weeks to months of life. Seventy percent of cases are diagnosed within the first 2-5 months of life. Infantile hemangiomas vary in size, location, rate of growth, depth and degree of complication. Most IHs do not require medical or surgical intervention.

Proliferating IHs are referred to a Dermatologist as early as possible. Twenty-four percent of cases may lead to ulceration, cardiac or airway compromise and permanent disfigurement. Historically, treatment has included corticosteroids, interferon- $\alpha$ , vinca alkaloids, beta-blockers, surgical excision or laser surgery. Oral propranolol, a nonselective beta-adrenergic blocker, has become a well-accepted, FDA-approved treatment option for proliferating IH. However, systemic side effects accompany treatment including hypotension and bradycardia, hypoglycemia and hyperkalemia. Topical application of timolol has gained favor by providing similar results as oral propranolol without exhibiting systemic side effects.

A retrospective chart review was performed on 6 patients with infantile hemangiomas in the Neonatal Intensive Care Unit. I report the use of the ophthalmic solution, Timoptic (timolol 0.5%) applied topically to hemangiomas of 5 preterm and 1 term infant. Gestational age ranged from 23 weeks - 37 weeks and birth weight ranged between 0.43kg and 3.8kg. IHs were seen on the thigh, wrist, below the lip, labia, chest and forehead. Timolol 0.5% was prescribed by the Dermatologist. One drop was applied topically to the hemangioma 2-3 times a day. Five of the 6 patients (83%) received topical timolol three times a day; 1 patient received treatment twice daily. Timolol was applied by the bedside nurse until complete resolution of the infantile hemangioma. The 6 infants were 1.5 - 6 months old when topical timolol was initiated and received on average 68 treatment days. One infant completed therapy before discharge, 3 were discharged home on topical timolol, 1 infant was transferred back to a referring hospital on timolol and 1 infant remains on timolol at time of submission. Topical timolol was well tolerated by all 6 patients and no side effects including cardiovascular variances or skin irritation was noted at any time during treatment. In conclusion, Timoptic is a modern, therapeutic option when treating superficial infantile hemangiomas in both term and preterm infants. Since timolol was applied topically, systemic side effects were not seen compared to oral propranolol use. Timoptic was well tolerated and produced adequate, rapid results. Topical timolol is truly a modern, safe approach in treating infantile hemangiomas.

#### IMPACT OF EXPANDED RESPIRATORY VIRAL TESTING ON ANTIMICROBIAL USAGE AND LENGTH OF STAY

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**Introduction:** Diagnostic testing for respiratory viruses offering more robust information confirming a viral etiology may result in less antibiotic usage, less intensive care and shorter hospital stays. After our institution

implemented an expanded respiratory viral panel capable of detecting seven organisms not tested for on the previous panel, we examined its impact on antimicrobial usage, ICU length of stay (LOS) and hospital LOS.

**Methods:** The current study is retrospective cohort study of 617 patients admitted to CAMC Women & Children's Hospital during a two year period. To be enrolled, subjects had to be less than five years of age and have had a respiratory viral panel (RVP) performed within 24 hours of admission. Patients with culture confirmed bacterial infection were excluded. At the midpoint of the study period, the institution replaced its existing RVP using a direct fluorescence antibody (DFA) detection method capable of detecting nine viral pathogens with a polymerase chain reaction (PCR) method which detects sixteen viral and bacterial pathogens. For each subject, the study reviewed medical records and collected data on demographics, RVP results, antimicrobial usage, ICU LOS and hospital LOS.

**Results:** Thirty-one percent (103/329) of patients in the DFA group had positive RVP findings, compared to 74% (214/288) in the PCR cohort [ $p < 0.001$ ]. Almost all of the increased number of positive results was due to Rhinovirus ( $n=109$ ). Antimicrobial use was high in both groups but subjects in the PCR group were somewhat less likely to have antimicrobial therapy initiated than the DFA group (63% vs 71%,  $p < 0.05$ ). Duration of antibiotic therapy (PCR median 41 hrs [0-454], DFA median 42 hours [0-674]) and likelihood of a discharge antibiotic prescription was not significantly different between the groups. ICU admission was 20% in the PCR group compared to 37% in the DFA group ( $p < 0.001$ ). Median LOS was 2 days in both groups. ICU LOS was not different between the two groups.

**Conclusion:** These data suggest that the availability of a more comprehensive RVP may result in lower rates of antibiotic usage in children admitted to hospital with respiratory infections. The decrease in antimicrobial usage offers some cost savings but they are unlikely to offset the increased cost of the assay. However, even a modest reduction in microbial resistance evolutionary pressure may justify implementation. Subjects admitted during the expanded panel period required less frequent admission to ICU but it is unclear what role the assay played since ICU admission is a complex decision and not based on a single laboratory result. If the decrease in ICU admission is due to the assay's availability, this would result in cost savings and reduction in adverse events which would likely justify the cost.

#### PATTERNS OF ANTIBIOTIC USE IN CHILDREN ADMITTED FOR ASTHMA OVER THREE YEARS IN THE MIDST OF AN ANTIMICROBIAL STEWARDSHIP PROGRAM TARGETED FOR RESPIRATORY SYNCYTIAL VIRUS



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**Introduction:** Guidelines for treatment of asthma do not recommend antibiotic use during an acute exacerbation unless there is concomitant infection or co-morbid condition; however, antibiotics have been prescribed without justification in 16% to 22% in these instances. From 2012 to 2013, our institutional antimicrobial stewardship program (ASP) targeted antibiotic prescribing for Respiratory syncytial virus (RSV) infection. We hypothesize that this would also reduce unnecessary use of antibiotics in children presenting with asthma.

**Methods:** Charts of children admitted for asthma during peak asthma months, January, March, November, and December 2012, 2013, and 2014 were reviewed. This study was exempt from Institutional Review Board approval. Pediatric patients 6 months of age and older were included, while children with sepsis, pneumonia, immunosuppression, or neutropenic fever, were excluded. Data collected were demographics, co-morbid conditions, results of complete blood count, differential, culture results, body temperature, antibiotic(s) prescribed, dosage, duration of therapy, length of stay, and re-admission rates. Antibiotic prescribing was deemed justified for: 1) documented infection, and 2) possible infection based on at least two of the following: fever, elevated white blood cell count, altered neutrophil count, elevated band count, or evidence of pneumonia. Patient demographics and LOS were compared using the Kruskal-Wallis test. Pearson's chi-square test was used for the proportion of patients exposed to antibiotics, the proportion of justified use of antibiotics, and the readmission rate. We adjusted for multiple pair-wise comparisons of age, weight, and LOS.

**Results:** A total of 711 children satisfied study entry criteria, with 182 in 2012, 282 in 2013, and 247 in 2014. All data after January 2013 represented post-ASP intervention for RSV. There was a difference in age between cohorts of patients, median 6, 5, and 5 years, for 2012, 2013, and 2014, respectively ( $p=0.022$ ). Overall, antibiotics were prescribed in 184 children; 67 of those were unjustified based on pre-existing guidelines (36%). Antibiotic prescribing declined significantly from 39.6% in 2012, to 22.3% in 2013, and to 19.8% in 2014 (overall  $p<0.001$ ), but not significantly between 2012 and 2013 ( $p=0.551$ ). Rates of unjustified use of antibiotics did not decline significantly over the study period ( $p=0.431$ ). Ceftriaxone was most commonly prescribed, followed by azithromycin, then amoxicillin. Azithromycin use declined over the years ( $p=0.019$ ). We found a reduction in LOS, median 2 (2012) to 1 (2013) and 1 (2014) ( $p=0.009$ ). There was no difference in readmission rates: 12.1%

in 2012, 8.9% in 2013 and 10.5% in 2014 ( $p=0.529$ ). **Conclusion:** Rates of antibiotic prescribing and LOS for asthma were reduced over three years; however, unjustified use remained elevated. Prescribing patterns changed for azithromycin. Declines in antibiotic use did not affect re-admission rates. This study justifies launching a more targeted ASP for asthma.

#### MEDICATION SAFETY EDUCATION TO INCREASE AWARENESS OF DISTRACTIONS AND INTERRUPTIONS FOR PHARMACISTS AND NURSES

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**Introduction:** The safety of the medication process is directly affected by numerous factors, one being distractions and or interruptions in the work environment, leading to an increased error potential. Just one interruption increases the error rate by 12.7%, and 53% of the time that interruption occurs during the administration process. After observation of interruptions occurring in every day nursing and pharmacy practice an education module was developed to increase awareness of the risk of misdirected attention.

**Methods:** The Medication Safety Committee identified this educational opportunity through event review and observation of nursing and pharmacy practice during walk rounds. In conjunction with the Education Department a literature review was conducted and a fifteen minute mandatory computer based learning module for nurses and pharmacists throughout Intermountain Healthcare was developed. To review preconceived notions regarding interruptions, an optional pre-test was offered the quarter prior to the education and again offered the quarter following the education module. Responses were based on a Likert scale, and the results were compared to identify changes in perception.

**Results:** Nurses and pharmacists completed 1134 pre-tests and 3227 post-tests. When asked if distractions and interruptions are a major contributor to medication errors 10% more agreed or strongly agreed after the education. Prior to the education the questions regarding the most and least common source of distraction revealed work environment and families as the most common cause of distraction. Post education, the staff appropriately identified the most common source of distraction as work environment and co-workers while, families were identified as a distraction 14% less frequently. The staff commonly agreed with the question stating the importance of avoiding and minimizing distraction and interruption prior to the module, with a 7% increase in agreement after the education. When asked about knowing how to minimize interruptions nurses and pharm-

cists agreed 11% more after education was given. The last question stated multitasking is a necessary and important strategy for effectively carrying out the medication process. When combining the disagree and strongly disagree groups there was a 29% increase in staff that recognized the perils of multitasking after the educational intervention. **Conclusion:** A computer based education module about distractions and inattention improved the knowledge base of pharmacy and nursing staff related to the error risks of misdirected attention. After completion of the module pharmacists and nurses recognized the increased risk of error with interruptions and distractions, and the risks of multitasking. Further research needs to be completed to show if the increased awareness leads to an actual decrease in errors.

#### CHEMICAL STABILITY OF REPACKAGED PARENTERAL LEVETIRACETAM AND DILUTED PHENOBARBITAL FOR THE NEOLEV TRIAL

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**Introduction:** The NEOLEV trial is a multicenter, randomized, double blind study comparing parenteral levetiracetam and phenobarbital as first line agents for neonatal seizures. In order to carry out study procedures and to maintain study blinding, novel dilutions and repackaging with confirmatory stability testing was required. **Methods:** Phenobarbital sodium injection 130 mg/mL was diluted with normal saline in glass vials to 2.25 mg/mL, 7.5 mg/mL, and 15 mg/mL. Levetiracetam in sodium chloride injection 15 mg/mL was repackaged into glass vials and hard plastic syringes. Samples were stored under refrigeration (2-8°C). Analyses for concentration were performed on day 0, 14, and 90 after sample preparation. Repackaged syringes were tested on day 0 and 14 only. Phenobarbital was analyzed using HPLC-UV dynamic absorbance detection. Levetiracetam was analyzed using liquid chromatography-tandem mass spectrometry. **Results:** Each sample retained >90% of its original concentration at all times tested. **Conclusions:** Stability testing of study medications was a crucial step in NEOLEV study design and development. These results have wider applicability in routine neonatal care where dosage form flexibility is often restricted by a lack of stability data.

#### IMPACT OF PEDIATRIC PHARMACISTS ON MEDICATION RECONCILIATION UPON UNIT TRANSFER WITHIN HOSPITAL ADMISSION: A PILOT STUDY

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**Introduction:** The Institute of Medicine's Crossing the Quality Chasm report identified transitions of care between different health care teams or environments as fraught with challenges and adverse events. This study aimed at evaluating the impact of pharmacist driven medication reconciliation on transitions of care within the hospital admission. **Methods:** A prospective pilot study was conducted from January 1 to February 28, 2015 at a 144-bed children's hospital. The units included were the pediatric intensive care unit (PICU), acute care units, neonatal intensive care unit (NICU), and the newborn nursery. The pediatric pharmacists ran a daily report of unit transfers and completed a thorough medication chart review. Results of the medication reconciliation were documented in the electronic medical record using a standardized template. Discrepancies and recommendations were discussed and reconciled with the medical team. **Results:** During the study period, 168 patients transferred units within the children's hospital during a single admission. The most common unit transfer was from the PICU to the acute care units and represented 96 (57%) of unit transfers. Medication reconciliation was performed on 70 of the 168 patients who transferred units. Twenty two (31%) of the medication reconciliations were performed within 12 hours and thirty three (47%) were completed within 12 to 24 hours of unit transfer. The average amount of time spent performing unit transfer medication reconciliation was  $9.4 \pm 2.2$  min. The average number of medications prescribed at time of unit transfer was  $5.2 \pm 4.7$  medications. Of the standardized pharmacist significance evaluations, four (6%) were considered high or critical requiring intervention. Significant errors prompted reconciliation with the medical team. **Conclusions:** This pilot study demonstrates the potential for pediatric pharmacists to identify and prevent medication errors between unit transfers within a hospital admission.

#### CONTINUOUS INFUSION VANCOMYCIN VIA INSTILLATION OF VANCOMYCIN INTO THE DIALYSATE SOLUTION

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**Introduction:** Vancomycin remains first line therapy for the treatment of life-threatening infections caused by methicillin resistant *Staphylococcus aureus* (MRSA) and ampicillin resistant *Enterococci*. Further, current evidence suggests that vancomycin trough levels of 15-20 mg/L are needed to maximize outcomes. Many factors can affect the pharmacokinetics of vancomycin in the pediatric intensive care unit (PICU) including sepsis, extra-corporeal life support, and continuous renal replacement therapy (CRRT). The purpose of this study was to evaluate the ability to achieve therapeutic vancomycin concentrations in the setting of CRRT by utilizing continuous infusion vancomycin via instillation of the vancomycin into the dialysate solution.

**Hypothesis:** The addition of vancomycin into the dialysate solution to facilitate continuous infusion vancomycin will result in therapeutic vancomycin concentrations >15 mg/L.

**Methods:** This was a retrospective chart review of patients receiving CRRT from 4/1/2009-5/31/14. All patients that had vancomycin added to the dialysate solutions were reviewed. Data collected included PRISM and pRIFLE scores, modality of CRRT, CRRT anti-coagulation, concentration of vancomycin added to the dialysate solution and vancomycin concentrations obtained while receiving CRRT.

**Results:** There were a total of 21 patients that received CRRT during the study period. Of the 21, 11(52.3%) received vancomycin in the CRRT dialysate solution. The mean PRISM score was  $16.6 \pm 6.5$ . The mean eGFR at the start of CRRT was  $44.7 \text{ mL/min/1.73m}^2$ . The median (range) concentration of vancomycin added to the dialysate was 25 mg/L (18-35 mg/L). The mean vancomycin serum concentration was  $22.8 \pm 3.3 \text{ mg/L}$ . All patients achieved a serum vancomycin concentration >15 mg/L. There were no adverse events related to adding vancomycin to the dialysate.

**Conclusion:** The addition of vancomycin to the dialysate solution is an effective modality to deliver a continuous infusion and ensure therapeutic vancomycin serum concentrations in the setting of CRRT. Further study is required to evaluate whether this delivery method can lead to improved patient outcomes.

#### POPULATION PHARMACOKINETICS OF MEROPENEM IN CRITICALLY ILL CHILDREN

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**Introduction:** Meropenem (MER) is a frequently prescribed antibiotic in pediatric intensive care units (PICU) but pharmacokinetic (PK) data to justify the optimal dosing regimen are sparse in critically ill children.

**Methods:** Blood samples (2-3 per child) were col-

lected from 11 children ages 3 mo to 9 yrs admitted to the PICU who were receiving standard MER dosing regimens to treat infections. MER concentrations were measured by a bioassay and the population PK modeled using Pmetrics, a non-parametric pharmacometric modeling and simulation package for R. Multiple models were tested to determine the best fit of the data. A 1000 patient Monte Carlo simulation (MCS) was performed to determine the probability of target attainment (PTA) for the following MER dosing regimens (40 mg/kg every 8 hr as 0.5 and 4 hr infusions. The percent of the dosing interval the free drug is above the minimum inhibitory concentration (MIC) (fT>MIC) was calculated over a range of MICs from 0.25-32 mg/L. The bactericidal target attainment was defined as  $\geq 40\%$  fT>MIC for MER. PTA  $\geq 90\%$  at each MIC was defined as optimal. **Results:** A 2-compartment model best fit the MER concentration data with weight a covariate. Mean  $\pm$  SD population estimates for clearance (CL), volume of the central compartment (Vc), and intercompartment transfer constants were  $0.21 \pm 0.22 \text{ L/hr/kg}$ ,  $0.18 \pm 0.22 \text{ L/kg}$ ,  $3 \pm 1.42 \text{ h}^{-1}$ , and  $1.53 \pm 1.1 \text{ h}^{-1}$ , respectively. This resulted an elimination half-life of  $0.69 \pm 0.23 \text{ hr}$  and a total volume of distribution estimate of  $0.45 \pm 0.36 \text{ L/kg}$ . The R<sup>2</sup>, bias and precision for the individual predicted versus observed concentrations were 0.998, -0.279, and  $0.407 \text{ mg/L}$ , respectively. PTAs for the MER dosing regimens are as follows:

MIC	40 mg/kg as 0.5 hr infusion	40 mg/kg as 4 hr infusion
0.25	99	100
0.5	99	100
1	98	100
2	96	100
4	90	100
8	71.5	99.6
16	43.5	71.3
32	22	30.7

**Conclusion:** These are the first population PK data of MER in critically ill pediatric patients (3 mo to 9 yrs of age). Based on these data, 40 mg/kg every 8 hr doses administered as 0.5 hr infusions will provide optimal PTA up to MER MICs of 4 mg/L, whereas prolonged 4 hr infusions will increase optimal PTA up to MICs of 8 mg/L.

#### PHARMACOKINETICS OF CONTINUOUS INFUSION MEROPENEM WITH CONCURRENT EXTRA-CORPOREAL LIFE SUPPORT AND CONTINUOUS RENAL REPLACEMENT THERAPY

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**Introduction:** Meropenem, a broad-spectrum carbapenem, is commonly utilized in the pediatric intensive care unit. Pharmacokinetic (PK) parameters such as the volume of distribution (Vd) and clearance (CL) can be significantly altered for individuals receiving extra-corporeal life support (ECLS) in addition to continuous renal replacement therapy (CRRT). Therefore, an understanding of the PK changes in critically ill children on ECLS and CRRT is crucial to determining an optimal anti-microbial regimen.

The purpose of this case report is to describe the pharmacokinetics of continuous infusion meropenem in a single patient on ECLS with concurrent CRRT.

**Methods:** Retrospective single patient chart review.

**Results:** A 2.8 kg, 10 day old full-term infant born via spontaneous vaginal delivery who presented with hypothermia, lethargy, and a ~ 500 gram weight loss from birth and was admitted to rule out a serious bacterial infection. She was found to have adenovirus (+). Her respiratory status worsened and she progressed to respiratory failure on HD#2. She further progressed to sepsis, DIC, and liver failure as a result of disseminated adenoviral infection. By HD#6, she started to develop acute kidney injury (AKI) and was >1500 mL (+) for the admission. On HD6-7 she was placed on ECLS for lung protection and to facilitate fluid removal. On HD 7 she was initiated on CRRT. On HD 12, a blood culture returned positive and subsequently grew *Pseudomonas aeruginosa* with a minimum inhibitory concentration for meropenem of 0.25 mg/L. As a result of the positive blood culture, she was initiated on a regimen of vancomycin, meropenem, and amikacin. Meropenem was started with a 40 mg/kg bolus given over 30 min after which a continuous infusion of 10 mg/kg/hr (240 mg/kg/day) was initiated. On HD 15 (ECLS day 9) a meropenem of 21 mg/L was obtained, corresponding to a clearance of 7.9 mL/kg/minute, drastically higher compared with 4 mL/kg/min reported in the package insert. Repeat cultures from HD 13-15 (ECLS day 7-9) were sterile.

**Conclusion:** A meropenem regimen of a 40 mg/kg bolus followed by a continuous infusion of 240 mg/kg/day was successful in providing a target attainment of 100% for serum concentrations above the MIC for at least 40% of the dosing interval and was associated with a sterilization of blood in this complex patient on concurrent ECLS and CRRT circuits.

#### NEONATAL TOXICITY VS. WITHDRAWAL FROM ESCITALOPRAM USE IN PREGNANCY

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**Case Report:** Selective serotonin reuptake inhibitor (SSRI) exposure during pregnancy can result in symptoms of serotonergic syndrome or serotonin withdrawal. The symptoms of each often overlap making it difficult to distinguish between the two, thus these symptoms are often referred to as serotonin behavioral syndrome (SBS). In contrast to other SSRIs, reports of serotonin behavioral syndrome (SBS) following in utero exposure to escitalopram and citalopram are limited. Citalopram toxicity in children has been previously described to include symptoms of lethargy, tachycardia, QTc prolongation, altered consciousness, hypertonia and seizures. We report a case of escitalopram exposure and suspected toxicity in a term infant exposed to 20 mg of escitalopram during pregnancy. The infant transferred to our neonatal intensive care unit (NICU) at 9 hours of life for further evaluation of lethargy, weak cry, bradycardia and non-reactive pupils. Hypoxic ischemic encephalopathy was suspected upon presentation, despite APGAR scores from the referring institution of 8 and 9. Maternal history was significant for depressive disorder treated with escitalopram throughout pregnancy. Upon admission, symptoms progressed to signs of hypertonia, irritability, high-pitched crying and posturing. The patient was loaded with phenobarbital (20 mg/kg) for empiric management of suspected seizures versus drug withdrawal. Both EEG and CT scans were normal, however an EKG revealed a prolonged QTc interval of 531ms. Signs of irritability and QTc prolongation continued through day of life (DOL) 5. The infant was discharged on DOL 10 with no further symptoms. We hypothesize that this represented a case of serotonin toxicity due to in utero exposure and recommend close monitoring for such symptoms of infants exposed to escitalopram during pregnancy.

#### ASSESSMENT OF INPATIENT INFliximab UTILIZATION: AN APPROACH TO DEVELOPING APPROPRIATE USE GUIDELINES

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**Introduction:** Acute severe exacerbations of inflammatory bowel disease (IBD) are potentially life-threatening. While there is limited clinical data to support the use of infliximab for acute exacerbations, guidelines include infliximab as second-line medical management following steroid failure in an attempt to avoid surgery in pediatric patients. Concern for unnecessary



inpatient infliximab use includes cost, as inpatient use is not reimbursed at our institution. The objective of this study was to assess our institution's infliximab utilization as a way to develop guidelines that allow for its use in appropriate patients and prevent overutilization in those who could be managed as outpatients.

**Methods:** This study was conducted as a retrospective chart review. Patients were identified through a drug utilization summary of inpatient pediatric infliximab use between January 1, 2011 and June 30, 2014. Patients were excluded if infliximab was administered for an indication other than IBD. Data collected included baseline demographics, past medical history, *Clostridium difficile* (C. diff), cytomegalovirus (CMV), and tuberculosis screening, surgical consults and interventions, infliximab dose and duration of therapy, concomitant medications, steroid use, and rates of surgical intervention. For ulcerative colitis (UC) patients, severity of the acute exacerbation was assessed utilizing the pediatric ulcerative colitis activity index (PUCAI). The primary outcome of interest was colectomy rates prior to discharge.

**Results:** A total of 38 inpatient infliximab infusions were reviewed representing 35 unique hospitalizations. In regards to the primary endpoint, approximately 48.6% of admissions had a surgical consult; however, a surgical procedure was only performed 11.4% of the time. Two additional patients required surgery post-discharge. While our data suggest early administration of infliximab may prevent or delay colectomy in certain patients, our study also identified areas for improvement in proper patient selection. Appropriate screening for tuberculosis was completed in 32 (91.4%) patients; however, screenings for C. diff and CMV were only performed in 29 (82.8%) and 13 (37.1%) patients, respectively. Additionally, steroid therapy was administered for less than three days in 16 (42.1%) patients, with a mean PUCAI score of  $55.6 \pm 14.6$  on the day of infliximab administration.

**Conclusion:** Based on these findings, the following recommendations for appropriate use were submitted to the pediatric pharmacy and therapeutics subcommittee: all patients should be screened for C. diff with a confirmed negative result, screening for tuberculosis should be completed for patients who have not been tested within the previous year, steroid failure (defined as three consecutive days of steroid administration, or prior use of maintenance steroids as an outpatient) must be documented and, for UC patients, disease severity should be quantified and documented using the PUCAI scoring system with a score of greater than or equal to 65 needed to qualify for infliximab therapy.

#### IBUPROFEN LYSINE (IL) STABILITY IN A RECENTLY INTRODUCED SiO<sub>2</sub> COATED VIAL

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**Introduction:** Particulates can place neonates at risk for complications. In 2010, Lundbeck Inc. voluntarily recalled IL (10 mg/mL, parenteral) when it discovered particulates during routine stability testing. Particulate matter was identified as an aluminum (AL) IL salt, a result of the interaction of IL with the standard glass vial inner wall. Corrective action led to the selection and reintroduction (October 2012) of IL in the Schott Type I vial (SCHOTT), coated interiorly with SiO<sub>2</sub> to minimize AL leaching. The purpose of this study was to evaluate the stability of ibuprofen lysine in SCHOTT.

**Methods:** This evaluation utilized several different tests to assess IL stability in SCHOTT under varied temperature (°C) and relative humidity (RH) conditions (25°C/60% RH, 40°C/75% RH, 60°C/60% RH) over a period out to 9 mo. Inductively coupled plasma mass spectrometry (ICPMS) measured AL IL content in solution. Infrared spectroscopy (IS) detected microscopic particles of AL IL. The light obscuration test (USP <788>) assessed changes in particulate concentrations at >10µ/container and >25µ/container. Scanning electron microscopic (SEM) evaluated inner vial surface changes. Studies used IL in a standard Type I glass vial (STD) as a control for evaluating AL content in solution and for microscopic detection of AL IL.

**Results:** ICPMS for SCHOTT found: 1) <9 mg/L, baseline (all conditions); 2) <9 mg/L, 9 mo (25°C/60% RH); 3) <9 mg/L, 6 mo (40°C/75% RH); and 3) 63 mg/L, 1 mo, and 92 mg/L, 6 mo (60°C/60% RH). ICPMS for STD revealed: 1) 45 mg/L, baseline (40°C/75% RH, 60°C/60% RH); 2) 137 mg/L, 1 mo, 165 mg/L, 2 mo, 207 mg/L, 3 mo, and 311 mg/L, 6 mo (40°C/75% RH); and 2) 198 mg/L, 1 wk and 198 mg/L, 1 mo (60°C/60% RH). IS for SCHOTT detected: 1) no particles, 9 mo (25°C/60% RH); 2) no particles, 1 and 6 mo (40°C/75% RH); and 3) particles (<60 mg), 1 mo (60°C/60% RH). IS for STD found particles, 1 month (60°C/60% RH). Particulate testing for SCHOTT did not find any change from baseline for >10µ/container through 9 mo and >25µ/container through 6 mo. SEM did not observe any vial surface changes for SCHOTT under all conditions.

**Conclusion:** IL in SCHOTT remained stable with respect to changes in particle formation and AL content in solution. STD showed significant increases of AL content in solution. SCHOTT provides protection from particulate generation with IL, yielding a safer product.

#### COMPARISON OF AMIKACIN PHARMACOKINETICS IN NEONATES PRE AND POST A DOSING PROTOCOL CHANGE

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**Introduction:** Aminoglycosides are commonly used for treatment of early and late onset sepsis in neonates. Although gentamicin or tobramycin are often first-line, some clinicians have utilized amikacin due to *Escherichia coli* antimicrobial resistance. However, there is limited data with amikacin in the neonatal population. The purpose of this study was to compare amikacin goal concentrations pre- and post- a dosing protocol change in our facility.

**Methods:** This was an IRB-approved retrospective study of neonates receiving amikacin during two time periods: January – December of 2013 (Group 1) and January – December of 2014 (Group 2). Group 1 included patients who received an amikacin dose consistent with published neonatal dosing recommendations while Group 2 received dosing from a modified protocol. Patients were included if they had an amikacin peak and trough concentration drawn. Concentrations were excluded if drawn prior to the second dose of amikacin or identified as an abnormal drug concentration, defined as a calculated volume of distribution (Vd) that was 30% greater than or less than the expected population Vd estimate. Data collected include demographic information, amikacin regimen, hearing screen results, renal function markers, microbiology results, and concomitant medications. The primary objective was to assess the change in frequency of goal peak concentration attainment (20-35 mg/L). Pharmacokinetic data was calculated with subgroup analysis based upon postmenstrual age (PMA), postnatal age (PNA), and presence of congenital heart disease. Secondary objectives included the description of sub- and supra-therapeutic peak concentrations and supra-therapeutic trough concentrations. Between-group analysis was performed using Wilcoxon-Mann-Whitney test, Student's t-test or Chi-square, or Fisher's exact analysis as appropriate with a p-value < 0.05.

**Results:** 278 neonates were included for analysis (Group 1: n=144; Group 2: n=134). The majority of patients were male (60%) and admitted for prematurity or respiratory distress (77%). The median gestational age in Group 1 was 34.4 wks (30.0-37.9) versus Group 2 at 36.9 wks (31.4-38.9). The PNA was similar between both groups at 4 days while the PMA was 35.7 wks (31.0-38.5) and 37.4 wks (33.7-39.4) in Group 1 and Group 2 respectively. There was a significant increase in goal peak concentration attainment between Groups 1 and 2, 34% vs. 84%, p<0.001. There was a decrease in supra-therapeutic peak concentra-

tions between groups, 65% vs. 12%, p<0.001. There was no significant difference in sub-therapeutic peak or supra-therapeutic trough concentrations.

**Conclusion:** A modified neonatal dosing protocol resulted in increased peak concentration attainment of amikacin compared to published neonatal dosing recommendations. Future research should focus on determination of the optimal dosing regimen in neonates.

#### ADHERENCE TO ANTI-INFECTIVE PRESCRIBING RECOMMENDATIONS IN INSTITUTIONAL FEBRILE NEUTROPENIA GUIDELINES

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**Introduction:** Infection is a major cause of morbidity and mortality in patients with severe neutropenia. In order to optimize patient outcomes and prevent the development of antibiotic resistance, it is important to select optimal anti-infective therapy when appropriate. In 2012, the clinical practice guideline for patients with febrile neutropenia at a free-standing children's hospital was updated to reflect the most current medical evidence. It is unknown whether anti-infective prescribing behaviors are consistent with guideline recommendations or if deviation from the guideline is well-documented by prescribers. The objective of this study was to determine prescribing adherence to the updated febrile neutropenia clinical practice guideline. Secondary objectives included characterizing factors that influenced non-adherence and describing prescribers' practices for documenting rationale for occurrences of non-adherence.

**Methods:** This was a retrospective cohort study of patients admitted to a free-standing children's hospital who had febrile neutropenia. Patients were identified using pharmacy reports to select patients with an absolute neutrophil count < 500 cells/mm<sup>3</sup> who received at least one of the antimicrobials included in the institutional clinical practice guideline from January 1, 2013 to December 31, 2013. Descriptive statistics were used for frequencies of empiric drug selection, de-escalation, and/or discontinuation that were adherent to the clinical practice guideline. Spearman correlation was utilized to determine association between patient variables and guideline non-adherence.

**Results:** One hundred thirty-three patients with febrile neutropenia were included. Twenty incidents (15%) of guideline non-adherence were noted, resulting in overall adherence of 85%. There was no correlation between specific patient variables and guideline non-adherence. Cefepime and vancomycin were the drugs most often associated with guideline non-adherence, accounting for 35% (n=7) and 30% (n=6) of the inci-

dents, respectively. For all instances of guideline non-adherence involving vancomycin, rationale for empiric addition of vancomycin could not be located in the electronic medical record. It could not be determined if the patient truly did not meet guideline criteria for empiric vancomycin or if empiric vancomycin was appropriate, but documented rationale was absent. **Conclusion:** Overall adherence to the institutional clinical practice guideline for febrile neutropenia was good at 85%. Cefepime and vancomycin were responsible for most inconsistencies, so it may be beneficial to focus educational efforts on recommended use of these specific antibiotics. Since documentation for the empiric use of vancomycin was inadequate, encouraging prescribers to document clinical justification for the empiric use of vancomycin may increase ability to determine adherence in the future. For future guideline updates, it may be useful to include objective measures for the determination of factors including measures for degree and severity of mucositis and hemodynamic instability.

#### A RETROSPECTIVE ANALYSIS OF CLINICAL OUTCOMES WITH CONTINUOUS VERSUS INTERMITTENT NAFICILLIN INFUSIONS IN CHILDREN

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**Introduction:** The efficacy of nafcillin therapy is associated with the percentage of time that the free drug concentration remains above the minimum inhibitory concentration (fT>MIC) of the infecting organism. Traditional intermittent doses are administered every 4 to 6 hours, but continuous infusions may allow for more steady drug concentrations and therefore increased fT>MIC, and may decrease pharmacy and nursing time. Minimal experience with continuous infusion anti-staphylococcal beta-lactams has been published. The primary objective of this study was to compare the efficacy and safety outcomes of continuous versus intermittent nafcillin infusions. **Methods:** This was a retrospective cohort study performed at a freestanding, tertiary care children's hospital. Subjects were included if they were at least 30 days old and received more than one dose of nafcillin dosed by intermittent infusion (II; 30 min infusion every 4 or 6 hrs) or continuous infusion (CI) from January 1, 2009 to December 31, 2012. Clinical and microbiological data were extracted from the medical record. Documented nafcillin-associated adverse reactions were recorded. Treatment success was defined by any one of the following without the presence of conflicting data: microbiologic cure,

prescriber documented treatment success, or normalization of abnormal clinical or laboratory parameters. **Results:** 177 subjects (40 in the CI and 137 in the II group) with median (IQR) ages of 9 yrs (2.3-12) in the CI and 2 years (0.75-9.5) in the II groups were included. Overall treatment success was observed in 92.5% vs. 93.4% of CI vs. II patients, respectively (p=0.735). Similar rates of microbiologic cure (CI: 91.3%; II: 94.4%; p=0.63) and median [IQR] length of stay (days) were observed (CI: 7 [5 – 21.75]; II: 11 [5 – 24.5]; p=0.696). Extended lengths of stay were less common in CI vs. II patients, with 37.5% vs. 56.2% of patients admitted to the hospital for ≥10 days (p=0.037). Adverse reactions were documented in 42.5% vs. 41.6% of CI and II subjects, respectively (p=0.92) with no statistical difference in specific reactions. Patients receiving CI tended to have a higher likelihood of bone marrow suppression/neutropenia than II patients (88.2% vs. 63.2%; p=0.073). **Conclusions:** In this pediatric cohort, overall treatment success and microbiologic cure were similar between CI and II recipients. Patients receiving CI nafcillin may be less likely to experience extended hospital stays as compared to patients receiving II nafcillin. Continuous infusion nafcillin appears to be an acceptable alternative to II nafcillin in children.

#### RISK FACTORS IN PEDIATRIC HEART TRANSPLANT PATIENTS ASSOCIATED WITH INCREASED MYCOPHENOLATE MOFETIL TOXICITY

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**Introduction:** Mycophenolate mofetil (MMF) is the anti-proliferative agent of choice for maintenance immunosuppression in heart transplant patients. Its significant adverse effect profile includes gastrointestinal intolerances and hematologic toxicities that can lead to either dose reduction or discontinuation. The primary objective is to identify risk factors in pediatric heart transplant patients associated with an increased incidence of adverse effects that necessitate discontinuation of MMF in the first 12 months of therapy. **Methods:** Pediatric patients aged 0-18 years that received a heart transplant at our institution between January 1, 2009 and December 31, 2013 and were initiated on MMF therapy were identified. Patient chart review was conducted to identify discontinuation of MMF within 12 months. The reason for discontinuation, patient age, height, weight, MMF dose, MMF dosage formulation, concomitant calcineurin inhibitor, and cytomegalovirus (CMV) status was also recorded. **Results:** A total 93 patients were screened with 35 meeting criteria for inclusion whose mean age at transplant was 8.3 (range, 0-18) yrs. Seventeen (48.6%) patients initiated on MMF discontinued therapy in the first year after a mean of 2 mo (range, 0-7). Diarrhea

and nausea/vomiting were the two most common documented reasons for discontinuation of therapy, occurring in 8 (47%) and 6 (35%) patients, respectively. Mean dose and dosage form were similar between groups at discontinuation of MMF or 12 months of therapy.

**Conclusions:** Adverse effects associated with MMF necessitating discontinuation remains a significant challenge for pediatric heart transplant patients. Neither age, MMF dose, nor dosage formulation were associated with interruption of therapy in our patient population. Further investigation is needed to identify patient risk factors for MMF discontinuation.

#### UNEXPECTED CARDIAC TOXICITY FROM A CHEMOTHERAPY REGIMEN INCLUDING BORTEZOMIB FOR ACUTE MYELOID LEUKEMIA: TWO CASE REPORTS

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**Introduction:** Each year, Children's Hospital Colorado cares for approximately six children with a new diagnosis of acute myeloid leukemia (AML). AAML1031 is a Children's Oncology Group Phase III trial to study the effectiveness of bortezomib and sorafenib in AML. Patients enrolled in Arm B receive bortezomib in both induction and intensification phases of chemotherapy. Bortezomib inhibits 26S proteasome cellular activity, which affects multiple signaling cascades within the cell, thus leading to apoptosis of tumor cells.

**Case Summaries:** We report two cases of cardiac toxicity during the intensification phase of AAML1031 Arm B in children with no history of cardiovascular disease. The first case occurred in a 14-yr-old female admitted for chemotherapy with high-dose cytarabine, mitoxantrone, and bortezomib. Her course was complicated by persistent fevers and neutropenia, pancytopenia, bacteremia, hypertension, and acute heart failure. This patient had increasing tachycardia over two weeks with heart rates up to 130 beats per minute. On physical exam, she was fluid positive and had crackle lung sounds. Chemistry labs were concerning for poor end-organ perfusion (SCr 1.12, AST 255, ALT 79) and ECHO revealed significantly low ejection fraction (24%). A second case occurred in an 18-year-old male admitted for chemotherapy with high-dose cytarabine, etoposide, and bortezomib. This patient's course was complicated by rash, fevers in the setting of neutropenia, acute kidney injury, and severe, localized chest pain that started on day 18 of his chemotherapy regimen. Chest pain began to worsen with breathing, and an EKG revealed a newly prolonged QT interval. ECHO showed evidence of pericardial effusion and repeat EKG revealed ST elevations consistent with pericarditis.

**Discussion:** According to the manufacturer's prescribing information of bortezomib, a warning of

worsening or development of cardiac failure has been reported, including in patients with no preexisting heart conditions. There is one case report published describing a pericardial effusion after bortezomib in a 56-yr-old female with multiple myeloma. The incidence of any treatment-related cardiac disorder seen in a study in adults with multiple myeloma was 8% when bortezomib was used. There is currently no safety information in pediatric patients.

**Conclusions:** We describe unexpected cardiac toxicity in two adolescent patients during the intensification phase of AML chemotherapy while using bortezomib. It is unclear if toxicities resulted from bortezomib, past anthracycline use, or a combination of both. More information is needed to determine safety information of bortezomib in pediatric patients.

#### NATIONAL SURVEY OF TREATMENT STRATEGIES FOR ACUTE BRONCHIOLITIS

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**Introduction:** Acute bronchiolitis is a leading cause of infant hospitalizations. The primary objective of this study was to characterize the pharmacologic and non-pharmacologic treatment strategies used for acute bronchiolitis across U.S. children's hospitals, and secondarily, to determine if treatment aligns with American Academy of Pediatrics (AAP) recommendations and evidence-based medicine. **Methods:** A 19-item survey instrument was developed to assess treatment practices for acute bronchiolitis in infants and children <2 yrs of age without a history of wheezing, reactive airway disease, or asthma across U.S. children's hospitals. A total of 203 U.S. children's hospitals were identified via <http://www.childrenshospitals.net> and [http://www.health-guideusa.org/childrens/childrens\\_hospitals.htm](http://www.health-guideusa.org/childrens/childrens_hospitals.htm). Contact information for pediatric pharmacists and pediatric pharmacy faculty members was retrievable for 145/203 hospitals via the: ACCP member directory; ASHP member and residency directories; PPAG member and residency directories; and, individual hospital and/or affiliated pharmacy school websites. Assuming a 95% confidence level and a confidence interval of 5, a sample size of 137 hospitals was deemed necessary. Hospitals were randomly selected for inclusion. The survey was pilot-tested and distributed via SurveyMonkey on 4/17/2014. Frequency and descriptive statistics were used to characterize responses: frequency of treatment use was categorized as high (>75%), moderate (=50-74%), or low (<50%).

**Results:** 38 hospitals responded to the survey (response rate 27.7%). A high proportion of hospitals reported using non-pharmacologic treatments: nasal suctioning (97%), oxygen (97%), hydration (94%) and



chest physiotherapy (CPT) (80%), for the management of acute bronchiolitis. At least 80% of hospitals reported using nasal suctioning, oxygen, and hydration 'often' or 'always', while 54% of hospitals reported using CPT 'often' or 'always'. A high proportion of hospitals reported using beta-2 agonists (100%), racemic-epinephrine (92%), systemic antibiotics (87%), systemic corticosteroids (82%), and hypertonic saline (HS) (81%); a moderate proportion of hospitals reported using inhaled corticosteroids (65%) and isotonic saline (61%); and, a low proportion of hospitals reported using dornase alfa (49%), inhaled antibiotics (35%), montelukast (35%), and ribavirin (16%), for the management of acute bronchiolitis. Beta-2 agonists, racemic-epinephrine, HS, and systemic corticosteroids were used 'often' or 'always' used by 49%, 47%, 40%, and 20% of hospitals, respectively. In contrast, systemic antibiotics and ribavirin were used 'rarely' or 'sometimes' by 91% and 100% of hospitals, respectively. The major limitation of this study is the response rate <60%, which increases risk for nonresponse bias. **Conclusions:** The use of non-pharmacologic treatments for acute bronchiolitis across U.S. children's hospitals was common, and with the exception of CPT, aligned with AAP recommendations and evidence-based medicine. The use of pharmacologic treatment across U.S. children's hospitals was also common. This suggests medication overuse, given the relative lack of supporting data for this indication; however, the frequency of medication use within these hospitals suggests practice somewhat aligns with AAP recommendations and evidence-based medicine.

#### EVALUATION OF MEASURING DEVICES PACKAGED WITH PRESCRIPTION ORAL LIQUID MEDICATIONS

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**Introduction:** The method by which parents and caregivers measure liquid medications for children has long been identified as potentially problematic. Provision of a measuring device with the medication can help alleviate this problem. The Food and Drug Administration (FDA) issued a non-binding guidance for measuring devices packaged with oral liquid over the counter (OTC) medications stating manufacturers should include a measuring device that bears relevant markings and instructions. A previous study reported that 74% of OTC medications were packaged with measuring devices prior to the publication of the FDA guidance. No such guidance is available for prescription oral liquid medications. The purpose of this study was to evaluate whether oral liquid prescription products are packaged with appropriate measuring devices.

**Methods:** This was a descriptive study of prescription oral liquid medications dispensed during a six month period at a community pharmacy. Product information was obtained from the National Library of Medicine's DailyMed database and from the products themselves. Endpoints included provision of a measuring device, the type of device, the maximum dose measurable, intervals on the provided device, and inclusion of instructions to the pharmacist. **Results:** A total of 382 liquid prescription medications were included in the study. Forty-nine of the 382 products (12.8%) were packaged with a measuring device. The most commonly provided device was a calibrated dropper (n=18; 36.7%), followed by an oral syringe with a bottle adaptor (n=9, 18.4%). Specific instructions on proper use of the provided measuring device were included with 20 products (40.8%). Among the products that did not provide a measuring device, only 70 of the 333 package inserts (21%) included instructions to the pharmacist regarding counseling the patient on proper administration. **Conclusion:** Packaging of prescription oral liquid medications is inconsistent and leaves room for vast variability in patient/parent administration practices. In the future, patterns of actual dispensing practices among pharmacies and pharmacists would help determine the true incidence of measuring device dispensing.

#### CHEMICAL CHARACTERIZATION OF COMMERCIAL SURFACTANT PRODUCTS USING LIQUID CHROMATOGRAPHY AND CORONA® CHARGED AEROSOL DETECTOR (CAD®)

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**Introduction:** Surfactant deficiency and dysfunction have been associated with numerous pulmonary conditions. In premature infants, surfactant deficiency leads to respiratory distress syndrome (RDS). The specific aims of this study were two-fold: (1) to characterize the lipid profile of Surfaxin® using a high-performance liquid chromatographic technique; (2) to compare Surfaxin® lipid profile to the lipid profile of the other natural (animal-derived) surfactants. **Methods:** Surfactant characterization was performed using a gradient mobile phase and high-performance liquid chromatography (Shimadzu High Performance Liquid Chromatography System) combined with Thermo CAD Detection. The CAD detector was selected for its high versatility to detect any nonvolatile or semivolatile analytes with or without a chromo-

phore. The HPLC-CAD method was transferred and qualified for use to simultaneously detect sinapul-tide (KL4), dipalmitoylphosphatidyl choline (DPPC), palmitoyloleoylphosphatidyl glycerol (POPG), and palmitic acid (PA). A factorial study design was used to characterize 4 commercially available surfactants (Curosurf, Infasurf, Surfaxin, and Survanta), 2 manu-facturer's lots of each surfactant, and each surfactant characterization was replicated 6 times. The resulting chromatograms were plotted and visually analyzed for differences between the respective surfactants.

**Results:** The chromatograms depict the chemical composition of each surfactant. Surfaxin® contains all four surfactant analytes (KL4, DPPC, POPG, and PA), Survanta contains only DPPC and POPG, Curosurf contains DPPC as the primary ingredient and POPG to a lesser extent, and Infasurf contains DPPC as the primary active ingredient. Differences between manufactured lots are also observed be-tween the natural surfactants. Whereas, numerous other undetermined ingredients are also observed in natural surfactants. Historically, neonatologists have desired to limit exposure of pharmacologic agents to neonates and young infants that are not proven to be safe and effective. Such desire has resulted secondary to reports of adverse effects occurring in neonates and young infants secondary to unlabeled or labeled ingredients that are contained in drug products, and generally recognized as safe (GRAS). Examples of pharmaceutical ingredients include aerosol propel-lants, preservatives, coloring agents, emulsifying or solubilizing agents, perfumes, ointments, and/or solvents; all have had reports of adverse effects. To this end, manufacturers who have developed new products for use in neonates and infants over recent years (e.g., caffeine citrate for prevention of apnea of prematurity) have limited or excluded the addition of pharmaceutical excipients to minimize risk of adverse events. The appearance of a degradation product of phospholipids, lysophosphatidylcholine (LPC), is observed in natural surfactant chromatograms. This observation is important as LPC is reported to inhibit surfactant surface tension-lowering effects.

**Conclusion:** Chemical characterization demonstrated distinct differences between commercial surfactants including 1) phospholipid composition, 2) manu-factured lot differences, and 3) phospholipid degradation products. We speculate that further chemical analyses of surfactants will provide new data for health care providers to evaluate when selecting surfactants for their respective clinical application.

#### SAFETY AND EFFICACY OF INHALED TOBRAMYCIN IN NON-CYSTIC FIBROSIS CHILDREN

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**Introduction:** Inhaled tobramycin has been used extensively in children with cystic fibrosis (CF) to reduce pulmonary exacerbations, improve lung function, and prevent subsequent hospital admis-sions. Clinical evidence to support the use of inhaled tobramycin to treat serious pulmonary infections by *Pseudomonas aeruginosa* in non-CF children is scarce. Aerosolized administration of tobramycin targets drug delivery to the endobronchial site with minimal systemic absorption. However, possible pharmacokinetic variations in non-CF children may result in significant tobramycin plasma levels and adverse effects. This study describes a single institu-tion's experience regarding the safety profile, dosing regimen, and treatment outcomes of inhaled tobra-mycin for pulmonary infections by *P. aeruginosa* and other Gram-negative bacteria in non-CF children.

**Methods:** A retrospective chart review of non-CF children ( $\leq 18$  yrs) who received at least 1 dose of tobramycin inhalation solution for the treatment of an active infection or eradication of pulmonary colonization by *P. aeruginosa* or other Gram-negative bacteria from November 1, 2009 to October 31, 2014 was conducted. The primary objective was to evaluate the safety of inhaled tobramycin in non-CF children, with a focus on acute kidney injury. Secondary objec-tives included describing the dosing and duration of inhaled tobramycin as well as its efficacy on the eradi-cation of *P. aeruginosa* or susceptible Gram-negative bacteria from the sputum. Inpatient cost associated with inhaled tobramycin usage was also evaluated.

**Results:** A total of 51 patient encounters was reviewed. The median age was 6 yrs (interquartile range (IQR): 1.9-11.0). Majority of patients were admitted to the pediatric intensive care unit (92.2%) with 11 patients (21.6%) receiving mechanical ventilation at therapy initiation. Twenty seven patients (52.9%) were tracheostomy dependent. Inhaled tobramycin therapy did not result in any clinically significant changes in the surrogate markers for renal function (BUN, SCr, eGFR, and urine output). There was no documentation of nephrotoxicity or ototoxicity associated with inhaled tobramycin. No patient experienced cough, dyspnea, or bronchospasm during drug administration. The manufacturer's recommended dose of 300 mg every 12 hrs for CF children was the most frequently prescribed dose (86.3%). Eradication of Gram-negative bacteria from the respiratory tract was achieved in 75% of the patients who had repeat cultures available for review.

**Conclusions:** Inhaled tobramycin appears to be safe in non-CF children based on our institution's 5-year experience. Future studies should evaluate the safety and cost effectiveness of inhaled tobramycin for the

treatment of pseudomonal respiratory infections in non-CF children with and without chronic underlying respiratory conditions.

#### A RETROSPECTIVE EVALUATION OF CURRENT DOSING & THERAPEUTIC DRUG MONITORING PRACTICES OF VORICONAZOLE AT CARDINAL GLENNON CHILDREN'S MEDICAL CENTER

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**Introduction:** Fungal infection is a leading cause of morbidity and mortality in immunocompromised pediatric patients. Voriconazole has a broad spectrum of activity against fungal pathogens such as *Aspergillus* and *Candida* species. Several studies recommend an initial dosage of 14-18 mg/kg/day IV for children. However, voriconazole exhibits wide inter- and intra-patient variability and genetic polymorphism and the optimum dosing regimen has yet to be established. During the study period, patients less than 12 yrs of age received a median dosage of 14 mg/kg/day (range 5-19 mg/kg/day) and patients 12 yrs and older received recommended adult dosing. The primary objective of this study was to determine if target voriconazole plasma levels were achieved with current dosing practices at Cardinal Glennon. Secondary objectives were to evaluate the effect of concomitant medications on voriconazole levels and to determine if there was any association between age or weight, and achieving voriconazole target levels. **Method:** This retrospective clinical study examined data from all patients who received voriconazole between June 1, 2010 and June 1, 2013 and had at least 1 voriconazole plasma concentration measurement. Dosage, start date, route of administration, voriconazole concentrations, and dose adjustments, interactive concomitant medications, and adverse effects were collected for all patients during the course of their therapy. **Results:** Twenty-four patients were included in this retrospective review; however, 3 patients received more than one course of voriconazole for a total of 27 patient-courses. Fifty percent of the patients were females. The most common underlying diagnosis were acute leukemia (54%), immune deficiency (12.5%), brain tumors (8%), and others (25%). The median age of patients was 8.35 yrs (range 0.17-18 yrs). Twelve patients out of 27 (44%) had voriconazole concentrations of  $\geq 1$ mg/L (median 1.9 mg/L; range 1.1-12.1 mg/L) at the first measurement. The median voriconazole dosage referenced to total body weight in these patients was 10.8 mg/kg/day and the median age

was 12.5 yrs. Patients with concentrations  $< 1$  mg/L (median 0.2 mg/L; range  $< 0.1$ -0.8 mg/L) received a median dosage of voriconazole of 11.7 mg/kg/day. The median age in this group was 5 yrs. Age was the only statistically significant difference between the two groups ( $p=0.001$ ). There was no statistically significant difference in dosage, concomitant medications, and adverse effects between the two groups. After dose adjustment, the majority of patients (66%) with subtherapeutic voriconazole plasma concentrations achieved therapeutic levels. The median dosage to achieve therapeutic levels in this group was 17.1 mg/kg/day (range 3-30.6 mg/kg/day). **Conclusion:** Younger patients require higher doses of voriconazole to achieve therapeutic plasma levels when compared to older patients.

#### ASSESSING THE IMPACT OF AMERICAN ACADEMY OF PEDIATRICS REQUIREMENTS FOR ELECTRONIC PRESCRIBING IN CHILDREN

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**Introduction:** The objective of the study is to assess electronic health records (EHR) for their ability to meet the American Academy of Pediatrics (AAP) requirements for safe and effective e-prescribing in children and to determine if prescribing errors could be decreased by these requirements. **Methods:** Investigators met with clinic personnel to discuss EHR specifics, assess system capabilities and determine the presence or absence of the AAP requirements. Scenarios for prescription ordering were entered into the system to determine the presence or absence of each of the 19 requirements outlined by the AAP. Additionally, the clinic generated a report of all prescriptions written in their pediatric clinic in September and October 2013. These prescriptions were independently reviewed for errors by 2 pharmacists. A physician also independently reviewed the prescriptions and adjudicated the final decision over error classification. Errors were further categorized as being preventable or not based on the AAP requirements. **Results:** The EHR was found to meet 4 of 19 AAP criteria. Four criteria were partially met. Of the 477 prescriptions reviewed, 63 (13.2%) contained an error. A coefficient of agreement calculation between reviewers is planned and will be presented at the meeting. If the system contained AAP requirements of indication-based dosing, dose recommendations, dose range checking, and medication-specific indications, 47 errors (74.6%) could have been avoided. If a custom medication list were created,

34 errors (53.9%) could have been avoided. Combined, this could have prevented 53 (84%) errors. **Conclusions:** While the assessment of additional EHR systems is planned, it appears that inclusion of AAP requirements for prescribing could help avoid some errors, although additional interventions will be needed to further reduce prescribing errors in pediatrics.

### PROVIDERS' PERSPECTIVES ON CAREGIVERS' CONCERNS WHEN INITIATING ADHD MEDICATION FOR THEIR CHILD

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**Introduction:** Approximately 8%-11% of school-aged children in the US are diagnosed with attention deficit/hyperactivity disorder (ADHD). Findings from the first and largest multi-modal treatment trial in pediatric psychopharmacology, the Multi-Modal Treatment of ADHD Study (MTA), indicated that intensive medication therapy management (MTM) was superior to routine community care or behavior therapy alone in managing the core symptoms of ADHD. The MTM group received monthly medication maintenance visits with pharmacotherapists who provided support, encouragement, practical advice, and monitored side effects. This landmark study reinforced the impact of MTM on improved outcomes and endorsed medication as first line ADHD treatment for children and adolescents. Despite the evidence of effective pharmacological MTM for ADHD, caregivers are reluctant to initiate medication for their child. Moreover, since ADHD symptom improvement was superior in the MTM group than in the community care group, it is evident that caregivers and their children may not be receiving routine medication counseling. This highlights the need to improve MTM service for caregivers and their children who are receiving outpatient care for ADHD. **Objective:** The objective of this study is to elicit providers' perspective on what they feel is the most important concern to caregivers when considering initiating ADHD medication for their child. **Methods:** A total of 37 providers were recruited from outpatient pediatric primary care, developmental and mental health practices across Maryland to complete an anonymous online survey. The survey has two sections: 16 questions that elicit preferences for caregivers' most important concerns and 11 demographic questions. Each preference elicitation question displays 6 statements, and providers select the one statement they feel is most important and the one statement they feel is least important to caregivers' treatment decisions. This forces individuals to weigh the relative

importance of one concern over another, and evokes trade-offs (i.e., weighing the statements jointly rather than individually). Mean scores are calculated from the responses and ranked by relative importance.

**Conclusion:** Determining what providers feel is most important to caregivers when considering initiating ADHD medication for their child can be used to identify congruence and conflict between caregivers and providers perceptions of important barriers to medication initiation. This should provide a better understanding of the factors that may influence ADHD medication non-adherence. Such information could be usefully applied to personalized MTM services so that pharmacists address the issues that are most concerning to caregivers. Ultimately, the patient-centered, personalized approach to MTM services could enhance outcomes for children managed in routine outpatient clinical practice settings.

### RATE OF PNEUMOCOCCAL IMMUNIZATION IN PEDIATRIC ASTHMA PATIENTS

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**Introduction:** Asthma is a chronic lung disease which increases the risk of experiencing exacerbations, or acute decompensations of lung function requiring hospitalization. The Centers for Disease Control and Prevention (CDC) recommend that asthma patients (ages 2-18 yrs) receive the pneumococcal immunization series (pneumococcal conjugate 7-valent, pneumococcal conjugate 13-valent, and pneumococcal polysaccharide 23-valent). This recommendation was been supported by a recent meta-analysis which showed a positive association between asthma and invasive pneumococcal disease (bacteremia, meningitis, and pneumonia with bacteremia). The current rate of PCV-7, PCV-13, and PPSV-23 immunization in pediatric patients with asthma in Utah is unknown. The purpose of this retrospective chart review is to determine the pneumococcal series immunization rate in patients hospitalized at Primary Children's Hospital with asthma. **Methods:** The asthma hospital admissions for the past two years (children ages 2-18 yrs) will be compared against the Utah Statewide Immunization System to determine the rate of PCV-7, PCV-13, and PPSV-23 immunization in these patients. The hypothesis is that the rate of PCV-13 and PPSV-23 immunizations amongst pediatric asthma patients in Utah is less than 50%. **Results:** A total of 2,630 patients (ages 2-18 yrs) diagnosed with asthma were admitted to Primary



Children's Hospital from January 1, 2011 to December 31, 2013. With the PCV-7 immunization, 1505 of these patients (58%) received the first dose of the PCV-7, 1352 patients (52%) received the second dose, 1216 patients (47%) received the third dose, and 847 (33%) received the fourth dose. With the PCV-13 immunization, 988 patients (38%) received the first dose of the PCV-13, 463 patients (18%) received the second dose, 383 patients (15%) received the third dose, and 294 patients (11%) received the fourth dose. With the PPSV-23 immunization, only 74 patients (<3%) received the immunization.

**Conclusion:** Even with CDC recommendations for immunization of asthma patients with the pneumococcal immunization series, the rate of pneumococcal immunization amongst asthma patients hospitalized in the past 2 years at Primary Children's Hospital is quite low. Only 38% of patients received at least one dose of PCV-13, and less than 3% of patients received PPSV-23. To help decrease the risk of potential complications of invasive pneumococcal disease in asthma patients, a conscientious effort to increase the number pneumococcal immunizations in asthma patients admitted to the hospital has been made.

#### ASSESSMENT OF IRON STATUS AND SUPPLEMENTATION NEEDS IN THE PREMATURE INFANT

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**Introduction:** Iron is essential for red blood cell production and neurodevelopment. Premature infants are at risk for iron deficiency, however excessive iron and free radical production may increase the risk of chronic disease such as bronchopulmonary dysplasia. Studies have not evaluated the serum iron (SI) and ferritin (FTN) levels throughout hospitalization of a premature infant or the effects of transfusions. No consensus exists for the monitoring or supplementation of iron in premature infants.

**Objectives:** The primary objective of this study was to evaluate the degree of iron deficiency in preterm infants. The secondary objective was to determine the impact of blood transfusions on serum iron and ferritin levels.

**Methods:** Infants <2500 gm and <34 wks birth weight (BW) gestational age (GA) were evaluated for enrollment in the prospective evaluation of the iron status and needs of premature infants. Baseline serum hemoglobin (Hgb), hematocrit (Hct), SI, and FTN were drawn at birth with standard admission labs. Hemoglobin (Hgb), Hct, SI, and FTN were evaluated weekly and following each blood transfusion. The impact of GA and BW on SI and FTN at birth and at 28 days were analyzed. Changes in FTN and

SI pre and post- blood transfusion were evaluated.

**Results:** 125 preterm infants were enrolled in this study at a mean GA of 31 6/7  $\pm$  3 2/7 wks and BW 1641 gm  $\pm$  533.5 gm. Mean indices at birth were: Hgb 16.1  $\pm$  2.1 g/dL, Hct 49.5  $\pm$  6.6%, FTN 134.9  $\pm$  166.7 ng/mL, SI 61.1  $\pm$  49.9 mcg/dL. The mean Hgb, Hct, and SI, levels at birth were lower for infants < 28 wks GA than those > 28 wks (14.3 vs 16.5 g/dL Hgb; 43.8 vs 50.6 %Hct; and 41 vs 66.2 mcg/dL SI, respectively). Mean FTN and SI values at 1 mo of age did not differ significantly between infants transfused within the first month of life (FTN 116.4  $\pm$  89.3 ng/mL; SI 109.5  $\pm$  31.9 mcg/dL) versus those who were not transfused (FTN 171.5  $\pm$  148 ng/mL; SI 98  $\pm$  32.2 mcg/dL). Pre and post blood transfusion iron studies were evaluated for 194 transfusions. Although the mean increase in SI post transfusion was minimal (6.62 mcg/dL), there was wide variability in response (+ 76.5 mcg/dL). **Conclusion:** Infants < 28 wks GA have lower SI levels at birth, however FTN levels were elevated likely due to stress and inflammation/infection. The SI and FTN at 1 month of age do not appear to be influenced by blood transfusions. Significant variability in SI increases occur post transfusion which may warrant monitoring in patients receiving blood transfusions.

#### COMPARISON OF WARMING TIMES FOR SURFACTANT PRODUCT ADMINISTRATION

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**Introduction:** Natural surfactant products (beractant, calfactant, poractant alfa) have specific manufacturer recommendations for warming either naturally or manually, while the synthetic surfactant, lucinactant, utilizes a warming cradle to warm to body temperature. The temperatures of the various surfactant products achieved prior to administration have not been documented in practice. Variations in surfactant product temperature prior to administration may influence the clinical response and administration reactions.

**Objectives:** The primary objective of this study was to compare surfactant product temperatures prior to administration following manufacturer recommend preparation procedures. The secondary objective was to compare the temperatures of surfactant products as a function of time. **Methods:** Five samples of each commercially available surfactant product (beractant, calfactant, poractant, and lucinactant) and vial size were warmed according to manufacturer recommended procedures. For comparison purposes, poractant was warmed using similar techniques as required for beractant since it does not have any manufacturer recommended warming procedures. Temperatures were measured

and recorded at 1 minute (min) intervals during the warming process and at each respective recommended endpoint. Final product temperatures were obtained and recorded of each product within the vial and once drawn into a syringe. Comparisons of end temperatures, achievement of target temperatures, and time to achieve such were analyzed.

**Results:** Each natural surfactant product (beractant, calfactant, poractant) achieved room temperature when warmed in a closed hand for 8 min. The mean temperature  $\pm$  standard deviation) achieved via hand warming for beractant was  $30 \pm 1.4^\circ\text{C}$  and  $23.3 \pm 1.5^\circ\text{C}$  for the 4 mL and 8 mL vial sizes respectively. Similarly, the mean temperature achieved at 8 min for calfactant was  $30.5 \pm 1.9^\circ\text{C}$  and  $23.6 \pm 0.8^\circ\text{C}$  for the 3 mL and 6 mL vials respectively. Poractant achieved room temperature within a hand in a mean of  $2.0 \pm 0.7$  min for the 1.5 mL vials and  $3.2 \pm 0.3$  min for the 3 mL vials. In contrast, when allowed to warm on a countertop for 20 min, none of the natural surfactant products reached room temperature. Poractant required a mean of  $27.5 \pm 3.3$  min to achieve room temperature on a countertop for the 1.5 mL vials and  $39.3 \pm 6.3$  min for the 3 mL vials. Lucinactant achieved a mean temperature of  $37.6 \pm 0.9^\circ\text{C}$  when warmed via a warming cradle for 15 min.

**Conclusions:** The natural surfactant products achieved room temperature when warmed in a closed hand for 8 min, but did not achieve room temperature via countertop warming within the suggested time. The vial size of the natural surfactant products influenced the warming temperature variability. Lucinactant consistently achieved body temperature via a warming cradle. The clinical impact on the newborn of administering of a surfactant product at body versus room temperature is yet to be determined.

#### RETROSPECTIVE EVALUATION OF ZIPRASIDONE (GEODON®) USE AND PATIENT SAFETY

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**Introduction:** Ziprasidone (Geodon) is a 5th generation atypical antipsychotic agent. Its exact mechanism of action is unknown, but it functions as an antagonist at the D<sub>2</sub>, 5-HT<sub>2A</sub> and 5-HT<sub>1D</sub> receptors and an agonist at the 5-HT<sub>1A</sub> receptor. It moderately inhibits reuptake of serotonin and norepinephrine. The role of ziprasidone in pediatric patients includes indications for schizophrenia, autism, bipolar I disorder, and Tourette's syndrome. However, its safety and effectiveness is undetermined, and its place in practice currently remains uncertain. Ziprasidone is associated with an increased risk for QTc prolongation and the potential to cause adverse cardiac events, including sudden death. This retrospective

review evaluates the non-formulary utilization of ziprasidone and assesses the indications for use and safety at a large free-standing children's hospital.

**Methods:** Patients were identified through an electronic medical record report that included all dispenses of ziprasidone from March 2013 to March 2014 in both the inpatient setting and Emergency Department. Information collected included: patient age, gender, weight, primary service, diagnosis, EKG results, ziprasidone dose, and duration of ziprasidone use.

**Results:** The 38 patients who were prescribed ziprasidone were on average  $14.5 \pm 2.7$  years old and weighed  $75.4 \pm 30.1$  kg. Their average daily dose was  $71.9 \pm 45.6$  mg. The most common indications were bipolar disorder (47%), mood disorder (10%), and unknown (32%). The Hospital Pediatrics service prescribed ziprasidone for 68% of the patients. EKG monitoring was obtained for 50% of the patients, with an average QTc of  $420.5 \pm 24.1$  milliseconds. None of the patients experienced QTc prolongation, which was defined as  $>480$  in females and  $>470$  in males.

**Conclusion:** Ziprasidone has been used in Hospital Pediatrics patients across a wide range of age groups at Nationwide Children's Hospital. Doses of ziprasidone started at normal or lower doses based on adult dosing guidelines because the safety and effectiveness in pediatric patients have not been established. The increased risk for dose-related QTc prolongation requires routine QTc monitoring, yet the challenge in maintaining monitoring through transitions of care makes ziprasidone an unfavorable agent.

#### THE USE OF NERONTIN (GABAPENTIN) FOR PAIN AND IRRITABILITY IN THE NEONATAL INTENSIVE CARE UNIT (NICU)

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**Introduction:** Treating pain and irritability (or neuro-irritability) in neonates is difficult and limited by a lack of guidelines as well as many safety considerations in this population. Patients with neurological impairment require a therapeutic regimen that is both safe and effective. To date, there are limited data regarding the use of gabapentin in infants and neonates for the adjunctive treatment of pain. Case reports have shown some efficacy with the addition of gabapentin for this indication however, further evaluation is needed to assess its efficacy and safety profile. The goal of this study was to evaluate the use of gabapentin in the neonatal intensive care unit (NICU) at the Cleveland Clinic, with the hope of determining the efficacy and safety of its use in this patient population.

**Methods:** This is a retrospective, non-interventional, medical chart review. The medical record data was

obtained through an EPIC report for all NICU patients that received gabapentin as an inpatient for pain or irritability in the past ten years. Baseline characteristics included: age, vitals, renal function, concomitant analgesic medications, and gabapentin dose and frequency. The following were assessed throughout gabapentin therapy: neonatal pain, agitation and sedation scale (N-PASS) scores, neonatal abstinence scores (NAS), duration of gabapentin use, adjunct medications for pain or agitation (dexmedetomidine, morphine, midazolam, lorazepam), and side effects of gabapentin therapy. **Results/Conclusions:** Twelve patients (8 males and 4 females) were evaluated and analyzed. The average inpatient duration of gabapentin use was 98.4 days. Seven patients were discharged from the NICU on gabapentin and one patient was still receiving gabapentin at the conclusion of data collection. Gabapentin was discontinued in two of the twelve patients before discharge, and two patients expired in the NICU. The average day of life for gabapentin initiation was 119 with an average starting dose of 4.63mg/kg/dose. Eight of the twelve patients had a gestational age less than thirty weeks. Three patients had a creatinine clearance <50 mL/min at the start of gabapentin therapy. The majority of patients were admitted to the NICU due to lung disease or respiratory issues. Multiple adjunct medications were reviewed. Lorazepam was the most common adjunct medication used at initiation and at discharge from NICU or discontinuation of gabapentin. Only one patient experienced an adverse event from gabapentin use. This patient developed nystagmus at day of life 178 (day 59 of gabapentin). Overall, the medication was well-tolerated, and further analysis is being run on efficacy outcomes.

#### UTILIZING STUDENTS AND TECHNICIANS TO AUTHORIZE MEDICATION REFILLS THROUGH A COLLABORATIVE PRACTICE

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**Introduction:** In October 2014, Baystate Children's Specialty Center approached the Baystate Health Outpatient Pharmacies seeking a solution for the overwhelming burden associated with medication refill requests. Due to this burden, nursing priorities had shifted from direct patient care to the processing of refill requests and prior authorizations. It was uncertain whether a collaborative practice agreement (CPA) could be successful given limited resources and a lack of available pharmacist hours. The decision was made to develop a CPA utilizing specially trained pharmacy technicians and students, granting them the ability to authorize refill requests on a per-protocol

basis, under the direct supervision of a prescriber. **Methods:** The pilot program was initiated in November 2014, beginning with formal agreements between the pharmacists of the Baystate Health Outpatient Pharmacies and the medical staff of both the Pediatric Gastroenterology and Neurology Departments. The gastroenterology protocol included 24 medications for the treatment of constipation, diarrhea, irritable bowel syndrome, and inflammatory bowel disease, while the neurology protocol included 33 medications for the treatment and prevention of seizures and headaches. The protocol mandated the following criteria: a Baystate specialist had seen the patient within the previous 12 mo, a follow-up appointment was scheduled, and the patient demonstrated a history of compliance with attending appointments. The medication, route, strength, and frequency were then verified in both the most recent provider note and the patient's electronic medication list. If all of these conditions were met the request could be authorized for an additional 6 mo. **Results:** Within three weeks of initiating the program, it was determined that a standard refill request, with no complications, took 5 to 10 min to process, accounting for 10 to 14 man hours per wk. For medications outside the protocol parameters, further information was required to be communicated between departments, adding time and increasing work hours by an additional 25 per wk. Prior authorizations, approximately 10 per wk, required an additional 10 hrs. During the first 4 months, an average of 200 medication refill requests and 10 prior authorizations were submitted per week. Of these refill requests 50% were authorized following the written protocols. **Conclusion:** Through this pilot program, trained pharmacy technicians and students have been utilized to authorize standard medication refills. As a result, medication-related burdens on nursing staff have decreased while pharmacy roles have increased. Preliminary anecdotal evidence has suggested increases in patient satisfaction and compliance. Furthermore, medication safety has increased via decreased therapeutic duplications, discontinuation of medications for resolved indications, and correction of prescribing errors. The future of this project is focused on employee and patient satisfaction surveys, optimization of transitions of care, and 30-day follow-up phone calls to further improve patient satisfaction and increase medication adherence.

#### NEONATAL ABSTINENCE SYNDROME (NAS) PROTOCOL REVISIONS AT AN ACADEMIC MEDICAL CENTER

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**Introduction:** Neonatal abstinence syndrome (NAS)

occurs when an infant is exposed in utero to maternal use of opiates and/or other addictive substances. This syndrome is characterized by central nervous system hyperirritability and autonomic nervous system dysfunction. The incidence of NAS has increased drastically over the past decade to epidemic proportions. In Kentucky, NAS has increased 11-fold from 2001 to 2011 and is still rising. NAS often requires pharmacotherapy and extended hospitalization to prevent life-threatening withdrawal symptoms. However, no standardized evidence-based treatment plans have been implemented. Our institution uses a NAS treatment algorithm utilizing modified Finnegan scoring as a guide to carefully escalate and/or wean medications based on response. An initial Medication Use Evaluation (MUE) project was conducted in May of 2014 to analyze patient outcomes after NAS algorithm implementation. Results indicated a higher initial morphine dose as well as the earlier addition of clonidine could potentially decrease length of stay (LOS) resulting in cost-savings. The revised NAS protocol was implemented in June 2014. The purpose of this study is to determine if revised NAS protocol improved patient outcomes and decreased LOS. Through this study, we hope to further fine-tune the NAS algorithm leading to better symptom control and decreased LOS. **Methods:** We conducted a retrospective chart review of NAS patients admitted to our institution for NAS treatment from June 2014 to November 2014. Each patient's treatment regimen was evaluated to determine the number of agents required for symptom control. We excluded patients who received less than 10 days of therapy (mainly preterm infants), started treatment prior to admission, NAS treatment not completed at the time of data collection, or transferred to another facility. Data collected included gestational age, hospital of birth, LOS, length of NAS treatment, number of dose escalations, number of weans, maximum morphine dose, weaning schedule, use of add-on agents, maternal substance of abuse, and discharge disposition. **Results:** 152 patients were included in this analysis. After exclusion criteria were applied, 124 patients remained. Comparing the two data sets, the new protocol did not decrease LOS as anticipated. The first data set contained 21.5% of patients on a multidrug regimen while the second data set increased to 40% on a multidrug regimen. Surprisingly, the early addition of clonidine failed to impact LOS. **Conclusion:** Based on this analysis, the NAS protocol was once again revised in March 2015. The updated protocol recommends the initial starting dose of morphine 0.05 mg/kg/dose orally every three hours when Finnegan scores >24 (three scores >8 or two scores >24). The protocol recommends dose escalations up to 1 mg/kg/day before adding a second medication. The caregiver should consider the specific maternal substances of abuse when choosing the secondary medication.

# IMPACT OF FENTANYL CONTINUOUS INFUSION DOSING ON TIME TO SEDATION AMONG CRITICALLY-ILL CHILDREN

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**Introduction:** Fentanyl is a common opioid continuous infusion (CI) in the PICU. Due to its lipophilicity, studies have noted utilization of actual body weight for dosing in obese adults could lead to over-sedation, but there is a paucity of data in children. The purpose of this study was to examine the association between fentanyl CI dosing and time to goal sedation among critically-ill children. **Methods:** This IRB-approved, retrospective cohort study included 77 children 2-17 years receiving fentanyl CI between January 1, 2012-May 31, 2014. Patients receiving neuromuscular blocker CI's were excluded. Sedation was assessed by the State Behavioral Scale (SBS). The primary objective was to examine the association between fentanyl dosing and time to goal sedation (3 consecutive SBS scores 0 to -1). The secondary objective was to determine factors associated with under, optimal, and over-sedation. Cox proportional hazards regression was used to examine association of fentanyl CI dose with time to goal sedation while controlling for potential modifying and confounding factors [age, gender, weight, BMI, Pediatric Risk Factor of Mortality (PRISM)-III scores, fentanyl CI dose changes and boluses, and concomitant sedatives]. Competing risk models were used to identify factors associated with under, optimal, and over-sedation. **Results:** The majority of children were male with a mean age of  $8.6 \pm 4.9$  yrs. The mean weight was  $31.0 \pm 19.9$  kg, with a BMI-percentile of  $49.1 \pm 37.9$ . The majority (70.1%) were <85th BMI-percentile; 20.8% were classified as obese (>95th BMI-percentile). Fifteen (19.5%) had a previous PICU admission. The mean PRISM-III was  $14.2 \pm 8.9$ . The mean initial fentanyl dose was  $1.53 \pm 0.65$  mcg/kg/hr and  $45.1 \pm 31.5$  mcg/hr. The median time to goal sedation was 11 hours (range 3.57-227.3). Among non-obese children, for every 10 mcg/hr increase in initial fentanyl dosing, children were 19% less likely to achieve goal sedation [adjusted hazard ratio (HR): 0.81; (95%CI: 0.70-0.93)]. Non-obese children who had one or more dose changes and boluses took longer to achieve goal sedation ( $p < 0.01$ ). Initial dosing was not associated with time to goal sedation in obese children [adjusted HR: 1.09; (95%CI: 0.93-1.28)]. Children with previous PICU admissions were 71% less likely to achieve goal sedation [adjusted HR: 0.29 (95% CI: 0.12-0.73)]. Receipt of additional boluses



and higher PRISM-III scores were associated with optimal goal sedation and over-sedation, respectively ( $p < 0.01$ ). Dose changes, older age, obesity were associated with lower risk of over-sedation ( $p < 0.01$ ). No factors were associated with under-sedation ( $p > 0.05$ ).

**Conclusions:** There was wide variability in time to achieve goal sedation. Children with previous PICU admission were less likely to achieve goal sedation. The data suggest that non-obese children were less likely to achieve goal sedation with initial fentanyl CI dose. Future prospective pharmacokinetic and pharmacodynamic studies should evaluate differences in sedation outcomes in obese and non-obese children.

#### OFF LABEL USE OF DORNASE ALFA IN THE PEDIATRIC INTENSIVE CARE UNIT

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**Introduction:** Dornase alfa is a mucolytic agent approved for use in cystic fibrosis patients. Practice has expanded in Pediatric Intensive Care Units to include the use of dornase alfa in mechanically ventilated patients without cystic fibrosis. Limited evidence is available that evaluates the efficacy of dornase alfa in this patient population. The postulated benefit is that by decreasing mucous viscosity there may be improved ventilation, decreased atelectasis, fewer ventilator days, and less re-intubations.

**Objectives:** The primary objective of this study is to analyze the off-label use of dornase alfa in patients without cystic fibrosis who are admitted to the pediatric intensive care unit. Secondary objectives seek to characterize dornase alfa dosing strategies and overall health care costs.

**Methods:** To determine these outcomes, a retrospective study ranging from January 2011 to December 2013 will be performed. Data collected from the electronic medical record includes patient age, weight, indication, dosing, and duration of dornase alfa therapy. Other data encompasses mechanical ventilator days, duration of intensive care unit stay, duration of total hospital stay, and overall hospital cost.

**Results:** Included in the study were 142 cases of dornase alfa administration. Preliminary results show the following indications for dornase alfa: thick secretions (52.8%), atelectasis (39.4%), viral bronchiolitis (29.6%), and pneumonias (38.7%). These values are due to patients having multiple indications. The mean length of dornase alfa therapy was  $6.01 \pm 6.25$  days, with a mean number of doses totaling  $10.23 \pm 11.65$  doses. The average patient cost related to dornase alfa therapy was \$900.45. The most common dosing strategy observed was 2.5 mg nebulized every 12 hrs. The total number of ventilator days was  $12.33 \pm 13.56$  days. Length of Pediatric Intensive

Care Unit stay averaged  $16.38 \pm 15.73$  days, while total length of hospital stay was  $23.13 \pm 21.57$  days.

**Conclusion:** As found in this analysis, dornase alfa is used for multiple indications in ventilated patients without cystic fibrosis. The utility of this practice has yet to be determined from high quality clinical trials, as current data is conflicting as to the efficacy of dornase alfa in this patient population. Additional comparative studies are needed to assess the efficacy endpoint of off-labeled use of dornase alfa in mechanically ventilated pediatric patients without cystic fibrosis.

#### ASSESSMENT OF SECOND-GENERATION ANTIPSYCHOTIC UTILIZATION AND METABOLIC PARAMETER MONITORING IN AN INPATIENT PEDIATRIC POPULATION

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**Introduction:** Second-generation antipsychotics (SGAs) are utilized in pediatric patients for a variety of indications. Metabolic side effects, such as weight gain and elevated fasting blood glucose, are known complications of SGA use, particularly in adult patients. Recent studies indicate that current practices for monitoring of SGA-induced metabolic side effects in pediatric patients are deficient. Therefore, the primary purpose of this study was to evaluate metabolic parameter monitoring in pediatric patients discharged from an inpatient psychiatric institution on SGA treatment.

**Methods:** This quality improvement initiative retrospectively assessed SGA utilization and metabolic parameter monitoring in a pediatric population. This project was reviewed and approved by the quality improvement committee at our institution. Patients under 18 yrs of age discharged from an inpatient psychiatric institution on scheduled SGA treatment were included. Electronic medical records (EMRs) from 11/01/2013 to 04/30/2014 were reviewed. Patient specific data collected were: age, height, weight, BMI, waist circumference, fasting blood glucose, triglycerides, HDL, and blood pressure. In addition, SGA specific pharmacy data were also evaluated and included: SGA prescribed and total daily dose. Waist circumference percentiles were calculated to determine patients' metabolic syndrome status according to International Diabetes Federation (IDF) criteria. Outcomes were measured by tracking: percent of patients with documentation completed for each metabolic monitoring parameter; percent of patients with existing metabolic syndrome according to IDF criteria; average total daily dose for individual SGAs; and frequency of use of individual SGAs.

**Results:** Of 243 pediatric patients prescribed a

scheduled SGA at discharge, only 14.8% (n=36) had completed documentation of all metabolic monitoring parameters (age, blood pressure, weight, triglycerides, HDL, fasting blood glucose, and waist circumference). Blood pressure was the most commonly completed metabolic parameter in 241 patients (99.2%). Waist circumference was the least commonly complete parameter documented in 68 patients (28%); 14 of these patients (20.6%) were in the >90th percentile and 3 of the 14 (21.4%) met IDF criteria for metabolic

syndrome. Risperidone was the most commonly prescribed SGA (41%; n=99; 1.92 mg average daily dose).

**Conclusions:** Documentation of several metabolic parameters (i.e., blood pressure, weight, lipids, and fasting blood glucose) was high; however, only 36 patients (14.8%) had completed documentation for all parameters and thus could be evaluated for metabolic syndrome. These results suggest that more vigilance is needed to ensure complete metabolic monitoring has occurred in pediatric patients prescribed SGA therapy.