ABSTRACTS

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ORIGINAL RESEARCH

These papers describe original research in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, pharmacoepidemiology, and pharmacogenomics.

ADR/Drug Interactions

1. Evaluating Adverse Drug Reactions Occurring in the Medical Intensive Care Unit Using Three Objective Instruments for Causality Assessment. Sandra L. Kane-Gill, Pharm.D., M.Sc.,[1] *Elizabeth A. Forsberg, Pharm.D. Candidate,*[1] Cassandra J. Bellamy, Pharm.D.,[2] Margaret M. Verrico, R.Ph.[3]; (1) University of Pittsburgh, Pittsburgh, PA; (2) Hospital of the University of Pennsylvania, Philadelphia, PA; (3) University of Pittsburgh Medical Center, Pittsburgh, PA

PURPOSE: Objective instruments are used to determine the occurrence of adverse drug reactions (ADRs). The preferred instrument for use in the intensive care unit (ICU) is not established. The purpose of this study was to compare the agreement between the Kramer algorithm, the Naranjo Probability Scale, and the Jones algorithm in the ICU for the detection of ADRs.
METHODS: Adult patients admitted to the medical ICU from July 1, 2005, to June 30, 2006, who received drugs designated "triggers," signals to alert clinicians to potential ADRs, were eligible. A random sample of 261 triggers was selected for retrospective chart review. Each trigger was individually evaluated for potential ADRs using the Kramer algorithm, the Naranjo Probability Scale, and the Jones algorithm. Percent agreement among the instruments for all levels of certainty was estimated using the intraclass correlation coefficient. In addition, the percent agreement among instruments for the conclusive determination of an ADR was calculated using agreement between two of three instruments with a score of possible, probable, or definite.
RESULTS: For 223 patients (51.6% men) having 261 triggers, the mean ± SD age was 58.8 ± 17 years. Mean SAPSII score was 49.6 + 16.4.

Table. Agreement Between Instruments for All Levels of Certainty

Instrument	Intraclass Correlation Coefficient (confidence interval)
Naranjo vs. Kramer	0.949 (0.936–0.960)
Naranjo vs. Jones	0.919 (0.898–0.936)
Kramer vs. Jones	0.912 (0.890–0.931)
Naranjo vs. Kramer vs. Jones	0.927 (0.911–0.940)

When categories (remote, possible, probable, and definite) varied between instruments, most cases differed by only one level of certainty. A total of 79 ADRs were conclusively detected. Agreement among instruments was 97.5, 98.7, and 98.7% for an ADR using the Kramer, Naranjo, and Jones instruments, respectively.
CONCLUSIONS: These instruments demonstrated similar results for detecting ADRs in the ICU. We recommend using the simplest instrument, namely the Jones algorithm.

2. Emerging Adverse Events with Aliskiren: Increased Blood Pressure and Angioedema. *Krystal K. Haase, Pharm.D., BCPS*, Chris Tawwater, Pharm.D., Eric J. MacLaughlin, Pharm.D., BCPS; Texas Tech University Health Sciences Center, Amarillo, TX

PURPOSE: Aliskiren is the first direct renin inhibitor approved for the treatment of hypertension. This agent provides a novel mechanism of action, but its role is unclear. Concerns regarding potential adverse events have been raised, including paradoxical increases in blood pressure and angioedema. However, few cases of angioedema and no cases of increased blood pressure were reported in published trials. We conducted a systematic evaluation of the U.S. Food and Drug Administration's Adverse Event Reporting System (AERS) database to determine the incidence and significance of these two unrelated adverse events.
METHODS: Case data were extracted from the AERS database for the last two quarters of 2007. All adverse events for aliskiren were screened for terms describing increased blood pressure and allergic reactions, including angioedema, using definitions from the *Medical Dictionary of Approved Regulatory Terms*. Frequency, case outcomes, concomitant medications, timing, and demographics were evaluated.
RESULTS: A total of 641 unique adverse event cases were identified. Of those, 23.9% described increased blood pressure or ineffective therapy, with the former representing 56% of the cases. Reported outcomes included target organ damage (6%), hospitalization (6%), life-threatening complications (3.9%), and death (1.3%). Angioedema was described in 8.42% of all cases. Median time to reaction was 2 days; 19% of patients required hospitalization. Patients with angioedema were more likely to be on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers compared with patients with rash alone (11.1% and 23.4% vs. 0% and 2.4%, respectively; $p<0.05$).
CONCLUSIONS: Increased blood pressure and angioedema are clinically relevant adverse events reported for aliskiren. Most events occurred early after initiation. In addition, hospitalization and other complications were reported in several cases. Aliskiren should be initiated with caution or avoided in patients at increased risk of high renin–associated hypertension or angioedema until additional safety data are available.

3. Acute Kidney Injury Following Exposure to Antibiotic-Laden Bone Cement. *Paul Thill, Pharm.D., BCPS*; Ferris State University College of Pharmacy, Saginaw, MI

PURPOSE: This pilot study investigated a possible correlation between antibiotic-laden bone cement (ALBC) and nephrotoxicity during the early postoperative period of joint replacement procedures.
METHODS: This was retrospective review of patients undergoing total orthopedic joint replacement procedures from January 2006 to January 2007 at a community hospital. Any patient receiving ALBC was included in the analysis. We collected all serum antibiotic and creatinine concentrations performed during the hospital admission. A patient experiencing a doubling of serum creatinine from the preoperative value was identified as having acute kidney injury (AKI).
RESULTS: Thirty-six patients were identified as receiving tobramycin; 33 of these patients also received vancomycin in the bone cement. Five (14%) of the 36 patients receiving ALBC met the criteria for AKI. Two of these patients had toxic tobramycin serum concentrations. The first patient had a random serum concentration of 5 µg/mL at 4 days postimplantation; this concentration steadily declined after the prosthesis and cement were removed on day 7 postoperation. A second patient had a random tobramycin concentration of 70 µg/mL at 4 days postoperation and remained critically elevated after 4 weeks postoperation because the patient was too unstable to tolerate removal of the prosthetic joint.
CONCLUSIONS: One explanation for the high serum tobramycin concentrations is that inadequate mixing was taking place, and voids containing unincorporated antibiotic powder allowed the release of large quantities into the systemic circulation. On discovery of this series of patients, we changed the procedure of mixing cement to involve mixing of the dry cement powder with the antibiotic powder before adding the liquid resin. We also implemented a procedure of checking serum tobramycin concentrations postoperatively. Since these changes, there have been no cases of elevated tobramycin serum concentrations or unexplained AKI.

4. Drug Interactions in Prescriptions for Outpatients. *Sukhyang Lee, Pharm.D., Ph.D.,*[1] Jung Hwa Lee, M.S.[2]; (1) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku,

Seoul, South Korea; (2) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, IA, South Korea

PURPOSE: The aim of this study was to analyze the pattern of drug interactions in outpatients' prescriptions and identify contributing factors for interactions. The significance of drug interactions was classified by "Drug Interaction Facts 2006." Searches were performed both within prescriptions and across prescriptions for each patient.

METHODS: During a 1-year period from March 2005 to February 2006 at a university hospital in Korea, the prescriptions for outpatients were reviewed for drug interactions including the number, department, and combination. The interaction significance was evaluated on the basis of "Drug Interaction Facts 2006."

RESULTS: There were 287,905 prescriptions with two or more drugs, of which 41,491 (14.4%) had drug interactions. Those of significance-1 level accounted for 14,640 (25.4%) prescriptions. The overall rate of drug interactions was highest in cardiology, with a rate of 45.2%, and was higher in the elderly. The most common significance-1 drug interaction was clopidogrel–acetyl salicylic acid. There were, in total, 120,782 prescriptions from the different departments during same period. There were 5570 prescriptions with drug interactions. Those of significance-1 level accounted for 1380 (15.8%) prescriptions. The overall rate of drug interactions was the highest in cardiology and endocrinology, with a rate of 12.9%, and was higher in the elderly. The most common prescription with significance-1 drug interaction was clopidogrel–acetyl salicylic acid.

CONCLUSIONS: Drug interactions both within and across prescriptions were included in routine therapy. An online computer-based system should monitor for incidences of adverse effects associated with drug interactions. The drug interaction information of the system should be used with consideration of prescription specification and with close monitoring.

5. Increased Risk of Significant Creatinine Kinase Elevation with High Dose Simvastatin Compared to Moderate Dose. *Ryan S. Stolcpart, Pharm.D.*, Kari L. Olson, Pharm.D., Thomas Delate, Ph.D., Jon R. Rasmussen, Pharm.D., Thomas F. Rehring, M.D., H. Whitton Hollis Jr., M.D., John A. Merenich, M.D.; Kaiser Permanente Colorado Region, Aurora, CO

PURPOSE: This study compared the risk of creatinine kinase (CK) elevation in patients on simvastatin 40 mg daily with other doses of simvastatin and lovastatin.

METHODS: This retrospective case-control study at Kaiser Permanente Colorado identified all patients who received a prescription for lovastatin or simvastatin between January 1, 1999, and June 30, 2006. Patients (n=183), those who developed a CK elevation of 2000 IU or more while taking the statin, were matched 1:10 to controls (n=1830) by the sold date of the statin prescription taken by the patients at the time of CK elevation. Multivariate, conditional logistic regression was used to identify demographic, comorbidity, laboratory, and medication use data associated with the CK elevation.

RESULTS: A total of 73,162 patients received 1,017,218 prescriptions for lovastatin or simvastatin during the study period. Elevations in CK of 2000 IU/L or greater occurred in 183 (0.25%) cases. Simvastatin use was associated with a higher risk of CK elevation than lovastatin (OR = 1.53; 95% CI: 1.01–2.31). Using simvastatin 40 mg daily as the referent, simvastatin 80 mg daily was associated with an increased risk of CK elevation (OR = 2.6; 95% CI: 1.1–4.4), whereas lovastatin 80 mg/day was not (OR = 1.8; 95% CI: 0.8–3.5). Concomitant use with medications known to interact with statins was associated with an increased risk of CK elevation (OR = 6.07; 95% CI: 4.05–9.08), particularly with 80 mg of either lovastatin (OR = 23.8; 95% CI: 7.7–74.0) or simvastatin (OR = 15.2; 95% CI: 5.2–44.1).

CONCLUSIONS: Our study suggests that, although the overall risk is low, simvastatin carries a higher risk of CK elevations than lovastatin and that simvastatin 80 mg daily carries a higher risk than simvastatin 40 mg daily. This risk is magnified when high doses of either simvastatin or lovastatin are used concurrently with interacting medications.

6. The Valproate Related Thrombocytopenia. *Ji Young Yun, M.S.,*[1] Sukhyang Lee, Pharm.D., Ph.D.[2]; (1) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, South Korea; (2) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, South Korea

PURPOSE: To investigate the incidence and potential risk factors of thrombocytopenia in hospitalized patients receiving valproate.

METHODS: We retrospectively studied adult inpatients treated with valproate between July and December 2007. The clinical data were collected for each patient's age, sex, weight, platelet count, bleeding tendency, valproate dose/day, dose/kg/day, and plasma valproate concentration. Thrombocytopenia was defined as a platelet count less than 130 x 103/mm^3. Valproate-related thrombocytopenia was evaluated based on Naranjo's algorithm with greater than probable and possible. Incidence and risk factors were assessed for the thrombocytopenia.

RESULTS: Eleven (5.4%) of all 204 patients developed thrombocytopenia. The plasma valproate concentration (91.6 ± 24.1 vs. 73.2 ± 22.7; p=0.02), dose/day (1390.9 ± 413.8 vs. 1134.7 ± 322.9; p=0.013), and dose/kg/day (26.4 ± 11.3 vs. 20 ± 6.4; p=0.003) were significantly higher in patients with thrombocytopenia. The plasma valproate concentration greater than 100 µg/mL was a significant risk factor of thrombocytopenia (p=0.014). The degree of thrombocytopenia was asymptotic and had no bleeding complications with dose reduction or dose discontinuation.

CONCLUSIONS: A plasma valproate concentration greater than 100 µg/mL should alert clinicians to the risk of developing thrombocytopenia. The platelet count should be followed for patients receiving a high valproate concentration.

Adult Medicine

7. Evaluating the Rate of Venous Thromboembolism (VTE) Prophylaxis and Percentage of Ordered Doses Administered in Medically Ill Patients. *Sheila M. Wilhelm, Pharm.D., BCPS,*[1] May Chang, Pharm.D., BCPS[2]; (1) Wayne State University, Detroit, MI; (2) Harper University Hospital, Detroit, MI

PURPOSE: In medically ill patients, venous thromboembolism (VTE) prophylaxis reduces VTE risk by at least 50%; however, it is underused. In a previous study at Harper University Hospital (HUH), medical staff education yielded appropriate VTE prophylaxis for 73.1% of eligible medically ill patients. To obtain optimal benefit, patients must receive all ordered doses of prophylactic medication. The aims of the current study are an assessment of the endurance of education regarding VTE prophylaxis through the determination of current VTE prophylaxis rates in medically ill inpatients and a determination of the percentage of ordered doses of VTE prophylactic medication administered.

METHODS: Patients admitted to the internal medicine service at HUH from August 1, 2007, to October 31, 2007, were retrospectively screened by chart review. Patients between 18 and 89 years old were enrolled. Demographics, VTE risk factors, bleeding risk factors, and VTE prophylaxis regimen—including the number of doses ordered and administered—were assessed. Eligibility for pharmacological VTE prophylaxis was based on the Detroit Medical Center VTE prophylaxis pathway.

RESULTS: A total of 531 patient records (41% men, mean age 61.5 years) were reviewed. Three hundred fifty-two were eligible for VTE prophylaxis, and 242 (68.8%) of those received appropriate prophylaxis. Forty additional patients had VTE prophylaxis regimens ordered but either were ineligible for prophylaxis (n=19) or received an inappropriate regimen based on institutional standards (n=21). Of 282 patients who had any prophylaxis doses ordered, 103, 162, and 212 received 100%, more than 90%, and more than 80% of ordered doses, respectively. Of 244 patients who received subcutaneous heparin 5000 units 3 times/day, 166 (68%) either missed or refused at least one dose. Eighty-six refused, and 126 missed one or more doses; 46 of these both refused and missed one or more doses.

CONCLUSIONS: Pharmacist-driven educational efforts have had a lasting impact on the rate of appropriate VTE prophylaxis. In

addition, most ordered prophylactic medication is administered.

8. Evaluation of an Argatroban Dosing Protocol and Identification of Dose-Altering Patient Characteristics. *Erin L. Schaaf, Pharm.D.*, Bridget Morse, Pharm.D., Tracy Sprunger, Pharm.D., BCPS; Community Health Network, Indianapolis, IN

PURPOSE: Current argatroban dosing, based on the manufacturer's guidelines, is weight based with decreased dosages in hepatic failure only. Community Health Network (CHN), in Indianapolis, IN, has experienced many activated partial thromboplastin time (aPTT) values outside the therapeutic range with its current protocol in accordance with these guidelines. Studies have shown that, together with hepatic dysfunction, other patient characteristics may influence argatroban dosing.

Objective: The primary study objective was to determine the percentage of therapeutic aPTTs for patients initiated on argatroban according to CHN's protocol. The secondary study objective was to determine the effect of renal dysfunction on the therapeutic argatroban dose.

METHODS: CHN patients who received argatroban from January 2003 to October 2007 were included. Baseline characteristics and comorbidities were collected in all patients together with identification of organ dysfunction on initiation of argatroban. Baseline aPTT values and subsequent numbers of aPTT levels under, at, or below target were collected for each patient.

RESULTS: Thirty-four of 70 patients initiated on argatroban were included in the study. The mean time to reach a therapeutic aPTT was 17 hours (SD ± 10 hours) with a mean dose of 1.9 µg/kg/minute (SD ± 1.5 µg/kg/minute). Fifty-one percent of patient aPTTs were therapeutic, and 28% and 21% were subtherapeutic and supratherapeutic, respectively. Baseline serum creatinine was elevated at 3.0 mg/dL (SD ± 3 mg/dL) with an estimated creatinine clearance (CrCl) of 39 mL/minute (SD ± 32 mL/minute). Patients with CrCl values less than 30 mL/minute required a dose of argatroban that was, on average, 1.7 µg/kg/minute less than patients with CrCl values more than 60 mL/minute (p=0.015).

CONCLUSIONS: A therapeutic aPTT was reached and maintained for 51% of the recorded values when dosed according to protocol. Estimated CrCl was the only significant predictor of the argatroban dose needed to maintain a therapeutic aPTT.

9. Ability of the Activated Partial Thromboplastin Time Versus the Antifactor Xa Assay to Maintain Unfractionated Heparin Within a Therapeutic Range. *Ryan D. Tabis, Pharm.D.*, Christopher J. Taylor, Pharm.D., BCPS; Carl T. Hayden VA Medical Center, Phoenix, AZ

PURPOSE: The primary objective of this study was to compare the ability of the activated partial thromboplastin time (aPTT) and anti-Xa assay to maintain a therapeutic concentration of heparin when used in a dosing protocol for acute venous thromboembolism (VTE). Secondary objectives included a comparison of bleeding rates between the tests and a comparison of the mean number of venipunctures (as required for monitoring) between the tests.

METHODS: This study was a retrospective cohort study. Patients receiving a continuous infusion of unfractionated heparin (UFH) from January 2001 to April 2008 were included. Patients who were monitored and had doses adjusted by a protocol using the antifactor-Xa test made up one group, and matching case-controls who were monitored and had dosages adjusted by an aPTT-based protocol served as the comparator group.

RESULTS: Seventy-four subjects were in the aPTT-monitored group, and 49 subjects were in the antifactor Xa–monitored group. For the primary end point, patients in the aPTT-monitored group had 45.1% of the tests within the therapeutic range, whereas 56.9% of the tests were within the therapeutic range in the antifactor Xa–monitored group (p=0.124). In addition, major bleeding was discovered in three patients in the aPTT-monitored group versus none in the antifactor Xa–monitored group. Finally, patients in the aPTT-monitored group received a mean of 8.69 venipunctures during the first 96 hours of therapy versus only 7.84 venipunctures in the antifactor Xa–monitored group.

CONCLUSIONS: Although patient recruitment will continue in the antifactor Xa–monitored group to reach a sample size that will provide appropriate statistical power, it appeared that using an antifactor Xa–based protocol to monitor and adjust UFH dosing resulted in a trend toward higher percentages of tests within the therapeutic range, fewer major bleeding events, and fewer venipunctures in the first 96 hours of therapy.

Ambulatory Care

10. A Method for Educating Patients and Documenting Smoking Status in an Electronic Medical Record. *Sarah Shrader, Pharm.D., BCPS*, Kelly Ragucci, Pharm.D., FCCP, BCPS, CDE; South Carolina College of Pharmacy – MUSC Campus, Charleston, SC

PURPOSE: Determine the rates of smoking cessation and movement along the transtheoretical model of change after implementation of a template in existing pharmacy-related progress notes within the electronic medical record.

METHODS: Patients who were routinely monitored by clinical pharmacists for anticoagulation and diabetes mellitus education at three university-based primary care clinics at the Medical University of South Carolina were included. At each visit, the pharmacist would ask questions, provide education related to smoking cessation status, and document this information in a newly designed smoking cessation template that was incorporated into existing progress notes. Data, including smoking cessation rates and movement along the continuum of change, were collected between April 2007 and March 2008. The McNemar chi-square test was used to compare the groups of patients achieving smoking cessation pre- and postintervention.

RESULTS: Of the 609 patients seen by clinical pharmacists, the patients' average number of visits was 12, and the average number of years smoked was 27 (20 cigarettes per day). Ninety patients (15%) were current smokers at the beginning of the study. Thirty-eight patients (42%) had moved to the action or maintenance phase by the end of the study period, and 52 (58%) patients had moved forward within the continuum of change. More specifically, 34 patients in the contemplation/preparation phase and 4 patients in the precontemplation phase pre-intervention achieved cessation at the end of the study period (p=0.03) Of the 38 patients who achieved smoking cessation, 12 (31%) used varenicline, 6 (16%) used nicotine replacement, 4 (11%) used bupropion, 15 (39%) used no drug therapy, and 1 (3%) used a combination of nicotine replacement and bupropion.

CONCLUSIONS: Incorporating a smoking cessation template in existing progress notes and providing education during existing pharmacy-referral visits is a simple and effective method to assist patients in achieving smoking cessation.

12. A Retrospective Look at the Effects of a Pharmacist-Run Tobacco Cessation Clinic. *Timothy C. Chen, Pharm.D.*, Erin Mikusky, Pharm.D., Khanh L. Nguyen, Pharm.D., Stacey Nguyen, Pharm.D., Jessica Harris, Pharm.D., Mark Bounthavong, Pharm.D.; Department of Veterans Affairs, San Diego, CA

PURPOSE: The prevalence of smokers in the Department of Veterans Affairs is significantly higher than in the general population (33% vs. 23%), suggesting that tobacco cessation programs are needed to assist veterans to prevent morbidity and mortality. The pharmacist-run tobacco cessation clinic at the VA San Diego Healthcare System was created in 2005 to improve overall access to tobacco cessation options and to improve follow-up. The purpose of this study was to evaluate the success of the clinic.

METHODS: In this retrospective chart review study, all patients who had received an initial pharmacist telephone call for smoking cessation products at the VA San Diego Healthcare System from January 1, 2007, to June 30, 2007, were evaluated. The primary outcome was to determine the success rate of the clinic by calculating the abstinence rates at 1, 3, and 6 months. Secondary outcomes included determining the abstinence rates for patients with psychiatric illness and determining the effect of follow-up telephone calls by the smoking cessation pharmacists on cessation rates. Cessation rates were calculated using Pearson's CHI^2 test.

Univariate analysis and logistic regression analysis were used to determine which factors were associated with a successful quit attempt.
RESULTS: A total of 503 patients were included in this analysis. Cessation rates at 1, 3, and 6 months were 37, 24, and 16%, respectively. No significant baseline factors were found between the two groups except for age. The number of follow-up calls was a significant factor in maintaining tobacco-free status.
CONCLUSIONS: The analysis demonstrated a 16% cessation rate at 6 months for the pharmacist-run clinic. Follow-up calls were a significant factor in improving cessation rates. Despite some limitations, the analysis suggests that pharmacist-run tobacco cessation clinics improve cessation rates in the veteran population.

13. Characteristics of Prescription Refill Requests in a Primary Care Clinic. *Devra K. Dang, Pharm.D., BCPS, CDE,*[1] Nina Yen, Pharm.D.,[1] Bruce E. Gould, M.D.,[2] Keith vom Eigen, M.D., MPH, Ph.D.[2]; (1) University of Connecticut, Storrs, CT; (2) University of Connecticut School of Medicine, Farmington, CT
PURPOSE: Responding to the increased volume of prescription refill requests has become an overwhelming task for health care providers in primary care and other settings. This study identified the extent of, and reasons for, the refill request burden in an urban primary care clinic.
METHODS: This study was conducted in an adult primary care clinic, and data were obtained on 10 different days between November 2006 and January 2007. Data were recorded each time a prescription renewal request was received and addressed by the on-site physician. Information collected included drugs requested, request method, possible causes for the request, how the request was managed, and time spent on each request. In addition, a convenience sample of patients who presented to the clinic was asked to complete an anonymous survey to describe their refill request habits, patterns, and satisfaction with the current refill process.
RESULTS: A total of 150 refill requests were reviewed, and 177 patient surveys were completed. Most requests were received by pharmacy fax (63.2%). An average of 16.4 (range 9–33) refill requests were received each day, with a mean of 8.1 minutes spent addressing each request. A provider issue contributed to 47.3% of refill requests, with the most common issue being no refills documented in the chart at the last visit (59.2%). A patient issue also contributed to 47.3% of requests, with missed appointments as the most common etiology (54.9%). Ninety-six percent of the patients reported being at least somewhat happy with the clinic's prescription renewal process.
CONCLUSIONS: Providers were spending up to 4.5 hours per day resolving refill requests that were mainly due to a provider- or patient-related etiology. Provider and patient education regarding better methods of requesting, managing, and documenting medication refills is needed.

14E. Effect of Depression on Diabetes Control and Medication Adherence in Underserved Patients. *Devra K. Dang, Pharm.D., BCPS, CDE,*[1] Michelle Flynn, Pharm.D.,[2] Charles Caley, Pharm.D., BCPP,[1] Thomas E. Buckley, R.Ph., MPH,[1] Neil J. Facchinetti, Ph.D.[1]; (1) University of Connecticut School of Pharmacy, Storrs, CT; (2) Saint Francis Hospital and Medical Center, Hartford, CT
PURPOSE: Concomitant depression may affect the ability of a patient with diabetes to adhere to treatment plans and, subsequently, the degree of diabetes control. This study (1) identified the prevalence and severity of depression in patients with diabetes at an urban primary care clinic and (2) evaluated correlations between depression and diabetes control, medication adherence, quality of life, and health use.
METHODS: A convenience sample of 100 consented patients were screened using the Patient Health Questionnaire (PHQ-9), a self-report of depressive symptoms, the Modified Morisky scale, a self-report on medication adherence behavior, and the SF-12 Health Survey, a self-report of general health and quality of life. Chart review of the 12 months before study entry was performed focusing on indicators of diabetes control. Patients with no to mild depression (PHQ-9 score less than 10) were compared with those having moderate to severe depression (PHQ-9 score of 10 or more).
RESULTS: Ninety-nine patients completed the study. PHQ-9 results showed that 66.7% were screened as having no to mild depression, and 33.3% were screened as having moderate to severe depression. Of those who did not have a diagnosis of depression before study entry, 21.6% reported moderate to severe depression. Compared with patients having no to mild symptoms, patients with moderate to severe depression reported lower medication adherence and health-related quality of life and had a higher number of clinic visits ($p<0.05$ for all parameters). More patients with moderate to severe depression received a diagnosis of peripheral neuropathy ($p=0.036$). No statistically significant differences were noted for mean glycosylated hemoglobin, blood pressure, or lipid panel values between the two patient groups.
CONCLUSIONS: The high rate of comorbidity between diabetes and depression makes it an essential issue for clinicians to address. Identification of depression and its severity in patients with diabetes is expected to lead to evaluation and treatment and potentially to improved medication adherence and outcomes.
Presented at the American Society of Health-System Pharmacists Midyear Clinical Meeting, Las Vegas, NV, December 2–6, 2007.

Bone Health/Osteoporosis

15E. Bone Mineral Density and Biochemical Marker Response Rates in Postmenopausal Women After Treatment with Zoledronic Acid. Pierre D. Delmas, M.D., Ph.D.,[1] I. Reid, M.D., M.B., Ch.B.,[2] René Rizzoli, M.D.,[3] Silvano Adami, M.D.,[4] Philip Sambrook, Ph.D.,[5] Erik F. Eriksen, M.D., D.M.Sc.,[6] *Peter Mesenbrink, Ph.D.,*[7] Richard Eastell, M.D.[8]; (1) Hôpital Edouard Herriot, Lyon, 69437 Lyon Cedex 03, Lyon, France; (2) University of Aukland, Auckland, New Zealand; (3) Geneva University Hospitals, Geneva, Switzerland; (4) University of Verona, Verona, Italy; (5) University of Sydney, Sydney, Australia; (6) Novartis Pharma AG, Basel, Switzerland; (7) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (8) University of Sheffield, Sheffield, UK
PURPOSE: Clinical monitoring of responses to treatment is important. In the HORIZON-Pivotal Fracture Trial, 7736 women received three annual infusions of zoledronic acid 5 mg (ZOL) or placebo; ZOL significantly reduced osteoporotic fractures of the spine, nonspine, and hip.
METHODS: Lumbar spine bone mineral density (BMD) was measured annually in a subset of 541 women. In another subset, bone turnover markers (C-telopeptides [CTX], bone alkaline phosphatase [bone ALP] [n=605], and procollagen type I intact N-terminal propeptide [n=1248]) were measured in serum at baseline and at 12, 24, and 36 months. CTX and bone ALP were also measured at 6 months. We assessed response rates to treatment in two ways: (1) fraction of patients showing expected deviation from baseline and (2) fraction of patients showing deviation from baseline in excess of the least significant change (LSC) for the given biomarker.
RESULTS: Lumbar spine BMD showed increases over baseline in 88.8, 92.4, 93.2, and 94.8% of patients at 6, 12, 24, and 36 months, respectively. Assuming an LSC of 3.0%, response rates at the same time points were 50.4, 61.9, 83.4, and 83.6%, respectively. Serum CTX (S-CTX) was the most sensitive biochemical marker; a decrease from baseline was observed in 96.0, 94.5, 89, and 86.2% of patients at 6, 12, 24, and 36 months, respectively. Assuming an LSC for CTX of 60%, response rates were 72.7, 52.5, 46.6, and 44.0%, respectively.
CONCLUSIONS: In conclusion, S-CTX assessment at 6 months provides excellent early monitoring of patient responses to ZOL, with 96% showing a decrease and 72.2% showing a clinically significant reduction. Spine BMD increases were observed in 92.4% of patients at 12 months and in 93.2% of patients at 24 months, and clinically significant BMD responses were observed in 61.9% at 12 months and in 83.4% at 24 months. ZOL had a favorable safety profile and was generally well tolerated.
Presented at the IBMS Davos Workshops: Bone Biology & Therapeutics; Davos, Switzerland, March 9–14, 2008.

Cardiovascular

16. Incremental Direct Treatment Cost of Atrial Fibrillation in the Medicare Population. Won Chan Lee, Ph.D.,[1] Gervasio A. Lamas, M.D.,[2] Sanjeev Balu, Ph.D., M.B.A.,[3] *James Spalding, Pharm.D., M.S.*,[4] Qin Wang, M.S.,[5] Chris Pashos, Ph.D.[6]; (1) Abt Bio-Pharma Solutions Inc., Bethesda, MD; (2) Mount Sinai Medical Center, Miami Beach, FL; (3) Abt Bio-Pharma Solutions, Lexington, MA; (4) Astellas Pharma US, Inc., Deerfield, IL; (5) Abt Bio-Pharma Solutions, Inc., Bethesda, MD; (6) Abt Bio-Pharma Solutions, Inc., Lexington, MA

PURPOSE: Atrial fibrillation (AF) is the most commonly sustained arrhythmia in adults and can involve costly treatment and complications. Still, there are few estimates of direct treatment cost data of AF in the Medicare population in the United States. This study investigated whether the direct treatment cost of Medicare patients having a diagnosis of AF would be higher than a matched cohort of non-AF patients.

METHODS: A Medicare claims database of a 5% random national sample was used to identify patients receiving a diagnosis of AF in 2003. These patients were matched on a 1:1 basis with a patient without AF by age, gender, and race. Claims for these patients were examined from 1 year before their index AF diagnosis to 1 year of follow-up postindex date. The incremental cost of treating AF was calculated with multivariable regression models controlling for covariates.

RESULTS: In 2003, 55,260 subjects developed new AF, of which 69% were 75 years or older, 54% were women, and 91% were white. The incremental treatment cost of AF was estimated to be $14,188 (95% CI: $13,197–$14,993; p<0.01). Stroke and heart failure (HF) were the most common complications at 1-year post-AF diagnosis, with a higher number of AF patients experiencing stroke (23.1% vs. 13.3%; p<0.01) and HF (36.7% vs. 10.4%; p<0.01) compared with non-AF patients. Incremental impact of stroke on AF treatment cost was estimated to be $7929 ($23,143 vs. $15,214, p<0.01), and HF had a much higher impact at $15,540 ($30,664 vs. $15,214; p<0.01) relative to an AF patient without stroke and HF, respectively.

CONCLUSIONS: Average incremental direct treatment costs for patients with AF were estimated to be greater than the previously reported estimate in the Medicare population. A substantial portion of attributed costs resulted from HF and stroke incidence in this population.

17. Evaluation of a Multidisciplinary Comprehensive Atherosclerosis Management Clinic. *Cynthia A. Jackevicius, B.Sc.Pharm., M.Sc., Pharm.D., BCPS, FCSHP*,[1] Hang Tran, Pharm.D.,[1] Freny Vaghaiwalla Mody, M.D.[2]; (1) Western University of Health Sciences, Pomona, CA; (2) Veteran Affairs Greater Los Angeles Healthcare System (VAGLAHS), Los Angeles, CA

PURPOSE: Despite the scientific evidence, tolerability, and availability of secondary prevention medication therapy for coronary heart disease, a large number of patients remain untreated. To address the underuse of secondary prevention treatment, a multidisciplinary specialty cardiology clinic, Comprehensive Atherosclerosis Management Program (CAMP), was implemented for patients who had been hospitalized for acute coronary syndromes (ACS). Patients are referred for a one-time CAMP clinic visit 2 months post-ACS. The objectives of the study were to evaluate the overall effectiveness of CAMP by comparing the (1) use of secondary prevention drugs and (2) risk factor parameters (e.g., lipids, blood pressure) in patients enrolled or not in the CAMP clinic 6 and 12 months posthospital discharge.

METHODS: We conducted a retrospective cohort study. Patients hospitalized for ACS between August 2003 and June 2006 were classified into CAMP and non-CAMP groups. Patients were evaluated using chart review for demographics, comorbidities, use of secondary prevention drugs, laboratory values, and clinical outcomes.

RESULTS: A total of 158 patients were included in the study. Baseline demographics were comparable between CAMP and non-CAMP patients. Although use of secondary prevention drugs declined in both groups over time, the CAMP group had higher rates of medication use at 6 and 12 months. CAMP patients had a lower low-density lipoprotein (LDL) and higher high-density lipoprotein (HDL) at 6 months but also had a higher hemoglobin A1C. At 12 months, CAMP patients retained a lower LDL and higher HDL, but differences were not as marked.

CONCLUSIONS: This study suggests that the CAMP clinic provides benefit to patients with ACS in medication use and lipid parameters. The benefit of CAMP appeared to decrease over time, suggesting the potential need for follow-up visits.

18. Circulating Aldosterone and Mineralocorticoid Receptor Genotype Are Predictive of Potassium Response to Spironolactone in Heart Failure. *Larisa H. Cavallari, Pharm.D.*, Vicki L. Groo, Pharm.D., Marlos A. Viana, Ph.D., Yang Dai, Ph.D., Shitalben R. Patel, M.S., Thomas D. Stamos, M.D.; University of Illinois at Chicago, Chicago, IL

PURPOSE: Spironolactone is a mineralocorticoid receptor (NR3C2) antagonist that improves survival in heart failure; however, its use is limited by an increased risk of hyperkalemia. We sought to identify patient-specific factors associated with spironolactone-induced potassium elevation in heart failure.

METHODS: Sixty-two patients with heart failure were started on spironolactone, with serum potassium and aldosterone determined at baseline and potassium repeated 1 week after spironolactone initiation and dose titration. Angiotensinogen G-6A and M235T and *NR3C2* C215G and I180V genotypes were determined using polymerase chain reaction and pyrosequencing or capillary sequencing. Demographic, clinical, and genetic data were compared between patients whose potassium increased by more than 0.5 mEq/L (high response group; n=15) and those with lesser potassium elevations (low response group; n=47). Variables potentially associated with potassium response on univariate analysis were entered in a multivariate logistic regression model to assess their predictiveness.

RESULTS: Patients in the high potassium response group had a higher median (interquartile range) aldosterone level (182 [127–222] vs. 92 [62–118] pg/mL; p=0.002) and frequency of the *NR3C2* 215G allele (50% vs. 22%; p<0.01) compared with patients in the low response group. Angiotensin and *NR3C2* I180V genotypes were similarly distributed between groups. Aldosterone concentration was positively correlated with diuretic dose (r=0.313; p=0.014) and negatively correlated with serum potassium (r = -0.319; p=0.012). On regression analysis, factors predictive of potassium increases greater than 0.5 mEq/L were aldosterone greater than 150 pg/mL (OR = 27.6 [95% CI: 2.8–277.3]) and *NR3C2* 215G carrier status (17.2 [1.6–183.3]).

CONCLUSIONS: Our data suggest that potassium should be monitored with particular caution when initiating spironolactone in patients with heart failure having evidence of elevated aldosterone, such as high diuretic requirements or low baseline potassium, or the *NR3C2* 215G allele.

19. Phenotypic Characterization of Endothelial Function in Individuals with Established Atherosclerosis Using Two Noninvasive Methods. *Almasa Bass, Pharm.D.*,[1] Melissa Caughey, R.V.T.,[2] J. Heyward Hull III, Pharm.D., M.S.,[1] George A. Stouffer, M.D.,[2] Alan L. Hinderliter, M.D.,[2] Craig R. Lee, Pharm.D., Ph.D.[1]; (1) Eshelman School of Pharmacy, UNC at Chapel Hill, Chapel Hill, NC; (2) School of Medicine, Division of Cardiology, UNC at Chapel Hill, Chapel Hill, NC

PURPOSE: Endothelial dysfunction contributes to atherosclerotic lesion development, and predicts risk of coronary events. Brachial artery ultrasound flow-mediated dilation (BAUS-FMD) is the gold standard noninvasive method to assess endothelial function; however, interuser variability limits its widespread use. Digital peripheral arterial tonometry (PAT) offers greater potential for multicenter use, including ambulatory settings where testing can be completed by pharmacists. We sought to evaluate the relationship between the BAUS-FMD and digital PAT measures of endothelial function in patients with established atherosclerosis.

METHODS: Using a cross-sectional design, 37 individuals with 50%

or more stenosis in one or more major epicardial artery were studied for 58 ± 27 (mean ± SD) days after their cardiac catheterization, after fasting overnight and withholding their morning medications. Brachial artery reactivity was assessed by ultrasonography by quantifying the peak percent change in arterial diameter (FMD%) and peak change in blood flow velocity-time integral (VTI-ratio) before and after induction of reactive hyperemia by forearm cuff occlusion for 5 minutes. The reactive hyperemia-induced change in digital pulse volume amplitude (PAT-ratio) was simultaneously measured using the *EndoPAT2000* device (Itamar Medical). All non-normally distributed data were log transformed. Relationships between log PAT-ratio, FMD, and log VTI-ratio were determined by regression analysis.
RESULTS: Subjects were 56 ± 10 years old, 70% men, and 78% white. In addition, 68% underwent revascularization, whereas 49, 84, and 95% were receiving angiotensin-converting enzyme inhibitors, b-blockers, and statins, respectively. No significant relationship was observed between log digital PAT-ratio and FMD ($r = -0.123$, $p=0.496$). However, a significant correlation existed between log PAT-ratio and log VTI-ratio ($r=0.598$, $p<0.001$). Similar relationships were observed after adjusting for age and gender ($p=0.410$ and $p<0.001$, respectively).
CONCLUSIONS: These findings suggest that BAUS-FMD and digital PAT-ratio measure different facets of endothelial function and represent distinct vascular phenotypes. Future studies in larger populations are necessary to validate these relationships and elucidate the prognostic utility of each phenotypic measure of endothelial function.

20. Efficacy and Safety of Aliskiren for the Treatment of Hypertension. *Benjamin W. Van Tassell, Pharm.D., BCPS,*[1] Mark A. Munger, Pharm.D.,[1] Anthony Yadao, M.D.[2]; (1) University of Utah, College of Pharmacy, Salt Lake City, UT; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ
PURPOSE: Direct renin inhibitors (DRIs) are the newest class of therapies available for the treatment of hypertension. Aliskiren is the first of the DRIs to be approved for the treatment of hypertension as either monotherapy or in combination with other antihypertensive agents.
METHODS: These data represent a pooled analysis of controlled studies of aliskiren conducted and completed before January 1, 2006. Additional studies of aliskiren combination therapy are also presented.
RESULTS: In pooled trials of more than 7000 patients with mild to moderate hypertension, once-daily aliskiren treatment (n=4704) for 6–8 weeks reduced mean sitting (ms) systolic/diastolic blood pressure from baseline by 8.7 to 13.0/7.8 to 10.3 mm Hg (150 mg) and 14.1 to 15.8/10.3 to 12.3 mm Hg (300 mg). When aliskiren 150 or 300 mg was added to hydrochlorothiazide (HCTZ) 12.5 or 25 mg, respectively, ms systolic blood pressure and ms diastolic blood pressure were lowered from baseline significantly more than either component monotherapy ($p<0.05$). Treatment for 8 weeks with aliskiren 150 mg and valsartan 160 mg (with forced titration to aliskiren 300/valsartan 320 at week 4) lowered ms systolic blood pressure and ms diastolic blood pressure from baseline by 17.2 and 12.2 mm Hg, respectively, both significantly greater than either agent alone ($p<0.0001$). The overall incidence of adverse events, most of which were mild or moderate, was similar between aliskiren (39.8%) and placebo (40.2%). The most common adverse events thought to be related to aliskiren were headache, diarrhea, and fatigue.
CONCLUSIONS: In patients with mild to moderate hypertension, aliskiren was well tolerated and effective in lowering blood pressure. Current and future studies will explore the effects of aliskiren on cardiovascular outcomes. One recently completed study showed an antiproteinuric effect in hypertensive patients with diabetes, independent of blood pressure lowering. The combination of aliskiren and losartan for 24 weeks reduced the mean urinary albumin-to-creatinine ratio an additional 20% (95% CI: 9–30%; $p=0.0009$) compared with losartan plus placebo.

21. Atmospheric Pressure and INR Variability – Are They Related? *Michael E. Ernst, Pharm.D.,*[1] Robert F. Shaw, Pharm.D., MPH,[2] Erika J. Ernst, Pharm.D.,[3] Bruce Alexander, Pharm.D.,[4] Peter J. Kaboli, M.D.[5]; (1) College of Pharmacy and Department of Family Medicine, Carver College of Medicine, The University of Iowa, Iowa City, IA; (2) College of Pharmacy, The University of Iowa; and, Department of Pharmacy, Iowa City VA Medical Center, Iowa City, IA; (3) College of Pharmacy, The University of Iowa, Iowa City, IA; (4) Department of Pharmacy and Department of Psychiatry, Iowa City VA Medical Center, Iowa City, IA; (5) Department of Internal Medicine, Carver College of Medicine; and CRIISP at the Iowa City VA Medical Center, Iowa City, IA
PURPOSE: Changes in atmospheric pressure (AP) influence hepatic blood flow and drug metabolism. Greater changes in AP are noted to occur during fall/winter months. Anecdotal experience suggests international normalized ratio (INR) variability in normally stable patients is temporally related to significant AP changes. We investigated whether this association could be observed within a large sample of patients with multiple INRs.
METHODS: This was a retrospective review of outpatient anticoagulation records from the Iowa City VAMC and affiliated outpatient clinics between October 1999 and July 2007. All patients receiving at least one prescription for warfarin and at least one INR 30 days or more from the date of their first warfarin prescription were identified. INRs during periods of hospitalization and vitamin K use were excluded. The dataset was then filtered to identify "index" or nontherapeutic INRs, which were identified as either a supratherapeutic or subtherapeutic INR that followed a previously therapeutic INR. To assign AP with index INR, proximity analysis (ARC-GIS v. 9.0) using geocoding of ZIP codes of identified patients to the nearest NOAA station was performed. Associations for APs from the preceding 48-hour (T-2), 24-hour (T-1), and index INR date ($T = 0$) were evaluated using Spearman's rho or Pearson's correlation.
RESULTS: A total of 1121 unique patients with 5256 index INRs were identified. No associations between ΔINR and ΔAP ($p=0.26$) or absolute INR and AP ($p=0.07$) were observed. ΔT-2 in AP demonstrated greater variation during fall/winter months than in spring/summer months (0.23 mm Hg vs. 0.13 mm Hg; $p<0.001$); however, ΔINR for the corresponding seasons was not significant ($p=0.136$). No significant difference was detected in the proportions of nontherapeutic INRs among the different seasons ($p=0.371$).
CONCLUSIONS: No correlation was observed between AP changes and INR variability. These negative findings refute the anecdotal experience seen in our anticoagulation clinic. A prospective design could more adequately control for additional factors known to influence INR variability.

22. Prevalence and Pattern of Caffeine Use in Heart Failure. Seung H. Lee, Pharm.D.,[1] Jennifer I. Park, B.A.,[1] Karine N. Danskey, B.S.,[1] Luanna Yang, B.S.,[1] Doris S. Rezvanpour, B.S.,[1] Katelyn Tran, R.D., CNSD,[1] Sheryl L. Chow, Pharm.D.,[2] Uri Elkayam, M.D.,[1] *Tien M.H. Ng, Pharm.D.*[1]; (1) University of Southern California, Los Angeles, CA; (2) Western University of Health Sciences, Pomona, CA
PURPOSE: Caffeine exerts pharmacological effects that could influence heart failure (HF) pathophysiology. Our purpose was to report the prevalence and pattern of caffeine intake and its association with patient and HF characteristics.
METHODS: Two hundred patients with HF (mean age 58 ± 12 years, 41% women) at LAC+USC Medical Center and Centinela-Freeman Medical Center, New York Heart Association functional class (NYHA FC) I–IV, were surveyed to delineate caffeine use, caffeine education received, and physician contacts (hospitalizations, emergency department visits, unscheduled office visits, and telephone calls to physician) for the past year and potential associations with patient and HF characteristics.
RESULTS: Most (83.5%) reported at least some caffeine use, and 66.5% reported regular caffeine use (at least 3 times/week). Coffee (48%) and soda (47%) were the most common sources of caffeine. Only 19% of patients received counseling on caffeine use. Average weekly caffeine intake in all patients was 908.2 ± 1144.9 mg. For the comparison of regular versus nonregular caffeine users, patient and HF characteristics were not different except for fewer HF years since diagnosis and lower blood pressures in regular caffeine users

(Table). The frequency of physician contacts in the previous year (Table) did not differ between regular and nonregular users. When analyzed by quintiles of weekly caffeine intake, no associations with characteristics or frequency of physician contacts existed. Furthermore, the number of emergency department visits and hospitalizations determined from chart review did not differ by caffeine use.

CONCLUSIONS: A high prevalence of caffeine use from multiple sources exists in patients with HF. In this preliminary study, incidence of caffeine use does not appear to be associated with HF characteristics or outcomes.

Select Characteristics	Regular Caffeine Users	Nonregular Caffeine Users	p-value
no.	133	67	
Age (years)	57 ± 12	59 ± 13	0.28
Women (%)	40	45	0.58
African American (%)	42	37	
SBP (mm Hg)	130.6 ± 26.2	140.4 ± 27.3	0.02
DBP (mm Hg)	77.4 ± 17.3	83.8 ± 17.4	0.01
Heart rate	87.7 ± 18.8	88.8 ± 22.3	0.73
Years since HF diagnosis	3.4 ± 5.6	6.0 ± 9.4	0.04
LVEF (%)	35 ± 17	34 ± 16	0.61
NYHA FC I (%)	23	22	0.99
NYHA FC II (%)	26	24	
NYHA FC III (%)	43	45	
NYHA FC IV (%)	9	9	
Mean no. of physician contacts	5.5 ± 5.0	5.6 ± 5.4	0.90

DBP = diastolic blood pressure; LVEF = left ventricular ejection fraction; SBP = systolic blood pressure.

23E. The Combination of Amlodipine/Valsartan (5/160 mg) Significantly Reduces the Incidence of Peripheral Edema Versus Amlodipine 10 mg in Hypertensive Patients Not Adequately Controlled with Amlodipine 5 mg. *Joachim Schrader, M.D.,*[1] Marianne Weisskopf, M.D.,[2] Lucy Keeling, M.S.,[2] Philippe Ferber, M.D.[2]; (1) St. Josef-Hospital, Department of Internal Medicine, Cloppenburg, Germany; (2) Novartis Pharma AG, Clinical Development & Medical Affairs, Basel, Switzerland

PURPOSE: To demonstrate the benefit of combination amlodipine-valsartan (A/V) 5/160 mg versus amlodipine (A) 10 mg in reducing peripheral edema for comparable mean sitting systolic blood pressure (MSSBP) reduction.

METHODS: Patients (55 years and older) not adequately controlled (MSSBP 130 mm Hg or more and 160 mm Hg or less) after a 4-week run-in with A 5 mg were randomized in a double-blind fashion to receive A/V 5/160 mg or A 10 mg for 8 weeks, followed by A/V 4 weeks for all patients. Coprimary efficacy variables included change in MSSBP from baseline to week 8 and proportion of patients with peripheral edema reported as adverse events. The resolution of peripheral edema was also assessed 4 weeks after switching patients from A 10 mg to A/V.

RESULTS: At randomization, MSSBP was 143.4 and 144.4 mm Hg for patients on A/V 5/16 mg (n=592) and A 10 mg (n=591), respectively. At week 8, a greater reduction in MSSBP was observed with A/V compared with A 10 mg (least square mean -8.01 vs. -6.30; p<0.001 for noninferiority). Significantly fewer patients in the A/V group experienced peripheral edema up to week 8 compared with A group (6.6% vs. 31.1%, respectively; p<0.001). MSSBP control and overall BP control at week 8 were significantly higher in A/V than in A (34% vs. 25% and 57% vs. 49%, respectively). In patients switched from A 10 mg to A/V 5/160 mg, edema resolved in 56%, with no increase in BP. Besides peripheral edema, both treatments were well tolerated.

CONCLUSIONS: In this study of patients not responding to A 5 mg, treatment with A/V 5/160 mg demonstrated a numerically greater antihypertensive effect than A 10 mg. Of importance, A/V induced significantly less peripheral edema than A 10 mg, with more than 50% of patients switched from A 10 to A/V showing resolution of their edema.

Presented at the Hypertension 2008 Conference (the Joint Congress of the 18th Scientific Meeting of the European Society of Hypertension and the 22nd Scientific Meeting of the International Society of Hypertension), Berlin, Germany, June 14–19, 2008.

24E. Is the Combination of Valsartan/Hydrochlorothiazide Regimen More Effective, Compared to Conventional Treatment with Amlodipine and Hydrochlorothiazide, in Lowering Ambulatory Blood Pressure (BP) in Patients with Stage 2 Hypertension? – The EVALUATE Study. Yves Lacourciere, M.D., FRCPC, FACP,[1] Jackson T. Wright Jr., M.D., Ph.D.,[2] *Rita Samuel, M.D.,*[3] Dion H. Zappe, Ph.D.,[3] Das Purkayastha, Ph.D.,[3] Henry R. Black, M.D.[4]; (1) Centre Hospitalier de l'Universite Laval, Sainte Foy, QC, Canada; (2) Case Western Reserve University, Cleveland, OH; (3) Novartis Pharmaceuticals Corporation, NJ; (4) New York University, School of Medicine, New York, NY

PURPOSE: Previous studies using fixed-dose combinations of angiotensin receptor blocker (ARB) and hydrochlorothiazide (HCTZ) have shown improved ambulatory blood pressure (ABP) reduction in patients with stage 2 hypertension. This treatment strategy, however, has not been compared with a strategy of calcium channel blocker (CCB) combined with HCTZ. The purpose of the current study was to compare both strategies.

METHODS: EVALUATE was a multicenter, double-blind, parallel-group, forced-titration study of patients with stage 2 hypertension (n=482, mean age = 58 years, mean seated blood pressure 171/98 mm Hg). After a 2-week washout period, eligible patients were randomized to either valsartan-HCTZ (V/HCTZ) (n=241) or amlodipine-HCTZ (A/HCTZ) (n=241) for 10 weeks. Treatment was initiated with V 160 mg or A 5 mg and then force-titrated at 2 weeks to V/HCTZ 160/12.5 mg or A 10 mg and at 4 weeks to the maximum dose of V/HCTZ 320/25 mg or A/HCTZ 10/25 mg. Change in mean 24-hour ambulatory systolic blood pressure from baseline was the primary end point.

RESULTS: After 10 weeks, mean ambulatory systolic blood pressure/ambulatory diastolic blood pressure was reduced by -21.1/-12.5 mm Hg in the V/HCTZ group versus -18.1/-9.7 mm Hg in the A/HCTZ group (p<0.0001 for both ambulatory systolic blood pressure and ambulatory diastolic blood pressure). Blood pressure control rates (less than 140/90 mm Hg) were greater (64.1%) in the V/HCTZ versus (57.8%) the A/HCTZ group. Adverse events reported were similar between the two groups: 39% in V/HCTZ versus 41.5% in A/HCTZ; however, peripheral edema was higher in the A/HCTZ group (12.4% vs. 3.3% in V/HCTZ).

CONCLUSIONS: The fixed-dose combination of V/HCTZ is a significantly more effective treatment regimen than A/HCTZ with similar tolerability. Current antihypertensive treatment guidelines stress the importance of the use of HCTZ in a combination therapy regimen. This study suggests that an ARB-based regimen with HCTZ is a more effective treatment strategy than the addition of HCTZ to CCB in lowering ABP in patients with stage 2 hypertension.

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25E. Metabolic Effects of Combination Angiotensin Receptor Blockade/Hydrochlorothiazide in Prediabetic, Obese, Hypertensive Patients. Leopoldo Raij, M.D.,[1] James R. Sowers, M.D.,[2] Ishwarlal Jialal, M.D., Ph.D.,[3] Brent M. Egan, M.D.,[4] Elizabeth Ofili, M.D., M.Ph.,[5] *Rita Samuel, M.D.,*[6] Dion H. Zappe, Ph.D.,[6] Das Purkayastha, Ph.D.,[6] Prakash Deedwania, M.D.[7]; (1) University of Miami Miller School of Medicine, Miami, FL; (2) University of Missouri–Columbia, Columbia, MO; (3) UC Davis Medical Center, Sacramento, CA; (4) Medical University of South Carolina, Charleston, NC; (5) Morehouse School of Medicine, Atlanta, GA; (6) Novartis Pharmaceuticals Corporation, NJ; (7) UCSF Fresno, Fresno, CA

PURPOSE: Thiazide diuretics are effective for treating obese, hypertensive patients, despite their negative metabolic effects. It is

unknown whether adding a renin-angiotensin system blocker to diuretics mitigates the negative effects on glucose metabolism in these patients. This 16-week randomized, multicenter study compared valsartan and hydrochlorothiazide (V/HCTZ) with amlodipine-HCTZ (A/HCTZ) on glucose metabolism in obese, hypertensive patients.

METHODS: A total of 412 obese (body mass index = 35 ± 7 [SD] kg/m^2; body weight = 98 ± 23 kg), hypertensive (seated blood pressure = 159 ± 8/94 ± 8 mm Hg) patients (age 56 ± 9 years, 66% women) entered double-blind treatment with V/HCTZ 160/12.5 mg or HCTZ 12.5 mg after a 4-week washout period. Patients were force-titrated to V/HCTZ 320/25 mg or A/HCTZ 10/25 mg, respectively. At week 16, changes were measured from baseline in fasting and 2-hour postprandial glucose and insulin after an oral glucose tolerance test (OGTT).

RESULTS: At end point, clinic blood pressure reductions were similar (p>0.05) in both groups. Fasting and 2-hour glucose increased (p<0.01) with A/HCTZ, resulting in a greater percentage of patients with impaired fasting glucose or impaired OGTT (Table). New-onset diabetes occurred in more patients in A/HCTZ than in V/HCTZ (21 [11%] vs. 3 [2%]; p<0.05), respectively.

	V/HCTZ (n=197)		A/HCTZ (n=204)	
Parameter	Baseline	Week 16	Baseline	Week 16
SBP/DBP (mm Hg)	160 ± 8/95 ± 8	129 ± 16/81 ± 10	159 ± 8/94 ± 8	131 ± 13/81 ± 9
Fasting glucose (mg/dL)	98.0 ± 16	98.1 ± 16	99.4 ± 19	102.8 ± 18*
Postprandial glucose at 2 hours (mg/dL)	123.9 ± 47	126.3 ± 50	127.7 ± 40	146.5 ± 57*
Fasting insulin (µU/mL)	19.7 ± 20	23.4 ± 26	20.4 ± 21	23.6 ± 19
Postprandial insulin at 2 hours (µU/mL)	92 ± 82	116 ± 13	96 ± 76	120 ± 100
Impaired fasting glucose N (%)	67 (34)	66 (38)	76 (38)	91 (50)
Impaired OGTT N (%)	70 (36)	49 (29)	70 (34)	87 (48)

*p<0.01 vs. *V/HCTZ*.
DBP = diastolic blood pressure; SBP = systolic blood pressure.

CONCLUSIONS: Compared with A/HCTZ, V/HCTZ reduced progression toward impaired fasting glucose, impaired glucose tolerance, and new-onset diabetes in obese hypertensive patients.

Presented at the Hypertension 2008 Conference (the Joint Congress of the 18th Scientific Meeting of the European Society of Hypertension and the 22nd Scientific Meeting of the International Society of Hypertension), Berlin, Germany, June 14–19, 2008.

27E. Clopidogrel Attenuates Coated-Platelet Formation in Patients Undergoing Elective Cardiac Catheterization. *Nicholas B. Norgard, Pharm.D.,*[1] Shoaib Saya, M.D.,[2] Thomas Hennebry, M.D.,[3] Callie Hann, B.S.,[2] George L. Dale, Ph.D.[2]; (1) University at Buffalo – School of Pharmacy and Pharmaceutical Science, Buffalo, NY; (2) University of Oklahoma Health Sciences Center, Department of Medicine, Oklahoma City, OK; (3) University of Oklahoma Health Sciences Center, Department of Medicine, Oklahoma City, OK

PURPOSE: Coated platelets are a subclass of highly thrombotic, activated platelets with an enhanced ability to generate thrombin. These cells are thought to play a major role in the initiation and maintenance of thrombotic occlusions, and excessive numbers of coated platelets are believed to increase thrombotic risk. A previous report showed that P2Y12 inhibition in vitro can attenuate coated-platelet formation. The aim of this study was to determine the effect of clopidogrel administration on coated-platelet formation.

METHODS: We enrolled 27 patients undergoing elective coronary angiography. Coated-platelet levels, expressed as percentage of total platelets, were determined before and after a 300-mg clopidogrel dose, and a postprocedure blood sample was drawn 6 hours after the coronary angiography in all patients. Platelet samples were stimulated with 500 ng/mL convulxin and 0.5 U/mL thrombin with or without 1.5 or 6 µM adenosine diphosphate (ADP).

RESULTS: Baseline levels of coated platelets were 40.0% ± 14.3% (mean ± 1 SD). After 24 hours of clopidogrel exposure, the convulxin plus thrombin coated-platelet level was 32.8 ± 13.6, representing a significant 7.2% absolute reduction (17.8% relative reduction; p<0.0001). Clopidogrel significantly lowered the convulxin, thrombin plus ADP coated-platelet production to 43.7 ± 14.9 (1.5 µM) and 47.7 ± 16.2 (6 µM), representing an 11.0% absolute reduction (20.1% relative reduction for 1.5 mM) and an 11.2% absolute reduction (19.1% relative reduction for 6 mM), respectively. Coated-platelet levels were not significantly altered by angiography or stent placement.

CONCLUSIONS: The administration of clopidogrel reduces coated-platelet formation. This is the first report on the impact of in vivo administration of a P2Y12 antagonist on coated-platelet formation. The significance of a partial attenuation in coated-platelet potential has yet to be determined, but this could represent a new antithrombotic mechanism of clopidogrel beyond inhibition of ADP-induced aggregation, specifically the reduction in coated-platelet potential.

Submitted for publication to Circulation Research.

28. Bivalirudin Alone or in Combination with Eptifibatide in Elective Percutaneous Coronary Intervention. *Abir O. Kanaan, Pharm.D.,*[1] Steve Anisman, M.D.,[2] Eddison Ramsaran, M.D.,[2] Jennifer L. Donovan, Pharm.D.[1]; (1) Massachusetts College of Pharmacy and Health Sciences, Worcester, MA; (2) Saint Vincent Hospital, Worcester, MA

PURPOSE: Antiplatelet and anticoagulant therapies are essential to the management of coronary artery disease. Bivalirudin, with provisional use of glycoprotein (GP) IIb/IIIa inhibitors, has demonstrated efficacy and safety in elective percutaneous coronary intervention (PCI). The addition of GP IIb/IIIa inhibitors to bivalirudin has increased at our institution when performing elective PCI. The objectives of this study were to (1) determine whether outcomes differed between combination therapy and bivalirudin monotherapy and (2) identify whether combination therapy was used in high-risk patients.

METHODS: A retrospective chart review was conducted in 255 consecutive patients undergoing elective PCI from January to December 2005. Patients received bivalirudin monotherapy (group B) or bivalirudin plus eptifibatide (group BE). The use of eptifibatide was at the discretion of the operating interventionalist and could be given either in a planned or provisional fashion. Primary end points included thrombosis and death during the 1-year follow-up. A statistical analysis was performed on the basis of intent to treat using Fisher's exact test.

RESULTS: A total of 138 (54%) and 117 (46%) patients were included in groups B and BE, respectively; 63 were lost to follow-up. Patients in groups B and BE were similar in age (67.75 ± 12.55 vs. 68.51 ± 10.42, respectively) and female gender (29.71% vs. 35.89%, respectively). There was no difference between B and BE groups in thrombosis (1% vs. 2%, respectively; CI: 0.06–1.72; p=0.25) or death (2% vs. 3%, respectively; CI: 0.14–1.62; p=0.35) at 1 year. Comorbidities, including hypertension, hyperlipoproteinemia, prior myocardial infarction, and prior coronary artery bypass grafting, were similar (p=NS) between groups; however, more patients with diabetes were in the BE group compared with the B group (29% vs. 18%; CI: 0.38–0.67; p<0.0001).

CONCLUSIONS: There was no difference in thrombosis and death between bivalirudin alone or in combination with eptifibatide. More patients with diabetes were in the combination group, justifying the therapy.

29. Influence of Albuterol on Alveolar-Capillary Membrane Conductance in Patients with Heart Failure. *Eric M. Snyder, Ph.D.,*[1] Maile L. Ceridon, B.S.,[2] Minelle L. Hulsebus, B.S.,[2] Bruce D. Johnson, Ph.D.[2]; (1) University of Arizona, Tucson, AZ; (2) Mayo Clinic College of Medicine, Rochester, MN

PURPOSE: Heart failure (HF) results in an impaired ability of the ventricular walls to contract and relax enough to move blood to the periphery as well as through the lungs and can result in the accumulation of blood and water in the lungs. The β-2 adrenergic receptors (ADRB2) are involved in lung fluid clearance through augmentation of ion transport across type I and II alveolar cells as

well as through relaxation of the pulmonary lymphatics. We sought to determine the effects of stimulation of the ADRB2 on alveolar-capillary membrane conductance (D_M, an index of lung water) in nine healthy subjects (age = 50 ± 13 years, height = 72 ± 10 cm, weight = 76 ± 16 kg, body mass index [BMI] = 26 ± 5 kg/m^2, mean ± SD) and six patients with stable HF (61 ± 13 years, height = 179 ± 7 cm, weight = 93 ± 16 kg, BMI = 29 ± 5 kg/m^2).

METHODS: We measured cardiac output (Q), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), diffusion capacity of the lungs for carbon monoxide (DLCO), D_M, and pulmonary capillary blood volume (Vc) before and 30 minutes after nebulized albuterol.

RESULTS: There were no changes in the cardiovascular parameters with albuterol (healthy: Q = 4.1 ± 0.4 to 4.5 ± 1.3 L/minute, HR = 65 ± 11 to 63 ± 17 beats/minute, SBP = 116 ± 13 to 114 ± 10 mm Hg, DBP = 81 ± 11 to 77 ± 10 mm Hg; HF: Q = 3.3 ± 1.0 to 3.6 ± 1.0, HR = 68 ± 10 to 71 ± 13, SBP = 123 ± 18 to 117 ± 15, DBP = 73 ± 12 to 75 ± 14). There were no significant changes in DLCO, D_M, or Vc in either group (healthy: DLCO = 22 ± 2 to 21 ± 3 mL/kg/minute, D_M = 35 ± 8 to 35 ± 9 mL/kg/minute, Vc = 42 ± 13 to 37 ± 7 mL; HF: DLCO = 19 ± 4 to 19 ± 4 mL/kg/minute, D_M = 31 ± 9 to 32 ± 7 mL/kg/minute, Vc = 35 ± 13 to 46 ± 5 mL), although Vc changed in opposite directions. D_M corrected for Vc increased in healthy subjects and in patients with HF (% change healthy = 11% ± 20%, HF = 10% ± 30%). The change in D_M/Vc was variable in HF and appeared linked to the use of β-blockers.

CONCLUSIONS: These data suggest that inhaled β-agonist exposure reduces Vc in healthy adults with evidence for improved D_M, whereas in HF patients, inhalation of the β-agonist increases Vc and D_M.

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30. Preoperative Statin Use Is Not Associated with a Reduced Risk of Atrial Fibrillation After Cardiac Surgery. *Brian J. Barnes, Pharm.D.,*[1] Patricia A. Howard, Pharm.D., FCCP, BCPS (AQ, CV),[1] Amit Kumar, M.D.,[2] Michael E. Gorton, M.D.,[3] Scott Solomon, M.D.,[2] Jeffrey B. Kramer, M.D.,[3] Gregory F. Muehlebach, M.D.,[3] James L. Vacek, M.D.[4]; (1) School of Pharmacy, The University of Kansas, Kansas City, KS; (2) The University of Kansas Hospital, Kansas City, KS; (3) Mid-America Thoracic and Cardiovascular Surgery, Inc., The University of Kansas Hospital, Kansas City, KS; (4) Mid-America Cardiology, The University of Kansas Hospital, Kansas City, KS

PURPOSE: Postoperative atrial fibrillation (POAF) is prevalent after cardiac surgery and is associated with significant morbidity and increased costs. Statins, which are commonly used in this population, have been identified as a potential preventive strategy. The objective of this study was to examine the effect of preoperative statin use on the risk of POAF after cardiac surgery.

METHODS: A retrospective, observational study was conducted using data from 489 adult patients who underwent cardiac surgery in 2003. Data sources included institution-specific data from the Society of Thoracic Surgeons national database plus medical and medication administration records. Univariate analyses and unconditional, logistic regression were used to determine the impact of preoperative statin use on the probability of developing POAF while controlling for the baseline risk of POAF and the use of amiodarone prophylaxis (AMP). A baseline risk index was calculated for each patient using a validated model (JAMA 2004;291:1720–9) consisting of 11 variables. Patients with chronic atrial fibrillation or missing data were excluded.

RESULTS: The mean patient age was 63 (SD = 13) years; 73% were men, 81% underwent coronary artery bypass grafting, and 29% underwent valve surgery. Baseline demographics were similar between those receiving and not receiving preoperative statins. Based on the calculated risk index, 51% were considered low risk for POAF, and 49% were considered moderate to high risk. POAF occurred in 27% of patients receiving statins and in 24% of those not receiving statins (p=0.3792). After controlling for baseline risk of POAF and the use of AMP, statins were not associated with reductions in POAF (OR = 1.19; 95% CI: 0.782–1.822; p=0.4118).

CONCLUSIONS: Multiple factors may affect the development of POAF after cardiac surgery, including patient demographics, comorbidities, and concomitant medications. In this study, after adjustment for these factors, the preoperative use of statins did not significantly influence the development of POAF.

31. Effects of Paroxetine on the Pharmacokinetics of Immediate- and Extended-Release Metoprolol. *Robert B. Parker, Pharm.D.,*[1] Judith Soberman, M.D.[2]; (1) University of Tennessee Department of Clinical Pharmacy, Memphis, TN; (2) University of Tennessee Division of Cardiovascular Diseases, Memphis, TN

PURPOSE: Depression is a commonly occurring comorbidity in patients with cardiovascular disease. This study seeks to determine the effects of the antidepressant paroxetine (PAR) on the pharmacokinetics of immediate- and extended-release metoprolol succinate.

METHODS: Fifteen healthy volunteers who were CYP2D6 extensive metabolizers were studied in an open-label crossover trial conducted in three phases administered in random sequence. Phase 1: Single dose of extended-release metoprolol succinate 100 mg (ER100) on day 1. On days 2–7, PAR 20 mg was given, and on day 8, it was coadministered with SR100. Phase 2: Identical to phase 1 except sustained-release metoprolol 200 mg (ER200) was given. Phase 3: Identical except that on days 1 and 8, two doses of immediate-release metoprolol 100 mg (IR100) were given 12 hours apart. *S*-metoprolol (active enantiomer) concentrations were determined by high-performance liquid chromatography. Pharmacokinetic parameters were determined by noncompartmental analysis.

RESULTS: *S*-metoprolol pharmacokinetic parameters (mean ± SD) are summarized below.

Phase	ER100	ER100+ PAR	ER200	ER200+ PAR	IR100	IR100+ PAR
C_{max} (ng/mL)	15.7 ± 7.0†	43.6 ± 9.6*‡	30.3 ± 17.4†	84.7 ± 20.6*‡	84.8 ± 54.3	173.3 ± 61.7*
T_{max} (hour)	7.4 ± 3.5†	12.6 ± 6.7*‡	7.9 ± 0.5*†	11.0 ± 3.9‡	1.4 ± 0.6	1.5 ± 0.6
AUC_{0-24} hour (ng*hour/mL)	258.5± 130.4†	828.4 ± 199.9*‡	512.4 ± 281.3	1590.1 ± 437.2*	463.5 ± 328.3	1430.4 ± 433.1*
*t*1/2 (hour)	-	-	-	-	3.5 ± 1.3	6.7 ± 1.1*

*p<0.05 vs. corresponding agent alone.
†p<0.05 vs. IR100.
‡p<0.05 vs. IR100+PAR.

CONCLUSIONS: (1) PAR markedly inhibits the metabolism of ER and IR metoprolol. (2) Although the relative effect of PAR on the pharmacokinetics of ER and IR metoprolol is similar, PAR exerts a larger absolute effect on IR metoprolol compared with ER metoprolol. (3) With coadministration of PAR or other potent CYP2D6 inhibitors, the risk of adverse effects from excessive β-blockade may be increased with IR metoprolol versus ER metoprolol.

32. Evaluation of Racial Disparities with Statin Use in Veterans Post-Myocardial Infarction. *Amy B. Hulsey, Pharm.D.,*[1] Robert B. Parker, Pharm.D.,[2] Kelly C. Rogers, Pharm.D.[3]; (1) VA Medical Center, Memphis, TN; (2) University of Tennessee Department of Clinical Pharmacy, Memphis, TN; (3) University of Tennessee College of Pharmacy, Memphis, TN

PURPOSE: Aggressive lipid lowering with statins is important for secondary prevention in post–myocardial infarction (post-MI) patients. Evidence indicates that African Americans (AA) are disproportionately affected by heart disease and that racial disparities exist in the use of evidence-based therapies. The purpose of this study was to determine if racial disparities existed in the use of statins in post-MI patients at the Memphis VA Medical Center.

METHODS: Patients were identified who experienced an MI between January 1, 2006, and December 31, 2006, and were discharged alive. Demographic data, date/type of MI, statin therapy, low-density lipoprotein at baseline and 12 months, adherence to drug therapy, all-cause use rates for emergency department and hospital admissions, reinfarctions, revascularizations, and death were recorded.

RESULTS:

	Whites (n=56)	African Americans (n=30)
Age (years)*	67 ± 11	65 ± 14
Receiving statins at discharge	54 (96%)	27 (90%)
Simvastatin dose* (mg/dL)	50 ± 27	45 ± 27
Admission LDL* (mg/dL)	99 ± 39	96 ± 36
LDL at 1 year* (mg/dL)	79 ± 33	89 ± 42
Achievement of LDL goal at 1 year	34 (61%)	18 (60%)
12-month adherence	22 (39%)	12 (40%)
ED use*	1.6±2.5	2.3 ± 2.5
All-cause hospitalizations*	0.9 ± 2.0	0.8 ± 1.0
All-cause mortality	10 (18%)	4 (13%)

*Mean ± SD; no variables statistically significant.

CONCLUSIONS: Statin use in post-MI veterans is high in this small cohort analysis. No differences were found in prescription of statins or intensity of dose given between races. Although admission LDL cholesterol was similar between groups, a trend toward a greater statin-mediated reduction in LDL at 1 year was noted in whites. Adherence rates and achievement of LDL goal at 1 year were similar. A trend toward more ED visits, but not hospitalizations, was observed in AA. In this high-risk veteran population, no racial differences in statin therapy were identified.

33. High Loading Dose 300 mg vs. 600 mg of Clopidogrel in Patients Undergoing Coronary Intervention. *Sukhyang Lee, Pharm.D., Ph.D.,*[1] Eun Jong Cheon, M.S.[2]; (1) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, South Korea; (2) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, IA, South Korea

PURPOSE: A loading dose of clopidogrel, administered at least 6 hours before percutaneous coronary intervention (PCI) is performed in patients with acute MI/angina, inhibits platelet aggregation within an early time. The recommended loading dose of clopidogrel for patients with PCI is currently 300 mg. Recent studies have suggested that a 600-mg loading dose inhibits platelet aggregation earlier and faster than 300 mg. In this study, we compared clinical outcomes of 600-mg loading dose of clopidogrel with those of 300 mg and evaluated bleeding complications.

METHODS: Data were retrospectively collected from medical charts of patients (n=158) who had undergone PCI and loaded with 300 or 600 mg of clopidogrel before the procedure, between May and November 2005. The primary end point was the occurrence of death, MI, cerebral infarction, or target vessel revascularization at 7 days, 30 days, and 6 month. The secondary end point was incidence of bleeding complications in the hospital at 7 days.

RESULTS: Patients were pretreated with 300 mg (n=79) or 600 mg (n=79) of clopidogrel before the procedure. At 7 days, 30 days, and 6 months, the primary end point was not significantly different between the two groups. The rate of bleeding complications was not different between the two groups.

Table. 6-Month Clinical Outcomes

	Clopidogrel Dose		
	300 mg (n=79), n (%)	600 mg (n=79), n (%)	p-value
Death	—	—	—
Recurrent MI	9 (%)	4 (%)	0.15
Target vessel revascularization	6 (%)	4 (%)	0.52
Cerebral infarction	1 (1.3%)	—	0.32

CONCLUSIONS: In patients undergoing PCI, pretreatment with 600 mg of clopidogrel did not lead to a statistically significant reduction in cardiovascular disease. A 300-mg clopidogrel loading dose given before PCI is sufficient.

34. Xanthine Oxidase Inhibition Attenuates Hypoxia-Induced Changes in Chemoreceptor Sensitization Pathways. *John M. Dopp, Pharm.D.,*[1] Noah J. Marcus, M.S.,[1] Cynthia B. Bird, B.S.,[1] Nathan Phillipi, B.S.,[1] John J.M. Moran, B.S.,[1] E. Burt Olson, Ph.D.,[1] Harold D. Schultz, Ph.D.,[2] Yulong Li, M.D., Ph.D.,[2] Barbara J. Morgan, Ph.D., PT[1]; (1) University of Wisconsin, Madison, WI; (2) University of Nebraska College of Medicine, Omaha, NE

PURPOSE: Intermittent hypoxia (IH) in patients with obstructive sleep apnea (OSA) increases carotid body (CB) chemoreceptor sensitivity and sympathetic output that contribute to the development of hypertension. Animal models suggest that chemoreceptor sensitization is mediated by superoxide, induced by angiotensin II activation of reduced nicotinamide adenine dinucleotide phosphate oxidase. Because angiotensin II also activates xanthine oxidase (XO), we hypothesized that XO contributes to oxidative stress mechanisms in the CB during IH.

METHODS: We randomized 21 adult male Sprague-Dawley rats to be exposed to 2 weeks of IH (alternating 21% and 10% oxygen every 2 minutes for 12 hours daily) or normoxia. Hypoxic and normoxic rats were further randomized to receive allopurinol 65 mg/kg/day or placebo by oral gavage for 1 week before and during 2 weeks of hypoxia or normoxia. After 2 weeks, CBs were excised under anesthesia and stored for analysis. Expression of CB proteins that promote (angiotensin type 1 receptor [AT1R]) and inhibit (neuronal nitric oxide synthase [nNOS]) chemoreceptor sensitivity were determined by Western blotting and normalized to glyceraldehyde phosphate dehydrogenase (GADPH). CB superoxide concentrations were measured using lucigenin fluorescence in two rats per group.

RESULTS: Mean ± SEM protein expression and superoxide generation are shown in the Table. IH increased oxidative stress, increased expression of proteins that promote chemoreceptor sensitivity, and decreased expression of proteins that inhibit chemoreceptor sensitivity. Allopurinol attenuated these hypoxia-induced changes.

CONCLUSIONS: XO inhibition attenuates IH-induced changes in superoxide production, AT1R, and nNOS proteins in rat CBs. Allopurinol may represent a novel approach to reduce exaggerated sympathetic activity and associated cardiovascular morbidity in patients with OSA.

	Normoxia-Placebo	Normoxia-Allopurinol	Hypoxia-Placebo	Hypoxia-Allopurinol
AT1R/GADPH	0.76 ± 0.18	0.42 ± 0.12	1.35 ± 0.18	0.52 ± 0.15
nNOS/GADPH	1.04 ± 0.15	0.70 ± 0.17	0.21 ± 0.09	0.82 ± 0.2
Superoxide (RLU/minute/100 µg of protein)	0.57 ± 0.05	0.54 ± 0.05	1.36 ± 0.17	0.62 ± 0.16

RLU = relative light unit.

35. Reductions in N-terminal Prohormone Brain Natriuretic Peptide Associated with Reduced Risk of Hospitalizations Among Chronic Heart Failure Patients in an Ambulatory Care Setting. *Daniel E. Zamarripa, Pharm.D.,*[1] Jessina C. McGregor, Ph.D.,[2] Jessie Chan, B.S.,[2] Harleen Singh, Pharm.D.[2]; (1) Portland VA Medical Center, Portland, OR; (2) Oregon State University/Oregon Health & Science University College of Pharmacy, Portland, OR

PURPOSE: N-terminal prohormone brain natriuretic peptide (NTproBNP) is a cardiac biomarker often used as a prognostic and diagnostic tool in heart failure (HF). Evidence suggests that using NTproBNP to titrate HF medications is useful. However, it is not known how the magnitude of change in NTproBNP correlates with patient morbidity and mortality. The objective of this study was to examine the relationship between changes in NTproBNP levels and clinical outcomes in patients with chronic HF in an ambulatory care setting.

METHODS: A retrospective cohort study was conducted of patients at the Portland VA Medical Center with one baseline NTproBNP level and at least one follow-up NTproBNP level between January 26, 2006, and January 1, 2008. Patients on dialysis were excluded from the study. Data were collected through electronic chart review. The primary outcome of interest was hospitalization within 90 days of the follow-up NTproBNP level. Logistic regression was used to model the association between changes in NTproBNP and hospitalization.

RESULTS: Of the 126 medical records reviewed, 79 met inclusion criteria. The median time between NTproBNP levels was 99 days.

Mean patient age was 68 years, and 98.7% of patients were men. Median NTproBNP was 1648 pg/mL at baseline and 1543 pg/mL at follow-up. The incidence of 90-day hospitalization was 25.3%. A reduction of at least 30% in NTproBNP was associated with a statistically significant decrease in the odds of 90-day hospitalization (OR = 0.23, 95% CI: 0.06–0.93). An increase in NTproBNP of at least 30% was not significantly associated with 90-day hospitalization (OR = 0.73; 95% CI: 0.23–2.41).
CONCLUSIONS: This study suggests that reductions in NTproBNP are associated with reduced risk of hospitalization. Larger studies are needed to further evaluate the association between the magnitude of change in NTproBNP and patient outcomes and how this information may facilitate the optimization of HF medications.

36. A Pilot Study to Evaluate the Safety and Efficacy of a Prothrombin Complex Concentrate to Reverse International Normalized Ratios > 2 in Patients Requiring Implantable Cardiac Devices. *Denise Pratt, Pharm.D.,*[1] Nathan Gerrish, Pharm.D. Candidate,[1] R.K. Thakur, M.D.,[2] Elizabeth Lojewski, B.S. Candidate[2]; (1) Sparrow Hospital, Lansing, MI; (2) Michigan State University, East Lansing, MI
PURPOSE: An open-label pilot study was designed to evaluate if protocol dosing of prothrombin complex concentrate (PCC) would adequately reverse the international normalized ratio (INR) values to less than 2.0 to allow implantation of cardiac devices without interruption of warfarin therapy and without significant bleeding or thrombotic event postprocedure and 30-day follow-up.
METHODS: A PCC dosing protocol was designed to administer specific doses of PCC based on a patient's INR on the day of procedure. After administration of PCC, the procedure was completed, and warfarin therapy was continued as previously prescribed. The percentage of patients with INRs less than 2 at the time of the procedure and the percentage of patients within an INR at goal range the following day were determined. Patients were monitored for thrombotic and bleeding complications at 24 hours, 7 days, and 30 days.
RESULTS: The protocol was evaluated in 19 patients. The mean age was 73.1 ± 11.25 years; 12 were men. The average baseline INR was 2.73 ± 0.45. The average dose of PCC was 6.8 ± 1.35 units/kg. The percentage of patients with an INR less than 2 at the time of the procedure was 57.9%. Percentage of patients with an INR within goal range the following day was 31.6%. All patients tolerated PCC without adverse events. A small pocket hematoma developed in one patient, which resolved spontaneously. A patient with atrial fibrillation (AF) developed paresthesia in the ulnar distribution of the left hand after replacement of a lead and cardiac defibrillator generator; the procedure involved induction and termination of one episode of ventricular fibrillation. He had a nonocclusive brachial artery lesion that was likely embolic and could have occurred because of underlying AF and/or PCC. No patient had any bleeding complications.
CONCLUSIONS: Protocol dosing of PCC can reverse warfarin effects to enable safe implantation of cardiac devices.

37. Assessment of the White-Coat Effect Among Established Hypertensive Patients Who Assert to Be Well Controlled. *David A. Bookstaver, Pharm.D.*, Christos Hatzigeorgiou, D.O., MPH; Eisenhower Army Medical Center, Fort Gordon, GA
PURPOSE: The purpose of this study was to determine the white-coat effect (WCE), defined as the mean difference in blood pressure in clinic and during the daytime interval, on 24-hour ambulatory blood pressure monitoring (ABPM) among patients referred for presumed white-coat hypertension (WCH). In addition, the impact of ABPM on the antihypertensive regimen was determined.
METHODS: Medical records of 222 consecutive patients referred for assessment of WCE were reviewed. Patients without a clinic visit since a medication change and those with less than 70% valid readings were excluded. Daytime mean blood pressure during ABPM was compared with mean prior clinic readings to determine the WCE. The prevalence of WCH was determined and defined as a daytime mean of 135/85 mm Hg or less on ABPM. Changes to antihypertensive therapy were determined for the 6-month period after the study.
RESULTS: Twenty-nine patients were excluded, and 77% of the remaining 193 patients met the definition of WCH, which was significantly higher than the hypothesized rate from a literature review of 40% ($p<0.01$). The WCE was 35 ± 14/9 ± 9 mm Hg in those meeting the definition of WCH and 18 ± 16/3 ± 9 mm Hg in patients who did not ($p<0.01$). Mean blood pressure at clinic visits was 158 ± 13/77 ± 10 mm Hg and 127 ± 12/70 ± 9 mm Hg during the daytime on ABPM ($p<0.01$). Therapy was unchanged 6 months after ABPM in 83% of patients meeting the definition of WCH and in 89% of those who were at goal during the test despite a mean post-ABPM blood pressure of 151/74 mm Hg.
CONCLUSIONS: Clinical suspicion of a significant WCE was highly accurate, and ABPM led to no change in therapy for most patients.

38. Evaluation of Triple Antithrombotic Therapy After Percutaneous Coronary Intervention (PCI) in Veterans. *Lan K. Ngo, Pharm.D.,*[1] Shannon W. Finks, Pharm.D., BCPS,[2] Robert B. Parker, Pharm.D.,[3] Kelly C. Rogers, Pharm.D.[2]; (1) Veterans Affairs Medical Center, Memphis, TN; (2) University of Tennessee College of Pharmacy, Memphis, TN; (3) University of Tennessee Department of Clinical Pharmacy, Memphis, TN
PURPOSE: Dual antiplatelet therapy (DT) with aspirin (A) and clopidogrel (C) is recommended after percutaneous coronary intervention (PCI) with stents. The use of these agents is complicated when patients also have indications for warfarin (W) therapy. The safety and efficacy of this triple therapy (TT) remain unclear. The purpose of this study was to evaluate veterans receiving W who undergo PCI and to assess outcomes associated with their prescribed post-PCI antithrombotic regimen.
METHODS: Patients at the Memphis VA Medical Center receiving W at the time of PCI between January 2006 and August 2007 were identified. Demographic data, antithrombotic regimen (TT or DT with either A+C, A+W, or C+W), W indication, stent type, rates of thrombolysis in myocardial infarction (TIMI) major or minor bleeding, blood transfusions, repeat revascularizations, emergency department visits, and hospitalizations in the 12 months post-PCI were recorded.
RESULTS: Thirty-nine patients were identified (25 TT; 14 DT). The rate of overall bleeding among patients receiving TT and DT at 12 months was 44% versus 57%, respectively. Rate of TIMI minor bleeding among patients receiving TT and DT at 12 months was 24% versus 14%, respectively. A total of five major bleeds occurred in the TT group—all in patients receiving 325 mg of A versus 81 mg ($p=0.026$). Four major bleeds occurred in the DT group (two patients receiving 81 mg of A and two receiving 325 mg of A).
CONCLUSIONS: In patients receiving TT, an A dose of 325 mg was associated with increased risk of major bleeding. Additional evaluation is warranted to further understand the safety and efficacy of TT in this population. Developing an in-house registry assessing the risks associated with triple therapy would be a valuable tool. Future analysis will include blood transfusions, repeat revascularizations, emergency department visits, and hospitalizations.

39E. Sodium Derangement and Associated Clinical and Financial Outcomes: Analysis of 115,969 Acute Heart Failure Admissions in 2004–2005. Andrew F. Shorr, M.D., MPH, FCCP,[1] Ying P. Tabak, Ph.D.,[2] Stephen G. Kurtz, M.S.,[2] James Spalding, Pharm.D., M.S.,[3] *Vikas Gupta, Pharm.D., BCPS*[2]; (1) Washington Hospital Center, Washington, DC; (2) Cardinal Health Information Services, Marlborough, MA; (3) Astellas Pharma US, Inc., Deerfield, IL
PURPOSE: Acute heart failure (AHF) remains a leading cause of morbidity and mortality. Derangements in serum sodium are common in patients presenting with AHF, but the clinical implications of sodium derangements and associated altered mental status (AMS) changes on admission are unknown. We sought to evaluate the association between sodium derangements and morbidity, mortality and cost burden for hospitalized AHF patients.
METHODS: We retrospectively analyzed a large database of 115,969 AHF admissions in the United States across 185 hospitals (teaching and nonteaching) in 2004–2005. We categorized patients into one of four cohorts based on admission laboratory data:

sodium equal to 130 mEq/L or less as severe hyponatremia; 131–135 mEq/L as hyponatremia; and more than 145 mEq/L as hypernatremia; we used sodium 136–145 mEq/L (normonatremic) as the reference group. We estimated excess risks for mortality, AMS, LOS, and cost using multivariable analysis.
RESULTS: Overall, the median age was 77; 55% were women. Crude mortality was 3.6%. The prevalence of severe hyponatremia, hyponatremia, and hypernatremia was 5.3, 15.9, and 3.2%, respectively. The corresponding crude mortality was 7.6, 4.9, and 6.7% compared with 2.9% for the normonatremic group. After controlling for confounding risk factors, all three levels of sodium derangement were independent predictors for mortality, AMS, and excess LOS (see Table). Both hyponatremia levels were also independent predictors for excess cost.

	≤ 130	131–135	136–145	> 145
Cases, %	5.3	15.9	75.6	3.2
Mortality, OR (CI)	1.8 (1.6–2.0)	1.3 (1.2–1.4)	ref	1.6 (1.3–1.8)
AMS, OR (CI)	1.3 (1.2–1.4)	1.1 (1.0–1.1)	ref	2.1 (1.9–2.2)
Excess LOS, days (CI)	1.1 (1.0–1.3)	0.5 (0.4-0.6)	ref	0.3 (0.1–0.4)
Excess cost, $ (CI)	1363 (994–1732)	595 (368–821)	ref	(314) [(779)–151]

CONCLUSIONS: About one-fourth of patients with AHF presented to hospitals with deranged sodium levels, which were associated with adverse clinic and economic outcomes.
Presented at the American College of Cardiology 57th Annual Scientific Session, Chicago, IL, March 29–April 1, 2008.

40. Evaluation of Skeletal Troponin-I as an Early Serum Marker for Statin-Induced Myopathies. *Armine Khachatryan, Pharm.D.*, Donna Agan, Ed.D., Harminder Sikand, Pharm.D., Paul Phillips, M.D.; Scripps Mercy Hospital, San Diego, CA
PURPOSE: A significant limiting side effect associated with statin therapy is muscular pain, which can range from myalgia to myositis and rhabdomyolysis. Early muscle toxicity, such as myositis, is often below the detection threshold of currently available laboratory serum markers. Creatine kinase (CK) is the most commonly used marker; however, it is limited by specificity and sensitivity for early muscle toxicity. Several preliminary studies demonstrated that skeletal troponin-I (sTnI) was a sensitive and specific serum marker of skeletal muscle injury regardless of etiology.
METHODS: This pilot study assessed the utility of sTnI for detecting statin-induced myopathies. Patients who were statin naïve or who had not been on statin therapy for the previous 6 months and who did not meet the exclusion criteria were consented and enrolled prospectively. Blood samples were drawn within 24 hours of statin therapy initiation and after 6 weeks of therapy. Each patient served as his/her own control. The results of the investigational assays for fast and slow isoforms of sTnI were compared against standard CK measurements. At the third and fifth weeks, patients were called to address compliance with therapy and to remind them of their upcoming appointment. At the sixth week of follow-up, patients completed a self-reported questionnaire that characterized the type of muscular symptoms experienced during this trial.
RESULTS: The research-based assay used in this study has an analytic sensitivity of 0.39 ng/mL and a specificity of 99%. Of the 129 patients screened, 118 were excluded on the basis of study criteria. Eleven patients consented and enrolled. Interim analysis demonstrates that 92% of the variance in CK can be explained by fast sTnI (adj. r^2=0.92, p<0.001). Final results will be presented.
CONCLUSIONS: sTnI appears to be a promising alternative serum marker for the evaluation of statin-induced myopathies; however, a larger study is needed to fully assess its potential.

Clinical Administration

41. Academic and Training Requirements in Advertisements for Pharmacy Management and Clinical Director Positions: A Follow-up. *John E. Murphy, Pharm.D.*, Jade Ashby, Pharm.D.; University of Arizona College of Pharmacy, Tucson, AZ
PURPOSE: To determine academic and training requirements found in advertisements for pharmacy department manager/director, assistant/associate director, and clinical director positions and to compare the results with those of a previous study.
METHODS: Advertisements appearing in the *American Journal of Health-System Pharmacy* (AJHP) were analyzed for academic and training criteria that were either preferred or required for pharmacy department manager/director, assistant/associate director, or clinical pharmacy director positions. Included advertisements were for pertinent positions found in AJHP between January 2002 and December 2007. Some of the requirements or preferences that appeared in the advertisements analyzed included type of pharmacy or other degree, postgraduate training including residencies and/or fellowships, and previous experience qualifications.
RESULTS: Four hundred twenty-six advertisements met inclusion criteria. Results were listed in percentages of advertisements either requiring or preferring a certain qualification. A large portion of advertisements sought applicants who had completed a residency (24% – pharmacy manager/director, 50% – clinical director, and 47% – assistant/associate manager). Preferences and requirements of the Pharm.D. or M.S. degree qualification decreased in percent from a previous study. However, there was an increase in the relative number of advertisements with an M.B.A. preference (9% [n=27]) compared with the previous study. When experience was required or preferred, an average of at least 4 years was suggested for each of the position types.
CONCLUSIONS: Many of the results from this study were similar to previous studies that examined job qualifications for pharmacy manager and clinical director positions. It remains evident that education, training, and experience play a major role in meeting the qualifications associated with obtaining a position as a pharmacy department manager/director, clinical director, or assistant/associate director, with residencies required or preferred more often in the latter two categories.

Community Pharmacy Practice

42. Attitudes of Physicians Toward Pharmacist-Provision of Medication Therapy Management Services (MTMs) as Part of the Medicare Part D Benefit. *Fadi M. Alkhateeb, Ph.D.*, David A. Latif, Ph.D., Renee McCafferty, Pharm.D.; University of Charleston, Charleston, WV
PURPOSE: The implementation of Medicare Part D in 2006 has the potential to improve patient care, lower health care costs, and advance the profession of pharmacy through pharmacist-provided medication therapy management (MTM) services. However, a dearth of research has evaluated physicians' attitudes toward pharmacist-provided medication management services, and little is known about factors that may affect these attitudes. Investigating the attitudes of physicians is especially relevant because the success or failure of some MTM services will still be dependent on physicians' attitudes and their collaboration with pharmacists. Therefore, our objective for this study was to test a model of physicians' attitudes toward pharmacist-provided MTM services as a part of Medicare Part D.
METHODS: A mail survey was sent to a random sample of 500 physicians practicing in West Virginia. Multiple linear regression was used to test the model. The independent variables included were prescription volume; specialty type; years of practice; gender; academic affiliation; practice size; physicians' attitudes toward collaborative agreement; physician-pharmacist communication frequency regarding patient medications, new prescription suggestions, and refill; and control variable (age).
RESULTS: A total of 102 responses were received for a response rate of 22.1%. The mean for physicians' attitudes toward support providing MTMs by pharmacists was 2.86 of 5 (anchored at 5 = strongly agree and 1 = strongly disagree). The overall physicians' attitudes model for providing MTMs by pharmacists was significant (R^2=0.55). Physicians' attitudes toward collaborative agreement, specialty, years of practice, physician-pharmacist communication, frequency regarding patients' drugs, and gender had significant influences on physician attitudes toward MTMs' provision by pharmacists (p<0.05).
CONCLUSIONS: The proposed model is useful to explain physicians' attitudes toward providing MTMs by pharmacists.

43. Patterns of Pharmacy Use Among HIV Positive Women in San Francisco. *Tracy P. Hsu, Pharm.D.*, Jennifer M. Cocohoba, Pharm.D., Ruth M. Greenblatt, M.D.; University of California, San Francisco, San Francisco, CA

PURPOSE: Community pharmacies are an important bridge between receiving a prescription and taking antiretroviral therapy. Breakdowns in the patient-pharmacy relationship may result in suboptimal therapy and an increased risk of treatment failure. Few studies have examined the relationship between outpatient pharmacy use and human immunodeficiency virus (HIV)-associated outcomes. The objectives of the study were to determine patterns of community pharmacy use of women enrolled in the San Francisco Women's Interagency HIV Study and to assess whether patterns of pharmacy use correlate with patient characteristics or treatment outcomes.

METHODS: This was a prospective study nested within a large natural history cohort. The nested study included a survey of pharmacy use and was administered biannually between 2004 and 2007. Poisson regression methods were used to assess the associations between patient characteristics and pharmacy use patterns. Repeated-measures linear and logistic regression models were used to assess the relationships between the numbers of pharmacies used, CD4 count, and HIV viral load. Analyses were adjusted for potential confounders.

RESULTS: Three hundred fifty-two women, of whom 71% were HIV positive, were included in the analysis. Most reported using an average of one pharmacy during each 6-month period. HIV infection was associated with using multiple pharmacies (p=0.04), although the association was not statistically significant when adjusted for employment. Among women who were HIV positive and taking antiretroviral therapy, using multiple pharmacies was associated with a lower CD4 count (p=0.04), but the association was not statistically significant when adjusted for other factors. Using multiple pharmacies was not associated with virologic treatment failure.

CONCLUSIONS: HIV status may be an important predictor of patterns of outpatient pharmacy use. Women who were HIV positive who used multiple pharmacies had lower immunologic recovery, but this relationship was not independent of other factors. Individuals taking more drugs may tend to use multiple pharmacies, which, if supported by future studies, may aid in planning pharmacy services.

44E. Initiative to Convert Patients from Nebulized Respiratory Medications to Portable Inhalers: Analysis of Pharmacist Claims for a Professional Fee to Optimize Therapy in Nova Scotia, Canada. *Susan K. Bowles, Pharm.D., M.Sc.*,[1] Chris Cameron, B.Sc., M.Sc.,[2] Charmaine C. Cooke, B.Sc. (Pharm.), M.Sc.,[3] Ingrid Sketris, Pharm.D., MPA (HSA),[4] Priti Flanagan, Pharm.D.[3]; (1) Dalhousie University and Centre for Health Care of the Elderly, Halifax, NS, Canada; (2) Department of Community Health and Epidemiology, Dalhousie University, Halifax, NS, Canada; (3) Population Health Research Unit, Dalhousie University, Halifax, NS, Canada; (4) College of Pharmacy, Dalhousie University, Halifax, NS, Canada; (5) Fraser Health Authority, Vancouver, BC, Canada

PURPOSE: To determine the involvement of pharmacists from Nova Scotia, Canada, in the initial years of the wet nebulization respiratory medication conversion initiative (2000–2004). This policy initiative provided pharmacists with a professional fee for the provision of patient education around the use of spacer devices in combination with portable inhalers for eligible beneficiaries of the Nova Scotia Pharmacare Programs.

METHODS: A retrospective population-based study was performed using claims from the Nova Scotia Pharmacare Program administrative database for January 1, 2000, through December 31, 2004. The study population consisted of those who received drug benefits through the Seniors' and Family Benefits' Pharmacare Programs. Claims by pharmacists for the professional fee were identified using specified billing codes for spacer devices.

RESULTS: During the 5-year evaluation period, 21,590 spacer device claims were billed to Pharmacare Programs. Spacer device claims from 2000 to 2004 were 5299, 4582, 4017, 3946, and 4016, respectively. The proportion of spacer device users per 1000 respiratory medication users from 2000 to 2004 was 137, 127, 150, 155, and 166, respectively.

CONCLUSIONS: The policy initiative of paying pharmacists a professional fee to provide spacer devices has had a significant and sustained uptake in Nova Scotia. However, more beneficiaries of the Pharmacare program could potentially benefit from receiving a spacer device in combination with portable inhalers for their respiratory medications, as well as education from pharmacists on the correct use of these devices.

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Critical Care

45E. Comparison of Estimated Creatinine Clearance Using Modified Diet in Renal Disease, Cockroft-Gault or 24-Urine Equations in Critically Ill Surgical Patients. *Anthony T. Gerlach, Pharm.D., BCPS,*[1] Sheela Thomas, M.S., R.D.,[1] Joseph Dasta, M.S.,[1] Steven Steinberg, M.D.,[1] Charles Cook, M.D.,[1] Jessica Benson, Pharm.D.[2]; (1) The Ohio State University Medical Center, Columbus, OH; (2) The Cleveland Clinic Foundation, Columbus, OH

PURPOSE: Assessment of renal function and adjustment of renally eliminated drugs are fundamental tasks of critical care practitioners, especially pharmacists. In patients with chronic kidney disease, the use of the four-variable (M4) or six-variable (M6) Modification of Diet in Renal Disease Study equations produced more accurate glomerular filtration rate (GFR) estimates than the Cockroft-Gault (CG) equation. This cohort study compared the M4, M6, and CG equations with an estimation of creatinine clearance with a 24-hour urine creatinine collection in surgical ICU (SICU) patients.

METHODS: Patients admitted to the SICU with 24-hour urine collection were evaluated retrospectively for age, gender, race, serum creatinine, blood urea nitrogen, and albumin between July 2004 and December 2006. Creatinine clearance estimation with CG used ideal body weight and was normalized to 1.73 m^2. Patients were excluded if they were pregnant, received concurrent dialysis, or did not have an albumin within 7 days of 24-hour urine collection. Statistical analysis was performed by analysis of variance.

RESULTS: Fifty nine patients were included for analysis (30 men; mean age 63.7 years). The mean estimated creatinine clearance values (±SD) for M4, M6, 24-hour urine, and CG were 99.4 (±81.6), 64 (±54.9), 77.9 (±78.1), and 38.5 (±51.1) mL/minute/1.73 m^2, respectively (p=0.007).

CONCLUSIONS: In critically ill surgical patients, there is a wide variation in estimation of creatinine clearance using M4, M6, CG, and 24-hour urine collection. Further studies are needed to define the optimal formula for estimation of renal function and for drug dosage adjustments.

Presented at the 37th Society of Critical Care Medicine Critical Care Congress, Honolulu, HI, February 2–6, 2008.

46. Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers Reduce Mortality in Septic Patients. *Paul P. Dobesh, Pharm.D.*, Donald G. Klepser, Ph.D., M.B.A., Timothy R. McGuire, Pharm.D., Craig Morgan, Pharm.D. Student, Keith M. Olsen, Pharm.D.; University of Nebraska Medical Center, Omaha, NE

PURPOSE: Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have proven ability to have a positive effect on several inflammatory markers in patients with diabetes, hypertension, and heart failure. Many of the same inflammatory markers are associated with the syndrome of sepsis. ACEIs/ARBs may be able to protect against the excessive inflammatory response in severe sepsis. ACEIs/ARBs have been studied in patients with pneumonia but not in patients with sepsis. Therefore, we evaluated the effect of ACEIs/ARBs on in-hospital mortality in patients with sepsis.

METHODS: This retrospective cohort study included all patients older than 40 years with a diagnosis of sepsis and an intensive care

unit admission at our academic medical center from January 1, 2005, to December 31, 2006. ACEI/ARB use, patient demographics, and APACHE II score at the time of sepsis were collected from patient charts. We used a multiple logistic regression model to evaluate the association between ACEI/ARB use and in-hospital mortality after controlling for age, gender, and severity of illness.
RESULTS: We identified 188 patients who met the inclusion criteria for this study. Of these patients, 84 (45%) had exposure to ACEI/ARB use. ACEI/ARB and non-ACEI/ARB patients were similar in age (66.5 ± 13.1) and APACHE II scores (26 ± 5.6). In the univariate comparison, ACEI/ARB users had a 46% relative reduction in mortality compared with non-ACEI/ARB users (26.2% vs. 56.7%; p<0.001). In the multivariate regression, ACEI/ARB use had a protective effect (OR = 0.214; CI: 0.105–0.433; p<0.001), whereas age (OR = 1.041; CI: 1.014–1.069; p=0.003) and APACHE II score (OR = 1.115; 95% CI: 1.046–1.188; p=0.001) were associated with increased mortality.
CONCLUSIONS: In this analysis, the use of ACEIs/ARBs had a protective effect on patients with sepsis by significantly reducing mortality compared with patients not receiving ACEIs/ARBs. These data will be used to develop a more systematic evaluation of ACEI/ARB use in patients with sepsis.

47. Clinical and Economic Outcomes of Involving Pharmacists in the Direct Care of Critically Ill Patients with Thromboembolic Disorders. *Robert MacLaren, Pharm.D.,*[1] C.A. Bond, Pharm.D.[2]; (1) University of Colorado School of Pharmacy, Aurora, CO; (2) Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX
PURPOSE: This study explores associations between the involvement of clinical pharmacists in the care of critically ill Medicare patients with thromboembolic events (TEs) and mortality rates, length of intensive care unit (ICU) stay, Medicare charges, and drug charges. Outcomes of bleeding complications (BCs) are also delineated according to the involvement of clinical pharmacists.
METHODS: ICU pharmacy services were obtained from a 2004 national survey. Clinical pharmacy service was defined as having some pharmacist time specifically devoted to the direct care of ICU patients. TEs and BCs were defined using ICD-9-CM codes. Intensive care unit outcome data were drawn from 2005 MEDPAR.
RESULTS: The involvement of clinical pharmacists was evaluated in 110,309 patients with TEs, accounting for 7987 BCs. Mortality rates in ICUs that did not have clinical pharmacists were higher by 37% (OR = 1.41; 95% CI: 1.36–1.46; 183 extra deaths) and 32% (OR = 1.35; 95% CI: 1.13–1.61; six extra deaths) for TEs and BCs, respectively. Lengths of stay in ICUs without pharmacists were longer by 14.8% (7.28 ± 8.17 vs. 6.34 ± 7.80 days; p<0.0001; 59,429 extra ICU days) and 15.8% (12.4 ± 13.28 vs. 10.71 ± 9.53 days; p=0.008; 7478 extra ICU days) for TEs and BCs, respectively. The absence of clinical pharmacists was associated with extra Medicare charges of $215,397,354 (p<0.001) and $63,175,725 (p<0.0001) for TEs and BCs, respectively. Extra drug charges were $26,363,674 (p<0.0001) and $2,610,750 (p<0.001), respectively. In the absence of clinical pharmacists, BCs increased by 48% (OR = 1.53; 95% CI: 1.46–1.60; 131 extra BCs), resulting in 39% more patients with BCs (OR = 1.47; 95% CI: 1.28–1.69; 25 extra patients) receiving more transfusions (6.77 ± 10.35 vs. 3.06 ± 2.64 blood units/patient, p=0.006; 93 extra blood units).
CONCLUSIONS: The involvement of clinical pharmacists in the care of critically ill Medicare patients with TEs is associated with reduced mortality, improved clinical and economic outcomes, and fewer BCs.

48E. Hypernatremic Hyperosmolar State (HHS) in Acute Brain Injury (ABI): Effect on Intracranial Pressure. *Denise H. Rhoney, Pharm.D.,*[1] Dennis Parker, Pharm.D.,[1] Xi Liu-DeRyke, Pharm.D.,[1] Lisa Forsyth, Pharm.D.,[2] William M. Coplin, M.D.,[1] J. Ricardo Carhuapoma, M.D.[3]; (1) Wayne State University, Detroit, MI; (2) William Beaumont Hospital, Royal Oak, MI; (3) Johns Hopkins University, Baltimore, MD
PURPOSE: Osmotherapy is a mainstay intracranial pressure (ICP) treatment. We sought to evaluate efficacy, adverse effects (ADRs), and patient outcomes of two maintenance fluid approaches using hypernatremic hyperosmolar state (HHS) versus eunatremic euvolemic state in patients with acute brain injury (ABI).
METHODS: Patients with ABI with elevated ICP values were prospectively randomized to either 3% sodium chloride/acetate (HTS) (n=14) to achieve sodium (Na) of 150–155 mEq/L and serum osmolarity 315–320 mmol/L or 0.9% sodium chloride (NS) (n=12) for 72 hours (1–2 mL/kg/hour). Routine care/ICP management was standardized. Hemodynamics and ICP were monitored and recorded hourly.
RESULTS: Thirty-nine percent of patients had brain trauma, and 15% had subarachnoid hemorrhage. Groups were similar for admission in Glasgow Coma Scale, ICP, mean arterial pressure, serum Na+, APACHE II, gender, and age. Average highest serum Na+ and osmolarity in HTS patients was 155.7 mEq/L and 326.9 mmol/L, respectively; 43% reached goal in 24 hours or less and 79% in 48 hours or less. Percent time ICP less than 20 mm Hg during the study period was similar between groups (NS 69.5% vs. HTS 82.9%; 95% CI: -35.2, 9.4) Average cerebral perfusion pressure was more than 70 mm Hg in both groups during the study period. Hemodynamics were also similar between groups. Fluid balance during the study period was 886 mL (NS) and 3490 mL (HTS). HTS patients received significantly fewer interventions for ICP control (1.9 vs. 6.6; p=0.02).There were no differences between the NS and HTS groups in length of stay (15.5 vs. 10 days, respectively) or modified Rankin (4 vs. 6, respectively) at discharge. ADRs were similar between groups.
CONCLUSIONS: Inducing HHS within the first 72 hours after ABI maintains ICP, requiring significantly fewer additional interventions without an increase in ADRs. Further study will better qualify outcome differences.
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49. Conversion of Critically Ill Patients from Continuous Insulin Infusions to Subcutaneous Insulin. *Kyle A. Weant, Pharm.D.,*[1] Alim Ladha, M.D.[2]; (1) UK HealthCare, Lexington, KY; (2) University of North Carolina at Chapel Hill, Chapel Hill, NC
PURPOSE: Continuous insulin infusions have become a standard of care in most intensive care units; however, methods for transitioning patients to other insulin therapies during transfer to floor beds have not been extensively evaluated.
METHODS: A searchable pharmacy database was used to retrospectively identify adult patients admitted to the neurosurgery service and prescribed a continuous insulin infusion between May 2007 and February 2008. All patients were transitioned to subcutaneous (SC) insulin on floor transfer. Patients were stratified according to the dose of SC insulin as a percentage of their prior 24-hour continuous insulin requirement and then analyzed on the rate of achievement of goal blood glucose (BG) values, 80–150 mg/dL, within the first 48 hours.
RESULTS: A total of 769 BG values from 79 patients were recorded during the study period. Data analysis demonstrated lower median BG values with the use of 60–70% of insulin infusion requirements compared with all other groups. For patients without a history of diabetes mellitus (DM), the use of 60–70% of the prior insulin requirement resulted in a significantly greater percentage of patients within the target range compared with other groups (78%; p<0.05). For those with a history of DM, insulin doses of more than 70% yielded the most frequent achievement of target values, although there was substantial variability within this group. No significant difference was noted in the incidence of hypoglycemia (less than 80 mg/dL) between groups.
CONCLUSIONS: Methods currently used to transition patients off insulin infusions vary widely. Initial data suggest that using 60–70% of the 24-hour insulin requirement would result in BG values of 80–150 mg/dL 80% of the time. Further study is necessary to adequately assess the optimal insulin infusion transition protocol for critically ill patients to ensure both safety and efficacy.

50. Inpatient Cardiac Arrest Outcomes at Two Major Medical Centers with a Focus on Vasopressin. *Brooke L. Baltz, Pharm.D.,*

Lynda Tanagi, Pharm.D.; UW Medicine, Seattle, WA

PURPOSE: This study examined sympathomimetic use in the cardiac arrest setting to determine if vasopressin had comparable effects with epinephrine on return of spontaneous circulation (ROSC) and survival at end of code. In addition, the following were investigated: (1) whether drug choice affected rhythm outcomes, (2) whether sequence of drug administration affected survival at end of code, and (3) whether advanced cardiac life support (ACLS) guidelines were being followed. Following ACLS guidelines was defined as vasopressin replacing either the first or second dose of epinephrine.
METHODS: Code records of 524 patients experiencing cardiac arrest between January 1, 2003, and October 11, 2007, at two academic centers were reviewed. Initial rhythm, order of drug administration, ROSC after drug administration, and survival at end of code were documented. Data were analyzed using the random-effects logistic regression method.
RESULTS: Epinephrine alone was administered in 462 codes (88%), and 62 patients received both agents. ROSC was 5.8 ± 7.4 times higher with vasopressin than epinephrine (p=0.165). The time variable was significant (p<0.001), with the odds of ROSC for each additional administration of drug 16% lower (1.0–0.84) than for the previous administration. The between-person variability was significant (p<0.001), accounting for 33% of the variance. Survival rate was 55% for epinephrine versus 36% for patients receiving both drugs. Outcomes according to initial rhythms resulted in no significant findings. Of 62 codes that used vasopressin, advanced cardiac life support (ACLS) guidelines were followed in 14 situations (23%), with a survival rate of 50% versus 29% if ACLS guidelines were not followed. The odds of survival was 3.1 if the guidelines were followed (p=0.07).
CONCLUSIONS: With this study alone, there is insufficient evidence to recommend one sympathomimetic over the other because it appears that epinephrine and vasopressin were not the deciding factors with regard to outcome.

51. Propylene Glycol Accumulation in Patients Receiving Intravenous Lorazepam Infusions. *Erica L. Horinek, Pharm.D.*, Robert MacLaren, Pharm.D., Tyree H. Kiser, Pharm.D., Doug N. Fish, Pharm.D.; University of Colorado School of Pharmacy, Aurora, CO

PURPOSE: To evaluate the accumulation of propylene glycol (PG) in critically ill patients receiving lorazepam by continuous infusion (CI) and determine factors associated with accumulation.
METHODS: This study was an observational safety assessment of adult patients admitted to the medical intensive care unit receiving lorazepam by CI for 12 hours or more. PG serum concentrations were obtained 24 hours or more after initiating lorazepam CI and every 3–5 days thereafter. PG accumulation was defined as 25 mg/dL or greater, as measured by the hospital laboratory. Groups with and without PG accumulation were compared using the unpaired t-test. Correlation analyses used linear regression.
RESULTS: Thirty-three patients had 48 PG serum samples. Age was 46 ± 14 years; APACHE II score was 26 ± 9; 16 patients had renal dysfunction; and 10 patients had hepatic dysfunction. PG concentrations were 75 ± 104 mg/dL (median of 21 mg/dL; interquartile range of 8.5–88 mg/dL). Fourteen patients (42%) had PG accumulation, representing 23 (48%) serum samples. Twenty-one (88%) of the 23 serum samples were associated with lorazepam CI of 4 mg/hour or more. Only the lorazepam dosing regimen differed between patients with and without PG accumulation. Factors correlating with PG serum concentrations were the rate of lorazepam infusion when PG samples were collected (r^2=0.81, p<0.0001; rate of 7.5 ± 7.9 mg/hour) and cumulative lorazepam dose in the 24-hour period preceding the collection of PG samples (r^2=0.71, p<0.0001; 24-hour dose of 149 ± 151 mg). Patient characteristics and other dosing parameters did not correlate with PG serum concentrations. Seven patients (21%) developed renal dysfunction after lorazepam CI was initiated, but associated causes were indeterminable. Other possible PG-associated side effects were not observed.
CONCLUSIONS: PG serum concentrations correlated with the rate of lorazepam CI and cumulative 24-hour lorazepam dose. Extrapolation of these results to other intensive care unit populations needs validation. Despite the absence of confirmed PG-associated side effects, clinicians should be aware that PG accumulation may occur with lorazepam CI.

52. Patients Receiving Chronic Warfarin Therapy Admitted to the Intensive Care Unit: What Are the Outcomes? Gregory J. Peitz, Pharm.D.,[1] *Mark Malesker, Pharm.D.*,[2] Carolyn McDonald, M.D.,[1] Lee E. Morrow, M.D.[1]; (1) Creighton University Medical Center, Omaha, NE; (2) Creighton University School of Pharmacy, Omaha, NE

PURPOSE: There is a paucity of data concerning outcomes of chronically anticoagulated patients requiring intensive care unit (ICU) admission. This study was designed to assess the ICU outcomes of these patients relative to patients not receiving warfarin therapy and to identify predictors of mortality.
METHODS: Data were retrospectively collected on patients (n=1472) admitted to a combined medical/surgical/trauma ICU during a 1-year period. Baseline data including international normalized ratio (INR) values, APACHE II scores, and medical history were recorded. Relative in-hospital events were captured for the remaining hospital course. Statistical analyses were performed to compare pertinent outcomes between the cohorts.
RESULTS: Chronic warfarin therapy was documented in 100 patients' medical histories (6.8% of all ICU admissions). Patients receiving warfarin had a higher incidence of in-hospital mortality than patients not receiving warfarin (34.9% vs. 30.5%, p=0.03). Compared with the aggregate ICU population, patients receiving warfarin were older (69.9 vs. 56.6 years, p<0.001), had a higher incidence of fresh frozen plasma and red blood cell administration (36% vs. 12%, p<0.001, and 40% vs. 27%, p<0.001, respectively), had experienced more infectious and bleeding complications (24% vs. 18%, p=0.004, and 19% vs. 7%, p<0.001, respectively), and had experienced fewer thromboembolic complications (0% vs. 2%, p=0.003). Using multivariate logistic regression to adjust for the effects of covariates, predictors of death in patients on chronic warfarin therapy included the INR value on ICU admission, the initial APACHE II score, and the amount of vitamin K administered. This model found that mortality risk increased 27.3% with each international unit increase in the INR (p=0.033); 10.3% with each 1-point rise in APACHE II score (p=0.013); and 6.5% with each 1 mg of vitamin K administered (p=0.023).
CONCLUSIONS: Patients receiving warfarin requiring ICU admission have higher mortality than their nonanticoagulated critically ill counterparts. These data demonstrate a direct relationship between INR values and mortality risk.

53. Lipid Administration in the VELOCITY Trial: Safety and Efficacy of Clevidipine Butyrate Intravenous Emulsion in Acute, Severe Hypertension. *Joseph F. Dasta, M.Sc., R.Ph.*,[1] Jay M. Mirtallo, M.S., R.Ph.[2]; (1) University of Texas, Hutto, TX; (2) The Ohio State University Medical Center, Columbus, OH

PURPOSE: VELOCITY was an open-label, multicenter, single-group trial evaluating the safety and efficacy of clevidipine butyrate intravenous emulsion (CLV), a rapid-acting calcium channel blocker, for treatment of severe hypertension.[1] Because CLV is an intravenous lipid emulsion, we additionally evaluated infusion volume, duration, and 24-hour lipid load and their effects on triglyceride concentrations.
METHODS: Patients 18 years and older presenting with systolic blood pressure (SBP) more than 180 mm Hg and/or diastolic blood pressure more than 115 mm Hg on two successive measurements 15 minutes apart were eligible. CLV was administered at 2.0 mg/hour for the first 3 minutes. If the prespecified patient-specific target reduction in SBP was not achieved, the dosage was doubled at investigator discretion every 3 minutes to a maximum of 32.0 mg/hour. Triglyceride concentrations were measured at baseline, every 24 hours during infusion, and 6 hours postinfusion.
RESULTS: Target SBP was achieved within 30 minutes of CLV infusion in 89% of patients in the efficacy population (n=117). In the safety population (n=126), median infusion duration was 20.66 hours, median total volume infused was 336.33 mL, and median

maximum 24-hour lipid dose was 0.74 g/kg/day (range 0.0–4.3 g/kg/day). The recommended maximum lipid dose of 2.5 g/kg/day was exceeded in 11 (8.7%) patients. The median change in triglyceride concentration from baseline to 6 hours postinfusion was 0 (n=57).[1] Triglyceride concentration increased in 47.4% of patients, decreased in 47.4%, and did not change in 5.2% during this period. No correlation was found between total lipid dose and change in triglyceride concentration from baseline to 6 hours postinfusion. No hyperlipidemic adverse events were noted.
CONCLUSIONS: In acute, severe hypertension, CLV rapidly achieved target blood pressure without exceeding the recommended 24-hour lipid load in a majority of patients. Total lipid dose infused did not correlate with changes in triglyceride concentration.
[1]Ann Emerg Med 2008; (June 6 e-pub).

54. Clinical Characteristics and Outcomes of Critically Ill Patients with Carbapenem-Resistant Acinetobacter baumannii Bacteremia or Pneumonia: A Single-Center Experience. *Justin K. Rak, Pharm.D.*, Neil E. Ernst, Pharm.D., Eric W. Mueller, Pharm.D.; The University Hospital, Cincinnati, OH
PURPOSE: Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is increasingly associated with nosocomial infection. We sought to describe local definitive antibiotic regimens and evaluate clinical and microbiologic outcomes in critically ill medical and surgical patients with CRAB bacteremia or pneumonia.
METHODS: Adult medical and surgical intensive care unit (ICU) patients admitted to The University Hospital between August 2005 and February 2008 with blood or significant lower respiratory cultures positive for CRAB and clinical signs/symptoms of infection were reviewed. Pregnant, hospice, and cystic fibrosis patients were excluded. Clinical and microbiologic cure, as well as in-hospital outcomes, was recorded.
RESULTS: Twenty-eight patients were included (13 pneumonia, 10 pneumonia/bacteremia, and 5 bacteremia). Twenty-one (75%) patients were male and had surgical diagnoses. Median (range) ICU admission APACHE II score was 20 (11–33), infection day sequential organ failure assessment 8 (5–16), and mean ICU length of stay 35 ± 22 days. Eleven (39%) patients had recent hospital admission, 28 (100%) required mechanical ventilation, and 16 (57%) required vasopressors. Time from hospital admission to infection was 14 ± 9 days; 27 (96%) infections were polymicrobial. Of tested isolates, susceptibility rates were colistimethate 100% (n=14), tobramycin 31% (n=54), ampicillin-sulbactam 11% (n=54), and tigecycline (minimum inhibitory concentration [MIC] of 2 or less) 0% (n=15). Seven (25%) patients received adequate empiric antibiotic therapy. Of treated patients (n=26), 13 (50%) received combination antibiotic therapy, and 15 (58%) received a colistimethate-based regimen (six intravenous only, seven inhaled only, and two both). Duration of definitive antibiotic therapy was 9.5 ± 5.6 days. Of treated patients, 8 (31%) demonstrated clinical cure, and 11 (85%) of 13 patients with follow-up cultures had microbiologic cure; 10 (36%) patients experienced reinfection. Overall, five (18%) patients died.
CONCLUSIONS: Critically ill patients with CRAB bacteremia or pneumonia have moderate-high severity of illness, polymicrobial infections, and extended duration of ICU stay. Colistimethate demonstrated the highest in vitro activity, whereas tigecycline resistance was high among tested isolates. Continued research is needed to identify effective antibiotic strategies for CRAB-related infections in critically ill patients.

Drug Information

55E. Lacosamide: Efficacy and Safety as Oral Adjunctive Treatment in Adults with Partial-Onset Seizures. *Steve Chung, M.D.*,[1] Michael Sperling, M.D.,[2] Victor Biton, M.D.,[3] Gregory Krauss, M.D.,[4] Margaret Beaman, B.Sc.,[5] David Hebert, Ph.D.,[5] SP754 Study Group, Ph.D.[5]; (1) Barrow Neurological Institute, Phoenix, AZ; (2) Thomas Jefferson University, Philadelphia, PA; (3) Clinical Trials, Inc., Little Rock, AR; (4) John Hopkins Hospital, Baltimore, MD; (5) SCHWARZ BIOSCIENCES, Inc. (a member of the UCB Group), Raleigh, NC
PURPOSE: To investigate the efficacy and safety of oral adjunctive lacosamide in subjects with partial-onset seizures taking one to three concomitant antiepileptic drugs, a multicenter, randomized, placebo-controlled trial was performed.
METHODS: Subjects (n=405) reporting eight or more seizures with less than a 21-day seizure-free period during an 8-week baseline were randomized (1:2:1) to placebo and 400 or 600 mg/day lacosamide (given 2 times/day), respectively. Efficacy was evaluated by seizure frequency data (12-week maintenance vs. baseline). Safety was evaluated by adverse events (AEs), electrocardiograms, vital signs, clinical laboratory values, and body weight.
RESULTS: Median percent reduction in seizure frequency was 20.8, 37.3, and 37.8% for placebo, 400 mg/day, and 600 mg/day lacosamide groups, respectively. Lacosamide significantly reduced seizure incidence over placebo (400 mg/day, p=0.008; 600 mg/day, p=0.006). The 50% responder rates were 18.3, 38.3, and 41.2% for placebo and 400 and 600 mg/day for lacosamide groups, respectively, with both lacosamide doses showing statistical significance over placebo (p<0.001). AEs appearing to be dose related included dizziness, nausea, diplopia, blurred vision, vomiting, tremor, abnormal coordination, and nystagmus.
CONCLUSIONS: In this trial, oral administration of adjunctive lacosamide (400 and 600 mg/day) significantly reduced seizure incidence in patients with uncontrolled partial-onset seizures. AEs were consistent with previous trials.
Presented at the American Academy of Neurology, Chicago, IL, April 12–19, 2008.

56. Analysis of the Changing Incidence of Non-Inferiority Trials. *Anne Hurley, Pharm.D.*, Trevor McKibbin, Pharm.D., M.Sc., BCPS, Katie Suda, Pharm.D.; University of Tennessee Health Science Center, Memphis, TN
PURPOSE: There has been growing concern regarding the noninferiority trial design and application of clinical trial results to patient care decisions (JAMA 2006;295:1172–4). In this study, we evaluated the incidence of noninferiority trials to (1) compare the publication rates of noninferiority trials from 1997 to 2007 and (2) evaluate the incidence of noninferiority trials by therapeutic category.
METHODS: Original articles with a noninferiority study design were identified through PubMed and Embase. The key word noninferiority was used in both databases, limited to clinical trials. Data were collected on articles published between 1997 and 2007. Noninferiority trials that did not evaluate medications were excluded.
RESULTS: A total of 215 articles were identified using our search criteria. There was a consistent increase in the yearly incidence of published clinical trials with a noninferiority study design, with only one trial in 1998, compared with 78 in 2007. Of the articles identified, 22% were in the therapeutic category of infectious disease, followed by cardiology (10%). Of the journals identified, the *Lancet* had the highest incidence of publication of trials with a noninferiority design, with 13 (6%) of the identified trials published in this journal. The median impact factor of the journals publishing noninferiority trials was 2.85 (interquartile range 1.58–4.02). Of the trials with an identified funding source (n=136), 70% listed industry as the only funding source.
CONCLUSIONS: The publication of noninferiority trials has increased during the past 10 years, particularly in infectious diseases. Most of these trials are conducted with industry funding and published in journals with a lower impact factor.

57E. Evaluation of Lacosamide in Diabetic Neuropathic Pain Trials. Aziz Shaibani, M.D., FACP,[1] Sabine Bongardt, M.S.,[2] Kenneth Sommerville, M.D.,[3] *Tracy Durgin, Ph.D.*[4]; (1) Nerve and Muscle Center, Houston, TX; (2) SCHWARZ BIOSCIENCES GmbH (a member of the UCB Group), Monheim, Germany; (3) formerly employed at SCHWARZ BIOSCIENCES, Inc. (a member of the UCB Group), Raleigh, NC; (4) UCB, Inc., Smyrna, GA
PURPOSE: To evaluate the efficacy and safety of the investigational antinociceptive and anticonvulsant drug lacosamide dosed at 400 mg/day in the treatment of diabetic neuropathic pain, data were

collected from phase II and III double-blind, randomized, placebo-controlled trials.
METHODS: Three fixed-dose trials (SP742, SP743, and SP768) contained a 12-week maintenance period; the phase II flexible-dose trial (SP614) consisted of a 4-week maintenance period. Primary outcome was within-subject change in average daily pain score (11-point pain scale) from baseline to the last 4 weeks of maintenance for the fixed-dose trials and from baseline to the end of maintenance for the flexible-dose trial.
RESULTS: Subjects receiving lacosamide 400 mg/day (n=426) showed numerically reduced pain scores over placebo (n=291) in all trials. Results were statistically significant in two trials (SP614, p=0.04; SP742, p=0.01) and at the level of significance in SP768 (p=0.0507) for the primary variable. Significance was not reached in SP743 because of a strong placebo effect at the final visit. When using the secondary variable of change from baseline to the entire maintenance phase, lacosamide 400 mg/day significantly reduced pain over placebo in the fixed-dose trials (p=0.02, p=0.01, and p=0.007 for SP742, SP743, and SP768, respectively). Treatment with 400 mg/day lacosamide resulted in the occurrence of four adverse events with an incidence of more than 5% and greater than placebo: dizziness (13.8%), fatigue (7.7%), nausea (6.8%), and tremor (5.6%).
CONCLUSIONS: Lacosamide 400 mg/day significantly reduced pain and showed good tolerability in clinical trials of diabetic neuropathic pain.
Presented at the American Academy of Neurology, Chicago, IL, April 12–19, 2008.

Education/Training

58. Development and Assessment of Internet Case Based Multi-disciplinary Infectious Disease Workshops as a Learning Tool in Antimicrobial Therapeutics. Angela Wilks, Ph.D., *Neha U. Sheth, Pharm.D.*, Shannon Tucker, M.S.; University of Maryland School of Pharmacy, Baltimore, MD
PURPOSE: (1) To create an online infectious disease workshop (IDW) that maximizes the skills and competencies of student pharmacists in the experimental and therapeutic principles of infectious diseases and (2) to provide a framework to assess student synthesis of these principles as a result of completing the workshop.
METHODS: The IDW incorporated patient assessment, laboratory simulations (Kirby-Bauer, MIC, and synergy), and the required interpretation of data from laboratory tests to demonstrate the student pharmacist's ability to determine patient-appropriate empiric therapy and treatment. Virtual laboratory exercises assessed the students' ability in data reading, calculations, reporting of results, and development of a patient-appropriate therapeutic plan.
RESULTS: By analyzing student performance on the IDW against student performance on infectious disease questions in the current and prerequisite microbiology courses, we have shown the incorporation of this problem-based learning activity improves a student's ability both to retain knowledge and develop informed patient-specific therapeutic plans. Student perceptions of the IDW as a learning tool were obtained by an assessment questionnaire.
CONCLUSIONS: Infectious diseases and antimicrobial therapeutics is a particularly challenging arena in pharmaceutical care for several reasons, not the least of which is the increased complexity of the discipline. The IDW allows development of a flexible knowledge base of basic science to be integrated in the therapeutic decision-making process. The students' performance in the IDW assessment of basic science concepts in a problem-based learning therapeutic situation improved their overall performance in a subsequent examination of the material in case-based formats.

59. Accreditation Council for Graduate Medical Education Duty Hour Compliance and Awareness Among Postgraduate Year 1 Pharmacy Residents. Jennifer D. Canady, Pharm.D.,[1] Melanie W. Pound, Pharm.D., BCPS,[2] Dana Blecke, Pharm.D., BCPS,[3] Beth Beasley, Pharm.D.,[3] *Susan M. Miller, Pharm.D., BCPS*[4]; (1) Southern Regional Area Health Education Center and Cape Fear Valley Health System, Fayetteville, NC; (2) Campbell University School of Pharmacy and Cape Fear Valley Health System, Fayetteville, NC; (3) Cape Fear Valley Health System, Fayetteville, NC; (4) University of North Carolina at Chapel-Hill School of Pharmacy, Southern Regional AHEC and Cape Fear Valley Health System, Fayetteville, NC
PURPOSE: In 2005, the American Society of Health-System Pharmacists (ASHP) incorporated the Accreditation Council for Graduate Medical Education (ACGME) duty-hour standards into accreditation guidelines. The purpose of this study was to assess ASHP-accredited postgraduate year 1 (PGY1) pharmacy residency programs' compliance with each ACGME duty-hour rule within the standards. Secondary end points included assessing PGY1 pharmacy residents' awareness of ACGME duty-hour standards and assessing compliance rates to duty-hour standards across various PGY1 residency program settings.
METHODS: PGY1 pharmacy residents in ASHP residencies completed a Web-based survey between January and March 2008. The survey described each ACGME duty-hour rule and assessed compliance with each rule. Furthermore, it assessed the number of hours that pharmacy residents work on residency-related activities and the emotional impact of adherence to the standards.
RESULTS: About 17% of PGY1 pharmacy residents nationally participated in the survey (n=259). Overall, the rule with the highest rate of compliance (98.4%) was the rule restricting residents to less than a 30-hour shift. The rule with the lowest rate of compliance (31.9%) was the rule requiring residents to take full 10-hour breaks between each shift. Academic and community hospital settings were less likely to be in compliance with each of the rules. Predominantly outpatient residency program settings had a higher rate of compliance with each of the rules. Pharmacy residency programs co-located with medical residency programs had a lower rate of compliance with duty-hour rules than programs not in this same type of environment.
CONCLUSIONS: Compliance with ACGME duty-hour standards is required for ASHP residency accreditation. Although programs state compliance with duty-hour standards, open-ended comments suggest that individual rules are not well understood, making it difficult to assess the true compliance of residency programs. Residency programs may require changes in curriculum and expectations to meet ACGME standards.

60E. Impact of an Introductory Leadership Course on Student Leadership Beliefs and Behaviors. *W. Greg Leader, Pharm.D.*, Scott A. Baggarly, Ph.D., Mary L. Caldwell, M.Ed., LPC, Laurel L. Andrews, Pharm.D., Lesa W. Lawrence, Ph.D.; University of Louisiana at Monroe College of Pharmacy, Monroe, LA
PURPOSE: The purpose of this study was to evaluate the impact of an introductory leadership course on leadership behaviors and beliefs of pharmacy students.
METHODS: The study used a pretest-posttest design. Pharmacy students actively participating in leadership roles in professional organizations within the college were invited to enroll in a 3-credit-hour introductory leadership course. On the first and last day of the course, students completed a 17-question leadership belief survey, the Kouzes and Posner Student Leadership Practices Inventory (SLPI), a 30-question survey that evaluates the frequency of student leadership practices and behaviors in five areas, and a leadership concept questionnaire based on course objectives. All surveys used a 5-point Likert-type scale. Changes in pre- and postcourse survey scores were compared using a paired Student's t-test with statistical significance defined a priori (p<0.05).
RESULTS: Seventeen students completed the study. After completion of the course, students demonstrated a significant increase in leadership belief scores (73.6 post vs. 69.5 pre; p=0.013) and significant increases in positive leadership behaviors in all five areas measured by the SLPI (Model the Way, p=0.0003; Inspire a Shared Vision, p=0.0002; Challenge the Process, p=0.0002; Enable Others to Act, p=0.03557, and Encourage the Heart, p=0.00305). Students also reported greater understanding of leadership concepts after course completion (survey scores: 80.3 post vs. 65.3 pre; p<0.0001).
CONCLUSIONS: This project evaluated the impact that a

leadership course may have in the development of future leaders for the pharmacy profession. After completion of the course, students had significantly increased understanding of leadership concepts, positive changes in beliefs concerning leadership, and an increase in practices associated with effective leadership. If leadership skills can be learned, students with the potential to be future leaders in the profession should be given opportunities to develop these skills.
Published in Am J Pharm Educ 2007; 71:42. Article 60.

61. A Quizzical Approach to Innovative Experiential Teaching. *Amy M. Lugo, Pharm.D., BCPS, BC-ADM,*[1] Mina S. Willis, Pharm.D., PA-C,[1] Cynthia J. Boyle, Pharm.D., FAPhA[2]; (1) National Naval Medical Center, Bethesda, MD; (2) University of Maryland School of Pharmacy, Baltimore, MD
PURPOSE: The purpose of the study was to assess whether creative teaching strategies would increase the desire to learn and allow improved knowledge retention.
METHODS: A survey of fourth-year student pharmacists completing an advanced pharmacy practice experience in internal medicine was conducted to assess the use of quizzes on learning and retention. The primary objective was to determine whether having students create a quiz on a specific topic would increase their knowledge simply by doing the assigned task. Secondary objectives of the survey included assessing the timing of quizzes in relation to the corresponding topic discussion, as well as which topic discussions were most useful. In addition, we assessed the students' overall perceptions of their learning experience.
RESULTS: Eighteen (100%) student pharmacists completed the 5-point Likert survey. Twelve students (67%) had never created a quiz on a specific topic, and almost all (89%) felt that generating a quiz increased their knowledge and depth of understanding. When surveyed about the timing of quizzes (before, after, or both) in relation to topic discussions, results showed that most (94%) considered taking a quiz before the topic discussion the most beneficial for learning. The reviews most helpful on an internal medicine rotation were infectious diseases, renal failure, heart failure, and laboratory tests. Seventeen (94%) students perceived that they had an overall excellent learning experience.
CONCLUSIONS: Having students generate quizzes on a specific topic and complete quizzes designed by their peers was a very effective teaching strategy. This teaching method can be used in various practice settings, and the results allow continuous quality improvement of advanced pharmacy practice experiences.

62. Evaluation of a Medicare Part D Community Outreach Train-the-Trainer Program for Pharmacy Faculty. *Marilyn Stebbins, Pharm.D.*, Timothy W. Cutler, Pharm.D., Robin L. Corelli, Pharm.D., Amanda R. Smith, MPH, Helene Levens Lipton, Ph.D.; University of California, San Francisco, San Francisco, CA
PURPOSE: Despite large-scale educational campaigns launched by the Centers for Medicare and Medicaid Services (CMS), many Medicare beneficiaries lack sufficient knowledge and skills to navigate the complex and confusing Medicare Part D (Part D) prescription drug benefit. *Partners in D*, a collaborative research initiative of the seven California schools of pharmacy, was developed to help underserved Medicare beneficiaries improve their understanding and use of Part D. We assessed the outcomes of the *Partners in D* train-the-trainer (TtT) program in which pharmacy faculty learned how to train student pharmacists to conduct one-on-one counseling sessions during community outreach events targeted toward vulnerable Medicare beneficiaries.
METHODS: Three outcomes were measured using a pre-post survey of 17 faculty participants from six schools: (1) knowledge of the Part D benefit structure and design; (2) skill in using the Medicare Prescription Drug Plan Finder tool (Plan Finder), an online resource for evaluating Part D plan options; and (3) faculty members' confidence in their ability to train student pharmacists. Follow-up interviews were conducted to evaluate the adoption of the *Partners in D* community outreach curriculum and determine the number of Medicare beneficiaries reached.
RESULTS: The TtT program significantly improved the faculty's knowledge of Part D, mastery of the Plan Finder, and confidence in teaching the material to student pharmacists. Within 8 weeks after the program, five of six schools trained adopted *Partners in D* coursework (both its didactic and outreach components) and initiated teaching. Four months after the program, 240 students from participating schools had completed 21 outreach events reaching 186 Medicare beneficiaries.
CONCLUSIONS: Improvements in pharmacy faculty knowledge of Part D and the Plan Finder increased confidence in training student pharmacists; the ease of curriculum integration into schools of pharmacy statewide indicates that the TtT program is practical and effective and that it merits serious consideration as a national model.

63E. Academic and Training Requirements in Advertisements for Pharmacy Practice Academic Positions. *John E. Murphy, Pharm.D.*, Lisa Hawkey, Pharm.D.; University of Arizona College of Pharmacy, Tucson, AZ
PURPOSE: To evaluate required and preferred qualifications for pharmacy practice faculty in advertisements and to compare with previous study results.
METHODS: A descriptive retrospective study of qualifications described in advertisements for academic positions in pharmacy practice in the United States. Educational and postgraduate training requirements were determined. Advertisements published in three nationally distributed pharmacy journals and newsletters between January 2002 and December 2006 were evaluated for required or preferred degree(s), completion of residencies and/or fellowships, years of work experience, board certification, and other postgraduate training and education. Advertisements were separated by whether they were for tenure-track, nontenure-track, or nontenure positions as well if the track was not stated. Moreover, the advertisements were separated for rank including assistant, associate, assistant/associate, and full professor.
RESULTS: Of 426 advertisements for nonadministrative faculty positions, only 297 (69.7%) specifically required a residency or equivalent experience. Postdoctorate training, including postgraduate year 1 (PGY1) residencies, postgraduate year 2 (PGY2) residencies, and fellowships, or their equivalent in experience, was required in 77% of the 426 advertisements for pharmacy practice faculty. Board certification was required in only four advertisements; however, board certification was preferred in 11% of advertisements, and eligibility was noted in an additional four advertisements. Fifty-one advertisements assessed were for administrative faculty positions. Advertisements for tenured positions did not have more extensive requirements listed than those for nontenured positions, nor did advertisements for assistant, associate, or full professors compare with advertisements for assistant professors. Advertisements for department chair positions, for the most part, lacked enumeration of qualifications. For most categories, the requirements have increased compared with the results from a previously published study.
CONCLUSIONS: Compared with a previous study, colleges and schools of pharmacy have increased the required or preferred qualifications needed to secure a pharmacy practice faculty position. Of importance to ACCP, residencies are still not required for all pharmacy practice faculty positions.
Presented at the American Association of Colleges of Pharmacy Annual Meeting, Chicago, IL, July 20–21, 2008.

64. Communicating Value to the Patients We Serve – An Educational Workshop for Pharmacy Students. *Celia MacDonnell, Pharm.D.,*[1] Colleen Moffitt, Pharm.D.[2]; (1) University of Rhode Island, College of Pharmacy, Kingston, RI; (2) Pfizer, Inc., Wakefield, RI
PURPOSE: A workshop using patient-pharmacist encounter situations commonly experienced in community pharmacy settings was conducted with third-year (P3) pharmacy students. The vignettes presented opportunities for the pharmacist to educate patients about the value of medicine as well as provide pharmaceutical care. This project is aimed at evaluating pharmacy students' attitudes about their value as future health care providers.
METHODS: "Unlocking the Value: Communicating Value to the

Patients We Serve" is an educational workshop developed by the Institute for the Advancement of Community Pharmacy. This workshop was conducted annually at the University of Rhode Island, College of Pharmacy, from 2005 to 2007. Three video vignettes were discussed: (1) communicating the importance of adherence; (2) explaining why filling a prescription takes time; and (3) discussing medication costs. Participants completed a pre- and postlecture survey regarding patients' attitudes and their own attitudes about their value.

RESULTS: Responses related to "Clinical/Accuracy," Cost/Insurance," or "Customer Service" were grouped. Students reported providing clinical information or accuracy as most important 70, 75, and 83% between 2005 and 2007. However, respondents indicated that patients viewed customer service as most important, 42, 32, and 51%.

Drug expense and insurance queries were reported as the most frustrating questions. In 2006 and 2007, participants indicated that prescription cost disputes declined; however, managing insurance issues remained an area of frustration.

More than 90% of participants reported they learned new techniques for communicating their value and felt more confident in addressing the most frustrating questions they were asked.

CONCLUSIONS: "Unlocking the Value: Communicating Value to the Patients We Serve" demonstrates how training pharmacy students in the areas of communication and patient-centered care can increase professional self-awareness. This, is turn, enhances patient interaction and reveals the value of the pharmacist in drug therapy.

65. Perceived Benefits and Negative Aspects of Postgraduate Pharmacy Training. *Cara L. Léos, Pharm.D., BCPS*, Laura C. Smoot, Pharm.D., BCPS; Auburn University Harrison School of Pharmacy, Auburn University, Auburn, AL

PURPOSE: Pharmacy students often seek the advice of their faculty mentors regarding the utility and value of postgraduate education (residencies or fellowships). Concerns about this training often include the personal time investment, financial disparity between resident and pharmacist salaries, possible relocation, and necessity of additional training compared with their personal career goals. This study was conducted to provide faculty and other student advisors with data from pharmacists with careers across the profession regarding their perceptions of their postgraduate training experience. To address these student concerns, the authors designed a survey to evaluate the perceived benefits and negative aspects of postgraduate pharmacy training.

METHODS: A 22-question online survey was distributed to various listserves from the American Association of Colleges of Pharmacy and the American College of Clinical Pharmacy. Only pharmacists who had completed residency and/or fellowship training were invited to participate. Participants were asked to identify the three greatest benefits and three most negative aspects of their training.

RESULTS: About 3321 pharmacists were invited to participate. Of the 681 responses, the most commonly identified positive perceptions were educational opportunities not otherwise encountered, increased competence/confidence, and a solid foundation in pharmaceutical care. Negative results included insufficient stipends, time away from family, and salaries on completion not reflecting additional training. Eighty-four percent stated that, in retrospect, they would still complete their training.

CONCLUSIONS: The recent vision statements put forth by pharmacy's professional organizations are requiring mandatory postgraduate training for pharmacists to have direct patient contact. This study reveals greater positive perceptions of the experience and professional value.

66. Assessment of Pharmacy Residency's Formal Training in Teaching. *Lauren E. Keyser, Pharm.D.*, Nancy S. Yunker, Pharm.D., Craig F. Kirkwood, Pharm.D., Jaime R. Robles, Ph.D.; Virginia Commonwealth University Medical Center, Richmond, VA

PURPOSE: Many pharmacy residency programs offer formal training in teaching and learning. The objective of this study was to examine if pharmacy residency programs provide the education that current residents and new pharmacy faculty members consider important and necessary to become successful.

METHODS: This project used two computerized surveys: one for current residents and one for faculty who completed residency training within 5 years. The resident survey documented educational session offerings and teaching experiences and their perceived importance. The faculty survey assessed if previous residency training provided the background necessary for successful faculty performance. The resident survey was e-mailed to American Society of Health-System Pharmacists–listed programs, and the faculty survey was e-mailed to American Association of Colleges of Pharmacy-listed pharmacy schools.

RESULTS: Overall, 515 residents and 145 faculty members completed the surveys. Current postgraduate year 1 (PGY1) residents at academic teaching hospitals who anticipated practicing as a hospital-based clinician comprised most resident respondents. The types of educational sessions offered varied considerably among resident respondents, but more than 40% believed that all listed sessions were important or very important. More than 70% of residents responded that their programs offered a variety of teaching experiences, and 40% stated these experiences were required. Most classified these experiences as important or very important. Ninety-nine percent of faculty respondents were assistant professors, with 40.5% completing a PGY1 residency. A large variation was noted in the types of educational sessions offered, and less than 50% of respondents felt that 14 of 18 educational sessions listed were adequately addressed. More than 50% of faculty respondents had teaching experiences during their residency.

CONCLUSIONS: Most current resident and new faculty respondents experienced some type of formal training in teaching during residency training. A dichotomy exists between the offered educational sessions and the perceived needs of respondents. Teaching experiences appear to be offered widely and adequately meet respondents' needs.

67. Actively Engaging Students in the Art of Peer Review. *Wendy I. Brown, Pharm.D., MPAS, PA-C, AE-C*; North Dakota State University College of Pharmacy, Nursing and Allied Sciences, Fargo, ND

PURPOSE: To educate pharmacy students on effective peer review, provide opportunities to practice peer review, and assess learned skills.

METHODS: Students were educated on the process of peer review through didactic lectures as part of a pharmacy elective course. During the course, students were required to evaluate peers' posters and research proposals using standardized rubrics. A computerized assessment center was used to collect and tabulate results of the rubrics. This familiarized student reviewers with an online submission process and helped maintain confidentiality. Student authors were given a computer-generated report of two reviewers' comments and had the opportunity to revise their projects before submitting for evaluation by the course instructor. Pre- and postsurveys were given to students to assess their beliefs about peer review.

RESULTS: Students had a greater understanding of the concept of peer review as it related to scientific publications ($p<0.0003$). There was increased recognition of the peer reviewer's accountability to the editor ($p<0.006$) and the author ($p<0.02$) for appraisal of the manuscript. A common challenge for students giving peer review was the amount of time it took to create constructive comments that would be meaningful for the author compared with relying on generalities. The most helpful aspect about giving and receiving peer review was that it improved students' own work compared with being only part of the class requirements.

CONCLUSIONS: Graduate programs teach students how to identify and criticize logical flaws; however, no formal training is given on peer review. Providing peer reviews that are useful to the author is a learning process that must be practiced. By educating students on effective peer review, students learned to constructively improve an author's work. This initial exposure will help promote young professionals to give and receive peer review.

68. A Comparison of Patient Recall of Medication Information With and Without Pharmacist Discharge Counseling. *Laura Roman, B.S., R.Ph.*,[1] Luke Probst, Pharm.D., BCPS,[1] Domenica Pacific, Pharm.D.[2]; (1) University Hospital, Upstate Medical University, Syracuse, NY; (2) Central New York Psychiatric Center, Marcy, NY

BACKGROUND: Investigators have demonstrated that patients interviewed at the time of discharge have little knowledge or information regarding their medications. Discharge planning that includes medication counseling at our institution is traditionally performed by our nursing staff. At our institution, drug information sheets are given to patients together with a standard discharge form, which provides drug name, route, frequency, and a brief explanation of the medication's intended use. Barriers, including lack of time and inadequate staff and resources, have been cited as reasons for a reduced role by pharmacists in counseling patients before hospital discharge. Presently, our pharmacists infrequently provide discharge medication counseling for similar reasons.

PURPOSE: We sought to determine the impact of pharmacist counseling before hospital discharge compared with nursing-based mediation education. Patient knowledge was determined by recall of the following information of each discharge medication: name, indication, dose/frequency, and at least one possible side effect.

METHODS: After institutional review board approval of the study, we enrolled 87 patients. Subsequent to informed consent, patients were randomized by computer-generated sampling to receive standard medication education by nurse- or pharmacist-provided medication counseling, generally within 24 hours of discharge. Follow-up telephone interviews with the patient by a pharmacist who did not participate in the study occurred within 7 days of discharge. The pharmacist queried the patient using scripted messages and collected response data on a standardized form to determine the patient's knowledge of medications.

RESULTS: Eighty-seven patients consented to study participation, and data for 64 were evaluable; 46.9% of patients were pharmacist counseled. Recall of information for pharmacist-counseled versus nurse-counseled patients was drug name 85.2 versus 77.1%; indication 80.3 versus 67.8%; frequency 85.8 versus 70.9%; and side effect 32.7 versus 24.6%.

CONCLUSIONS: Pharmacist medication counseling resulted in better patient recall of discharge medication information.

69. Time Study of Pharmacy Faculty in Family Medicine Residency Programs. *Sarah M. Westberg, Pharm.D., BCPS*, Jean Y. Moon, Pharm.D., Chrystian R. Pereira, Pharm.D., Lisa M. Hlavenka, Student Pharmacist; University of Minnesota College of Pharmacy, Minneapolis, MN

PURPOSE: To evaluate a time study of pharmacy faculty during their time in family medicine residency program clinics to better understand the faculty contributions to patients, family medicine, and pharmacy. To compare results of direct observation with self-report of activities.

METHODS: Direct observation time-and-motion studies were conducted with three pharmacy faculty members at family medicine residency clinics. Observations were completed by a student pharmacist in January 2008. Each faculty member was asked to complete a self-report of activities during the period of observation. A half-day pilot observation was conducted initially to verify the appropriateness of activity categories. The categories used were patient care, supervising patient care, teaching pharmacy learners, teaching medical learners, other professional, and miscellaneous. A total of six half-day sessions were observed for a total of 23.75 hours. Self-reports from faculty were received for five half-day sessions and totaled 23.3 hours.

RESULTS: The observation data indicated 58% of time spent in patient care, 2% in teaching pharmacy learners, 21% in other professional activities, and 19% in miscellaneous activities. The self-reported data indicated 49% in patient care, 2% in supervising patient care, 1% in teaching pharmacy learners, 1% in teaching medical learners, 30% in other professional, and 18% in miscellaneous activities. Differences between the self-reported data and the observation data were noted.

CONCLUSIONS: This study provides evidence that most faculty time is spent on patient care-related activities. It also illustrated that it is difficult to complete self-reported time studies in an accurate manner because distinct differences were seen between self-report and direct observation. Because this time study was conducted during a break for advanced practice pharmacy experiential students, it is not a complete picture of the pharmacy faculty's teaching activities. Further time studies by direct observation while pharmacy students are completing experientials on-site are planned.

70. Outcomes of an Initial Preceptor Experience for Fourth Year Pharmacy Students. *Courtney Krueger, Pharm.D.*, Kristen L. Goliak, Pharm.D.; University of Illinois at Chicago, College of Pharmacy, Chicago, IL

PURPOSE: The University of Illinois at Chicago College of Pharmacy initiated a shadowing program in the fall of 2007 to provide 40 introductory pharmacy practice experience hours for first-year (P1) students. The fourth-year (P4) students served as primary preceptors for the P1 students during this week-long experience.

OBJECTIVES: The objective of this abstract is to present the impressions of the P4 students after completing this introductory preceptor experience.

METHODS: A two-page anonymous survey was administered to the P4 students after their experience. They were asked to voluntarily provide feedback on questions using a 5-point Likert scale and were also able to provide answers and comments to qualitative questions.

RESULTS: Ninety-seven (81%) fourth-year (P4) students responded to the survey. For the quantitative questions, 92% agreed or strongly agreed that this was a positive experience, 95% agreed or strongly agreed that they worked well with the P1 student, and 94% agreed or strongly agreed that they felt comfortable being shadowed by a P1 student. In addition, comments from the P4s reflected a positive experience. Overall, P4 students felt this experience improved their understanding of precepting and increased their desire for future precepting opportunities. Some of the challenges noted by the P4s included maintaining the interest of the P1 students, incorporating the P1 students into all areas of practice, and determining appropriate activities for the P1 students.

CONCLUSIONS: The P4 students had a positive experience as first-time preceptors. This opportunity increased their awareness of the challenges their current preceptors face. Overall, this was a constructive activity for the P4 students; however, the program could benefit from an enhanced, formalized training program for P4 students.

71. Teaching Medication Errors: A Computer-Based Approach. *Michael J. Peeters, Pharm.D., BCPS*, Gayle L. Kamm, Pharm.D.; University of Toledo College of Pharmacy, Toledo, OH

PURPOSE: Pharmacists deal with medication errors often. Following Joint Commission standards, technical medication order errors are reviewed and tracked within health care institutions. Meanwhile, medication error instruction has been taught to varying degrees in pharmacy schools. A computer-based module was developed for pharmacy students to identify and remedy physician order errors.

METHODS: The computer-based module used the Blackboard platform. It consisted of several exercises and a Flash presentation (with audio). This 20-minute Flash presentation (1) defined medical, medication, and medication order errors; (2) reviewed Institute of Medicine suggestions and Joint Commission standards; (3) reviewed common types of medication order errors; and (4) gave specific institutional examples for illustration. The exercises consisted of 10 questions, with two parts to each question. With a specific institutional error, the first question was to identify the error type, and the second question was to fix the error into a correct order. Error types were wrong or missing information (e.g., drug, dose, frequency, route, as needed without an indication), unapproved abbreviations, and double-range orders. Students were randomized into two groups. Both groups completed a series of three different quizzes. Group 1 completed quiz A, the module, and then quizzes B and C. Group 2 took quizzes A and B, the module, and then quiz C.

RESULTS: Quiz results were not normally distributed. Group 1 scored median 50% (quiz A), 62.5% (quiz B), and 66.7% (quiz C). Group 2 scored median 50% (both quizzes A and B) and 66.7% (quiz C). Quizzes A and C did not differ (p=0.2396 and p=0.978, respectively); however, quiz B did (p=0.0014).
CONCLUSIONS: This randomized, controlled methodology describes a successful module that taught students to identify and resolve medication order errors. Even though only technical medication order requirements were addressed, these are very common and are an ongoing concern for pharmacists.

72. Incorporation of Wiki Technology into an Elective Course. *Priti N. Patel, Pharm.D., BCPS*, Olga Hilas, Pharm.D., BCPS, CGP; St. John's University, Queens, NY
PURPOSE: To incorporate wiki technology into a didactic setting and to assess student perceptions of wiki-based assignments.
METHODS: Students were required to complete two assignments involving the creation of disease state wiki pages in a sixth-year elective course. These assignments were given as teaching tools in lieu of traditional lectures. Voluntary and anonymous surveys assessing their perceptions of these assignments were distributed. Perceptions were evaluated using a 10-point Likert scale (1 being least useful/valuable and 10 being most useful/valuable) in addition to open-ended comments.
RESULTS: A total of 35 students completed the survey. Overall, students rated the usefulness of these assignments and the level of learning positively (median scores = 7). Despite these favorable perceptions, students were not interested in the incorporation of these types of assignments for other topics in this course (median score = 4.5) or other courses (median score = 4). Students also indicated that they preferred lecture-based learning (median score = 8.5), but a number would have liked these assignments in addition to, rather than in lieu of, a lecture. Positive comments regarding the assignments included increased learning as a result of active research, use of an innovative teaching method, and enjoyment of the collaborative and creative aspects. Negative comments included students' reluctance to review and edit others' work, the time-consuming and labor-intensive nature of the assignments, lack of follow-up discussions, and difficulties for students with limited computer proficiency.
CONCLUSIONS: Although wikis are useful tools for increased active learning, enhancement of lectures using this type of technology might have been better received. Wiki-based assignments were easily incorporated into the course and were generally viewed positively by the students.

73. Email vs. Face-to-Face: Faculty and Students' Perceptions of Tone and Content. *Pamela A. Foral, Pharm.D., BCPS*,[1] Jennifer J. Merkel, Pharm.D. Student,[2] Paul D. Turner, Ph.D.,[1] Thomas L. Lenz, Pharm.D.,[1] Michael S. Monaghan, Pharm.D.,[1] Ryan W. Walters, M.S.[1]; (1) Creighton University School of Pharmacy and Health Professions, Hixon-Lied Science Building, Omaha, NE; (2) Creighton University School of Pharmacy and Health Professions, Omaha, NE
PURPOSE: The prevalence of e-mail communication in higher education is undeniable. Furthermore, the emergence of distance/Web education has created a unique learning environment requiring the overwhelming majority of student-faculty communication to be electronic. The objective of the current study was to investigate the perceptions of students and faculty within a professional pharmacy program comparing the tone and content of e-mail communication with face-to-face communication.
METHODS: Data were collected by survey using three parallel questionnaires with phrasing tailored specifically for the campus student, distance student, or faculty member. Statistical analyses were guided by a table of specifications. Omnibus effects were tested by Kruskal-Wallis tests, and post hoc analyses were conducted using Mann-Whitney *U* tests. Appropriate Bonferroni adjustments were used to reduce the probability of type I errors.
RESULTS: More than 70% of those surveyed responded (N=566; n=194, 324, and 48 for distance, campus, and faculty, respectively). Significant differences were indicated in the perception that e-mail communication from students to faculty has the same tone and content as face-to-face communication, Z=75.89, p<0.001, and Z=48.41, p<0.001, respectively, with both campus and distance students agreeing significantly more than faculty. In addition, distance students agreed significantly more than campus students regarding both tone and content (Z=2.66, p=0.008, and Z=3.49, p<0.001, respectively). No significant differences were indicated regarding the tone and content of e-mail from faculty to students.
CONCLUSIONS: A paucity of literature exists exploring the perceptions of faculty and students using e-mail communication in a professional program. The current study found significant differences in these perceptions and provided novel data beneficial to faculty and students. Future research should uncover how e-mail communication differs from face-to-face communication in professional programs, regardless of learning environment.

74. Implementation of a Weight-Based Basal/Bolus Insulin Use Strategy Improved Glycemic Control in Hospitalized Diabetic Patients on an Internal Medicine Service. *Stephen J. Schafers, Pharm.D.*, Eli Deal, Pharm.D., Hemal Gada, M.D., Shivak Sharma, M.D., Donna B. Jeffe, Ph.D., Mitchell G. Scott, Ph.D., Debaroti Borschel, M.D., Melvin Blanchard, M.D., Garry Tobin, M.D.; Barnes-Jewish Hospital at Washington University Medical Center, St. Louis, MO
PURPOSE: Control of hyperglycemia in noncritically ill hospitalized patients has traditionally been poor because of insufficient medical attention and reliance on sliding-scale insulin protocols as the primary management strategy. A study investigating the effect of a pharmacist-recommended weight-based basal/bolus insulin use strategy was implemented on an internal medicine service in a large academic medical center to evaluate physician acceptance and patient blood glucose control.
METHODS: Thirty-six internal medicine resident-physicians attended an endocrinologist-led, 1-hour interactive case-based insulin dosing session conducted by the residency training program. After the inservice, two clinical pharmacists provided insulin dosing recommendations to study physicians during three 1-month rotating periods that emphasized a prospective weight-based basal/bolus insulin use strategy. Patients were identified for pharmacist intervention if they had two blood glucose concentrations more than 180 mg/dL within 24 hours or if insulin therapy was limited to sliding-scale insulin. When recommendations were provided, resident-physicians were also asked to complete an insulin order form for a mock patient case and subsequently were provided feedback on their mock case insulin use plan.
RESULTS: Pharmacists' recommendations were accepted in 41 (67%) of 61 study patients. Among patients with dosage recommendations fully implemented compared with those without full implementation, blood glucose concentrations demonstrated a lower mean concentration (176 vs. 206 mg/dL; p=0.02) without a significant increase in hypoglycemia (blood glucose less than 70 mg/dL; 2.5% vs. 1.8%, p=0.45). In addition, only 45% of resident-physicians achieved scores within 10% of the expert answer for insulin use on their mock patient case survey.
CONCLUSIONS: The study's insulin use strategy was generally well accepted and associated with improved glycemic control in noncritically ill hospitalized patients with diabetes. More sustained physician training efforts are needed to optimize patient benefit.

Emergency Medicine

75E. A Pharmacist Can Improve Timely Administration of Medications to Boarded Patients in the Emergency Department. *Victor Cohen, Pharm.D., BCPS, CGP*,[1] Samantha P. Jellinek, Pharm.D., BCPS, CGP,[2] Lydia B. Fancher, Pharm.D., BCPS,[2] Antonios Likourezos, M.A., MPH,[2] Fred Cassera, R.Ph., M.B.A.[2]; (1) Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY; (2) Maimonides Medical Center, Brooklyn, NY
PURPOSE: The purpose of this study is to describe, quantify, and compare medication administration discrepancies in boarded

patients (admitted, awaiting bed placement) in the emergency department (ED) cared for by ED nurses versus nurses dedicated to these patients (K1 nurses). The impact of a pharmacist in improving timely administration of medications will be quantified.
METHODS: This was a prospective observational study including boarded patients who were age 18 years or older and had medication orders. A pharmacist in the ED (8:00 A.M. to 11:00 P.M.) determined patients who were eligible and if medications were given in a timely manner (plus or minus 1 hour from the scheduled administration time). If medications were not given, the pharmacist carried out an intervention to facilitate medication administration and then determined the effectiveness of the intervention.
RESULTS: There was a statistically significant difference in medications administered in a timely manner between ED and K1 nurses (65% vs. 85%, respectively; p=0.002). During the morning period (6:00 A.M. to 11:59 A.M.), there were significantly more drugs not administered on time by ED nurses in comparison with K1 nurses (31.4% vs. 17.1%, p=0.041). The pharmacist intervened by clarifying orders with the physician, expediting medications from the pharmacy (requesting/retrieving missing medications from the pharmacy), giving the medications to the nurse, educating the nurse, and procuring the medication. Intervention of the pharmacist was successful with both the ED and K1 nurses (95.5% and 94.1%).
CONCLUSIONS: Medication administration discrepancies exist between variations of nursing staff in the ED. A pharmacist can positively affect the timely administration of medications to boarded patients in the ED.
Presented at the New York ACEP 2008 Scientific Assembly at the Sagamore Hotel in Bolton Landing, New York, NY, on July 7, 2008.

76. Factors Affecting Morphine Dosage in Treating Severe Pain in the Emergency Department. Adam D. Biggs, Pharm.D., *Asad E. Patanwala, Pharm.D.*, Brian L. Erstad, Pharm.D., Peter Chase, M.D.; University of Arizona, Tucson, AZ
PURPOSE: The purpose of this investigation was to determine if patient weight is an independent predictor of intravenous morphine requirements in patients presenting to the emergency department (ED) in severe pain.
METHODS: Medical records of 2677 patients prescribed intravenous morphine in the ED between August 1, 2007, and October 31, 2007, were evaluated. Patients satisfied criteria for inclusion if they were 18 years or older with severe, nontraumatic abdominal pain. Patients who received analgesics other than intravenous morphine were in the ED for less than 4 hours, lacked demographic data, or had taken opioids before presentation were excluded. A total of 105 patients were included in the final analysis. Demographic data were collected together with pain scores, morphine doses, time of dose administration, and adverse events for the first 4 hours after the initial morphine dose was administered. Stepwise multiple regression analysis was performed to determine the independent variables predictive of morphine requirements.
RESULTS: Patient weight, age, sex, height, and race were not predictive of morphine requirements in the ED. Average pain score during the first 4 hours of morphine treatment was the only predictor of morphine requirements (p=0.0006).
CONCLUSIONS: Patient weight is not an independent predictor of intravenous morphine requirements in patients presenting to the ED in severe pain. Dosing strategies based on patient weight or other demographic variables are not warranted in this patient population.

Endocrinology

77. Comparison of Glycemic Management with the Implementation of a Standardized Sliding-Scale Insulin Dosing Form in a Community Hospital. *Crystal L. Hoffmann, Pharm.D.,*[1] Tyson W.A. Brooks, Pharm.D.,[2] Way Huey, Pharm.D.[1]; (1) St. Luke's Hospital, Chesterfield, MO; (2) St. Luke's Hospital and St. Louis College of Pharmacy, Chesterfield, MO
PURPOSE: To compare the safety and efficacy of blood glucose management before and after the implementation of a standardized sliding-scale insulin dosing form in general medicine patients.
METHODS: A retrospective chart review was conducted to compare glycemic control between two groups of general medicine patients. The control group consisted of 100 patients who had sliding-scale insulin ordered before the implementation of the standardized form, while the treatment group contained 100 patients who had sliding-scale insulin ordered using the standardized form. The primary outcome was to compare the measurement of blood glucose in the targeted glycemic range of 70–180 mg/dL, hyperglycemic range greater than 180 mg/dL, and hypoglycemic range of less than 70 mg/dL between the two study groups.
RESULTS: A total of 2635 and 2232 blood glucose measurements were collected for the control and treatment groups, respectively. The treatment group had more blood glucose measurements within the targeted range of 70–180 mg/dL compared with the control group (74% vs. 65%, p<0.005). Although the number of hypoglycemic events was similar between the two groups, there were fewer hyperglycemic readings in the treatment group (23.5% vs. 32%, p<0.005). Mean blood glucose readings were significantly lower for the treatment group compared with controls (147.6 ± 54.76 mg/dL vs. 160.4 ± 64.36 mg/dL, p<0.005). Similar findings were obtained in the following patient subsets: patients with steroid-induced hyperglycemia, patients on concurrent oral diabetic medications, and patients on concurrent basal insulin regimens.
CONCLUSIONS: Glycemic control was significantly better for general medicine patients when sliding-scale insulin was ordered using the standardized form. The form provided structure and consistency that led to a 13-mg/dL average decrease in blood glucose readings for the treatment group. These findings further strengthen the American Diabetes Association recommendation to use standardized insulin order forms.

78E. Use of Colesevelam HCl with Concomitant Statin Therapy in Type 2 Diabetes Mellitus Improves Glycemic Control and the Lipid Profile. *Allison B. Goldfine, M.D.,*[1] Vivian A. Fonseca, M.D.,[2] Stacey Abby, Pharm.D.,[3] Michael Jones, Ph.D.[3]; (1) Joslin Diabetes Center, Boston, MA; (2) Tulane University Health Sciences Center, New Orleans, LA; (3) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: In patients with primary hypercholesterolemia, colesevelam HCl in low-density lipoprotein cholesterol (LDL-c) by as much as 48%. Recently colesevelam HCl was approved for improving glycemic control in patients with type 2 diabetes mellitus (T2DM) when added to existing antidiabetes therapy. Because statins are commonly used to lower LDL-c in patients with T2DM, the A1C and LDL-c effects of colesevelam HCl in patients with T2DM on existing statin therapy is of interest. We report the results of an evaluation of the A1C and lipid effects of colesevelam HCl in patients with T2DM receiving concomitant statin therapy.
METHODS: A post hoc analysis was conducted of data from three double-blind, placebo-controlled primary studies wherein colesevelam HCl 3.75 g/day was added to metformin, insulin, or sulfonylurea-based therapy, respectively, in patients with inadequately controlled T2DM (A1C 7.5–9.5%). Data for patients who received statins were pooled (N=476 [about 47% of the overall study population]) and analyzed to determine if the beneficial A1C and lipid effects reported with colesevelam HCl were consistent in this population.
RESULTS: In patients with T2DM receiving statin therapy, the addition of colesevelam HCl resulted in significant least-square mean treatment differences in A1C (-0.45%; p<0.0001), LDL-c (-15.6%; p<0.0001), non–high-density lipoprotein cholesterol (HDL-c) (-6.1%; p=0.0112), total cholesterol (-4.5%; p=0.0108), and apolipoprotein B (-5.0%; p=0.0150). Although median triglyceride concentrations increased significantly with colesevelam HCl relative to placebo (19.5%; p<0.0001), this has been previously reported in studies with bile acid sequestrants.
CONCLUSIONS: It has been shown that improvement in glucose control and the lipid profile is associated with better outcomes in patients with T2DM. This analysis suggests that in patients with T2DM on existing statin therapy, the addition of colesevelam HCl consistently and effectively improves glycemic control and further improves the lipid profile.
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79. Psychological Barriers to Insulin Use in a Veteran Population. *T. Christopher Little, Pharm.D.,*[1] Frank J. Svete, Pharm.D., BCPS,[2] Todd Lee, Pharm.D.[2]; (1) Department of Veteran's Affairs, Chicago, IL; (2) Hines VA Hospital, Hines, IL

PURPOSE: The purpose of this study was to compare the attitudes of patients willing and unwilling to begin insulin as it relates to the components of psychological insulin resistance. A secondary purpose was to determine if education, ethnicity, or length of diabetes diagnosis influences a patient's willingness to start insulin.

METHODS: Individuals with diabetes who had not used insulin, were younger than 90 years, and had a hemoglobin A1C greater than 9% completed an anonymous survey about their attitudes toward insulin. Our tool was adapted from a validated survey developed in "Petrak F, Crispin AA, Stridde E, et al. Development and validation of a new measure to evaluate psychological resistance to insulin treatment. Diabetes Care 2007;30:2199–204." The topics evaluated were fear of injections and self-testing, expectations regarding positive insulin-related outcomes, expected hardship, stigmatization by insulin injections, and fear of hypoglycemia. Other information collected included education, ethnicity, and duration of diagnosis.

RESULTS: Ninety-eight qualifying surveys were collected. A comparison of willing and unwilling patients showed no differences in education, ethnicity, or length of diabetes diagnosis. The two groups showed significant differences for all topics, with 13 of the 14 study questions showing statistically significant differences. Multivariate analysis showed that opinion of insulin's effectiveness (OR = 1.94, p=0.044) and ability to prevent long-term complications (OR = 1.55, p=0.032) predisposed patients to be willing or unwilling to use insulin.

CONCLUSIONS: Patients willing to use insulin have significantly different feelings about the components of psychological insulin resistance. Patient opinion of insulin's effectiveness and ability to prevent long-term complications may be the most important because it will determine if a patient is willing to use insulin.

80. Evaluation of Converting Patients from Insulin Glargine to Insulin Detemir. *Ginelle A. Schmidt, Pharm.D.,*[1] Deanna L. McDanel, Pharm.D.,[2] Kathleen E. Horner, Pharm.D.,[2] Erin N. Newkirk, Pharm.D.,[3] Karen Farris, Ph.D.[4]; (1) The University of Iowa Hospitals and Clinics, Iowa City, IA; (2) University of Iowa Hospitals and Clinics, Iowa City, IA; (3) Froedtert & the Medical College of Wisconsin, Milwaukee, WI; (4) University of Iowa, Iowa City, IA

PURPOSE: Conflicting evidence regarding the conversion of patients from glargine to detemir exists despite manufacturer recommendations to convert patients on a unit-for-unit basis. The purpose of this study was to evaluate the dose and frequency of detemir required when converting patients with type 1 or type 2 diabetes mellitus from glargine to detemir. Secondary objectives were to compare glycemic control, weight gain, and risk of hypoglycemia.

METHODS: A retrospective analysis was performed evaluating 31 patients converted from glargine to detemir by usual practice between January 2006 and March 2007. Patients were identified using electronic medical records, and data were collected for 12 months after conversion.

RESULTS: At the end of 12 months, mean basal insulin doses were higher with detemir compared with baseline glargine doses (60.0 vs. 48.1 units/day, p=0.009; 0.60 vs. 0.46 units/kg, p=0.007). Patients also required higher total (basal plus bolus) insulin doses (90.0 vs. 74.3 units/day; p=0.004), and more patients required twice-daily detemir compared with glargine (48% vs. 13%, p=0.043). Patients with type 2 diabetes (n=21) required an increase in detemir doses during the study, whereas a decreased dose was observed in patients with type 1 (n=10) diabetes (18.0 vs. -0.90 units/day, p=0.042). No significant change in hemoglobin A1C was observed (9.49 vs. 9.56; p=0.124) despite the use of higher detemir doses. A trend toward weight loss (1.4 kg) and decreased hypoglycemia (19.4% vs. 41.9%) was observed, although it was not significant (p=0.87 and p=0.54, respectively).

CONCLUSIONS: Treatment with detemir appears to require higher doses compared with glargine, with an average of 25% higher doses observed in this study. These findings suggest that a unit-for-unit conversion from glargine to detemir, as suggested by the manufacturer of detemir, is not adequate in all patients, particularly in patients with type 2 diabetes.

81. Correlation of Thiazide-Induced Potassium Changes with Glucose Changes. Shawn D. Anderson, Pharm.D.,[1] Hua Feng, M.D., M.S.,[1] Rhonda M. Cooper-DeHoff, Pharm.D.,[1] *Steven M. Smith, Pharm.D.,*[1] Kent Bailey, Ph.D.,[2] Stephen T. Turner, M.D.,[2] Arlene Chapman, M.D.,[3] Julie A. Johnson, Pharm.D.,[1] John G. Gums, Pharm.D.[1]; (1) University of Florida, Gainesville, FL; (2) Mayo Clinic, Rochester, MN; (3) Emory University, Atlanta, GA

PURPOSE: Thiazide diuretics (TDs) are recommended as initial antihypertensive therapy by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; however, concern about incident diabetes may limit their use. A recent analysis correlated (r = –0.37) study concentration serum potassium (K+) with fasting blood glucose (FBG), and it has been suggested that maintenance of normal serum K+ prevents TD-induced dysglycemia. However, this correlation has not been replicated at the patient level. The primary objective was to investigate the correlation of serum K+ changes with FBG changes in hypertensive patients after hydrochlorothiazide (HCTZ) treatment.

METHODS: Participants were aged 17–65 with mild to moderate hypertension without significant comorbidities in the HCTZ arm of the Pharmacogenomics Evaluation of Antihypertensive Responses study. After a 3- to 6-week washout, HCTZ was initiated at 12.5 mg and titrated to 25 mg after 4 weeks. Fasting serum K+, FBG, and insulin were measured at baseline and after about 9 weeks. Mean changes from baseline were tested using a paired *t*-test. The required sample size for 85% power was 111. Correlations were determined for patient-level changes from baseline using Spearman's rho. Significance was set at p<0.05.

RESULTS: Mean changes from baseline were –0.32 ± 0.37 mEq/L (p<0.0001) for serum K+ (n=118), 2.35 ± 14.5 mg/dL (p=0.091) for FBG (n=111), and 2.46 ± 14.95 mIU/mL (p=0.089) for insulin (n=109). There was no significant correlation between changes in serum K+ and FBG (r=0.037 [95% CI: –0.157, 0.215], p=0.696) or with changes in serum K+ and insulin (r = -0.106, p=0.274). A significant positive correlation was found between changes in FBG and insulin (r=0.468, p<0.0001).

CONCLUSIONS: One proposed mechanism of diuretic-induced dysglycemia is through reduced insulin secretion secondary to serum K+ depletion. Our results suggest that no correlation exists between serum K+ changes and either FBG or insulin changes. Prevention of incident diabetes may require exploring alternative causal relationships for TD-induced dysglycemia.

82E. Improved Glycemic Control with Real-Time Continuous Glucose Sensors in Patients with Type 1 Diabetes. *Sam Ellis, Pharm.D.,*[1] Mary Voelmle, ANP,[2] Satish Garg, M.D.[2]; (1) University of Colorado School of Pharmacy C238-L15, Aurora, CO; (2) Barbara Davis Center for Diabetes, Aurora, CO

PURPOSE: This retrospective study evaluated patients initiated on continuous glucose monitors (CGMs) for (1) change in hemoglobin A1C values at 3 and 6 months and (2) changes in total hypoglycemic episodes, nocturnal hypoglycemia, insulin use, weight, and average blood glucose.

METHODS: All patients receiving real-time CGM training between April 2006 and June 2007 at the Barbara Davis Center for Diabetes were included in this study. Patients had to be 18 years old, have type 1 diabetes, and have documented baseline and 3-month A1C values. Pregnant women were excluded from this study. Data collected included medical history, indication for sensor use, self-reported hypoglycemia, and days of sensor use per month.

RESULTS: A total of 75 patients were included. Baseline characteristics included 55 (73%) women and age 38.4 years (range 18–72). Duration of diabetes was 22.4 ± 14.6 years, and average A1C was 7.37% ± 0.98%. Average sensor use was 16 ± 10 days/month (range 1–30). Hemoglobin A1C values decreased

significantly at 3 and 6 months (7.37 vs. 7.15 vs. 7.2%, p<0.001), despite no difference in overall insulin dose (45.2 vs. 45.9 units). Self-reported weekly hypoglycemic events decreased 27% (6.13 vs. 4.45 events/patient/week; p<0.001), and nocturnal hypoglycemic events were reduced by 35% (1.23 vs. 0.80; p=0.03). Severe hypoglycemic events requiring assistance decreased 68% during the first 3 months of sensor use (0.34 events/patient vs. 0.11 events/patient; p=0.10). Patients wearing the sensor for more than 15 days per month were 2.4 times as likely to achieve an A1C goal of less than 7%.

CONCLUSIONS: Use of a real-time continuous glucose sensor significantly improved A1C values while reducing overall and nocturnal hypoglycemic events after 3 and 6 months. This technology can aid pharmacists and other health care providers in adjusting the pharmacotherapy of patients with diabetes.

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Geriatrics

83E. Longitudinal Analysis of the Relationship Between Concomitant Anticholinergic Drug Use and Response to Donepezil in Mild-to-Moderate Alzheimer's Disease. *Susan K. Bowles, Pharm.D., M.Sc.*,[1] Swarna Weerasinghe, Ph.D.,[2] Sketris Ingrid, Pharm.D., MPA (HSA),[2] Kenneth Rockwood, M.D., FRCPC[1]; (1) Dalhousie University and Centre for Health Care of the Elderly, Halifax, NS, Canada; (2) Dalhousie University, Halifax, NS, Canada

PURPOSE: Anticholinergic (ACH) drugs and cholinesterase inhibitors (ChEIs) are often used together. Using data from the 52-week ACADIE study, we (1) describe patterns of concomitant ACH use; (2) assess longitudinal associations of ACH burden; and (3) assess longitudinal association between exposure type and donepezil response in mild-moderate Alzheimer's disease.

METHODS: Concomitant ACH use was defined as regular ACH use 2 weeks before each visit, with the ACH Drug Scale used to quantify ACH burden. The primary outcome was a change in the cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-Cog); goal attainment scaling (GAS) was a secondary measure. Data were analyzed using descriptive statistics and longitudinal regression, adjusted for confounding variables.

RESULTS: A total of 100 patients were enrolled in ACADIE. Three ACH exposure types were identified: none (69 of 100), continuous (13 of 100), and intermittent (18 of 100). Individuals in the intermittent group had more severe disease as indicated by higher baseline ADAS-Cog and lower mini-mental status examination scores. Concomitant ACH use occurred in 31% of study patients. ACH burden was low (defined as less than 4) in 42–50% of ACH users across the study duration, reflecting that most ACH agents were level 1 drugs. No association between ACH burden and outcome was identified for either ADAS-Cog or GAS. Similarly, no association was observed between exposure type and response using ADAS-Cog. However, a trend for association between intermittent exposure and response using GAS (OR = 0.52, 95% CI: 0.27–1.00) was seen.

CONCLUSIONS: Concomitant ACH use was not associated with an attenuated response to donepezil in this population during a 1-year timeframe. However, this may be a reflection of the low ACH burden in most patients. Further research is needed to explore the relationship between ACH burden and ChEI response and to determine if baseline disease severity is an important factor for response when concomitant ACHs are used.

Presented at the Canadian Society of Hospital Pharmacists Professional Practice Conference, Toronto, ON, Canada, February 2008.

84. Medication Adherence in Low Socioeconomic Status (SES) Seniors. *John T. Johnson, Pharm.D., CDE*, Sally Huston, Ph.D., R.Ph., Amber Watts, Pharm.D., William Guffey, Pharm.D.; University of Georgia College of Pharmacy, Athens, GA

PURPOSE: The purpose of the study was to identify medication adherence levels among low socioeconomic status (SES) seniors and to determine if cost was identified as a barrier to medication adherence.

METHODS: Attendees at 10 senior day care centers in northwest Georgia were offered individual brown bag medication reviews and a medication adherence system, Identimed. Each center was visited twice, with 4 weeks' minimum time separating visits. Seniors scoring below 23 (n=15) on the administered mini-mental status examination were excluded from the questionnaire. Demographic data (e.g., income, education level, population group, lived alone or not) were collected. Respondents were asked if cost was a factor with regard to medication adherence. Adherence was assessed for the previous 4 weeks using five previously validated questions and 6-point Likert-like scales. Scores were summed, with 5 indicating the best possible adherence and 30 indicating the worst possible adherence.

RESULTS: The initial survey was completed by 120 seniors. Annual incomes of less than $25,000 per year were reported by 60 (68.2%), and annual incomes between $25 and $50,000 per year were reported by an additional 19 (21.6%). A total of 38 (33.9%) had less than a high school education, and 43 (38.4) reported completing high school. The sample included 101 (90.2%) whites and 9 (8.0%) African Americans. A total of 99 respondents (72.3%) said that cost was not a factor in whether they took their drugs. With 5 being the best score, the mean summed self-reported adherence score for the first visit (n=111) was 7.3 (±3.1), and the mean score for the second visit (n=31) was 7.5 (±3.8).

CONCLUSIONS: Self-reported medication adherence levels were very good among these low SES seniors. Cost did not appear to be a barrier for most.

85. Impact of a Geriatric Palliative Care Service on Suboptimal Prescribing. *Erin M. Suhrie, Pharm.D.*,[1] Sherrie Aspinall, Pharm.D., M.Sc.,[1] Joseph T. Hanlon, Pharm.D., M.S.,[1] Mary Ann Sevick, Sc.D., R.N.,[1] Christine Ruby-Scelsi, Pharm.D.,[2] Emily Jaffe, M.D., M.B.A.[1]; (1) VA Pittsburgh Healthcare System, Pittsburgh, PA; (2) University of Pittsburgh, Pittsburgh, PA

PURPOSE: The primary aim of this study was to determine whether a geriatric palliative care team improves suboptimal prescribing for older veteran nursing home patients.

METHODS: This was a before-after intervention study involving patients who were admitted to, and subsequently died on, the Geriatric Palliative Care Unit between August 1, 2005, and July 31, 2007. Evidence of suboptimal prescribing was determined using the total number of scheduled medications and the Unnecessary Drug Use Measure, which contains three questions from the Medication Appropriateness Index on indication, effectiveness, and duplicate therapy. These measures were evaluated at two points: (1) on transfer/admission to the palliative care unit and (2) at the last 30-day medication review before death. Paired t-tests were used to compare medication use at the two points.

RESULTS: Eighty-nine patients were identified for this study. Average length of stay on the unit was 123.6 ± 222.8 days. Average number of chronic medical conditions was 8.4 ± 4.3. A majority of patients were male (97.8%) and white (78.7%). Number of scheduled medications decreased from 9.7 ± 4.3 at admission to 7.4 ± 3.6 at closeout (p<0.001). Number of unnecessary medications decreased from 1.7 ± 1.5 at admission to 0.6 ± 0.8 at closeout (p=0.003).

CONCLUSIONS: This geriatric palliative care unit reduced the overall number of drugs, as well as the number of unnecessary drugs taken by older veteran nursing home patients. Future studies should assess the impact of reducing unnecessary medication use on clinical outcomes such as quality of life.

86. Evaluation of Factors Influencing Fall Risk in a Community Hospital Setting. *Tracy L. Sprunger, Pharm.D.*,[1] Sandra K. Lemon, Pharm.D.,[2] Katherine M. Malloy, Pharm.D.,[2] Heather Mihalek, Pharm.D.,[2] Christina M. Papillon, Pharm.D.[2]; (1) Community Health Network/Butler University, Indianapolis, IN; (2) Community Health Network, Indianapolis, IN

PURPOSE: Patient falls are a serious complication to care in hospital settings. Recently, many hospitals have implemented fall prevention

programs; however, most have been unsuccessful at lowering the percentage of falls per year. Several studies have cited factors that may increase risk of falls including medications, ratio of nurses to patients, concomitant disease states, and environmental factors. The objective of this study was to evaluate medication classes as well as concomitant disease states that may increase the risk of falls in Community Hospital East's (CHE) elderly inpatient population.
METHODS: We conducted a case-control study of patients who experienced a fall, with or without injury, at CHE from January 1, 2007, through June 30, 2007. Control patients were matched to cases based on date of fall and same hospital unit in a 1:3 fashion. Data collected included patient demographics and medications within 24 hours of the fall, including benzodiazepines, antidepressants, antipsychotics, diuretics, and narcotics; data collected also included concomitant disease states such as stroke and Parkinson's disease. Statistical analysis was performed using SPSS v. 14.0.
RESULTS: A total of 80 fall cases were reviewed and matched with 276 controls. Patients taking antipsychotics and those receiving more than one dose of benzodiazepines within 24 hours of the fall were 3.7 and 3.8 times more likely to fall, respectively. White race and diabetes placed patients at reduced risk of falling, whereas a diagnosis of Parkinson's disease put patients at a 10-fold increased risk of falling.
CONCLUSIONS: Antipsychotics, multiple doses of benzodiazepines, and Parkinson's disease increased a patient's risk of falling at CHE, whereas patients with diabetes and white race had a decreased risk of falling.

Health Services Research

87. Pharmacist's Impact on Heart Failure Outcomes: Focus on Medication and Dietary Sodium Adherence. *Grace L. Earl, Pharm.D.*, Ruchi Banker, Pharm.D., Reena Thomas, Pharm.D., Neal Adams, Pharm.D., Andrew Peterson, Pharm.D.; University of the Sciences in Philadelphia/Philadelphia College of Pharmacy, Philadelphia, PA
PURPOSE: Dietary sodium indiscretions can lead to hospitalization for acute, decompensated heart failure. A pilot study evaluated the impact of a pharmacist educational program in an ambulatory care practice on reducing the mean daily dietary sodium intake by 33% or greater from baseline.
METHODS: Adult patients (older than 18 years) with chronic heart failure were instructed in achieving a sodium goal of 2000 mg or less per day. A 10-question food quiz was used to assess knowledge of high-sodium foods. A 24-hour dietary recall was used to assess sodium intake at four patient encounters. Data are presented as the mean (95% CI) and were analyzed by a paired *t*-test. The study was approved by an institutional review board.
RESULTS: Thirteen patients (age 55.4 years, ejection fraction 35.4%) had 5.2 of 10 questions correct on the baseline food quiz (95% CI: 3.4–7.0). The Morisky scale was 0.9 of 4 at visit 1 (95% CI: 0.351–1.467), and at visit 2, it was 0 (lower scores reflect greater likelihood of medication adherence). Sodium intake was 2166.5 mg (95% CI: 1443.6–2889.5) for 13 patients at baseline. Sodium intake in 10 subjects at visit 1 was 1788.7 mg (95% CI: 1071.3–2506.0), and at follow-up, it was 1617.0 (95% CI: 875.9–2358.1) (p=0.80). There was no difference in vital signs or weight at follow-up. Daily diuretic doses, using furosemide equivalents, were 65 mg (95% CI: 33.3–96.7) at visit 1 and 75 mg (95% CI: 41.5–108.5) at follow-up. There were three heart failure hospitalizations.
CONCLUSIONS: Patients with a moderate ability to recognize high sodium foods experienced a nonsignificant mean decrease in dietary sodium intake of 9.5%. From this pilot study, we observed that daily sodium intake of individuals is variable. Plans include developing a validated health literacy tool to assess competency in assessing knowledge and skills necessary for achieving dietary sodium adherence.

88E. Transfusion and Hospitalization Outcomes in Erythropoiesis Stimulating Agent (ESA)-Treated Cancer Chemotherapy Patients Based on Achieved Hemoglobin (Hb) Levels. Kay Larholt, Sc.D.,[1] Tanya Burton, M.S.,[1] David Hoaglin, Ph.D.,[1] Chris Pashos, Ph.D.,[1] Brahim Bookhart, M.B.A., MPH,[2] Mitra Corral, M.S., MPH,[2] Catherine Tak Piech, M.B.A.,[2] *R. Scott McKenzie, M.D.*[2]; (1) Abt Bio-Pharma Solutions, Inc., Lexington, MA; (2) Centocor Ortho Biotech Services, LLC, Bridgewater, NJ
PURPOSE: Recent changes in Medicare's erythropoiesis-stimulating agent (ESA) coverage policy have mandated that ESA administration in cancer chemotherapy patients be limited to those with a baseline hemoglobin (Hb) less than 10 g/dL and be contingent on specific achieved Hb concentrations. To understand the clinical implications of these coverage directions, data from an ongoing ESA registry were evaluated.
METHODS: Observational data from an ongoing, prospective registry of ESA-treated patients in 55 U.S. oncology clinics between December 2003 and November 2007 were analyzed. Hospital- and community-based outpatient practices were included. Data were analyzed from adult chemotherapy-treated oncology patients with at least two ESA doses and Hb concentration less than 10 g/dL before ESA administration. Transfusion and hospitalization-related outcomes were categorized into three cohorts based on mean Hb values achieved during ESA treatment: 9.1–10, 10.1–11, or 11.1–12 g/dL.
RESULTS: A total of 330 patients met inclusion criteria, with 36, 45, and 19% categorized into mean achieved Hb concentrations of 9.1–10, 10.1–11, and 11.1–12 g/dL. The mean achieved Hb concentrations were 9.6, 10.5, and 11.4 g/dL, respectively. Age, gender distribution, and ESA treatment duration were similar between groups. The proportion of patients transfused was 39, 23, and 19%, respectively. Logistic regression analysis suggested that, as the mean achieved Hb concentration increased, the risk of transfusion decreased (OR = 0.580, 95% CI: 0.401–0.839). The proportion of patients requiring hospitalization was 28, 26, and 19%, respectively. The number of hospitalizations per 100 ESA treatment days was 0.42, 0.40, and 0.29 in the respective cohorts.
CONCLUSIONS: Lower mean achieved Hb concentrations during ESA treatment were associated with significantly increased transfusion requirements and a trend toward higher hospitalization rates in the ESA-treated cancer chemotherapy patients with anemia (baseline Hb less than 10 g/dL). These findings on the clinical and resource implications of limiting ESA coverage to defined Hb concentrations should prove informative to health care providers.
Presented at the American Society of Health-System Pharmacists (ASHP) Summer Meeting and Exhibition, Seattle, WA, June 8–11, 2008.

89. Drug Utilization and Costs for Erythropoietic Stimulating Agents in Patients with Breast, Lung, or Gastrointestinal Cancer Receiving Chemotherapy. Gosselin Antoine, M.A.,[1] Marie-Hélène Lafeuille, B.A.,[1] Brahim Bookhart, M.B.A., MPH,[2] Patrick Lefebvre, M.A.,[1] *R. Scott McKenzie, M.D.*,[2] Francis Vekeman, M.A.,[1] Catherine Tak Piech, M.B.A.[2]; (1) Groupe d'Analyse, Ltée., Montreal, QC, Canada; (2) Centocor Ortho Biotech Services, LLC, Bridgewater, NJ
PURPOSE: To understand current use patterns and costs for epoetin alfa (EPO) and darbepoetin alfa (DARB) across tumor types in managed care cancer patients receiving chemotherapy.
METHODS: Medical claims from the Ingenix Impact National Managed Care Database between January 2005 and June 2007 were analyzed. Patients included were 18 years or older, had one or more claim for cancer within 90 days before treatment initiation, were newly initiated on EPO or DARB with two or more doses of either drug, and received chemotherapy during treatment. Mean cumulative erythropoiesis-stimulating agent (ESA) dose was used to calculate drug cost (based on October 2007 wholesale acquisition cost) and dose ratio (units EPO:µg DARB). Stratified analyses for breast, lung, and gastrointestinal cancer patients were also conducted.
RESULTS: A total of 3685 EPO and 5959 DARB patients formed the study population. The EPO group was older (58.5 vs. 56.1 years, p<0.001), had a lower proportion of women (65% vs. 69%, p<0.001), and had slightly longer treatment durations (EPO 60 days; DARB 56 days; p<0.001) compared with DARB patients. Mean cumulative doses (EPO 316,355 units; DARB 1169 µg) yielded a dose ratio of 271:1, corresponding to drug costs 27% lower for EPO

than for DARB (EPO $3961; DARB $5409; p<0.001). Stratified analyses by tumor type resulted in similar lower drug costs for EPO (breast 28%, lung 25%, gastrointestinal 25%, respectively; p<0.001).
CONCLUSIONS: This observational study of 9644 cancer patients reported a dose ratio of 271:1, which resulted in a 27% lower drug cost in the EPO group compared with the DARB group. Stratified analyses by major tumor types yielded similar drug costs.

90E. Transfusion Outcomes Among Oncology Patients Initiated with Erythropoiesis-Stimulating Agents (ESAs) at Baseline (BL) Hemoglobin (Hb) of <10 v 10–11g/dL: Data from the Dosing and Outcomes Study of Erythropoiesis-Stimulating Therapies (DOSE) Registry. Tanya Burton, M.S.,[1] Kay Larholt, Sc.D.,[1] Chris Pashos, Ph.D.,[1] Cyrus Peake, M.S.,[1] Brahim Bookhart, M.B.A., MPH,[2] Mitra Corral, M.S., MPH,[2] Catherine Tak Piech, M.B.A.,[2] *R. Scott McKenzie, M.D.*[2]; (1) Abt Bio-Pharma Solutions, Inc., Lexington, MA; (2) Centocor Ortho Biotech Services, LLC, Bridgewater, NJ
PURPOSE: Limited real-world data exist on transfusion patterns in patients initiated with erythropoiesis-stimulating agents (ESAs) at different baseline hemoglobin concentrations. Transfusion outcomes were investigated in chemotherapy-treated oncology patients initiated on ESAs at baseline hemoglobin of less than 10 g/dL versus 10–11 g/dL.
METHODS: Observational data from an ongoing, prospective registry of ESA-treated patients in 59 U.S. oncology clinics between December 2003 and November 2007 were analyzed. Hospital- and community-based outpatient practices were included. Data were analyzed from adult chemotherapy-treated oncology patients with two or more ESA doses.
RESULTS: A total of 1059 patients (ESA-initiated hemoglobin less than 10 g/dL, n=384, ESA-initiated hemoglobin 10–11 g/dL, n=675) from 59 sites were included. Baseline characteristics were similar for both groups. A significantly greater proportion of patients required transfusion with baseline hemoglobin less than 10 g/dL. Mean number of units per transfused patient was similar between groups. However, overall blood use for all enrolled patients was significantly greater for patients with baseline hemoglobin less than 10 g/dL (Table). Trends were maintained when data were analyzed from day 28 to the end of study (EOS).
CONCLUSIONS: Blood use was lower in patients with ESAs initiated at baseline hemoglobin of 10–11 g/dL compared with less than 10 g/dL. Differences were associated with the proportion of transfused patients rather than the use in transfused patients.

Baseline Hemoglobin (n=1059)	< 10 g/dL (n=384)	10–11 g/dL (n=675)	p-value
Patients requiring transfusions day 1-EOS	31%	15%	< 0.0001
Patients requiring transfusions day 28-EOS	16%	10%	0.0004
Mean (SD) units/ transfused patient day 1-EOS	2.9 (1.8)	3.2 (2.2)	0.68
Mean (SD) units/ transfused patient day 28-EOS	2.7 (1.5)	3.0 (2.0)	0.59
Mean (SD) units transfused/study patient, day 1-EOS	0.9 (1.7)	0.5 (1.4)	< 0.0001
Mean (SD) units transfused/study patient, day 28-EOS	0.4 (1.2)	0.3 (1.1)	0.004
Mean (SD) ESA treatment duration, days	58 (35)	58 (34)	0.88

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Hematology/Anticoagulation

91. Enoxaparin for Deep Vein Thrombosis Prophylaxis in Obese Patients. *Ayana K. Rowley, Pharm.D.*, Michelle Lilliston, Pharm.D., BCPS, Barbara Hammer, Pharm.D., BCPS; Moses Cone Health System, Greensboro, NC
PURPOSE: Expert opinion suggests an adjusted enoxaparin dose of 0.5 mg/kg every 24 hours is warranted for prevention of deep vein thrombosis (DVT) in obese patients (body mass index 30 or more). Moses Cone Health System has incorporated this dosing strategy into its anticoagulation protocol. The primary objective of this medication use evaluation was to determine the effectiveness of this dose. Secondary objectives were to determine if the adjusted dose correlated with targeted anti-Xa concentrations (0.3–0.6 IU/mL) and if a mathematical method of dose adjustment (ratio-proportion [R-P]) was effective.
METHODS: We prospectively collected data from December 2005 to May 2006 on all obese inpatients with enoxaparin ordered for DVT prophylaxis. The clinical pharmacy staff recorded specific clinical end points, implemented dose adjustments if needed, and monitored the patient until discharge or therapy discontinuation. Pharmacists adjusted nontherapeutic levels using an R-P equation and obtained new levels at steady state.
RESULTS: Forty-nine patients were evaluated. There were no reports of DVT or adverse bleeding events during hospitalization. Six-month readmission rate for DVT was zero. Overall, 70% of patients reached targeted anti-Xa concentrations without further dose adjustments. In a subanalysis of patients with reduced renal clearance (less than 30 mL/minute; n=9), 89% reached targeted anti-Xa levels ranging from 0.4 to 0.5. No patient had a supratherapeutic anti-Xa level. In patients not reaching targeted goals, the R-P consistently overestimated the dose required to correlate with predicted anti-Xa goals.
CONCLUSIONS: This medication use evaluation supports the use of an adjusted enoxaparin dose in obese patients with normal renal function. However, because patients with end-stage renal disease are at a higher risk of bleeding, monitoring with anti-Xa levels is warranted with consideration given to DVT risk factors for dose determination.

92. Age and Ethnicity Influence Warfarin Maintenance Dose; a Comparison of Elderly African American and White Patients. *Candice L. Garwood, Pharm.D.,*[1] Jennifer L. Clemente, Pharm.D.,[2] George N. Ibe, Pharm.D. Student,[1] Vijay A. Kandula, Pharm.D. Student,[1] Peter Whittaker, Ph.D.[3]; (1) Wayne State University, Detroit, MI; (2) Harper University Hospital, Detroit, MI; (3) Wayne State University School of Medicine, Cardiovascular Research Institute and Department of Emergency Medicine, Detroit, MI
PURPOSE: Warfarin doses required to maintain consistent therapeutic anticoagulation (AC) decrease with age; however, this conclusion is derived from studies enrolling predominantly white (W) patients. Consequently, universal application of dosing paradigms based on these studies may be confounded because ethnicity also influences dose; middle-aged African Americans (AA) require higher warfarin doses than W patients. Therefore, we compared warfarin maintenance doses in AA and W patients as a function of age.
METHODS: In a retrospective chart review, we examined 111 patients (75 AA, 36 W) who attended a pharmacist-managed AC clinic, were not receiving amiodarone, and had achieved therapeutic AC. We calculated the average weekly dose used to maintain therapeutic international normalized ratio for 8–24 consecutive clinic visits (observation period 363 ± 12 days). Average dose was determined for the following ranges: younger than 50, 50–59, 60–69, and older than 70 years.
RESULTS: Indications for therapy were 32% atrial fibrillation, 47% venous thromboembolism, 16% valve replacement, and 5% other. There was no difference between groups for indication or gender (female; AA 55%, W 53%). We found a negative correlation between dose and age (AA r = –0.89, p=0.04; W r = –0.96, p=0.01); thus, dose decreased with age, and at any given age, doses were greater for AA patients. Specifically, for those older than 70 years, weekly doses were higher in AA than in W patients (37.1 ± 2.7 mg vs. 26.5 ± 2.6 mg; p=0.01); there was a significant decrease from 55.6 and 49.1 mg, respectively, in patients younger than 50 years (p<0.01).
CONCLUSIONS: We confirmed the previously reported age-associated decreases in warfarin dose for W patients and demonstrated a similar relationship in AA patients. The 40%

increase in required dose for older AA versus W patients was clinically significant and indicates that strategies to estimate starting warfarin doses in elderly patients based on results from studies enrolling mainly W patients result in insufficient AC in AA patients and hence increase the risk of thromboembolism.

93. Risk Factors for Major Bleeding in Patients with Heparin-Induced Thrombocytopenia Treated with Argatroban: A Retrospective Analysis. *Catherine Verme-Gibboney, Pharm.D.,*[1] Marcie J. Hursting, Ph.D.[2]; (1) GlaxoSmithKline, Philadelphia, PA; (2) Clinical Science Consulting, Austin, TX

PURPOSE: To identify risk factors for major bleeding associated with the direct thrombin inhibitor argatroban in patients treated for heparin-induced thrombocytopenia (HIT).

METHODS: We retrospectively characterized major bleeding events and their risk factors among 269 patients with clinically diagnosed HIT treated with argatroban (2 µg/kg/minute initial dose, adjusted to achieve activated partial prothrombin times (aPTTs) 1.5–3 times baseline) from a prospective, multicenter study.

RESULTS: Patients received a median (range) argatroban dose of 1.9 (0.23–9.7) µg/kg/minute for 5.7 (0.1–16) days. Average aPTT values during therapy were 61.6 (37–182) seconds. Major bleeding, most commonly gastrointestinal, occurred in 19 (7.0%) patients during therapy. Another patient suffered intracranial hemorrhage 4 days after argatroban cessation. Bleeding was fatal in two (0.7%) patients; each received multiple anticoagulants and thrombolytic therapy. Major bleeding was more likely to occur in patients with HIT-related thrombosis (OR = 2.9, p=0.039), pulmonary impairment (OR = 20.3, p<0.001), or an aPTT greater than 100 seconds (OR = 3.7, p=0.010). Major bleeding rates were 5–9% when the average aPTT was 90 seconds or less and 22% when more than 90 seconds. No significant effects of patient demographics, other baseline illnesses including hepatic or renal impairment, argatroban dose, or treatment duration were detected on major bleeding.

CONCLUSIONS: Risk factors for major bleeding in HIT patients treated with argatroban include baseline HIT-related thrombosis and pulmonary impairment. For minimizing bleeding risk during argatroban therapy in HIT, the aPTT should be routinely monitored and maintained less than 90 seconds.

Herbal/Complementary Medicine

94. The Effect of Black Cherry Juice Concentrate on Serum Uric Acid in Patients with Heart Failure. *Anne P. Spencer, Pharm.D., BCPS,*[1] Maria Jose Pallares, Pharm.D.,[2] Adrian Van Bakel, M.D., Ph.D.[3]; (1) Roper Saint Francis Healthcare, Charleston, SC; (2) Miami VA Medical Center, Miami, FL; (3) Medical University of South Carolina, P.O. Box 250132, Charleston, SC

PURPOSE: The consumption of black cherry juice concentrate is reported to have a salutary effect on the treatment of gout, and patients with heart failure have limited treatment options. However, there are limited data to support the use of black cherry juice for the treatment of gout or hyperuricemia. The objectives of this study were to assess tolerability and determine the effect of black cherry juice concentrate on serum uric acid concentrations in patients with heart failure having hyperuricemia.

METHODS: In an open-label fashion, patients with systolic heart failure and serum uric acid concentrations greater than 6.5 mg/dL consumed 30 mL of black cherry juice concentrate daily for about 1 month. Baseline and posttreatment uric acid concentrations were obtained. Tolerability was assessed during the 30-day study period.

RESULTS: Twenty-one patients were enrolled, and 14 (67%) completed the study. Four patients were lost to follow-up, two dropped out because of side effects, and one was withdrawn because of noncompliance. The mean baseline uric acid concentration was 8.8 ± 1.58 mg/dL. After an average of 32 days of therapy, the mean uric acid concentration increased to 9.2 ± 2.17 mg/dL, which did not reach statistical significance. There was a 96% compliance rate with the black cherry juice concentrate. Of the 21 patients who consumed at least one dose of black cherry juice, 11 (52%) reported at least one potential associated side effect. Six (29%) complained of diarrhea, and three (14%) suffered from nausea and/or vomiting. Infrequently reported discomforts include taste disturbances, dizziness, stomach complaints, constipation, and dry mouth.

CONCLUSIONS: Black cherry juice concentrate has no beneficial effect on serum uric acid concentrations in patients with systolic dysfunction and hyperuricemia. Because of this lack of effect and the possibility of side effects, black cherry juice concentrate should not be recommended for the treatment of gout.

HIV/AIDS

95E. Low Incidence of Suspected Abacavir Hypersensitivity (ABC HSR) After Implementation of HLA-B*5701 Screening: Results from the ARIES Study. Benjamin Young, M.D., Ph.D.,[1] Kathleen Squires, M.D.,[2] Parul Patel, Pharm.D.,[3] Edwin DeJesus, M.D.,[4] Nicholas C. Bellos, M.D.,[5] Daniel S. Berger, M.D.,[6] Daniel Murphy, M.D.,[7] Denise H. Sutherland-Phillips, M.D.,[3] Qiming Liao, Ph.D.,[3] Paul G. Wannamaker, B.S.,[3] *Mark S. Shaefer, Pharm.D.*[3]; (1) Division of General Internal Medicine, University of Colorado, Denver, CO; (2) Thomas Jefferson University, Philadelphia, PA; (3) GlaxoSmithKline, Research Triangle Park, NC; (4) Orlando Immunology Center, Orlando, FL; (5) Southwest Infectious Disease Associates, Dallas, TX; (6) Northstar Medical Center, Chicago, IL; (7) Clinique Medicale l'Actuel, Montreal, QC, Canada

PURPOSE: The *HLA-B*5701* allele is a highly sensitive marker for abacavir hypersensitivity (ABC HSR); its high negative predictive value suggests that exclusion of patients with *HLA-B*5701* before initiating ABC will significantly reduce the incidence of ABC HSR. ABC HSR in *HLA-B*5701*–positive patients typically occurs within the first few weeks after initiation of ABC. The effect of open-label *HLA-B*5701* screening on the rate of ABC HSR in a prospective clinical study in a racially diverse population has not been determined.

METHODS: The ARIES study compares the safety and efficacy of a 36-week induction regimen of atazanavir plus ritonavir in combination with abacavir/lamivudine (ABC/3TC), followed by 48 weeks of the initial regimen or simplification to atazanavir alone plus ABC/3TC fixed-dose combination in a population of HIV-infected, antiretroviral-naïve, *HLA-B*5701*-negative subjects in the United States and Canada. Subjects with suspected ABC HSR underwent ABC skin patch testing and continued in the study on an alternative regimen. Results are reported through January 11, 2008.

RESULTS: Forty-one (5.7%) of 725 subjects screened for enrollment were *HLA-B*5701* positive and excluded from the study: 32 (7.2%) of 443 whites, 7 (2.8%) of 246 blacks, and 2 (5.6%) of 36 individuals of other races. Five hundred sixteen subjects were enrolled between March 28, 2007, and September 7, 2007; four (0.8%) subjects reported suspected ABC HSR with an onset time of 8, 10 (2), and 12 days from initiation of study medications. No subject had a positive skin patch test result.

CONCLUSIONS: After screening and exclusion of *HLA-B*5701*–positive subjects, clinically suspected ABC HSR was rarely reported through at least 18 weeks of study (0.8%) and was substantially lower than rates in previous studies that did not use *HLA-B*5701* screening. Thus, routine implementation of prospective *HLA-B*5701* screening reduces the rate of ABC HSR and should be considered in ABC-naïve subjects.

Presented at the 17th Annual Canadian Conference on HIV/AIDS Research, Montreal, QB, Canada, April 24–27, 2008.

96E. Tenofovir Effect on Renal Function Factoring in Both MDRD-Calculated Glomerular Filtration Rate (GFR) and Spot Urine Protein-to-Creatinine (UPC) Ratio. Thanes Vanig, M.D.,[1] Qiming M. Liao, Ph.D.,[2] *Belinda Ha, Ph.D.*,[2] Carol Williams, FNP[1]; (1) Spectrum Medical Group, Phoenix, AZ; (2) GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: Because serum creatinine may underestimate renal impairment, we investigated whether proteinuria assessed by urine protein-to-creatinine (UPC) ratio might predict early renal disease in a real-world cohort of antiretroviral (ARV)-treated HIV-positive patients.

METHODS: This retrospective analysis compared patients on tenofovir (TDF)- versus non–TDF-containing highly active

antiretroviral therapy (HAART) between 2006 and 2007. Baseline measurements included demographics, comorbidities, ARV history, serum creatinine, UPC ratio, CD4 count, and viral load. These measurements were followed through December 2007. We calculated glomerular filtration rate (GFR) (mL/minute/1.73 m^2) by the modification-of-diet-in-renal-disease equation and defined proteinuria as UPC ratio more than 200 mg/g. We report hazard ratios (HRs) by Cox proportional hazards model with multiple predictors, including comorbidities.

RESULTS: We analyzed 253 TDF and 122 non-TDF patients (n=375; 94% men; 4% black). Median time on treatment before baseline was 2.2 and 3 years, respectively, for the TDF and non-TDF patients. At baseline, both groups had similar proportions of patients with comorbid conditions (diabetes and hypertension); the TDF group had slightly fewer patients reporting a history of kidney disease (1% vs. 5%) and absence of hepatitis coinfection (86% vs. 90%). The TDF group had fewer patients with viral load less than 50 c/mL (68% vs. 88%) and lower median CD4 (440 vs. 554 cells/mm^3) and more patients with proteinuria (22% vs. 9%). Among patients with a baseline UPC ratio more than 200 mg/g, median GFR declined (from 81 to 71) in the TDF group and was relatively unchanged in the non-TDF group (from 79 to 84) during follow-up. In multivariate analyses, TDF use (HR = 2.13, p=0.008), diabetes (HR = 2.2, p=0.006), and age (p=0.001) were associated with time-to-UPC ratio more than 200 mg/g. TDF use (HR = 1.99, p=0.002) and age (p=0.001) were factors associated with time to GFR less than 60 or UPC ratio more than 200 mg/g.

CONCLUSIONS: In this retrospective study, TDF use was associated with decline in renal function as defined by reduced GFR and/or proteinuria measured by UPC ratio.

To be presented at the International AIDS Conference, August 2008.

97. Simplified Maintenance Therapy with ABC/3TC+ATV After ABC/3TC+ATV/RTV Induction: 48 Week Results. Richard Elion, M.D.,[1] Daniel S. Berger, M.D.,[2] Gary Richmond, M.D.,[3] Michael Sension, M.D.,[4] Edwin DeJesus, M.D.,[5] Paul Cimoch, M.D.,[6] Linda H. Yau, Ph.D.,[7] *Belinda Ha, Ph.D.*[7]; (1) George Washington University, Washington, DC; (2) Northstar Medical Center, Chicago, IL; (3) Broward General Medical Center, Fort Lauderdale, FL; (4) Comprehensive Care Center, Fort Lauderdale, FL; (5) Orlando Immunology Center, Orlando, FL; (6) Center for Special Immunology, Fountain Valley, CA; (7) GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: Several studies have suggested that the use of ritonavir (RTV) continues to be associated with increased lipid abnormalities, principally hypertriglyceridemia. We hypothesize that protease inhibitor–based therapy without RTV after induction with an RTV-boosted regimen of atazanavir (ATV)/RTV and abacavir/lamivudine (ABC/3TC) will simplify therapy, maintain virologic suppression, and reduce development of hypertriglyceridemia.

METHODS: In this open-label, prospective, multicenter study, 29 antiretroviral-naïve adults, each of whom received ATV 300 mg/RTV 100 mg + ABC/3TC once daily as initial therapy for 24 weeks or more and had HIV-1 RNA less than 50 c/mL, simplified their regimen to ATV 400 mg plus ABC/3TC once daily for a 48-week maintenance period.

RESULTS: Two subjects prematurely discontinued the study: one withdrew and one was lost to follow-up. At week 48 of maintenance, 83% (24 of 29) of subjects maintained HIV-1 RNA less than 50 c/mL, and 90% (26 of 29) of subjects maintained HIV-1 RNA less than 400 c/mL by missing-equals-failure analysis. One subject experienced unconfirmed virologic rebound to more than 400 c/mL. Median CD4+ cell count increased 16 cells/mm^3 from baseline. Mean fasting lipids at week 48 (percent change from start of maintenance) were 179 mg/dL (-11%) for total cholesterol, 105 mg/dL (-11%) for low-density lipoprotein cholesterol, 50 mg/dL (2%) for high-density lipoprotein cholesterol, and 117 mg/dL (-25%) for triglycerides.

CONCLUSIONS: Simplification to ABC/3TC+ATV through 48 weeks after induction with ATV/RTV+ABC/3TC maintained virologic suppression in most subjects and improved fasting lipids. Larger, randomized studies are needed to determine if this strategy provides an opportunity both for reducing long-term metabolic complications and simplifying antiretroviral therapy.

98E. Efficacy and Safety of Abacavir/Lamivudine (ABC/3TC) Compared to Tenofovir/Emtricitabine (TDF/FTC) in Combination with QD Lopinavir/Ritonavir (LPV/r) Through 48 Weeks in the HEAT Study. Parul Patel, Pharm.D.,[1] Kimberly Y. Smith, M.D.,[2] Derek M. Fine, M.D.,[3] Nicholas C. Bellos, M.D.,[4] Louis Sloan, M.D.,[5] Phillip Lackey, M.D.,[6] Denise H. Sutherland-Phillips, M.D.,[1] Cindy Vavro, B.S.,[1] Qiming M. Liao, Ph.D.,[1] *Mark S. Shaefer, Pharm.D.*[1]; (1) GlaxoSmithKline, Research Triangle Park, NC; (2) Rush University Medical Center, Chicago, IL; (3) Johns Hopkins University School of Medicine, Baltimore, MD; (4) Southwest Infectious Disease Associates, Dallas, TX; (5) North Texas Infectious Disease Consultants, Dallas, TX; (6) ID Consultants, Charlotte, NC

PURPOSE: The HEAT study was the first head-to-head trial to evaluate the efficacy and safety of dual nucleoside reverse transcriptase inhibitor (NRTI) backbones, abacavir/lamivudine (ABC/3TC) and tenofovir/emtricitabine (TDF/FTC), with a boosted protease inhibitor as part of recommended first-line treatments in HIV-1–infected subjects.

METHODS: Randomized, double-blind, placebo-matched, multicenter, 96-week study. HIV-1–infected, antiretroviral (ART)-naïve subjects had a plasma HIV-1 RNA (VL) of 1000 c/mL or more (stratified less than or 100,000 c/mL or more), and any CD4+ count. Subjects received either blinded ABC/3TC or TDF/FTC with open-label lopinavir/ritonavir soft gel capsules (LPV/r SGC) once daily. Virologic failure (VF) was defined as failure to achieve VL less than 200 c/mL by week 24 or confirmed rebound to 200 c/mL or more. Primary efficacy end point was proportion with VL less than 50 c/mL at week 48 (intent to treat [ITT], M = F, switch included analysis). A 95% confidence interval for the difference in treatment responses was calculated to show noninferiority using a 12% margin. Within-class switches were allowed for toxicity. *HLA-B*5701* screening was not performed.

RESULTS: A total of 688 subjects were randomized, with a mean age of 38 years, 49% nonwhite, and 18% women.

Baseline Characteristics	ABC/3TC+ LPV/r n=343	TDF/FTC+ LPV/r n=345	95% CI of Difference	P-value
Median HIV-1 RNA (log) c/mL				
e 100,000 c/mL	4.90	4.84		
	45%	41%		
Median CD4+, cells/mm^3	214	193		
Week 48 results				
HIV-1 RNA < 50 c/mL				
ITT-E, M = F, switch included	68%	67%	(-6.63, 7.40)	0.913
TLOVR	63%	61%	(-5.75, 8.78)	0.683
Observed	84%	87%	(-8.44, 3.34	
HIV-1 RNA < 400 c/mL				
ITT-E, M = F, switch included	75%	71%	(-2.71, 10.56)	0.246
TLOVR	71%	66%	(-2.46, 11.44)	0.206
Observed	94%	92%	(-2.69, 5.89)	0.467
Median CD4+ (_BL), cells/mm^3	429 (+201)	370 (+173)		
Virologic failure	12%	13%		
Premature withdrawal due to AEs	13 (4%)	20 (6%)		
Drug-related grade 2–4 AEs	154 (45%)	152 (44%)		
Suspected ABC HSR	14 (4%)	3 (1%)		
Proximal renal tubular dysfunction	0	3 (1%)		

BL = baseline; HSR = hypersensitivity reaction; TLOVR = time of loss of virologic response.

CONCLUSIONS: ABC/3TC was noninferior to TDF/FTC when combined with once-daily LPV/r. Median CD4+ increase was greater with ABC/3TC at week 48. Rates of drug-related grade 2–4 adverse events (AEs) were comparable. Both regimens proved efficacious in this ART-naïve population through 48 weeks.

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99. Improved Triglycerides After Reducing the Ritonavir (RTV) Boosting Dose from 200 mg to 100 mg Once Daily (QD) in HIV+ Patients Stabilized (Viral Load < 50 c/mL) on QD RTV-Boosted Fosamprenavir (FPV) 1400 mg + Abacavir (ABC) 600 mg/ Lamivudine (3TC) 300 mg. Dushyantha T. Jayaweera, M.D.,

MRCOG,[1] *Gary E. Pakes, Pharm.D.*[2]; (1) University of Miami Miller School of Medicine, Miami, FL; (2) GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: Clinical efficacy/safety after reducing once-daily ritonavir (RTV)-boosting doses from 200 to 100 mg has undergone little study in patients who are HIV positive and stabilized on fosamprenavir (FPV) 1400 mg once-daily regimens.

METHODS: In a 52-week, phase 4, open-label, single-center pilot study, 26 antiretroviral-naïve patients positive for HIV with viral loads (VL) greater than 1000 c/mL received induction with FPV 1400 mg/RTV 200 mg plus abacavir (ABC) 600 mg plus lamivudine (3TC) 300 mg every day for 28 weeks. Patients achieving VL less than 50 c/mL at week 28 were given maintenance therapy for 24 subsequent weeks with half the RTV dose (100 mg) plus the usual FPV, 3TC, and ABC doses. End points were the percentage of patients with VL less than 50 c/mL, CD4+ cell count change-from-baseline (BL), and change in safety/fasting lipid profile.

RESULTS: In the 26 patients enrolled (12 M, 14 F; 16 black, 10 white [including 5 Hispanics]), BL median VL was 4.93 log c/mL, and CD4+ count was 110/mm^3. Twelve patients completed the induction and maintenance study phases, with 14 prematurely discontinued for loss to follow-up (6), protocol violation (4), moving away (2), or suspected ABC hypersensitivity (2). In the 12 completers, 10 (83%) had VL less than 50 c/mL by maintenance—week 24, and CD4+ count increased from a median of 110/mm^3 (BL) to 292/mm^3 (induction – week 28) to 296/mm^3 (maintenance – week 24). Adverse event (AE) incidence/type did not notably change between induction, week 28, and maintenance, week 24, although few AEs were reported during the second half of the induction phase anyway. Median fasting total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides (TG) remained below National Cholesterol Education Program cutoff concentrations. BL/induction – week 28/maintenance – week 24 median total cholesterol (TC) was 130/177/183 mg/dL, LDL cholesterol was 78/107/114 mg/dL, high-density lipoprotein (HDL) cholesterol was 33/41/43 mg/dL, TC:HDL cholesterol was 3.9/4.3/4.3, and TG was 93/145/119 mg/dL.

CONCLUSIONS: In this pilot study, reducing the RTV-boosting dose from 200 to 100 mg/day in patients positive for HIV stabilized on once-daily FPV/ABC/3TC generally maintained virologic suppression, enhanced CD4+ count, and improved TG. Large-scale studies are needed to further evaluate the trends observed in this small study.

100. Foot Fracture Characteristics in HIV-Infected Patients Previously Treated with Tenofovir (TDF)- vs Non-TDF-Containing HAART: Results of Case-Series Study COL109415. Arash A. Horizon, M.D.,[1] Robert J. Joseph, DPM,[2] Qiming Liao, Ph.D.,[3] Steven T. Ross, M.S.,[3] *Gary E. Pakes, Pharm.D.*[3]; (1) Cedars-Sinai Health System, Los Angeles, CA; (2) Surgical Podiatry, Los Angeles, CA; (3) GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: Osteopenia in patients positive for HIV (frequency 22–50%) increases the risk of bone fractures, especially of the hip and spine. We characterized foot fractures diagnosed in patients positive for HIV in the Los Angeles Cedars-Sinai Health System.

METHODS: In this retrospective case-series study, the medical records of all male patients infected with HIV with magnetic resonance imaging-confirmed foot fractures (n=30) were examined. Data regarding demographics, HIV history, comorbidities, highly active antiretroviral therapy (HAART)/non-HIV drug prescription history, dual-energy x-ray absorptiometry (DEXA) bone mineral density scores, and fracture type were collected on Excel sheets and analyzed by logistic regression with stepwise selection.

RESULTS: Proportionally more patients with foot fractures had received tenofovir (TDF)-containing HAART (17 [57%]) than non–TDF-containing HAART (13 [43%]) prefracture. At fracture diagnosis, these two groups were similar regarding median age (49 years/48 years), HIV-1/RNA (both 1.7 log c/mL), time between HIV diagnosis and foot fracture (both 17.0 years); incidence of metatarsophalangeal fracture (12%/15%) and vertebral fracture (12%/15%); family history of bone diseases (24% vs. 23%); frequency of malabsorption syndrome, renal failure, calcium deficiency and vitamin D deficiency; and concurrent use of bisphosphonates (65%/69%), calcitonin, and diuretics. However, the TDF-treated group had more osteoporosis (35%/8%), stress-type fractures (53%/31%) other concurrent fractures (12%/0%), wasting syndrome (29%/15%), centripetal obesity (18%/8%), chronic cigarette smoking of more than 1 pack/day (35%/8%), DEXA T-scores less than -2.4 (denoting osteoporosis) in femur (24%/9%) and spine (47%/36%), and lower frequency of alcoholism (12%/31%) and anemia of chronic disease (0%/23%). More TDF-treated patients concurrently received protease inhibitors (71%/46%), non-nucleoside reverse transcriptase inhibitors (24%/0%), prednisone (24%/0%), calcium supplements (100%/85%), vitamin D (100%/85%), testosterone (47%/23%), and teriparatide (29%/8%). Median time from TDF initiation until fracture was 2.57 years (range 1.17–5.69 years). Logistic regression analysis showed relationships between femur DEXA T-scores less than 1.5 and body weight (p=0.036) and serum glucose (p=0.034).

CONCLUSIONS: This small pilot study suggests a greater incidence of foot fractures in HIV-infected patients on TDF- than non–TDF-containing HAART. Comorbidities and/or coadministered drugs may have influenced the occurrence of these fractures.

Hypertension

101E. Combination of Amlodipine Besylate + Olmesartan Medoxomil Provides Numerically Greater Reductions in Blood Pressure Compared with Component Monotherapies in Race and Ethnic Subgroups. *Suzanne Oparil, M.D.,*[1] David Ramstad, M.D.,[2] Michael Melino, Ph.D.,[3] James Lee, Ph.D.,[3] Reinilde Heyrman, M.D.[3]; (1) University of Alabama at Birmingham School of Medicine, Birmingham, AL; (2) Lakeview Medical Center, Suffolk, VA; (3) Daiichi Sankyo, Inc., Parsippany, NJ

PURPOSE: Hypertension prevalence is generally higher among black versus white or Hispanic/Latino patients. This study investigated if there were racial or ethnic differences for amlodipine besylate plus olmesartan medoxomil (OM) combination therapy versus respective monotherapy components in lowering blood pressure in patients with hypertension.

METHODS: A randomized, double-blind, placebo-controlled factorial-design study was conducted in patients with hypertension to determine if amlodipine (AML) 5–10 mg/day plus OM 10–40 mg/day (12 treatment arms) for 8 weeks had significant efficacy benefits versus monotherapy components. The primary efficacy variable was change from baseline in diastolic blood pressure at week 8. Secondary end points included change from baseline systolic blood pressure and attainment of blood pressure goal (less than 140/90 or less than 130/80 mm Hg for patients with diabetes).

RESULTS: Of 1940 patients, 1385 (71.4%) were white, and 481 (24.8%) were black. Ethnicity was asked separately from race: 245 (12.6%) were Hispanic/Latino. Subgroups had similar mean baseline blood pressure measurements of about 163/101 mm Hg. In black people, mean blood pressure reductions were greater with AML+OM versus OM monotherapy ($p<0.05$) and in nonblacks versus both OM and AML monotherapy ($p\leq0.0004$). The nonblack group had numerically greater mean reductions in blood pressure for the combination treatment versus the black group. For the ethnic subgroups Hispanic/Latino versus non-Hispanic/Latino, both had numerically greater blood pressure reduction for combination versus monotherapy. The responses were similar for both subgroups. For all four subgroups, the greatest mean blood pressure reductions were with AML+OM 10 + 40 mg treatment, with mean reductions of 29/16 mm Hg in blacks; 31/20 mm Hg in nonblacks; 29/21 mm Hg in Hispanics/Latinos, and 30/19 mm Hg in non–Hispanics/Latinos. All subgroups showed similar trends in achieving blood pressure goals.

CONCLUSIONS: In black and Hispanic/Latino patients, combination therapy resulted in numerically greater mean blood pressure reductions compared with monotherapy, with greatest mean blood pressure reductions occurring with AML+OM 10 + 40 mg. The blood pressure–lowering response was less in blacks versus nonblacks and was similar among the ethnic subgroups.

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102E. High Dose Combination of Amlodipine Besylate + Olmesartan Medoxomil Provides Greater Reduction in Blood Pressure Compared with Component Monotherapies in Subjects With and Without Diabetes. *George Bakris, M.D.,*[1] Stefano Mion-Bet, M.D.,[2] Sulekha Karki, BAMS,[3] James Lee, Ph.D.,[3] Reinilde Heyrman, M.D.[3]; (1) University of Chicago School of Medicine, Chicago, IL; (2) The Community Research of South Florida, Hialeah, IL; (3) Daiichi Sankyo, Inc., Parsippany, NJ

PURPOSE: Patients with diabetes often have difficulty achieving blood pressure goal. Coadministration of amlodipine besylate and olmesartan medoxomil (OM) may improve the blood pressure–lowering efficacy in these patients. This study investigated if amlodipine (AML)+OM had clinically significant benefits versus component monotherapies in lowering the blood pressure in patients with/without diabetes.

METHODS: A randomized, double-blind, placebo-controlled factorial-design study was conducted in patients with hypertension to determine if AML 5–10 mg/day and OM 10–40 mg/day (12 treatment arms) for 8 weeks had significant efficacy benefits versus monotherapy components. The primary efficacy variable was change from baseline in diastolic blood pressure at week 8. Secondary end points included change from baseline systolic blood pressure and attainment of blood pressure goal (less than 140/90 or less than 130/80 mm Hg for patients with diabetes).

RESULTS: Of 1940 patients, 261 (13.5%) had diabetes and a higher mean baseline blood pressure of 169/101 mm Hg versus 163/102 mm Hg for patients without diabetes. Each active treatment produced a statistically significant mean blood pressure reduction from baseline to week 8 ($p<0.0001$), with no differences in overall mean reductions between the two subgroups. AML+OM 10 + 40 mg produced the greatest blood pressure reductions (diabetes, 30/18 mm Hg; nondiabetes, 30/19 mm Hg). Lower percentages of patients with diabetes (0.0–13% with AML+OM 5 + 20 and 10 + 40 mg, respectively) reached the blood pressure goal of less than 130/80 mm Hg with combination therapy at week 8 compared with 39–60% (with AML+OM 5 + 10 mg and 10 + 20 mg, respectively) of nondiabetic patients achieving a blood pressure goal of less than 140/90 mm Hg. For comparison, 33–46% of patients with diabetes achieved a blood pressure of less than 140/90 mm Hg with AML+OM 10 + 20 mg or 10 + 40 mg. Combination therapy was safe and well tolerated.

CONCLUSIONS: Similar blood pressure reductions between the subgroups indicated similar responsiveness, although blood pressure goals were more easily achieved in nondiabetic patients, even when the goal was set similar among the two subgroups. Combination of AML and OM generally produced greater blood pressure reductions and enabled more patients to achieve their blood pressure goal compared with monotherapy.

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103E. An Olmesartan Medoxomil-Based Treatment Algorithm Safely and Effectively Reduces Blood Pressure Compared with Placebo in Patients with Hypertension. *Suzanne Oparil, M.D.,*[1] Steven G. Chrysant, M.D.,[2] Dean J. Kereiakes, M.D.,[3] Jianbo Xu, M.S.,[4] Kathleen J. Chavanu, Pharm.D.,[4] William F. Waverczak, M.S.,[4] Robert Dubiel, Pharm.D.[4]; (1) University of Alabama at Birmingham School of Medicine, Birmingham, AL; (2) Oklahoma Cardiovascular and Hypertension Center and the University of Oklahoma School of Medicine, Oklahoma City, OK; (3) The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, OH; (4) Daiichi Sankyo, Inc., Parsippany, NJ

PURPOSE: Assess blood pressure (BP)-lowering efficacy and safety of an olmesartan medoxomil (OM)-based treatment algorithm.

METHODS: This double-blind, randomized, placebo-controlled, titration study was conducted in 276 patients with hypertension. After a 3-week placebo run-in, patients were randomized to placebo (12 weeks) or OM 20 mg/day (3 weeks). If BP remained 120/80 mm Hg or higher, patients were uptitrated every 3 weeks as follows: OM 40 mg/day, OM/hydrochlorothiazide (HCTZ) 40/12.5 mg/day, and OM/HCTZ 40/25 mg/day. Patients with BP less than 120/80 mm Hg at any visit during active treatment continued their current therapy. Primary end point: change from baseline in mean systolic blood pressure (SBP) at study end. Secondary end points included change from baseline in mean diastolic blood pressure (DBP) and percentage of patients achieving BP goals less than 140/90, less than 130/85, less than 130/80, and less than 120/80 mm Hg at each titration period and study end.

RESULTS: Mean baseline BP: 157/94 and 155/94 mm Hg for the active treatment and placebo group, respectively. OM 20 mg/day reduced mean SBP by 11 mm Hg ($p<0.0001$) with further dose-dependent decreases to a maximum of 23 mm Hg ($p<0.0001$) with OM/HCTZ 40/25 mg/day versus a maximum reduction of 5 mm Hg ($p<0.001$) with placebo (weeks 7–9). At study end, cumulatively, 74% ($p<0.0001$) of patients achieved a BP goal less than 140/90 mm Hg (31% with placebo), and 27% ($p<0.0001$) achieved BP normalization of less than 120/80 mm Hg (2% with placebo). Active treatment was well tolerated, with an adverse event rate similar to placebo at all doses.

CONCLUSIONS: An OM-based regimen, with or without HCTZ, is safe and effective in achieving BP control.

		ΔSBP/ΔDBP	Cumulative No. of Patients Achieving BP Goal, n (%)[b]		
	no.	mm Hg[a]	< 140/90	< 130/80	< 120/80
OM 20	137	-11*/-5*	31 (22)***	9 (7)***	3 (2)
Placebo	137	-2***/-0.5	17 (12)	1 (1)	-
OM 40	132	-13*/-7*	58 (42)*	24 (17)*	13 (9)**
Placebo	126	-3**/-2***	24 (18)	4 (3)	1 (1)
OM/HCTZ 40/12.5	118	-21*/-11*	88 (63)*	44 (32)*	26 (19)*
Placebo	112	-5**/-3**	37 (27)	7 (5)	1 (1)
OM/HCTZ 40/25	88	-23*/-12*	103 (74)*	61 (44)*	38 (27)*
Placebo	94	-3/-0.4	42 (31)	9 (7)	2 (2)

[a]Mean change from baseline at study end (LOCF).
[b]Total number of patients in cohort used as denominator.
*$p<0.0001$; **$p<0.01$; ***$p<0.05$.

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104E. Combination of Amlodipine Besylate and Olmesartan Medoxomil Significantly Reduces Blood Pressure in Patients with Hypertension Independent of Age. *Steven G. Chrysant, M.D.,*[1] James Rhyne, M.D.,[2] Michael Melino, Ph.D.,[3] James Lee, Ph.D.,[3] Reinilde Heyrman, M.D.[3]; (1) Oklahoma Cardiovascular & Hypertension Center Center and the University of Oklahoma School of Medicine, Oklahoma City, OK; (2) The Lipid Center, Statesville, NC; (3) Daiichi Sankyo, Inc., Parsippany, NJ

PURPOSE: Systolic blood pressure typically increases with age, and blood pressure control is often a challenge in the elderly (65 years and older). This study investigated age-related differences in lowering blood pressure with amlodipine besylate and olmesartan medoxomil (OM) combination therapy versus respective components in patients with hypertension.

METHODS: A randomized, double-blind, placebo-controlled factorial-design study was conducted in patients with hypertension to determine if amlodipine (AML) 5–10 mg/day plus OM 10–40 mg/day (12 treatment arms) for 8 weeks had significant efficacy benefits versus monotherapy components. Efficacy included change from baseline in diastolic blood pressure at week 8 (primary); blood pressure goal rate (less than 140/90 or less than 130/80 mm Hg for patients with diabetes); and change from baseline systolic blood pressure (secondary).

RESULTS: Of 1940 patients, 384 (19.8%) were 65 years or older. Mean baseline blood pressure was 161/102 mm Hg (younger than 65 years) versus 174/100 mm Hg (65 years or older). Blood pressure reductions were generally larger for combination therapy than for respective monotherapies. For patients younger than 65 years, all comparisons were statistically significant ($p<0.0001$). In patients 65 years and older, all systolic blood pressure reductions were greater in combination therapy groups and judged clinically relevant. Not all comparisons reached statistical significance (smaller patient numbers). Responses for combinations were generally similar among the age cohorts. Mean systolic blood pressure reductions were numerically greater at highest dosages and in patients 65 years and older. For the AML+OM 10 + 40 mg group, blood pressure was reduced by 29/19 mm Hg (younger than 65

years) and 34/21 mm Hg (65 years and older). For patients younger than 65 years, 51–56% achieved their blood pressure goal on AML+OM 10 + 10–40 mg versus 21–44% with AML+OM 10 + 20–40 mg in patients 65 years and older. Combination therapy was safe and well tolerated.
CONCLUSIONS: Combination therapy with AML+OM allowed significant, dose-dependent blood pressure reductions in patients younger than 65 and 65 years and older. Blood pressure reductions appeared numerically greater in patients 65 years and older at the highest dose combinations; however, achievement of blood pressure goals was lower because baseline blood pressures were higher.
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105E. An Olmesartan Medoxomil-Based Treatment Algorithm Safely and Effectively Reduces Blood Pressure Compared with Placebo in Patients with Stage 1 Hypertension. *Steven G. Chrysant, M.D.,*[1] Suzanne Oparil, M.D.,[2] Dean J. Kereiakes, M.D.,[3] Kathleen J. Chavanu, Pharm.D.,[4] Jianbo Xu, M.S.,[4] William F. Waverczak, M.S.,[4] Robert Dubiel, Pharm.D.[4]; (1) Oklahoma Cardiovascular and Hypertension Center and the University of Oklahoma School of Medicine, Oklahoma City, OK; (2) University of Alabama at Birmingham School of Medicine, Birmingham, AL; (3) The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, OH; (4) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: Assess blood pressure (BP)-lowering efficacy/safety of an olmesartan medoxomil (OM)–based treatment algorithm.
METHODS: In a prespecified subgroup analysis of 130 patients with stage 1 hypertension (systolic blood pressure [SBP] 140–159 mm Hg or diastolic blood pressure [DBP] 90–99 mm Hg) from a double-blind, randomized, placebo-controlled study, patients were randomized to placebo (12 weeks) or OM 20 mg/day (3 weeks) after a 3-week placebo run-in.. If BP remained 120/80 mm Hg or higher, patients were uptitrated every 3 weeks as follows: OM 40 mg/day, OM/hydrochlorothiazide (HCTZ) 40/12.5 mg/day, and OM/HCTZ 40/25 mg/day. If BP was lower than 120/80 mm Hg at any visit during active treatment, patients continued their current treatment. Primary end point: change from baseline in mean SBP at week 12. Secondary end points: included change from baseline in mean DBP at week 12; percentage of patients achieving BP goals less than 140/90, less than 130/85, less than 130/80, and less than 120/80 mm Hg at each titration period and study end.
RESULTS: Mean baseline BP: 151/90 mm Hg (active treatment), 150/91 mm Hg (placebo). OM 20 mg/day reduced mean SBP by 9 mm Hg (p<0.0001), with further dose-dependent decreases to a maximum of 21 mm Hg with OM/HCTZ 40/25 mg/day (p<0.0001) versus a maximum -4 mm Hg with placebo (weeks 7–9, p=0.015). At study end, cumulatively, 81% (p<0.0001) of patients achieved BP goals of less than 140/90 mm Hg (43% with placebo), and 45% (p<0.0001) achieved BP normalization of less than 120/80 mm Hg (1% with placebo). At all doses, active treatment was well tolerated, with an adverse event rate similar to placebo.
CONCLUSIONS: An OM-based regimen is safe and effective in controlling BP in patients with stage 1 hypertension.

		ΔSBP/ΔDBP,	Cumulative No. of Patients Achieving BP Goal, n (%)[b]		
	no.	mm Hg[a]	< 140/90	< 130/80	< 120/80
OM 20 mg	56	-9***/-3*	21 (36)**	8 (14)*	3 (5)
Placebo	72	-2/0	12 (17)	1 (1)	-
OM 40 mg	57	-13***/-6***	34 (59)*	20 (35)***	10 (17)*
Placebo	70	-2/-1	19 (26)	3 (4)	1 (1)
OM/HCTZ 40/12.5 mg	50	-18***/-9***	44 (76)***	29 (50)***	19 (33)***
Placebo	67	-4**/-2**	29 (40)	4 (6)	1 (1)
OM/HCTZ 40/25 mg	29	-21***/-10***	47 (81)***	35 (60)***	26 (45)***
Placebo	62	-0.7/1	31 (43)	5 (7)	1 (1)

[a]Mean change from baseline at study end.
[b]Total number of patients in cohort used as denominator (LOCF).
*p<0.01; **p<0.05; ***p<0.0001.

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106E. An Olmesartan Medoxomil-Based Treatment Algorithm Safely and Effectively Reduces Blood Pressure Compared with Placebo in Patients with Stage 2 Hypertension. *Dean J. Kereiakes, M.D.,*[1] Suzanne Oparil, M.D.,[2] Steven G. Chrysant, M.D.,[3] Jianbo Xu, M.S.,[4] Kathleen J. Chavanu, Pharm.D.,[4] William F. Waverczak, M.S.,[4] Robert Dubiel, Pharm.D.[4]; (1) The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, OH; (2) University of Alabama at Birmingham School of Medicine, Birmingham, AL; (3) Oklahoma Cardiovascular and Hypertension Center and the University of Oklahoma School of Medicine, Oklahoma City, OK; (4) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: Assess blood pressure (BP)-lowering efficacy/safety of an olmesartan medoxomil (OM)-based treatment algorithm.
METHODS: In a prespecified subgroup analysis of 146 patients with stage 2 hypertension (systolic blood pressure [SBP] of 160 mm Hg or more or diastolic blood pressure [DBP] of 100 mm Hg or more) from a double-blind, randomized, placebo-controlled study, patients were randomized to placebo (12 weeks) or OM 20 mg/day (3 weeks) after 3 weeks of placebo run-in. If BP remained 120/80 mm Hg or more, patients were uptitrated every 3 weeks as follows: OM 40 mg/day, OM/hydrochlorothiazide (HCTZ) 40/12.5 mg/day, OM/HCTZ 40/25 mg/day. If BP was less than 120/80 mm Hg at any visit during active treatment, patients continued on their current treatment. Primary end point: change from baseline in mean SBP at week 12. Secondary end points included change from baseline in mean DBP and percentage of patients achieving BP goals less than 140/90, less than 130/85, less than 130/80, and less than 120/80 mm Hg.
RESULTS: Mean baseline BP: 161/97 mm Hg (active treatment) and 162/97 mm Hg (placebo). OM 20 mg/day reduced mean SBP by 12 mm Hg (p<0.0001) with further dose-dependent decreases to a maximum of 25 mm Hg with OM/HCTZ 40/25 mg/day (p<0.0001) versus a maximum 6-mm Hg reduction with placebo (weeks 10–12; p=0.034). At study end, 69% (p<0.0001) of OM-treated patients achieved BPs less than 140/90 mm Hg (17% with placebo), and 15% (p<0.01) achieved less than 120/80 mm Hg (2% with placebo). Patients with baseline SBP of 160 mm Hg or more/DBP of 100 mm Hg or more (n=37) achieved a mean SBP reduction of 36 mm Hg on OM/HCTZ 40/25 mg/day (p<0.0001) (mean 0.1-mm Hg reduction with placebo). At all doses, the active treatment was well tolerated.
CONCLUSIONS: An OM-based regimen is safe and effective in controlling BP in patients with stage 2 hypertension.

		ΔSBP/ΔDBP,	Cumulative No. of Patients Achieving BP Goal, n (%)[b]		
	no.	mm Hg[a]	< 140/90	< 130/80	< 120/80
OM 20	81	-12*/-7*	10 (12)	1 (1)	-
Placebo	65	-3/-1	5 (8)	-	-
OM 40	75	-13*/-7*	24 (30)**	4 (5)	3 (4)
Placebo	56	-4**/-2	5 (8)	1 (2)	-
OM/HCTZ 40/12.5	68	-23*/-13*	44 (54)*	15 (19)***	7 (9)***
Placebo	45	-6**/-3***	8 (12)	3 (5)	-
OM/HCTZ 40/25	59	-25*/-14*	56 (69)*	26 (32)**	12 (15)*
Placebo	32	-6***/-2	11 (17)	4 (6)	1 (2)

[a]Mean change from baseline at study end (LOCF).
[b]Total number of patients in cohort used as denominator.
*p<0.0001; **p<0.01; ***p<0.05.

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107E. Long-Term Efficacy of a Combination of Amlodipine Besylate Plus Olmesartan Medoxomil: Treating Black Patients to Blood Pressure Goal. *Suzanne Oparil, M.D.,*[1] James Lee, Ph.D.,[2] Michael Melino, Ph.D.,[2] Reinilde Heyrman, M.D.[2]; (1) University of Alabama at Birmingham School of Medicine, Birmingham, AL; (2) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: Dual therapy with antihypertensive agents from different classes (e.g., calcium channel blocker plus angiotensin receptor blocker) may increase the number of black patients

achieving blood pressure goal. This study examined the long-term efficacy and safety of coadministration of amlodipine (AML) and olmesartan medoxomil (OM) in black and nonblack patients with hypertension.
METHODS: Patients with mild to severe hypertension who completed an 8-week, double-blind trial of AML 5–10 mg/day and OM 10–40 mg/day alone or in combination entered a 44-week open-label treatment period to assess the long-term efficacy and tolerability of AML+OM (n=1684). Initial therapy was AML+OM 5 + 40 mg/day. After 2 weeks, patients not achieving recommended blood pressure goal (less than 140/90 mm Hg or less than 130/80 mm Hg if diabetic) were titrated to AML+OM 10 + 40 mg/day. If required, hydrochlorothiazide (HCTZ) 12.5 mg/day, and then 25 mg/day, was added.
RESULTS: Mean blood pressure for black patients (n=413) decreased from 163.3/102.2 mm Hg at baseline to 132.6/83.5 mm Hg at week 52. Mean blood pressure for nonblack patients (n=1271) decreased from 163.7/101.3 mm Hg at baseline to 130.7/81.3 mm Hg at week 52. By week 52, the recommended blood pressure goal (less than 140/90 mm Hg or less than 130/80 mm Hg if diabetic) was achieved in 66.7% of black (56 of 84, mean blood pressure 132.8/84.0 mm Hg) and 82.5% of nonblack (364 of 441, mean blood pressure 126.7/80.4 mm Hg) patients receiving AML+OM 5 + 40 mg/day; 73.3% of black (66 of 90, mean blood pressure 130.6/83.4 mm Hg) and 69.8% of nonblack (201 of 288, mean blood pressure 131.1/82.0 mm Hg) patients receiving AML+OM 10 + 40 mg/day; 72.0% of black (59 of 82, mean blood pressure 129.6/82.8 mm Hg) and 64.4% of nonblack (132 of 205, mean blood pressure 131.2/80.3 mm Hg) patients receiving AML+OM+HCTZ 10 + 40 + 12.5 mg/day; and 49.7% of black (73 of 147, mean blood pressure 135.9/83.7 mm Hg) and 44.5% of nonblack (121 of 272, mean blood pressure 137.3/83.3 mm Hg) patients receiving AML+OM+HCTZ 10 + 40 + 25 mg/day.
CONCLUSIONS: AML+OM±HCTZ therapy was effective in reducing blood pressure, enabling most black and nonblack patients to achieve blood pressure goals.
Published in J Clin Hypertens (Greenwich) 2008;10(suppl 10):A29.

108E. The Long-Term Effect of a Combination of Amlodipine Besylate Plus Olmesartan Medoxomil Therapy on Achieving Blood Pressure Goals in Patients with Diabetes. *George Bakris, M.D.,*[1] Sulekha Karki, BAMS,[2] James Lee, Ph.D.,[2] Reinilde Heyrman, M.D.[2]; (1) University of Chicago School of Medicine, Chicago, IL; (2) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: Guidelines recommend a lower blood pressure goal (less than 130/80 mm Hg) for patients with diabetes, who often need more aggressive blood pressure lowering than patients without diabetes to reach goal. This study examined the efficacy of coadministration of amlodipine besylate and olmesartan medoxomil (OM) in patients with and without diabetes.
METHODS: Patients with mild to severe hypertension who completed an 8-week, double-blind trial of amlodipine (AML) 5–10 mg/day and OM 10–40 mg/day alone or in combination entered a 44-week open-label treatment period to assess the long-term efficacy and tolerability of AML+OM (n=1684). Initial therapy was AML+OM 5 + 40 mg/day. After 2 weeks, patients not achieving the recommended blood pressure goal (less than 140/90 or less than 130/80 mm Hg if diabetic) were titrated to AML+OM 10 + 40 mg/day. If required, hydrochlorothiazide (HCTZ) 12.5 mg/day, and then 25 mg/day, was added.
RESULTS: Mean blood pressure for patients with diabetes (n=228) decreased from 168.2/100.9 mm Hg at baseline to 134.0/81.0 mm Hg at week 52. Mean blood pressure for nondiabetic patients (n=1456) decreased from 162.8/101.6 mm Hg at baseline to 130.7/82.0 mm Hg at week 52. By week 52, the recommended blood pressure goal (less than 140/90 mm Hg or less than 130/80 mm Hg if diabetic) was achieved in 36.1% of patients with diabetes (13 of 36, mean blood pressure 130.7/80.2 mm Hg) and 83.2% of nondiabetic patients (407 of 489, mean blood pressure 127.4/81.1 mm Hg) receiving AML+OM 5 + 40 mg/day; 20.0% of patients with diabetes (6 of 30, mean blood pressure 132.8/82.2 mm Hg) and 75.0% of nondiabetic patients (261 of 348, mean blood pressure 130.8/82.4 mm Hg) receiving AML+OM 10 + 40 mg/day; 34.1% of patients with diabetes (15 of 44, mean blood pressure 132.1/79.3 mm Hg) and 72.4% of nondiabetic patients (176 of 243, mean blood pressure 130.5/81.3 mm Hg) receiving AML+OM+HCTZ 10 + 40 + 12.5 mg/day; and 21.1% of patients with diabetes (23 of 109, mean blood pressure 136.8/81.9 mm Hg) and 55.2% of nondiabetic patients (171 of 310, mean blood pressure 136.8/84.0 mm Hg) receiving AML+OM+HCTZ 10 + 40 + 25 mg/day.
CONCLUSIONS: Despite availability of up-titration and larger decreases in blood pressure from baseline, fewer patients with diabetes achieved the more stringent blood pressure goal of less than 130/80 mm Hg.
Published in J Clin Hypertens (Greenwich) 2008;10(suppl):A10.

109E. Diurnally Adjusted Trough:Peak Analysis of Diastolic Blood Pressure for a Combination of Amlodipine Besylate and Olmesartan Medoxomil. *Shashank Rohatagi, Ph.D.,*[1] Reinilde Heyrman, M.D.,[1] Antonia Wang, Ph.D.,[1] Timothy Carrothers, Sc.D.[2]; (1) Daiichi Sankyo, Inc., Parsippany, NJ; (2) Pharsight Corporation, Mountain View, CA
PURPOSE: Sufficient blood pressure control during the entire 24-hour period is critical to antihypertensive therapy, but excessive pharmacological effects at peak should be avoided. Trough-to-peak ratios are therefore reported because they provide insight into how well blood pressure is controlled during the entire dosing interval.
METHODS: A randomized, double-blind, placebo-controlled factorial-design study was conducted in patients with hypertension to determine if amlodipine (AML) 5–10 mg/day plus OM 10–40 mg/day (12 treatment arms) for 8 weeks had significant efficacy benefits versus monotherapy components. Seated diastolic blood pressure measurements were performed at baseline and three times at steady state (predose, 0.5–2 hours postdose, and 4–10 hours postdose) for 546 subjects in the pharmacokinetic study subset. Diastolic blood pressure was modeled as $DBP_{ij} = baseline_i + diurnal_t + placebo + drug\ effect_i + variation_{ij}$. $Diurnal_t = \sum_i \{amplitude_i \cdot \cos[(t \cdot i \cdot 2 \cdot \pi/24) + phase\ shift_i]\}$, where t is time of day in hours, and $i = 1, 2, \ldots$ to the extent supported by the data. Diurnal models reported in the scientific literature were used to adjust diastolic blood pressure measurements for time of day because diurnal changes may confound the calculation of trough-to-peak ratios. In the primary analysis, a single "typical" pattern with blood pressure lower at night and higher in the day was used.
RESULTS: Mean trough-to-peak ratios for each treatment, corrected for time of day and placebo, were as follows: AML 5 mg/day, 0.76; AML 10 mg/day, 0.77; OM 10 mg/day, 0.72; OM 20 mg/day, 0.81; OM 40 mg, 0.80; AML+OM 5 + 10 mg/day, 0.76; AML+OM 10 + 10 mg/day, 0.75; AML+OM 5 + 20 mg/day, 0.75; AML+OM 10 + 20 mg/day, 0.76; AML+OM 5 + 40 mg/day, 0.76; and AML+OM 10 + 40 mg/day, 0.74. When corrected for time of day and placebo, the diastolic blood pressure trough-to-peak ratio remained constant across treatment groups. Because the diurnal patterns of systolic blood pressure and diastolic blood pressure are generally parallel for an individual subject, these results are also applicable to systolic blood pressure.
CONCLUSIONS: Reductions in diastolic blood pressure and systolic blood pressure are smooth and constant across clinically relevant doses of AML, OM, and AML+OM.
Published in J Clin Hypertens (Greenwich) 2008;10(suppl):A32.

In Vitro Testing of Novel Anticancer Agents

110E. Targeting Ras with False Prenyl Analogs. *Bojana Stevich, Pharm.D., M.S.,*[1] Cynthia Mattingly, B.S.,[1] David L. DeRemer, Pharm.D.,[2] Peter Spielmann, Ph.D.,[1] Val Adams, Pharm.D.[1]; (1) University of Kentucky, Lexington, KY; (2) Medical College of Georgia, Augusta, GA
PURPOSE: Ras is an integral protein to signal transduction pathway, and it is mutated in about 30% of cancer cells. Ras needs to be prenylated to become active. In this study, we screened unique false prenyl analogs to identify a lead anticancer compound. We performed additional studies to confirm the designed mechanism of action and activity in combination with other chemotherapy agents.

METHODS: Compounds were screened for cytotoxic activity in MDA-MB-231 (wild-type Ras, epidermal growth factor receptor overexpression), H460 (K-ras oncogene), and A549 (K-ras oncogene) cell lines. Concurrent exposures to nontoxic concentrations of lovastatin or escalating concentrations of paclitaxel were performed. All cytotoxic assays exposed cells for 48 hours, and cells were quantified with an SRB (sulforhodamine B) assay. Synergy was calculated with the Chou method. Western blots were performed using antibodies against A549 cell lines to determine if the proposed mechanism of action was trough inhibition of the mitogen-activated protein kinase (MAPK) pathway.
RESULTS: Two lead compounds (15-18 and 119-3) were identified. In H460s (human non-small cell lung carcinoma), the GI50 was 10 ± 1 mM for the 15-18 compound and 24.4 ± 4.9 mM for the 119-3 compound. Lovastatin sensitized cells by lowering the GI50 by 15% and 19%, respectively. Western blot analysis showed that the proposed mechanism of action of false prenyl analogs could be caused by inhibition of the MAPK pathway. At most concentrations tested, paclitaxel was synergistic with the lead compounds.
CONCLUSIONS: The lead false prenyl analogs (15-18 and 119-3) are modestly active against different cancer cell lines. Lovastatin sensitized the cells to the lead compounds, supporting their activity as false prenyl inhibitors. One of the proposed mechanisms of action of false prenyl analogs is through inhibition of the MAPK pathway. There is synergy between false prenyl analogs and paclitaxel.
Presented at Hematology/Oncology Pharmacists Association Annual Meeting, Anaheim, CA, June 18–21, 2008.

Infectious Diseases

111. Impact of Drug Allergy Label on a Patient's Clinical Course. *Lisa Charneski, Pharm.D., BCPS*; University of Maryland School of Pharmacy, Rockville, MD

PURPOSE: To assess whether hospitalized patients carrying a label of β-lactam "allergy" have worse clinical outcomes compared with patients who do not have this label.
METHODS: The pharmacy system was used to generate a daily report showing all antibiotic orders for patients separated by patients classified as β-lactam allergic and nonallergic. Eight weeks of reports were analyzed for the antimicrobials ordered, the number of antimicrobials ordered per patient, the number of hospital days, the number of readmissions within 6 weeks of discharge, and the number of patient deaths.
RESULTS: Five hundred sixty-three patients were prescribed antibiotics during the study period. Of these patients, 150 were labeled b-lactam allergic (26.64%). Number of days in the hospital was 12.49 ± 11.90 for the no-allergy group and 13.23 ± 12.19 for the allergy group (p=0.58). Percentages of readmissions within 6 weeks of discharge were 0.06 ± 0.26 for the no-allergy group and 0.09 ± 0.31 for the allergy group (p=0.2). Number of antimicrobials ordered per patient was 1.71 ± 1.08 drugs for the no-allergy group and 1.84 ± 1.50 drugs for the allergy group (p=0.31). In the no-allergy group, there were 17 deaths (4.1%) per 412 patients, and in the allergy group, there were 11 deaths (7.3%) per 150 patients (p=0.12). There was an obvious difference in the drugs prescribed for patients with allergy label versus those without (most notably clindamycin, cephalosporins, fluoroquinolones, and vancomycin).
CONCLUSIONS: The statistical analysis failed to show significance in the parameters examined. All parameters examined trended toward better outcomes for the nonallergic patients. The study limitation is that a small number of patients were monitored for only 8 weeks.

112. Discordant Minimum Inhibitory Concentrations (MICs) from VITEK2 and E-tests for Vancomycin Against Methicillin-Resistant *Staphylococcus aureus* (MRSA). *Scott J. Bergman, Pharm.D., BCPS,*[1] Lauren Moja, Pharm.D.,[2] Cheryl Drake, B.S.,[3] Joan Barenfanger, M.D., ABMM[3]; (1) Southern Illinois University Edwardsville, Box 19636, Springfield, IL; (2) Butler University, Springfield, IL; (3) Memorial Medical Center, Springfield, IL

PURPOSE: To evaluate whether there is a difference in vancomycin minimum inhibitory concentrations (MICs) for the same methicillin-resistant *Staphylococcus aureus* (MRSA) isolates when tested by two different methods. The Clinical Laboratory Standards Institute and, recently, the U.S. Food and Drug Administration both lowered the vancomycin MIC susceptibility breakpoint for MRSA to 2 µg/mL or less. Even with this new range, large decreases in clinical success rates have been observed with vancomycin treatment when MICs increase from 1 to 2 µg/mL.
METHODS: Forty-five unique MRSA samples were randomly selected from clinical blood cultures isolated during 2007. Vancomycin MICs were determined by automated microdilution using VITEK2 (bioMérieux, Inc., Durham, NC) and manual E-tests (AB Biodisk, Solna, Sweden). Results were read by two trained investigators. Any discrepancy was resolved by a third investigator.
RESULTS: All MRSA isolates were susceptible to vancomycin by both tests, but MICs varied by method (Table). For susceptible isolates, the VITEK2 AST-GP66 card reports vancomycin MICs for MRSA as either 1 or less or 2 µg/mL. Susceptible E-test results can be observed as 0.5, 0.75, 1, 1.5, and 2 µg/mL. Significantly more MICs greater than 1 µg/mL were detected by E-test compared with the results reported by VITEK2 (28.9% vs. 4.4%, p<0.001).
CONCLUSIONS: Differences exist between vancomycin MICs reported by VITEK2 and E-tests for MRSA. Clinicians should be aware of the method used to perform vancomycin MICs before making clinical decisions based on the test or comparing outcomes from published literature. To determine which of these two methods is more accurate, the results should be compared with manual broth dilution tests, which are considered the most reliable in vitro assessment of MIC.

MIC	VITEK2	E-test
(µg/mL)	n (%)	n (%)
0.5		1 (2.2)
0.75		4 (8.9)
1.0		27 (60)
≤ 1.0	43 (95.6)	
1.5		11 (24.5)
2.0	2 (4.4)	2 (4.4)

113. Epidemiology, Risk Factors, and Treatment of Candidemia at a Large Academic Medical Center: A Retrospective Study. *Brett H. Heintz, Pharm.D., BCPS*, Joanne C. Lee, Pharm.D., Siyuan Liu, Pharm.D., Judy Y. Kwak, Pharm.D.; University of California, Davis Medical Center, Sacramento, CA

PURPOSE: The primary objective of this study was to evaluate the epidemiology of *Candida* species, associated risk factors, and treatment of candidemia in critically ill and noncritically ill patients at the University of California Davis Medical Center (UCDMC). A secondary objective was to evaluate compliance with current candidemia treatment guidelines at UCDMC.
METHODS: We performed a retrospective chart review of all adult patients (n=112) who developed candidemia between August 2005 and August 2007.
RESULTS: *Candida albicans* was responsible for 46.8% of infections, whereas non-albicans *Candida* accounted for 53.2% of cases (*Candida glabrata* 19.8%, *Candida parapsilosis* 19.0%, and *Candida tropicalis* 7.1%). No significant difference in *Candida* species distribution was found when intensive care units (ICUs) were compared with non-ICU patient care areas. Fluconazole exposure was a significant risk factor for selection of non–*C. albicans* candidemia (p<0.005). All-cause mortality was significantly higher in patients in ICUs (42.9% vs. 13.2% in non-ICU patients), but no difference was found when *C. albicans* and non–*C. albicans* species were compared. Overall compliance with current UCDMC and national treatment guidelines was poor, including initial empiric therapy (antifungal selection and dosing), use of repeat blood cultures to guide therapy, and duration of treatment.
CONCLUSIONS: Non-*C. albicans* species accounted for 53.2% of candidemia cases, supporting the changing epidemiology of *Candida* and emergence of non-*C. albicans* species. Other than previous fluconazole exposure, there were no major differences in risk factors between *C. albicans* and non-*C. albicans* candidemia. Unexpectedly,

ICU stay showed no correlation to non-*C. albicans* candidemia. Adherence to current guidelines for the treatment of candidemia was poor at our institution. Revisions of current candidemia treatment guidelines at UCDMC are being developed with the aim of improving patient outcomes through optimal antifungal selection, dosing, and duration of therapy while decreasing the risk of resistance, potential adverse events, and overall costs.

114. Modeling Potential Spread Patterns for Shipboard Acute Gastroenteritis (AGE). *Michael D. Schwartz, Pharm.D.*; South University, Savannah, GA

PURPOSE: Model shipboard spread patterns of Norovirus acute gastroenteritis (AGE) using ultraviolet (UV)-fluorescent simulant powder.

BACKGROUND: Since 2000, reports of shipboard AGE have increased significantly. Highly publicized outbreaks have affected cruise ships, liners, and warships of various sizes. Much of AGE (acute nausea, vomiting, and diarrhea) may be attributed to Norovirus, one of the most prevalent viruses to infect humans outside the "common cold." The Centers for Disease Control and Prevention estimates Noroviruses cause more than 23 million cases of AGE in the United States annually. Spread is by the fecal-oral route (food/drink contamination or contact with contaminated inanimate objects), incubation ranges from 24 to 48 hours, and symptoms usually resolve in 1–3 days. Outbreaks have persisted on subsequent sailings in spite of attempts at extensive disinfection. Numerous literature sources report outbreaks and document methods to reduce outbreaks (e.g., vigilant handwashing, sanitizer gel use, surface cleaning); however, none describe modeling of potential spread patterns and associated timeframes.

METHODS: This at-sea study attempted to model potential close-quarters spread patterns onboard a 378′ U.S. Coast Guard Cutter. Appropriate military chain of command approval was preobtained. GloGerm UV-fluorescent nontoxic powder was placed on high-use surfaces (within two adjacent compartments): specifically, a hatch handle, doorknob, and ladder rail. This simulated a single source transferring the agent to onboard living areas. UV light was used to survey other compartments for evidence of dissemination. Timing of positive findings was also tracked.

RESULTS: Rapid simulant spread occurred. UV powder was found in four additional crew compartments only 10 minutes after application. Overall, 12 crew compartments on three of five decks (along an 80′ horizontal spread distance) were affected within 8 hours.

CONCLUSIONS: Using a nontoxic powder as a marker, this model of viral AGE showed rapid hand-to-object spread. Travelers should be advised about risks and prevention strategies for Norovirus.

115. Rifaximin Use in *Clostridium difficile* Infection (CDI). *Jamie M. Wilkerson, Pharm.D.*,[1] Paul Juang, Pharm.D.[2]; (1) Missouri Baptist Medical Center, St. Louis, MO; (2) St. Louis College of Pharmacy, St. Louis, MO

PURPOSE: Rifaximin has been shown to inhibit *Clostridium difficile* growth in vitro and was recently found to be effective in preventing recurrent *C. difficile* infection (CDI) in cases of vancomycin failure. The objectives of this study were to compare the use of rifaximin versus standard therapy in resolving CDI and preventing CDI recurrence.

METHODS: A retrospective data collection and analysis was conducted using an electronic data repository to identify patients 18 years and older with CDI determined by positive *C. difficile* toxin A test and/or pseudomembrane coli. Patients who received rifaximin for non–*C. difficile* indications were excluded. For primary outcomes, differences in mortality and colectomy between patients with CDI treated with rifaximin and patients treated with standard therapy were determined. For secondary outcomes, differences in hospital length of stay, *C. difficile*-directed antibiotic therapy duration, and discharge disposition between patients with CDI treated with rifaximin and patients treated with standard therapy were examined. In addition, the clinical use of rifaximin as primary or secondary therapy in the treatment of CDI at our institution was assessed. Fisher's exact test, the χ^2 test, and the Student's *t*-test were used as appropriate.

RESULTS: During the study period, 32 patients at our institution received rifaximin therapy for CDI. No significant differences in outcomes between groups were determined. On subgroup analysis of patients presenting with an initial CDI episode, no significant differences in outcomes between groups were detected. A trend toward significance with regard to duration of antibiotic therapy in favor of standard therapy was observed on further analysis of this subgroup (p=0.09).

CONCLUSIONS: In what is, to our knowledge, the largest analysis of rifaximin use for CDI, rifaximin was not associated with an improvement in outcomes versus standard therapy.

116E. Analysis of Appropriate Initial Antimicrobial Therapy in Community and Healthcare-Associated Pneumonia and Blood-Stream Infections. *Shawn J. Kram, Pharm.D.*,[1] Garrett E. Schramm, Pharm.D.,[1] Richard A. Fricker, B.A.,[1] Bekele Afessa, M.D., FCCP[2]; (1) Mayo Clinic, Rochester, Rochester, MN; (2) Division of Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine, Rochester, MN

PURPOSE: Timely and guideline-directed antimicrobial therapy has been shown to decrease mortality; however, the consequences of inappropriate therapy may force clinicians to overlook patient risk stratification and use broad-spectrum antimicrobials. The objective of this study was to evaluate the timeliness and appropriateness of evidence-based therapy for community- and health care-acquired pneumonia and bloodstream infections identified within 24 hours of admission.

METHODS: Retrospective study of patients admitted to Mayo Clinic (Rochester, MN) with either a community- or health care–acquired pneumonia or bloodstream infection from January 1, 2006, to December 31, 2006. Evidence-based therapy was defined using published guidelines and current literature for each infection type. Timeliness was defined as initiation of therapy within 6 hours of admission.

RESULTS: Eighty-four cases of pneumonia were identified and evaluated for timely, guideline-directed therapy. A significant difference between appropriate and inappropriate pneumonia therapy was found (17.9% vs. 82.1%, p<0.0001). Eighty-five bloodstream infections were identified and evaluated for timely, evidence-based therapy. Appropriate therapy occurred in 28.2% of the population, whereas inappropriate therapy occurred in 71.8% (p<0.0001). There was a significant correlation of receiving appropriate and timely evidence-based therapy with receiving appropriate and timely pathogen-specific therapy (p<0.0001).

CONCLUSIONS: The results of this study stress the importance of patient risk stratification and use of evidence-based therapy to provide pathogen-specific treatment.

Presented at the 34th Annual Midwest Pharmacy Residents Conference, Omaha, NE, May 8–10, 2008.

117E. Population Pharmacokinetics (PK) Analysis of Ceftaroline (CPT) in Volunteers and Patients with Complicated Skin and Skin Structure Infection (cSSSI). *Yigong Ge, M.D.*,[1] Sam Liao, Ph.D.,[2] George H. Talbot, M.D.[1]; (1) Cerexa, Inc., Alameda, CA; (2) PharMax Research, Inc., Somerset, NJ

PURPOSE: Ceftaroline (CPT) is a broad-spectrum cephalosporin exhibiting bactericidal activity against gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *Streptococcus pneumoniae* (MDRSP), as well as common gram-negative pathogens. CPT is currently in phase III development. This analysis was performed to (1) assess various baseline covariate factors that might alter CPT drug exposure, and thereby efficacy and safety, and (2) establish a population pharmacokinetics (PK) database to explore the probability of PK/pharmacodynamics target attainment by simulation.

METHODS: The population analysis was performed with PK data collected from 127 phase 1 and 2 study subjects (54 healthy, 23 renally impaired, and 50 with complicated skin and skin structure infection). Data were analyzed using the NONMEM program. A model was developed to identify covariates with a significant effect on CPT PK parameters.

RESULTS: The data fit well into a two-compartment PK model with zero-order input and first-order elimination. Creatinine clearance

was the primary factor predicting the clearance of CPT. The model-predicted PK profile closely resembled the observed profile of CPT. Validation and performance checks demonstrated the robustness of this population PK model to predict CPT concentration-time profiles in subjects with different levels of renal function. The key population PK parameters for CPT are summarized in the Table.

Parameters	Mean[a]	BSV (%)[b]
CLr (L/hour)	03.76 (9)	21 (14)
CLm (L/hour)	04.47 (7)	—
V1 (L)	17.3 (3)	26 (16)
V2 (L)	04.89 (5)	40 (19)
Q (L/hour)	01.83 (6)	58 (25)

[a]Expressed as coefficient of variation (% CV).
[b]BSV = between-subject variability calculated as variance (% CV).
CL_m = nonrenal clearance; CL_r = renal clearance; Q = intercompartmental flow rate between central (V1) and peripheral (V2) compartments.

CONCLUSIONS: A population PK analysis based on combined phase 1 and 2 data provided valuable information for use in Monte Carlo simulation for optimal dose selection as well as dosage adjustment recommendations.
Presented at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 17–20, 2007.

118E. Activity of Ceftaroline Against *Streptococcus pneumoniae* Bloodstream Isolates from Community-Acquired Pneumonia (CAP) in North America. *Yigong Ge, M.D.,*[1] J. Curry,[2] I. Morrissey,[2] R. Janes[2]; (1) Cerexa, Inc., Alameda, CA; (2) Quotient Bioresearch Limited, Microbiology, London, UK

PURPOSE: Ceftaroline (CPT) is a novel, parenteral, broad-spectrum cephalosporin exhibiting bactericidal activity against gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *Streptococcus pneumoniae* (MDRSP), as well as common gram-negative pathogens. CPT is currently in phase 3 development. We report the activity of CPT against 61 clinical isolates of *S. pneumoniae* collected between 2004 and 2006 from hospitalized patients in North America with defined community-acquired pneumonia (CAP).
METHODS: The activity of CPT was compared with that of eight other antimicrobial agents, and minimum inhibitory concentrations (MICs) were obtained using Clinical and Laboratory Standards Institute broth microdilution methods.
RESULTS: CPT was very active against all *S. pneumoniae* isolates tested. In both the United States and Canada, CPT consistently showed the lowest MICs versus β-lactam comparators, levofloxacin, and linezolid and comparable MICs versus tigecycline.

	MIC50/90 (µg/mL)				
S. pneumoniae (no. of isolates)	Ceftaroline	Amoxicillin-clavulanate	Ceftriaxone	Levofloxacin	Linezolid
Canada (10)	≤ 0.008/0.015	≤ 0.015/0.03	0.03/0.03	0.5/1	0.5/0.5
United States (51)	0.015/0.12	0.06/2	0.06/1	1/1	1/2
Total-North America (61)	≤ 0.008/0.12	0.03/2	0.03/1	1/1	1/2

CONCLUSIONS: These data extend and confirm previous findings on the activity of CPT against *S. pneumoniae*, a major respiratory pathogen. CPT has potential for treatment of CAP and other serious respiratory tract infections caused by *S. pneumoniae*.
Presented at the International Conference of the American Thoracic Society, Toronto, ON, Canada, May 16–21, 2008.

119. Molecular Mechanisms of Increased Expression of CDR1, PDH1, and SNQ2 in Fluconazole Resistant Clinical Isolates of *Candida glabrata*. *Kelly E. Caudle, Pharm.D.,*[1] Katherine S. Barker, Ph.D.,[1] Nathan P. Wiederhold, Pharm.D.,[2] P. David Rogers, Pharm.D., Ph.D.[1]; (1) University of Tennessee, Memphis, TN; (2) The University of Texas at Austin College of Pharmacy and The University of Texas Health Science Center at San Antonio, San Antonio, TX

PURPOSE: Recent reports have described the development of azole resistance in *Candida glabrata* isolated from immunocompromised patients during therapy. This has been shown to be caused by up-regulation of the multidrug transporter genes *CDR1*, *PDH1,* and *SNQ2*. We have shown that gain-of-function mutations in the transcriptional regulator gene *PDR1* result in the up-regulation of these transporters and high-level azole resistance.
METHODS: We sequenced the *PDR1* gene in four azole-susceptible and -resistant matched clinical isolate sets to identify novel gain-of-function mutations. Matched clinical isolates (and their respective susceptibilities to fluconazole) used in this study included 62-16 (minimum inhibitory concentration [MIC] = 1 µg/mL) and 62-17 (MIC more than 256 µg/mL); R-3562 (MIC = 16 µg/mL) and 03-2694 (MIC more than 64 µg/mL); 6856 (MIC = 32 µg/mL) and 6955 (MIC = 256 µg/mL); and SM1 (MIC = 8 µg/mL), SM2 (MIC = 256 µg/mL) and SM3 (MIC more than 64 µg/mL). The *PDR1* genes from isolates SM1 and SM3 were expressed in *C. glabrata* strain 66032D*pdr1,* and fluconazole resistance was measured. Expression of *PDR1* target transporter genes was measured by real-time RT-PCR (reverse transcriptase-polymerase chain reaction).
RESULTS: We identified four novel *PDR1* mutations resulting in amino acid substitutions in three sets of clinical isolates. The *PDR1* gene of one isolate (03-2694) was identical to its susceptible parent. Introduction of *PDR1* from SM3 into 66032D*pdr1* conferred fluconazole resistance and increased expression of *CDR1*, *PDH1*, and *SNQ2* compared with SM1.
CONCLUSIONS: Novel gain-of-function mutations in *PDR1* result in up-regulation of *CDR1*, *PDH1*, and *SNQ2*, as well as fluconazole resistance in *C. glabrata*. The lack of a mutation in *PDR1* for one of these matched isolate sets points to a yet-to-be-discovered mechanism of *CDR1*, *PDH1*, and *SNQ2*-mediated fluconazole resistance in this pathogen. Elucidation of the molecular basis of azole resistance in *C. glabrata* will facilitate the development of pharmacological strategies to circumvent this problem and to enhance the activity of this class of antifungal agents.

120. CAS5 Is Required for Fluconazole Tolerance in *Candida albicans*. Nathan P. Wiederhold, Pharm.D.,[1] Katherine S. Barker, Ph.D.,[2] *Jonathan Bain, B.S.,*[2] Vincent M. Bruno, Ph.D.,[3] Aaron P. Mitchell, Ph.D.,[3] P. David Rogers, Pharm.D., Ph.D.[2]; (1) The University of Texas at Austin College of Pharmacy and The University of Texas Health Science Center at San Antonio, San Antonio, TX; (2) University of Tennessee, Memphis, TN; (3) Columbia University, New York, NY

PURPOSE: Fungi respond to stressful conditions by activating specific transcriptional activation programs. To identify pathways activated by *Candida albicans* in response to azole antifungal stress, we examined changes in the gene expression profile of this pathogen on fluconazole exposure. Among the genes encoding transcription factors that were up-regulated was the gene encoding the transcriptional regulator of the cell wall damage response Cas5p. We hypothesized that Cas5p was required for fluconazole tolerance in *C. albicans*.
METHODS: *C. albicans* strain SC5314 was exposed to fluconazole at 4 µg/mL for 1, 6, and 24 hours. RNA was isolated, and messenger RNA abundance was measured by microarray (n=2) or real-time RT-PCR (reverse transcriptase-polymerase chain reaction) (n=3). The minimum inhibitory concentrations (MICs) and minimum fungicidal concentrations (MFCs) of *cas5*Δ/*cas5*Δ strain 1186, its complemented derivative 1190, and their parent strain BWP17 were determined by Clinical Laboratory Standards Institute microdilution and E-test. These strains were also subjected to time-kill analysis.
RESULTS: *CAS5* expression increased by 8.4-fold in response to 24-hour fluconazole exposure, with no increased expression at 1 or 6 hours. Disruption of *CAS5* had no influence on fluconazole MICs (0.125 vs. 0.25 mg/mL). However, the MFC for strain 1186 was markedly lower (4 µg/mL) compared with the parent and complemented strains (64 µg/mL). A clear zone of inhibition was observed for strain 1186 by E-test in contrast to reduced growth for strains BWP17 and 1190. The E-max value (log CFU/mL change at 24 hours from starting the inoculum by time-kill analysis) at 64 µg/mL was +1.22 for strain BWP17, -0.44 for strain 1186, and +1.02 for strain 1190.

CONCLUSIONS: Our findings demonstrate a direct role for Cas5p as a major transcriptional regulator of azole tolerance in *C. albicans*. Further study is needed to identify the Cas5p target genes directly responsible for this process, which may represent potential targets for improving the activity of the azole antifungals.

121. Daptomycin Use in Patients with Sepsis. *Keith J. Christensen, Pharm.D.,*[1] Scott A. McConnell, Pharm.D.,[2] Jack E. Brown, Pharm.D.,[2] Kenneth C. Lamp, Pharm.D.[2]; (1) Creighton University School of Pharmacy & Health Professions, Omaha, NE; (2) Cubist Pharmaceuticals, Lexington, MA

PURPOSE: Use data from a registry to elucidate the clinical experience of septic patients treated with daptomycin (DAP).

METHODS: CORE (2005–2006 program years) is a retrospective postmarketing study of DAP experience. Patients with sepsis who reported as an underlying disease process during DAP treatment and evaluable for outcome (cure, improvement, or failure) were selected. Sepsis was defined by the investigator based on data from the patients' records. Outcome was determined at the end of DAP therapy using protocol-defined definitions; success was defined as cure or improvement.

RESULTS: Of 171 patients identified with sepsis, 124 (73%) were evaluable for outcome. Patient characteristics were as follows: 32% older than 66 years, 38% with a creatinine clearance less than 30 mL/minute, and 24% on dialysis. Sixty-two percent had bacteremia, and 23% had complicated skin and skin structure infection. Commonly seen pathogens included *Staphylococcus aureus* (49%) and *S. enterococci* (34%). Eighty-two percent received prior antibiotic therapy—most commonly vancomycin (72%) or linezolid (16%). Forty-four percent of these patients were started on DAP because of treatment failure and/or resistance. The median (min, max) initial DAP dose was 5.5 mg/kg (2.9, 10) with a median (min, max) duration of 12 days (1, 79). The overall success rate was 86% (47% cure; 39% improved); the subset with methicillin-resistant *S. aureus* had a 78% success rate. Twelve adverse events (AEs) possibly related to DAP were reported in eight patients (6%); four of these AEs in two patients were assessed as serious. None of the 21 deaths (17%) were reported as possibly related to daptomycin.

CONCLUSIONS: DAP was associated with a successful clinical outcome in 86% of patients; almost half had previously experienced either treatment failure with DAP or resistance to a prior antibiotic. These data provide preliminary results on the use of DAP in this complicated patient population. Controlled studies are needed to best evaluate DAP for treatment of patients with sepsis.

122. Plasma Voriconazole Levels in Pediatric Patients and Potential Application to Therapeutic Drug Monitoring. *Maria E. Ceja, Pharm.D.*, Katherine Knapp, M.D., Jennifer L. Pauley, Pharm.D., Julie Richardson, Pharm.D., Kristine Crews, Pharm.D., BCPS, John C. Panetta, Ph.D., Patricia Flynn, M.D., M.S., James M. Hoffman, Pharm.D., M.S., BCPS; St. Jude Children's Research Hospital, Memphis, TN

PURPOSE: Therapeutic drug monitoring (TDM) may be useful to optimize voriconazole therapy, but no consensus exists regarding the therapeutic range. Data on voriconazole pharmacokinetics and TDM in children are limited. We evaluated the pharmacokinetics of voriconazole in patients with pediatric cancer and explored the potential application of voriconazole TDM.

METHODS: Plasma voriconazole levels, patient demographics, indication, and other data were retrospectively collected from patients who received voriconazole between June 2004 and November 2007. Pharmacokinetic parameters, including clearance and area under the curve (AUC), were calculated for patients with the three data points available (trough, peak, and 6-hour postdose).

RESULTS: Plasma voriconazole levels (60 trough, 29 peak, 11 random, and 29 six-hour postdose samples; total 129) from 48 patients (3 months to 20 years) receiving voriconazole as either prophylaxis (n=29) or treatment (n=19) were evaluated. The median (range) trough level was 0.25 (less than 0.2–10.00) µg/mL. Median dosage was higher in patients receiving voriconazole for treatment of an infection (4.3 mg/kg, 1.6–13 mg/kg) vs. those receiving prophylaxis (3.8 mg/kg, 2.2–5.7 mg/kg; p=0.014). However, median trough level did not differ in treatment group (less than 0.2, less than 0.2–8.4 µg/mL) versus prophylaxis group (0.40, less than 0.2–10.00 µg/mL; p=0.19). When trough levels were stratified by age, the median trough level in patients younger than 6 years (less than 0.2 µg/mL, less than 0.2–10.00 µg/mL; n=34), was lower than in older patients (0.62 µg/mL, less than 0.2–8.4 n=26; p≤0.001). For patients receiving intravenous voriconazole in whom pharmacokinetic parameters were calculated (n=6), the median clearance was 0.18 L/hour/kg, and the AUC (0, 12) was 25.54 mg·hour/L, which is comparable with published values.

CONCLUSIONS: Voriconazole trough levels were often undetectable in this cohort of patients. Patients younger than 6 years demonstrated lower median trough levels and may require more frequent dosing of voriconazole. TDM may have a role in optimizing voriconazole therapy, particularly for patients younger than 6 years.

123. A Pilot Study Evaluating the Timing of Linezolid Initiation After Clinical Failure of Vancomycin in Methicillin-Resistant *Staphylococcus aureus* Infections. Monica Domadia, Pharm.D.,[1] *Lee H. Nguyen, Pharm.D.*[2]; (1) Loma Linda University Medical Center, Loma Linda, CA; (2) Loma Linda University, School of Pharmacy, Loma Linda, CA

PURPOSE: This study evaluated the incidence of vancomycin failure in patients with methicillin-resistant *Staphylococcus aureus* (MRSA) and the outcomes associated with the timing of linezolid initiation after 7 days or less or more than 7 days of vancomycin therapy.

METHODS: Data were extracted from the medical charts of 273 adult patients infected with MRSA between May 26, 2006, and October 1, 2007. Patients were grouped by timing of linezolid therapy: early initiation (EI, 7 days or less) or late initiation (LI, more than 7 days). Patient variables and outcomes(total length of stay [LOS] after isolation, response [RE], achieved clinical stability [AS], time to stability [TTS], and infection-related mortality) were compared between groups.

RESULTS: Vancomycin failed in 17 subjects; they were converted to linezolid. The median time from vancomycin failure to linezolid initiation was 9 days. EI (n=6) and LI (n=11) groups were comparable in age (EI: 77 vs. 52 years, p=NS), APACHE II score (12 vs. 18.5, p=NS), and corrected vancomycin trough (11.8 vs. 11.8 mg/dL, p=NS). Most infections (82% [14 of 17]) were pneumonia and bacteremia. EI of linezolid did not statistically improve patient outcomes: LOS (EI: 14 vs. LI: 29 days, median), RE (EI: 34% vs. LI: 91%), AS (EI: 50%, 3 of 6, vs. LI: 82%, 9 of 11), TTS (EI: 11 vs. LI: 11 days, median), and mortality (EI: 50%, 3 of 6, vs. LI: 0%, 0 of 11).

CONCLUSIONS: Preliminary data suggest that early initiation of linezolid does not improve outcomes. However, continued research with a larger sample size is needed to better delineate the groups and understand the risk factors for vancomycin failure.

124. Daptomycin Treatment of Urinary Tract Infections. Graeme Forrest, MBBS,[1] *Jason A. Crompton, Pharm.D.,*[2] Donald S. North, Pharm.D.,[2] Brian J. Donovan, Pharm.D.,[2] Kenneth C. Lamp, Pharm.D.[2]; (1) University of Maryland, Baltimore, MD; (2) Cubist Pharmaceuticals, Lexington, MA

PURPOSE: The objective of this analysis was to characterize the use of daptomycin (DAP) in patients with urinary tract infections (UTIs) with or without noncatheter-related bacteremia (NCRB).

METHODS: Data are collected through an ongoing registry to characterize patterns of DAP use. Patients with a diagnosis of UTI and a positive urine culture for a gram-positive pathogen from 2005 and 2006 were selected for this analysis. Patients with NCRB were only included if they had a positive blood culture with the same pathogen as the UTI. Only patients evaluable for outcome were included. Outcome was determined at the end of therapy as cure, improved, or failure.

RESULTS: Forty-eight (44%) of 108 patients with UTIs met the criteria for inclusion. Seventy-five percent were female patients, and 88% were in the hospital 48 hours before receiving DAP. Success rate (cure plus improved) was 90%. Ten patients (21%) also had NCRB. Prior antibiotic therapy was used in 79% of patients, and the

most common were vancomycin (40%) and linezolid (19%). Prior antibiotic therapy was discontinued in 42% of patients because of the isolation of a resistant pathogen and in 19% of patients because of failure. The most common pathogens cultured from urine were enterococci (79%, of which 74% were resistant to vancomycin). From the urine of 19% of the patients, *Staphylococcal aureus* was isolated, of which 77% was methicillin resistant. Two-thirds of patients with *S. aureus* had positive urine and blood cultures. The median (min, max) DAP dosage and duration of therapy were 4 mg/kg (2.3, 11.4) and 8 days (2, 44), respectively. Thirty-five percent of patients received a DAP dose of 6 mg/kg or greater, and 63% of patients received an antibiotic together with DAP.
CONCLUSIONS: DAP appears to be an effective treatment for UTI, including patients with NCRB. These data support the previously published findings of DAP efficacy in patients with complicated gram-positive UTI.

125E. Daptomycin for the Treatment of *Staphylococcus aureus* Bacteremia. *Kenneth C. Lamp, Pharm.D.*, Brian J. Donovan, Pharm.D.; Cubist Pharmaceuticals, Lexington, MA
PURPOSE: To examine the outcomes of patients with *Staphylococcus aureus* bacteremia (SAB) treated with daptomycin.
METHODS: Patients with SAB and evaluable for outcome (cure, improved, or failure) were identified in a registry, CORE, 2005 and 2006 program years. Outcome was assessed at the end of daptomycin therapy using protocol-defined criteria. Patients with blood cultures positive for any other pathogen or for endocarditis were excluded. Success was defined as cure or improved.
RESULTS: Two hundred thirty-eight SAB patients met the selection criteria; 179 (75%) were evaluable; and success was reported in 157 (88% overall; 89% methicillin-resistant *S. aureus* [MRSA], methicillin-sensitive *S. aureus* [MSSA], n=119; 85% MSSA or methicillin susceptibility unreported, n=60). Comorbidities included diabetes (37%) and sepsis (20%). Twenty-six percent received daptomycin in an intensive care unit. Thirty-five percent of patients had an initial creatinine clearance of less than 30 mL/minute, with 65% receiving dialysis. The most common concurrent infections were skin (21%) and osteomyelitis (11%). Antibiotics were given before daptomycin in 83% of patients, most commonly vancomycin (72%). The success rate of daptomycin was 88%, irrespective of prior vancomycin exposure. The most common reason for stopping prior antibiotic therapy was failure (31%). Concomitant antibiotics (one or more doses) were used in 57% of patients, most often rifampin (26%) and vancomycin (25%). The receipt of concomitant rifampin or vancomycin did not affect success (83% with and 89% without, p=0.3). The median final daptomycin dose and duration of therapy was 6 mg/kg (60% received 6 mg/kg or more) and 15 days (range 1–84), respectively. Eight adverse events in eight (4%) patients were possibly related to daptomycin; three met the regulatory criteria for seriousness. The mortality rate was 6% (n=11); no deaths were reported as being possibly related to daptomycin.
CONCLUSIONS: In this population, daptomycin was effective for SAB. No apparent difference in success rates was seen between patients with MRSA or MSSA infections. Previous treatment with vancomycin did not influence the outcome of patients, nor did concomitant use of the antibiotics rifampin or vancomycin.
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126. Antifungal Drug Costs and Utilization Following Implementation of a Posaconazole Prophylaxis Protocol in Patients with Acute Myelogenous Leukemia. *Carrie W. Nemerovski, Pharm.D.*, Emily R. Mackler, Pharm.D., BCOP, Daryl D. DePestel, Pharm.D., Curtis D. Collins, Pharm.D., James G. Stevenson, Pharm.D.; University of Michigan, Ann Arbor, MI
PURPOSE: The objective of this study was to determine how implementation of a posaconazole prophylaxis protocol in adult patients with acute myelogenous leukemia (AML) would affect the cost of antifungal drug therapy as well as the cost and use of other antimicrobial agents.
METHODS: Medical records of patients with AML who received induction or reinduction chemotherapy between December 2006 and March 2008 were reviewed retrospectively. Antifungal, antimicrobial, and pharmacy cost and use data were compared before and after implementation of a posaconazole prophylaxis protocol. Before the prophylaxis protocol, patients were empirically treated with antifungal agents for persistent febrile neutropenia.
RESULTS: A total of 59 patients were included. Twenty-six patients received posaconazole prophylaxis after implementation and were compared with 33 patients before implementation. Groups were similar in comorbidities, disease severity, and fungal infection risk. Average antifungal drug cost was $2479 ± $2120 in the posaconazole group compared with $3655 ± $4693 in the preposaconazole group (p=0.21). Antimicrobial and pharmacy costs were similar between groups. Empiric or treatment doses of antifungal agents were required in 46.2% of patients in the posaconazole group compared with 90.9% of patients in the pre-posaconazole group (p=0.0003). A total of 16 (61.5%) patients in the posaconazole group required a change in antifungal therapy after a median of 10.5 days; 50% of those were switched because of an adverse drug reaction or inability to tolerate oral intake, including medications.
CONCLUSIONS: Implementation of a posaconazole prophylaxis protocol did not alter antifungal drug costs, though a trend toward a reduction in all evaluated costs was observed. A significant number of patients required empiric or treatment doses of antifungal agents before implementation of the prophylaxis protocol. A majority of patients were unable to complete antifungal prophylaxis with posaconazole and required a change to an alternative antifungal agent.

127. Promoting Pneumococcal Immunization in Medical Inpatients Through Educational Efforts. *Rani P. Patel, Pharm.D.*, Roopali Sharma, Pharm.D.; State University of New York (SUNY) Health Sciences Center at Brooklyn's University Hospital of Brooklyn, Brooklyn, NY
PURPOSE: It is estimated that only 10–20% of those at risk of pneumococcal disease receive the vaccine. The current national vaccination goal is 90% by 2010. At the State University of New York (SUNY) Health Sciences Center, a policy has been in place to screen all inpatients for eligibility. Nevertheless, the number of patients receiving the vaccine is quite low. The aim of this study was to identify eligible individuals and increase the use rate of vaccination by providing education to patients.
METHODS: All patients admitted to SUNY Health Sciences Center who were eligible to receive the pneumococcal vaccine were included in this prospective study. Patients were identified by reviewing admissions lists from two medical floors. Both groups were offered the vaccine by the nurse. If a patient refused the vaccine in the study group, he/she was provided with education and a simplified informational pamphlet by the pharmacist group. Reasons for refusal of the vaccine even after education were recorded as well as receipt of vaccine if the patient consented.
RESULTS: The study and control groups each had 45 patients. Eighty-seven percent of patients accepted the vaccine after education by the pharmacist compared with 4.4% of patients who received standard of care. Reasons for refusal even after education included disbelief in vaccine efficacy and fear that immunization would lead to active disease. All patients who accepted the vaccine from the nurse actually received it versus only 64% of the patients in the pharmacist education group.
CONCLUSIONS: Education provided by the pharmacist was beneficial in significantly increasing the acceptance rate of the pneumococcal vaccine in eligible patients, which strongly supports their role in this intervention. Discrepancies in vaccine acceptance from the pharmacist and vaccine receipt can be attributed to administrative issues. To reach vaccination goals, individuals must be assigned on the medical floors both to educate and administer the vaccine.

128E. In Vivo Assessment of the Activity of Ceftaroline (CPT), Linezolid (LZO) and Vancomycin (VAN) in a Rabbit Osteomyelitis Experimental Model (OEM) due to MRSA and GISA. *Cedric Jacqueline,*[1] J. Caillon,[1] G. Amador,[1] V. Le Mabecque, Yigong Ge, M.D.,[2] D. Biek, Ph.D.,[2] G. Potel,[1] A. Hamel[1]; (1) UFR Medicine, Nantes, France; (2) Cerexa, Inc., Alameda, CA

PURPOSE: The activity of a new broad-spectrum cephalosporin, ceftaroline (CPT), was compared with other anti-staphylococcal drugs in a rabbit osteomyelitis experimental model.

METHODS: Femoral trepanation of rabbits was performed, followed by injection of 10^9 CFU *Staphylococcus aureus* suspension into the knee cavity. A surgical debridement of the infected tissues was performed 3 days later, and animals were randomly assigned to no treatment (controls), CPT (simulating a human-equivalent [HE] dose of 10 mg/kg/12 hours), LZO (HE dose of 10 mg/kg/12 hours), and VAN (constant intravenous infusion to reach a 20 ´ minimum inhibitory concentration serum steady-state concentration). Surviving bacteria were counted in joint fluid (JF), bone marrow (BM), and bone (BQ) at day 3 and at the end of 4 days' treatment (day 7).

RESULTS:

Mean ± SD ± log CFU/g of Tissue (day 7-day 3)

	MRSA			GISA		
Treatment	JF	BM	BO	JF	BM	BO
Controls	0.10 ± 0.69	0.19 ± 0.68	0.10 ± 0.87	0.83 ± 0.35	0.64 ± 0.72	0.22 ± 0.55
CPT	-1.98 ± 1.0[b,d,e]	-2.95 ± 0.44[a,c]	-2.83 ± 1.50[a,c]	-1.55 ± 0.52[a]	-2.02 ± 0.93[a,c]	-2.01 ± 0.90[a,c]
LZO	-0.77 ± 1.39	-2.69 ± 1.92[b,d]	-2.25 ± 1.55[b,d]	-1.13 ± 1.25[b]	-2.59 ± 0.90[a,c]	-2.38 ± 1.08[a,c]
VAN	-0.19 ± 1.19	-0.39 ± 1.60	-0.52 ± 0.69	-0.68 ± 0.37[b]	-0.41 ± 0.47	-0.57 ± 0.47

[a]p<0.001 vs. controls.
[b]p<0.05 vs. controls.
[c]p<0.01 vs. VAN.
[d]p<0.05 vs. VAN.
[e]p<0.05 vs. LZO. Student-Newman-Keuls test after analysis of variance.

CONCLUSIONS: (1) Although VAN remains the standard treatment for methicillin-resistant *S. aureus* (MRSA) osteomyelitis, VAN was ineffective during a 4-day treatment of MRSA and poorly active against glycopeptide-intermediate *S. aureus* (GISA) infections in this model. (2) CPT and LZO showed significant in vivo activity in BM and BO. (3) CPT was the only drug to exhibit significant activity in MRSA-infected JF, (4) CPT is a promising therapeutic option for the treatment of severe MRSA infections.

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129E. Ceftaroline (CPT) Dose Adjustment Recommendations for Subjects with Mild or Moderate Renal Impairment (RI). *Yigong Ge, M.D.,*[1] Sam Liao, Ph.D.,[2] Dirk A. Thye, M.D.,[1] George H. Talbot, M.D.[1]; (1) Cerexa, Inc., Alameda, CA; (2) PharMax Research, Inc., Somerset, NJ

PURPOSE: CPT is a broad-spectrum cephalosporin for which renal excretion is the major route of elimination. To develop dosage adjustment recommendations for patients with renal impairment (RI), Monte Carlo (MC) simulation was used to explore various dosing regimens to optimize the probability of target attainment (PTA) without the risk of drug overexposure.

METHODS: With an advanced population pharmacokinetic model based on phase 1 and 2 data, including those from subjects with RI, MC simulations were performed by the S-Plus program to simulate CPT plasma concentrations in subjects with normal (creatinine clearance [CrCL] more than 80 mL/minute) renal function or mild (CrCl more than 50–80 mL/minute) or moderate (CrCl more than 30–50 mL/minute) RI, for a 600-mg every-12-hours intravenous infusion over 1 hour.

RESULTS: The observed CPT concentrations in all subjects were in agreement with the model-predicted concentrations. Simulation-predicted CPT maximum concentration (C_{max}) and area under the curve (AUC) at steady state in normal subjects and subjects with mild and moderate RI are summarized in the Table.

	Mean ± SD	
Renal Function	$AUC_{0-24\ hour}$ (hour·µg/mL)	C_{max} (µg/mL)
Normal	129 ± 29	23.09 ± 5.44
Mild impairment	163 ± 35	24.65 ± 5.85
Moderate impairment	187 ± 40	25.71 ± 6.17

Based on MC-predicted AUC and C_{max}, no dose adjustment is required for patients with mild RI, whereas dose adjustment (400 mg instead of 600 mg every-12-hour dosing regimen) is required for patients with moderate RI. The simulated % T greater than the minimum inhibitory concentration for the proposed dose regimens for RI subjects also met or exceeded the PTA for normal subjects.

CONCLUSIONS: Moderate RI has a notable effect on plasma concentrations of CPT. Accordingly, proper dose adjustment must be made for patients with significant RI to avoid drug overexposure while maintaining plasma concentrations sufficient to ensure antimicrobial efficacy. No dosage adjustment is recommended for mild RI; dosage adjustment to 400 mg every 12 hours intravenously for 1 hour is recommended for moderate RI.

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130E. In Vitro Activity of Ceftaroline Against a Collection of Recent Gram-Positive and Gram-Negative US Isolates. *Yigong Ge, M.D.,*[1] D. Biek, Ph.D.,[1] Daniel F. Sahm,[2] George H. Talbot, M.D.[1]; (1) Cerexa, Inc., Alameda, CA; (2) Eurofins Medinet Anti-Infective Services, Herndon, VA

PURPOSE: Ceftaroline (CPT) is a new broad-spectrum cephalosporin with excellent gram-positive coverage including methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin-resistant *Streptococcus pneumoniae* (PRSP). CPT is currently in late-stage clinical development for treatment of bacterial infections in the hospital. We report the activity of CPT against a collection of 4151 isolates of pathogens important in infections.

METHODS: Clinical isolates were collected in the United States during 2004–2005. Minimum inhibitory concentration (MIC) testing of CPT and 17 comparators was performed using Clinical Laboratory Standards Institute microbroth methods.

RESULTS: CPT showed excellent activity against staphylococci and streptococci, including MRSA and PRSP. CPT was highly active against the common gram-negative respiratory tract pathogens *Haemophilus influenzae* and *Moraxella catarrhalis*. Activity against gram-negative *Enterobacteriaceae* was similar to that of third-generation cephalosporins (i.e., very active against ceftazidime-susceptible [CAZ-S] strains but less active against extended-spectrum β-lactamase–producing isolates).

		MIC (µg/mL)		
Organism	n	MIC50	MIC90	Range
MSSA	348	0.25	0.25	≤ 0.03 to 1
MRSA	661	0.5	1	0.12 to 2
CNS (OXA-S)	201	0.06	0.12	≤ 0.03 to 0.5
CNS (OXA-R)	299	0.5	0.5	0.06 to 2
S. pneumoniae (PEN-S)	202	≤ 0.008	0.015	≤ 0.008 to 0.12
S. pneumoniae (PEN-R)	296	0.12	0.12	≤ 0.008 to 0.5
Viridans streptococci (PEN-R)	14	0.12	0.5	0.015 to 1
E. faecalis (VAN-R & S)	182	2	4	0.5 to 8
M. catarrhalis (β-lactamase-positive)	93	0.06	0.25	≤ 0.03 to 0.5
H. influenzae (β-lactamase positive)	101	0.015	0.03	≤ 0.008 to 2
Enterobacteriaceae (CAZ-S)	833	0.06	1	≤ 0.03 to > 16
Enterobacteriaceae (CAZ-NS)	220	> 16	> 16	0.12 to > 16

CAZ = ceftazidime; CNS = coagulase-negative staphylococci; MIC = minimum inhibitory concentration; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *S. aureus*; NS = nonsusceptible; OXA = oxacillin; PEN = penicillin; R = resistant; S = susceptible; VAN = vancomycin.

CONCLUSIONS: CPT exhibited broadly potent activity against a variety of gram-negative and gram-positive bacterial pathogens, including MRSA, PRSP, and β-lactamase–positive *H. influenzae*. This in vitro profile provides evidence that CPT has the potential to be effective in treating many community-acquired and hospital-

acquired bacterial infections.
Presented at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 17–20, 2007.

131E. Real-time Evaluation of Ceftaroline, a New Cephalosporin, Versus Vancomycin and Daptomycin in a Rat *S. aureus* Endocarditis Model Using In Vivo Bioluminescent Imaging.
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PURPOSE: Ceftaroline (CPT) is a new broad-spectrum cephalosporin with activity against both methicillin-sensitive *Staphylococcus aureus* and methicillin-resistant *S. aureus* (because of high PBP2a affinity). We evaluated the efficacy of CPT, vancomycin (VAN), and daptomycin (DAP) in real time using a rat model of aortic infective endocarditis (IE) caused by a bioluminescently engineered, biofilm-positive *S. aureus* strain.
METHODS: Rat IE was induced after transcarotid transaortic valve indwelling catheterization. Three days after intravenous infection with 10^5 CFU *S. aureus* Xen29, animals were randomized to receive (1) no therapy (control); (2) CPT, 20 mg/kg, intravenously, 2 times/day; or (3) VAN, 120 mg/kg, subcutaneously, 2 times/day; or intravenously) or DAP, 10 mg/kg, subcutaneously, once daily. All treatments were for 3 days. Bioluminescence signals (BLS) were detected and quantified daily using a sensitive in vivo imaging system. Twenty-four hours after the last antibiotic dose, animals were sacrificed, and target tissues were quantitatively cultured.
RESULTS: There were significant correlations between cardiac BLS and *S. aureus* densities in vegetations in all treatment groups (R^2=0.7623). CPT and VAN significantly decreased *S. aureus* densities and cardiac BLS versus controls. In addition, CPT had better efficacy in reducing *S. aureus* densities in all three target tissues (Table) and caused more rapid cardiac BLS decreases compared with VAN and DAP.

	Group log CFU/g Tissue ± SD		
Group (no. of animals)	Vegetation	Kidney	Spleen
Control (12)	9.87 ± 0.49	7.28 ± 0.59	6.53 ± 0.68
VAN (7)	6.76 ± 0.98*	4.15 ± 1.20*	4.28 ± 0.89*
DAP (6)	7.64 ± 0.32	5.53 ± 0.57*	5.49 ± 0.38
CPT (9)	4.88 ± 0.57**	4.09 ± 0.54**	3.63 ± 0.43**

*p<0.05; **p<0.0005 vs. control.

CONCLUSIONS: CPT treatment resulted in a more significant reduction of bacterial loads in vegetations than either VAN or DAP. CPT had excellent in vivo efficacy in this model of severe *S. aureus* infection (IE).
Presented at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 17–20, 2007.

132E. Sodium Derangement Among Hospitalized Pneumonia Patients: Prevalence and Association to Mortality and Prolonged Length of Stay.
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PURPOSE: Serum sodium (Na) derangements are common in patients presenting with pneumonia, but the clinical implications are unknown. We sought to evaluate the association between Na derangements and morbidity, mortality, and cost burden for hospitalized pneumonia patients.
METHODS: A large U.S. database of 86,488 pneumonia admissions across 185 hospitals (teaching and nonteaching) in 2004–2005 was explored. Based on empiric examination of the serum Na distribution on admission, we categorized patients into five cohorts: Na less than 130 mEq/L as severe hyponatremia; 131–135 mEq/L as hyponatremia; 144–145 mEq/L as hypernatremia; and more than 145 mEq/L as severe hypernatremia. We used Na 136–143 as the reference group and examined the relationship between Na derangements and both mortality and length of stay (LOS). We adjusted for multiple potential confounders (e.g., demographics, age, comorbidities) by multivariate analyses.
RESULTS: The median age was 73, and 53% were women with a crude mortality of 4.9%. Severe hyponatremia, hyponatremia, hypernatremia, and severe hypernatremia were present in 8.2, 25.9, 3.5, and 3.2% of cases, respectively. Patients with deranged Na levels had higher mortality and longer LOS compared with the reference group (all p<0.0001). After controlling for age, vital signs, laboratory findings, and other confounding risk factors, all four levels of Na derangement were independent predictors for mortality and excess LOS (all p<0.05). The independent, adjusted odds ratio for mortality associated with various Na derangements ranged from 1.1 to 1.7, and severe hyponatremia increased the risk of death by 40% (OR = 1.4, 95% CI: 1.3–1.6). The excess LOS associated with Na derangements varied from 0.21 to 0.73 day.
CONCLUSIONS: Na derangements are common in hospitalized pneumonia patients, and hyponatremia is seen in almost one-third of these individuals. Both hyponatremia and hypernatremia are associated with excess mortality and morbidity.
Presented at the International Conference of the American Thoracic Society (ATS) 2008 in Toronto, ON, Canada, May 16–21, 2008.

133E. Assessment of Vancomycin-Resistant Enterococcal Bacteremia in a Hematology and Bone Marrow Transplant Population: Outcomes and Risk Factors Associated with Treatment Failure.
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PURPOSE: To determine the possible risk factors associated with treatment failure of infection by vancomycin-resistant enterococcus (VRE) in hematology or bone marrow transplant patients by assessing treatment failure in patients receiving linezolid or daptomycin.
METHODS: The study included inpatients of the University of Michigan Health System who were older than 18 years; received chemotherapy for leukemia, lymphoma, or other hematologic cancers; had documented positive blood culture data indicating infection with VRE; and received primary therapy with at least 2 days of either linezolid or daptomycin. Patients included were treated between January 1, 2004, and January 1, 2007. Data collected included baseline characteristics such as demographic information, primary hematologic diagnosis, chemotherapy regimen, presence of other antibiotic or antifungal treatments, source of infection, and presence or removal of indwelling venous catheters. The effectiveness of the two treatments was based on microbiologic response to the two treatment options and the length of therapy required for a microbiologic response. Safety data were collected and assessed for both groups of patients. Data were analyzed by a Cox proportional hazards analysis to predict resolution of infection. This protocol was approved by the University of Michigan's institutional review board.
RESULTS: Data have been collected and analyzed from 72 patients who received daptomycin or linezolid. Acute myelogenous leukemia was the most common diagnosis (45.7% of patients). About 82% of patients cleared the VRE infection, and 70.5% of these patients had their central catheter pulled. Treatment failed in 14 patients (six had synergistic drugs added, two had therapy changed, and six died before clearing infection), and 42.9% had their central catheter pulled.
CONCLUSIONS: Daptomycin and linezolid are reasonable choices to treat VRE bacteremia. Pulling a central venous catheter may reduce failure rates in VRE bacteremia, and linezolid patients may be more likely to experience a transient increase in liver function tests.
Presented at the Hematology/Oncology Annual Meeting 2008, Anaheim, CA, June 18–21, 2008.

134E. Epidemiology of Serum Sodium Correction and Its Impact on Hospital LOS in Patients Admitted with Pneumonia and Hyponatremia.
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PURPOSE: Hyponatremia is present in about 30% of patients hospitalized with pneumonia and is associated with increased hospital length of stay (LOS). We hypothesized that the rate of correction of hyponatremia would affect this outcome.

METHODS: We analyzed 1026 hyponatremic (sodium [Na] less than 135 mEq/L) pneumonia patients hospitalized in 2003–2006 in 74 hospitals. Based on evaluation of hospital survival, we found a lower mortality with an Na rate of rise in the first 24 hours of 1–7 mEq/L (favorable group). The Wilcoxon nonparametric test for LOS and multivariate regression to estimate the effect of favorable Na management on LOS, controlling for admission severity, mortality status, interaction of mortality, and serum Na status, were used.

RESULTS: The overall in-hospital mortality was 11.8%, and the rate of favorable Na management was 50% (n=517), with the average baseline Na of 129.0 mEq/L (SD: 5.5 mEq/L) compared with 127.4 mEq/L (SD: 6.8 mEq/L) for the unfavorable group. In the favorable group, the crude average LOS was 7.4 days (SD = 5.8) compared with 8.2 days (SD = 7.2) for the unfavorable Na management group (p=0.34). After adjusting for confounders, the favorable Na group showed a 1-day reduction in the average LOS (95% CI: 0.2–1.9 days) compared with the unfavorable Na group (p=0.02).

CONCLUSIONS: Only 50% of pneumonia patients with admission hyponatremia are managed favorably with regard to the rate of serum Na correction. The adjusted mean marginal excess LOS of unfavorable Na management is 1 day. Recognition and institution of measures to ensure an appropriate and predictable rate of Na correction are needed to improve clinical and economic outcomes among hyponatremic patients with pneumonia.

Presented at the International Conference of the American Thoracic Society (ATS), Toronto, ON, Canada, May 16–21, 2008.

135. Clinical Outcomes and Nephrotoxicity Associated with Vancomycin Trough Concentrations During Treatment of Deep-Seated Infections. Elizabeth D. Hermsen, Pharm.D., M.B.A.,[1] *Monica Hanson, Pharm.D. Candidate,*[1] Jayashri Sankaranarayanan, M.Pharm., Ph.D.,[2] Julie Stoner, Ph.D.,[2] Marius C. Florescu, M.D.,[2] Mark E. Rupp, M.D.[2]; (1) The Nebraska Medical Center, Omaha, NE; (2) University of Nebraska Medical Center, Omaha, NE

PURPOSE: Higher vancomycin concentrations are thought necessary for treatment of deep-seated methicillin-resistant *Staphylococcus aureus* (MRSA) infection, yet this may result in a greater risk of nephrotoxicity. We evaluated the relationship between serum vancomycin trough concentration, nephrotoxicity, and efficacy for patients with deep-seated MRSA infection.

METHODS: A retrospective cohort study evaluated adults with MRSA pneumonia, endocarditis, or osteomyelitis who received vancomycin for 5 or more days from June 2005 to June 2007. Patients were stratified on the basis of mean vancomycin trough level (low [less than 15 µg/mL], high [15 µg/mL or more]). Outcomes were clinical response, mortality, length of stay (LOS), and nephrotoxicity. Three definitions of nephrotoxicity were used: (1) rise in serum creatinine (SCr) of 0.5 mg/dL or more; (2) 50% increase in SCr; and (3) 25% decrease in estimated creatinine clearance.

RESULTS: Fifty-five patients experiencing MRSA pneumonia (n=28), endocarditis (n=9), and osteomyelitis (n=20) (multiple infections, n=2) were stratified into low (n=39) and high (n=16) groups. High group patients were more likely to be septic (p=0.01) and have a higher APACHE II score (p=0.02). After adjustment for APACHE II score, clinical response rates did not differ significantly. Death occurred in 25 and 5% of the high and low group patients, respectively (p=0.05). LOS did not differ significantly between groups (p=0.73). Nephrotoxicity occurred in the low and high groups, respectively, for 18 and 37.5% (p=0.07) with definition 1, 15.4 and 37.5% (p=0.04) with definition 2, and 18 and 31.3% (p=0.1) with definition 3. After adjustment for APACHE II score, odds of nephrotoxicity were increased among high group compared with low group (OR = 3.42, 95% CI: 0.83–14.15; p=0.09).

CONCLUSIONS: Clinical response, mortality, and LOS did not differ significantly between high and low trough groups for deep-seated MRSA infections. Although not statistically significant, nephrotoxicity was consistently higher in the high trough group, regardless of the definition used.

136. Activity of Caspofungin Against Isolates of *C. parapsilosis*, *C. orthopsilosis* and *C. metapsilosis* by Time-Kill Methods. *Erika J. Ernst, Pharm.D.,*[1] Jesse Hollanbaugh, Pharm.D.,[2] Shawn Lockhart, Ph.D.,[2] Michael Pfaller, M.D.,[3] Daniel J. Diekema, M.D.[3]; (1) College of Pharmacy, The University of Iowa, Iowa City, IA; (2) University of Iowa, Iowa City, IA; (3) University of Iowa, Iowa City, IA

PURPOSE: *Candida parapsilosis* groups II and III have been proposed to be replaced with *Candida orthopsilosis* and *Candida metapsilosis*. The echinocandins are suggested to show decreased activity against *C. parapsilosis;* however, its activity versus *C. orthopsilosis* and *C. metapsilosis* determined time-kill methods has not been described.

METHODS: Isolates of *C. parapsilosis* (n=13), *C. orthopsilosis* (n=12), and *C. metapsilosis* (n=15) were identified. Minimum inhibitory concentrations (MICs) were determined by microdilution using Clinical Laboratory Standards Institute methods. Isolates were obtained from stored samples and subcultured twice on potato dextrose agar before testing. Fungal suspensions equal to a 0.5 McFarland standard were prepared in sterile water. One milliliter of this fungal suspension was added to RPMI 1640 with MOPS (3-morpholino-propane sulfonic acid) buffered to a pH of 7.0, providing a starting inoculum of 1×10^5 to 5×10^5 CFU/mL. Concentrations of caspofungin tested were 0.25–8 × MIC. Culture vials were incubated with agitation at 35ºC. At multiple time points during 24 hours (0, 2, 4, 8, and 24 hours), a 0.1-mL aliquot was removed from each culture vial and serially diluted in sterile water; 30 µL of this was plated for colony count determination after incubation at 35ºC for 24–48 hours.

RESULTS: Caspofungin MICs ranged from 0.12 to 1 µg/mL for *C. parapsilosis*, from 0.03 to 0.5 µg/mL for *C. orthopsilosis*, and from 0.03 to 1 µg/mL for *C. metapsilosis*. Against all 13 isolates of *C. parapsilosis*, caspofungin (8 x MIC) showed fungistatic activity, with an average 1.22-log reduction in CFU per milliliter from the starting inocula (range -0.3 to -1.9). For *C. orthopsilosis*, eight isolates showed fungistatic activity (a 0.3- to 1.9-log reduction), and four isolates showed no growth inhibition (a 0.86- to 1.44-log increase) at 8 × MIC. Twelve isolates of *C. metapsilosis* showed growth, whereas three showed minimal activity (a 0.2- to 0.7-log reduction in CFU per milliliter).

CONCLUSIONS: The antifungal activity of caspofungin against *C. parapsilosis*, *C. orthopsilosis,* and *C. metapsilosis* differed considerably from one another but did not appear to be related to the MIC.

137. The Effects of Antibiotic Administration on *Clostridium difficile*-Associated Diarrhea. *Kyung Sun Oh, M.S.,*[1] Sukhyang Lee, Pharm.D., Ph.D.[2]; (1) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Seoul, South Korea; (2) Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, South Korea

PURPOSE: The purpose of this study was to determine the risk factors of *Clostridium difficile*–associated diarrhea (CDAD) related to the administered antibiotics, including antibiotic classes and antibiotic treatment duration.

METHODS: We performed a retrospective case-control study in the patients with order of *C. difficile* toxin assay at I Hospital (Incheon, South Korea) from January 1, 2007, to December 31, 2007. Administrative, laboratory, and pharmacy data were collected from electronic medical databases.

RESULTS: The analysis included 129 reported *C. difficile* toxin assay results, with 42 positive cases and 87 negative cases. Significant antibiotic risk factors for CDAD included the use of fourth-generation cephalosporin (OR = 5.97, 95% CI: 1.37–25.98; p=0.017). Administration of metronidazole was protective against CDAD (OR = 0.30, 95% CI: 0.12–0.74; p=0.009). Prolonged antimicrobial therapy has been associated with an increased risk of

CDAD. Third-generation cephalosporins (OR = 3.81, 95% CI: 1.08–13.41; p=0.037) and aminoglycoside (OR = 5.50, 95% CI: 1.43–21.10; p=0.013) demonstrated a greater risk of CDAD for 15 days than under an 8-day treatment duration.
CONCLUSIONS: This study confirmed previous studies regarding the risk of acquiring CDAD. The fourth-generation cephalosporins were the significant risk factor compared with other antibiotics, whereas metronidazole appears to be protective.

Informatics/Clinical Decision Support

138. Improving Dyslipidemia Screening and Statin Prescribing in Diabetic Patients at a Community Hospital Using a Technology-Assisted Pharmacist Intervention. *Peggy S. McKinnon, Pharm.D.,*[1] Laura A. Noirot, B.S.,[2] Lisa Peters, Pharm.D.,[3] Stuti Sinha, Pharm.D.,[3] Richard M. Reichley, R.Ph.,[2] Kevin M. Heard, B.S.,[2] William D. Shannon, Ph.D.,[4] Dennis A. Bouselli, Pharm.D.,[3] Anne C. Goldberg, M.D.,[4] Wm. Claiborne Dunagan, M.D.,[4] Thomas C. Bailey, M.D.[4]; (1) Barnes-Jewish Hospital, St. Louis, MO; (2) BJC HealthCare, St. Louis, MO; (3) Missouri Baptist Medical Center, St. Louis, MO; (4) Washington University School of Medicine, St. Louis, MO
PURPOSE: Despite well-established evidence-based guidelines for dyslipidemia in patients with diabetes, therapy remains underused. We evaluated whether rates of dyslipidemia screening (low density lipoprotein cholesterol [LDL-c] testing) and adherence to guidelines for lipid-lowering therapy in patients with diabetes mellitus (DM) admitted to a community hospital were improved using a technology-assisted pharmacist intervention.
METHODS: The study was conducted between June 2006 and April 2008. Hospitalized patients with DM were identified using an automated clinical prediction rule. Alerts were generated for patients with DM without LDL-c testing or with an LDL-c of 100 mg/dL or greater. Medicine and cardiology practices were randomized to intervention or control groups. For patients with no LDL-c in the intervention group, the pharmacist recommended lipid profile testing. Statin therapy was recommended for intervention group patients with an LDL-c of 100 mg/dL or greater when no contraindications were present. Control group patients received usual care. Guideline adherence was defined as LDL-c testing within 24 hours of hospital admission (for the LDL intervention) or statin prescription at hospital discharge (for the statin intervention) or a valid exception for prescribing the medication. Differences in control and intervention groups were tested using a mixed model statistic (GLIMMIX, SAS, Cary, NC).
RESULTS: Five hundred sixty-four patients were evaluated for LDL-c testing, and 503 patients were evaluated for statin prescribing. Controlling for physician practice group and multiple patient visits, guideline adherence to LDL testing increased from 13.6 to 52.4% (p=0.0004) with pharmacist intervention. Guideline adherence for statin prescribing improved from 26.1% (control) to 57.6% (intervention) (p=0.0002).
CONCLUSIONS: A two-step intervention using an automated system to notify a clinical pharmacist and academic detailing of physicians improved the rate of dyslipidemia screening and use of statin therapy in patients with DM at a community hospital. However, there remains significant room for improvement.

Managed Care

139. Clinical Consequences of Suboptimal Clopidogrel Therapy After Stent Implantation in Acute Coronary Syndrome Patients: An Integrated Health Plan's Perspective. *Karina L. Berenson, MPH,*[1] Daniel Wiederkehr, B.S.,[1] Michelle R. Krukas, B.S.,[1] Lois E. Lamerato, Ph.D.,[2] Dinara Makenbaeva, M.D., M.B.A.,[3] Essy Mozaffari, Pharm.D., MPH,[4] John C. Corbelli, M.D.[5]; (1) Analytica International, New York, NY; (2) Department of Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, MI; (3) Bristol-Myers Squibb, Plainsboro, NJ; (4) Sanofi-Aventis, Bridgewater, NJ; (5) Buffalo Cardiology and Pulmonary Associates, PC, SUNY Buffalo School of Medicine and Biomedical Sciences, Buffalo, NY
PURPOSE: Clopidogrel has been shown to reduce the risk of recurrent acute coronary syndrome (ACS) hospitalizations in both randomized clinical trials (RCTs) and real-world observational studies. Although the composite end points of ACS recurrence or death have been examined in RCTs, the risk of such an end point has not been clearly quantified in observational data. This study examined the impact of clopidogrel on the risk of ACS recurrence and/or death in a real-world setting.
METHODS: We conducted a retrospective observational study to evaluate the clinical consequences of suboptimal clopidogrel therapy in patients with ACS undergoing stent insertion during 2002–2007. Patients were enrolled in an integrated commercial health plan that provides care across the continuum of inpatient and outpatient settings. After stent insertion during the initial hospitalization, the 2-year rate of ACS-related rehospitalization, procedure (e.g., stent, percutaneous coronary intervention [PCI], coronary artery bypass graft surgery [CABG]), or death was compared in patients receiving clopidogrel versus patients not receiving clopidogrel. Multivariate Cox regression was used to assess the association between clopidogrel use and risk of having one of the events while adjusting for demographics, comorbidities, procedures (e.g., CABG, PCI, stent), and follow-up time.
RESULTS: There were 720 patients who received stents during their first ACS hospitalization, of which 76.3% initiated clopidogrel after stent insertion. Unadjusted rates of 2-year ACS recurrence or death favored the clopidogrel group (26.8% vs. 36.6%; p=0.013). After adjusting for patient characteristics and follow-up time, the clopidogrel group was 25% less likely to have an ACS-related rehospitalization or death compared with those who did not receive clopidogrel (hazard ratio: 0.747; 95% CI: 0.567–0.985).
CONCLUSIONS: In this 2-year retrospective follow-up of patients with ACS receiving a coronary stent, the patients taking clopidogrel experienced a 25% lower risk of ACS-related rehospitalization or death compared with those not receiving clopidogrel.

140. Economic Consequences of Recurrent Acute Coronary Syndrome-Related Hospitalizations. *Karina L. Berenson, MPH,*[1] Augustina O. Ogbonnaya, MPH,[1] Roman Casciano, M.S.,[1] Dinara Makenbaeva, Pharm.D., M.D.,[2] Essy Mozaffari, Pharm.D., MPH,[3] Lois E. Lamerato, Ph.D.,[4] John C. Corbelli, M.D.[5]; (1) Analytica International, New York, NY; (2) Bristol-Myers Squibb, Plainsboro, NJ; (3) Sanofi-Aventis, Bridgewater, NJ; (4) Department of Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, MI; (5) Buffalo Cardiology and Pulmonary Associates, PC, SUNY Buffalo School of Medicine and Biomedical Sciences, Williamsville, NY
PURPOSE: Evaluate the cost of recurrent acute coronary syndrome (ACS)-related hospitalization in a real-world setting from a payer's perspective.
METHODS: Medical care encounters, resource use, and hospital charges were extracted from health care claims of patients hospitalized for new-onset ACS (defined by an ICD-9 code for unstable angina or myocardial infarction or a code for a coronary artery bypass graft [CABG], stent insertion, or percutaneous coronary intervention [PCI]) in an integrated regional health plan (1995–2007). Patients with an ACS-related rehospitalization during the following 2 years were identified. Mean rehospitalization charges were computed, and multivariate analysis identified drivers of higher ACS rehospitalization charges.
RESULTS: Of the total 11,266 patients with ACS, 3588 (32%) had at least one ACS rehospitalization. Rehospitalizations in which a CABG was performed were more costly than other ACS rehospitalizations, and charges were higher in the population age 65 and older across all rehospitalization procedures (CABG, stent insertion, and PCI; see Table). Multivariate analyses demonstrated that length of stay (LOS) and CABG were the strongest predictors of increased charges during the recurrence (p<0.0001). Patients with a history of diabetes, stroke, renal failure, or bleeding were significantly more likely to have increased LOS during the rehospitalization, as well as higher charges when not adjusting for LOS in the model.

Mean ACS Rehospitalization Charges

	All Ages		Younger Than 65		Older Than 65	
	Charge $	n	Charge $	n	Charge $	n
Any ACS rehospitalization	52,619	3588	50,813	1628	54,119	1960
CABG	125,431	550	118,931	262	131,343	288
Stent insertion	46,789	765	44,818	421	49,200	344
PCI	46,827	905	45,500	507	48,517	398

CONCLUSIONS: The costs of ACS-related rehospitalizations in a real-world setting are high, especially among older patients and patients with serious comorbidities. Reducing the risk of rehospitalization could lead to improved patient outcomes as well as substantial economic savings to payers.

141. Lipid Profile Changes Associated with Changing Available Formulary Statins.

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PURPOSE: To evaluate changes in a clinic population's lipid profiles after a formulary limited the availability of atorvastatin.

METHODS: A retrospective chart review identified patients enrolled in a select Medicaid-sponsored third party. Each patient's chart was reviewed for demographics as well as risk factors for coronary artery disease. The atorvastatin dose and fasting lipid panel documented in the medical records most immediately before January 2007 were considered baseline information. New statin, dose, and fasting lipid panels in the medical records at least 6 weeks after documented statin change were considered follow-up values. The time to documented change from atorvastatin was also recorded, with changes in January 2007 considered 0 month.

RESULTS: Overall, only the high-density lipoprotein cholesterol significantly increased from the pre–January 2007 lipid profiles and the post–January 2007 lipid profiles (42.5 vs. 44.1 mg/dL, p=0.018). Statistically significant changes were noted when computing total cholesterol values in patients changed from atorvastatin 20 mg (158.9 vs. 181.9 mg/dL, p=0.019), and triglycerides in patients changed from atorvastatin 80 mg (180.5 vs. 105.5 mg/dL, p=0.049). As well, 54.5, 20, 29, and 0% of atorvastatin 10-, 20-, 40-, and 80-mg treated patients (respectively) were appropriately converted during the changeover. The mean time to documented change was 2.9 (+3.1) months.

CONCLUSIONS: This analysis did not detect any major differences in lipid profiles when changing formulary statins. There are several potential confounders including medication adherence after change, drug cost, and provider communications that should be addressed and discussed before fully accepting this conclusion.

Medication Safety

142E. Epidemiology and Outcomes of Patients with Changes in Renal Function During Hospitalization That May Require Dosage Adjustment.

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PURPOSE: Failure to dose adjust for renal insufficiency during hospitalization can be a common cause of medication errors and is an important function for clinicians. We examined the prevalence, mortality, and length of stay (LOS) for cases that exhibited changes in renal function during hospitalization.

METHODS: We retrospectively analyzed 1,011,055 nondialysis admissions with at least two serum creatinine (SCr) values during a hospital stay across 74 hospitals that provided electronic laboratory results from 2003 to 2006. We used a modified Cockroft-Gault (140 – age)/serum creatinine (×0.85 for the female gender) to determine baseline and changing creatinine clearance (eCrCl, mL/minute). Cases were stratified on the basis of eCrCl as normal (81 mL/minute or more), mild (50–80 mL/minute), moderate (16–49 mL/minute), and advanced (15 mL/minute or less). Worsening or improvement was defined as cases that moved one or more eCrCl strata to another during hospitalization. Unadjusted hospital mortality (95% CI) and median LOS were evaluated.

RESULTS: On admission, 29.6% had normal, 34.4% had mild, 34.1% had moderate, and 1.9% had advanced eCrCl. Of these cases, the eCrCl remained the same in 79.2%, worsened in 11.6%, and improved in 9.2%. Mortality and median LOS was highest for worsening eCrCl (7.9 [CI: 7.8–8.1] and 6 days), followed by those remaining the same (2.8 [CI: 2.8–2.9] and 4 days) and those with improving eCrCl (1.8 [CI: 1.7–1.9] and 4 days). Cases with two or more strata worsening in eCrCl (0.5% of cases) had higher mortality and LOS (25.9 [CI: 24.7–27.1] and 10 days) than those with moderate (5.0 [CI: 4.9–5.1] and 5 days, 28.8% of cases) or advanced (13.3 [CI: 12.7–13.8] and 5 days, 1.5% of cases) eCrCl that remained the same.

CONCLUSIONS: Both improvement and worsening renal function necessitating potential dosage adjustment are common during hospitalization. Mortality and LOS were higher for cases with worsening renal function. Comprehensive renal dosing programs have the potential of improving medication safety and related outcomes.

Presented at the International Society for Pharmacoeconomics and Outcomes Research, Toronto, ON, Canada, May 3–7, 2008.

143E. Epidemiology and Outcomes of Patients Treated with Heparin During Hospitalization.

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PURPOSE: Current national patient safety goals call to reduce the likelihood of patient harm associated with the use of anticoagulation therapy. We examined the epidemiology, length of stay (LOS), and occurrence of bleeding in nonsurgical patients treated with heparin infusions during hospitalization.

METHODS: We retrospectively analyzed 1443 nonsurgical cases treated with heparin for at least 24 hours during hospitalization from four institutions that electronically provided laboratory and pharmacy data from 2004 to June 2007. Cases were categorized into the following groups based on serum activated partial thromboplastin time (aPTT) results: subtherapeutic (less than 51), therapeutic (51–75), above therapeutic (76–99), and supratherapeutic (100 or more). The number of cases meeting each aPTT category was compared at about 6 and 24 hours postheparin treatment. The actual to predicted hospital length of stay was compared for each aPTT category, with predicted LOS determined using previously described admission-based clinical models. Bleeding was assessed by the presence of diagnostic codes or laboratory results.

RESULTS: In those with aPTT measured, the percentage of cases at 6 and 24 hours were as follows: 19.6 versus 33.3 for subtherapeutic, 27.0 versus 35.7 for therapeutic, 20.6 versus 16.5 for above therapeutic, and 32.8 versus 14.5 for supratherapeutic. There was a 0.9-day excess LOS in the subtherapeutic group at 24 hours ($p<0.05$). Unadjusted bleeding rates were 19.8% in subtherapeutic, 18.3% in therapeutic, 20.8% in above therapeutic, and 19.1% in supratherapeutic cases at 24 hours.

CONCLUSIONS: One in three cases treated with heparin had a subtherapeutic aPTT at 24 hours, and these cases had a longer LOS. Clinicians responsible for ensuring anticoagulation safety should incorporate monitoring strategies for subtherapeutic aPTT results as diligently as those for supratherapeutic results.

Presented at the International Society for Pharmacoeconomics and Outcomes Research, 13th Annual International Meeting, Toronto, ON, Canada, May 3–7, 2008.

144. Impact of the Implementation of a Pharmacist-Run Discharge Medication Reconciliation Procedure.

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PURPOSE: Medication reconciliation at the time of hospital admission is of known importance within a health system. The Joint Commission 2008 National Safety Goal 8 has noted the importance

of accurately and completely reconciling medications across the continuum of care. This study evaluated an inpatient family medicine pharmacist-run medication discharge medication reconciliation procedure to determine if it (1) reduced discrepancies in medication profiles during transition from inpatient to outpatient and (2) improved physician satisfaction with the accuracy of medication profiles in the electronic medical record (EMR) after hospital discharge.
METHODS: The discharge medication reconciliation procedure was implemented in March 2008. Patients admitted to the service, while a pharmacist was present, during January 2008 were included in the preimplementation group, and patients admitted during April 2008 were included in the postimplementation group. To determine discrepancies, the dictated discharge summary was compared with the patient's outpatient EMR. Discrepancies included dose, route, frequency, duration, and medication (duplicate therapy, missing medication, or extra medication). Attending physicians completed a presurvey and postsurvey to assess satisfaction with the accuracy of medication profiles before and after implementation of the discharge medication reconciliation procedure, respectively. Differences were evaluated using the unpaired *t*-test and the Mann-Whitney *U* test.
RESULTS: Thirty-six patients were eligible for the preimplementation group, and 17 patients were eligible for the postimplementation group. There were 6.56 discrepancies per outpatient medication list in the preimplementation group and 1.71 discrepancies per outpatient medication list in the postimplementation group (p=0.0001). Before and after implementation of the procedure, physicians were somewhat unsatisfied and somewhat satisfied with the accuracy of medication profiles after hospital discharge, respectively (p=0.1834).
CONCLUSIONS: The implementation of an inpatient family medicine pharmacist-run discharge medication reconciliation procedure reduced discrepancies in medication profiles during transition from inpatient to outpatient. Physician satisfaction with the procedure did not significantly change.

145. Evaluation of a Computerized Physician Order Entry (cPOE) Weight-Based Unfractionated Heparin (UFH) Protocol at Beth Israel Deaconess Medical Center (BIDMC): Impact on Prescribing, Monitoring, Safety, and Achievement of Therapeutic Targets. *Adam B. Woolley, Pharm.D.*, Snehal H. Bhatt, Pharm.D., BCPS, Katherine Cunningham, Pharm.D., BCPS, M.S.; Beth Israel Deaconess Medical Center, Boston, MA

PURPOSE: Beth Israel Deaconess Medical Center implemented a weight-based unfractionated heparin (UFH) protocol in an effort to establish a safe practice model. A review of UFH orders indicated that this protocol was modified about 40% of the time because of physician perception that the protocol was too aggressive. Therefore, a review was warranted to evaluate the impact of prescribing variances on clinical and safety outcomes between protocol-based UFH and physician-modified dosing.
METHODS: A retrospective review was conducted to identify patients receiving UFH infusions between August and September 2007. Data collection included patient demographics, documentation of patient weight and congruence with the weight used in the protocol, indication for therapy, time between reported activated partial thromboplastin time (aPTT) and dose adjustment, time to target aPTT, instances the aPTT was outside the target range, and adverse effects. Collected data were used to determine differences in the time to therapeutic aPTT, duration of time outside target range, and incidence of UFH-related adverse effects between the protocol and the physician-modified dosing groups.
RESULTS: One hundred eighty-two patients were identified, of which 121 met inclusion criteria. There were no significant differences between weight-based and physician-modified dosing with regard to baseline characteristics or clinical and safety end points. Time to achieve target aPTT was 33.1 hours (10–69) in the protocol-based group versus 34.2 hours (11–79) in the physician-modified group (p=0.82) No differences between groups were observed in thrombolysis in myocardial infarction bleeding criteria 13 versus 10 (p>0.05). The number of rate adjustments because of variations outside the target range tended to be higher in the physician-modified group: 3.8 (1–11) versus 3.3 (1–9).
CONCLUSIONS: Use of a physician-modified UFH-based protocol did not improve clinical or safety end points compared with a weight-based protocol but resulted in a greater number of dose adjustments and wider variation outside the therapeutic range.

146. Pharmacist Driven Review and Upgrade of Alaris® Smart Pump Technology in the ICU. *Katie M. Muzevich, Pharm.D.*, Stacy A. Voils, Pharm.D.; Virginia Commonwealth University Health System, P.O. Box 980042, Richmond, VA

PURPOSE: In 2005, our institution converted all intravenous infusion pumps to Alaris Pump Module brand smart pumps with implementation of Guardrails Suite medication error prevention software v. 7. In July 2008, all pumps are scheduled to be upgraded from Guardrails Suite 7 to Guardrails Suite 9 for revision of the drug library, implementation of Guardrails parameters for intermittent infusions, and increase in the number of selections for intravenous fluid administration. The purpose of this study was to evaluate the current practice regarding administration of continuous-infusion intravenous medications in the intensive care unit (ICU) before pump upgrade.
METHODS: A one-time pump audit was conducted to assess current medication administration practices. To minimize potential confounders caused by the presence of clinical pharmacists on ICU services, the audit was conducted after a 2-day lapse in clinical pharmacist oversight. Data collection included intravenous medications administered without a documented order, ordered medications that were not being administered, and rate of Guardrails use.
RESULTS: Of the intravenous drugs actively infusing, 53% were not administered within Guardrails software; most of these (91%) were for intravenous fluids with limited Guardrails parameters. Two high-risk intravenous drugs (insulin and nitroglycerin) were infusing outside the Guardrails software. Of 114 administered intravenous drugs, 10.5% did not have a documented order. Twenty-nine percent of continuous intravenous drugs with active orders were not being used at the time of the audit.
CONCLUSIONS: Pharmacist participation in the review and upgrade of Alaris smart pump technology in the ICU has identified policy deviations and unsafe practices with regard to medication administration and documentation, which, in part, are secondary to Guardrails software limitations. Frequent audits should be conducted to assess the effect of increased pump functionality on medication administration practices.

147. An Analysis of Adverse Events Related to Peripheral Intravenous Catheter Use in Hospitalized Patients. *Brian A. Hemstreet, Pharm.D., BCPS*; University of Colorado Denver School of Pharmacy, P.O. Box 6511, Aurora, CO

PURPOSE: This prospective observational study evaluated peripheral intravenous catheter (PIVC) use in hospitalized adults. An analysis was performed to identify factors that increase the risk of developing catheter-related adverse events (CRAEs).
METHODS: Adult patients consecutively admitted to a general medicine floor of a tertiary care academic medical center were assessed daily for PIVC use during their hospital stay. Information collected included PIVCs used per patient, frequency and types of CRAEs, and outcomes or interventions related to CRAEs. Demographics and medical history were obtained from the patient's medical record. Evidence of CRAEs was assessed daily using computerized nursing records. CRAEs were defined as catheter occlusion, infiltration, extravasation, phlebitis, hematoma, infection, or thrombosis. Descriptive statistics were used for patient demographics and CRAE rates. A χ^2 test was used to compare differences across categoric variables. A Student's *t*-test was used to compare continuous variables. Odds ratios were obtained for factors associated with CRAE development using logistic-regression analysis. All patients signed an informed consent.
RESULTS: A total of 296 patients (51% male) were evaluated. Mean age and length of stay (LOS) were 54.3 years and 6.3 days. Fifty-five patients (18.6%) experienced one or more CRAEs. The average number of PIVCs used per admission was significantly greater in

patients who experienced a CRAE than in those who did not (3.1 vs. 1.5, p<0.001). Odds of developing a CRAE significantly increased based on the total number of PIVCs used (OR = 2.5, 95% CI: 1.9–3.31; p<0.0001) for each additional PIVC. Mean LOS was similar between patients who experienced CRAEs and those who did not (7.5 vs. 6.0 days, p=0.1248).
CONCLUSIONS: Risk of hospitalized patients developing CRAEs increases with the number of PIVCs used. Evaluating the need for PIVCs may reduce CRAEs by identifying patients who may alternatively receive oral fluids or drugs.

Nephrology

148E. Efficacy of Phosphorus Binding Between Chewed and Crushed Lanthanum Carbonate. *Priscilla How, Pharm.D.*, Darius Mason, Pharm.D., Jose Arruda, M.D., Alan Lau, Pharm.D.; University of Illinois at Chicago, Chicago, IL
PURPOSE: Lanthanum carbonate (LC) is an effective phosphorus (P) binder for the management of hyperphosphatemia and secondary hyperparathyroidism in chronic kidney disease. The manufacturer recommends that patients chew and take LC with/immediately after meals. However, some patients are unable to chew the tablets or prefer to crush the tablets and mix them with food. This study was conducted to compare the efficacy of P binding between chewed and crushed LC.
METHODS: Eleven healthy subjects (4 males and 7 females) were randomized in this crossover study to receive (A) a standardized meal containing 32 mmol/1 g of elemental P, which served as a dietary P load; (B) a single 1-g oral dose of LC that was chewed with the standardized meal; or (C) crushed into a fine powder using a pestle and mortar, mixed with applesauce, and taken with the standardized meal. Serum P concentrations were obtained at baseline and hourly for up to 8 hours after meal completion. Urine was collected at 2-hour intervals to determine the amount of P excreted. The changes in serum P, area under concentration-time curve (AUC), and urinary P excretion among the three arms were compared.
RESULTS: Subjects who received chewed (B) and crushed (C) LC with a meal had a smaller increase in serum P than those who received the meal alone (A). The increases in AUC from baseline for serum P were 4.7, 3.2, and 3.3 mg·hour/dL for arms A, B, and C, respectively (p=0.047). Of the seven subjects with detectable urine P concentrations, the total amounts of P excreted were 402, 356, and 344 mg for arms A, B, and C, respectively (p=NS).
CONCLUSIONS: The smaller change in serum P and AUC observed when LC was administered with the meal confirms that LC is an effective P binder. Chewed and crushed LC is similarly efficacious in binding dietary P.
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149. Outcomes Associated with Kidney Dysfunction in Cardiac Surgery Patients. *Judith L. Kristeller, Pharm.D.,*[1] Russell Stahl, M.D.[2]; (1) Wilkes University, Wilkes-Barre, PA; (2) Community Medical Center, Scranton, PA
PURPOSE: Kidney dysfunction is a risk factor for the development of postoperative kidney injury in cardiac surgery patients. The purpose of this study was to assess outcomes associated with baseline kidney dysfunction in patients undergoing cardiac surgery.
METHODS: Using our cardiothoracic surgery electronic database of 955 patients since 2005, we compared outcomes for patients with an estimated baseline glomerular filtration rate (GFR) less than 60 mL/minute/1.73 m^2 with outcomes for patients with an estimated GFR of 60 mL/minute/1.73 m^2 or greater. Using the modification-of-diet-in-renal-disease equation to estimate GFR, kidney dysfunction is defined as an estimated GFR less than 60 mL/minute/1.73 m^2.
RESULTS: Patients with an estimated GFR less than 60 mL/minute/1.73 m^2 have worse outcomes compared with patients having an estimated GFR of 60 mL/minute/1.73 m^2 or greater. The average 30-day mortality was higher in patients with kidney dysfunction (4.8% vs. 1.1%; p<0.001). The duration of hospital stay from the day of surgery to hospital discharge was longer in patients with kidney dysfunction (7.6 + 5.7 vs. 6.1 + 3.5 days; p<0.001). Total blood transfusions, defined as 1 unit of packed red blood cells, fresh frozen plasma, or pheresed platelets, were higher in patients with kidney dysfunction (4.4 + 5.3 vs. 2.0 + 4.0 units; p<0.001). Segment costs included variable costs or consumables (e.g., intravenous tubing, drugs) and direct costs or overhead expenses directly attributable to patient admission (e.g., days in the intensive care unit, use of the operating room). Segment costs were also higher in patients with kidney dysfunction ($23,519 + $9690 vs. $20,181 + $8686; p<0.001).
CONCLUSIONS: Based on our analysis demonstrating worse outcomes and higher health care resource allocation associated with impaired kidney function, it is prudent to target patients with an estimated GFR less than 60 mL/minute/1.73 m^2 for strategies to prevent worse outcomes.

150. Evaluation of Renal Dosing Recommendations in FDA Product Labeling Information of Approved and Marketed Drugs. *Thomas C. Dowling, Pharm.D., Ph.D.,*[1] Gary R. Matzke, Pharm.D.,[2] John E. Murphy, Pharm.D.,[3] Gilbert J. Burckart, Pharm.D.[4]; (1) University of Maryland, School of Pharmacy, Baltimore, MD; (2) Virginia Commonwealth University School of Pharmacy, Richmond, VA; (3) University of Arizona College of Pharmacy, Tucson, AZ; (4) Office of Clinical Pharmacology, CDER, FDA, Silver Spring, MD
PURPOSE: Dosing medications based on renal function is an important aspect of individualized pharmacotherapy. Recent adoption of estimated glomerular filtration rate (eGFR) using the modification-of-diet-in-renal-disease (MDRD) equation, new chronic kidney disease (CKD) classifications, and a calibrated creatinine assay has resulted in uncertainty among practitioners taking care of patients with impaired renal function (PIRF). The purpose of this study was to evaluate trends in the reporting of renal dosing information in U.S. Food and Drug Administration (FDA) Approved Product Labeling Information (PI).
METHODS: All new molecular entities (NMEs) approved during 1997–2007 for which dosing recommendations were proposed for PIRF were identified. All PI was reviewed to determine the methods to quantify renal function, the units of measure reported, and the use of CKD terminology.
RESULTS: A total of 45 NMEs included renal dosing recommendations in PI. The most common index of renal function was creatinine clearance (44 of 45); the Cockroft-Gault equation was specified in two cases, and GFR was measured in one. Standardization for body weight was rarely mentioned in any of the recommendations: the most common units of renal function measurement were mL/minute (34 of 45) and mL/minute/1.73 m^2 (4 of 45). No units of measure were reported for 7 of 45; rather, the general terms of mild/moderate/severe (6 of 45) or renal impairment were stated. The terms CKD, eGFR, and MDRD were not identified in PI.
CONCLUSIONS: Reporting of renal function methods and dosing recommendations for PIRF requires standardization to ensure optimal dosing. Substitution of eGFR for creatinine clearance for renal dosing is not supported by current PI and is not recommended at this time because of the lack of research. Studies evaluating the validity of using eGFR to predict drug clearance and thereby generate dosage recommendations are needed. **Disclaimer:** These comments are those of the authors and do not represent the official position of the FDA.

151. Compliance of the Pharmaceutical Industry with 1998 FDA Renal Guidance. *Gary R. Matzke, Pharm.D.,*[1] Thomas C. Dowling, Pharm.D., Ph.D.,[2] John E. Murphy, Pharm.D.,[3] Gilbert J. Burckart, Pharm.D.[4]; (1) Virginia Commonwealth University School of Pharmacy, Richmond, VA; (2) University of Maryland, School of Pharmacy, Baltimore, MD; (3) University of Arizona College of Pharmacy, Tucson, AZ; (4) Office of Clinical Pharmacology, CDER, FDA, Silver Spring, MD
PURPOSE: The 1998 U.S. Food and Drug Administration (FDA)

renal industry guidance provided the first regulatory expectation of when and how a pharmacokinetics (PK) study should be performed in patients with impaired renal function (PIRF).
METHODS: The package inserts for all FDA-approved new molecular entities (NMEs) from 1998 to 2007 were reviewed. The percentage of the NMEs excreted unchanged in the urine (% fe), the types of PK study, and any recommended dosage adjustments for PIRF were recorded. PK studies were categorized as full (more than four PIRF groups) or limited. The impact of the guidance was assessed by comparing the results with data from 1996 to 1997 (J Clin Pharmacol 2000;40:31–8).
RESULTS: Thirty-five of the NMEs had a % fe of more than 25, 11 had a % fe of 10–24.9, and the rest had a % fe of less than 10. Full or limited studies were conducted for 21 and 4, 7 and 2, and 22 and 19 of the NMEs in these respective categories. PK changes from full studies warranting dosage adjustment were noted for 68, 43, and 23% of the NMEs compared with 40, 0, and 32% when a limited study was done. The percentage of NMEs with a PK or hemodialysis study decreased from 56 and 15% in 1996–1997 to 42 and 10% in 1998–2007, respectively. The frequency with which full PK or hemodialysis studies were done in NMEs with a % fe greater than 25 increased from 25 and 15% in 1996–1997 to 64 and 48%.
CONCLUSIONS: An increase in PK studies or hemodialysis assessments was not noted among NMEs; however, more studies were conducted for NMEs that had the highest likelihood of needing dosage guidelines for PIRF.
Disclaimer: These comments are those of the authors and do not represent the official position of the FDA.

152. Medication Reconciliation in an Outpatient Hemodialysis Clinic. *Katie E. Pallotta, Pharm.D.,*[1] Darren W. Grabe, Pharm.D.,[1] Harold J. Manley, Pharm.D., BCPS,[2] Barbara E. Peck, R.N.[3]; (1) Albany College of Pharmacy, Albany, NY; (2) VillageHealth Disease Management, Albany, NY; (3) Albany Regional Kidney Center, Albany, NY
PURPOSE: Hemodialysis (HD) patients are at high risk of medication-related problems (MRPs). Relevant MRPs can only be found if an accurate medication list is available. Electronic medication records (EMRs) are often thought to improve medication reconciliation efforts. The goal of this study was to determine the accuracy of the EMR at an outpatient HD clinic.
METHODS: Medication reconciliation processes were applied at a local HD clinic to ensure accurate medication lists. A rigorous interview process was conducted to obtain medication lists for all clinic patients. The medication reconciliation process was completed by pharmacy interns during a 5-week advanced practice experience. Interns were trained and observed by a pharmacist preceptor. Reconciled medication lists were retrospectively compared with records from the EMR at the HD clinic. EMR medication entries were classified as correct or discrepant. HD clinic staff members were provided copies of reconciled medication lists, and initial findings were shared during an inservice presentation. Pharmacy students (different group) repeated the medication reconciliation process 6 months later, followed by the EMR comparison process.
RESULTS: Records from 164 patients were included in this analysis. One (less than 1%) patient medication record was completely accurate at baseline. A total of 507 (27%) individual medication entries at baseline were correct. After the inservice, medication list accuracy was statistically improved ($p<0.001$). Five (3.6%) patient medication records were completely accurate after 6 months. The number of correct individual medication entries increased to 37%.
CONCLUSIONS: Many discrepancies may occur in an EMR. Interventions to improve accuracy are needed to ensure patient safety. Pharmacy students were instrumental in collecting medication histories; however, further steps are needed to ensure updated EMR entries. Communicating the quantity and severity of discrepancies to clinic staff did not provide a clinically significant improvement in the accuracy of the EMR.

153. Role of Renal Function and Pharmacogenomics on Mycophenolic Acid Pharmacokinetics in Patients with Glomerular Diseases. *Melanie S. Joy, Pharm.D.,*[1] Jinzhao Wang, B.S.,[2] Tandrea Hilliard, B.S.,[2] Philip C. Smith, Ph.D.,[3] Mary Anne Dooley, M.D., MPH,[2] Ronald J. Falk, M.D.[2]; (1) University of North Carolina, Schools of Medicine and Pharmacy, UNC Kidney Center, Chapel Hill, NC; (2) University of North Carolina, School of Medicine, Chapel Hill, NC; (3) University of North Carolina, School of Pharmacy, Chapel Hill, NC
INTRODUCTION: Mycophenolic acid (MPA) is 98–99% protein bound, is metabolized by glucuronosyltransferases (UGTs), and undergoes enterohepatic recycling.
PURPOSE: To evaluate the effects of glomerular filtration rate (GFR) and UGT single nucleotide polymorphisms (SNPs) on the pharmacokinetics (PK) of MPA in glomerulonephritis.
METHODS: Heparinized plasma was obtained from 41 patients receiving MPA at 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours. MPA and major phenolic glucuronide (MPAG) were assayed by high-pressure liquid chromatography. DNA was isolated, and SNPs in UGT1A9 (T-275A, C-2152T, and T98C), UGT2B7 (C802T), and UGT1A7 (T622C) were assessed by allelic discrimination or direct sequencing. Statistics were analyzed by GraphPad Instat v. 3.0, and PK was analyzed by WinNonlin v. 4.1.
RESULTS: Demographics were race (25 W/16 nonwhite), gender (13 M/28 F), weight 85.0 ± 20.2 kg, GFR 97.2 ± 46.1 mL/minute, urinary protein-to-creatinine ratio 0.821, and albumin 4.18 ± 0.49 g/dL. PK differences by GFR are shown in the Table.

	GFR < 60 mL/minute (n=9)	GFR ≥ 60 mL/minute (n=32)
Cl/F (mL/minute)[a]	180 ± 96.1	349 ± 176*
$AUC_{0–12}$ (mg hour/L[b]	114 ± 69.8	51.2 ± 21.3*
$AUC_{6–12}$ (mg·hour/L)[b]	45.6 ± 32.0	17.8 ± 10.7
C_{trough} (µg/mL)[b]	8.84 ± 7.71	2.66 ± 1.94*
C_{max} (µg/mL)[b]	33.1 ± 30.6	17.9 ± 12.0
Cl_R (mL/minute)[a]	2.45 ± 2.81	4.59 ± 5.25
Cl/F unbound (L/minute)[a]	12.9 ± 7.65	37.1 ± 31.4*
MPAG $AUC_{0–12}$ (mg·hour/L)[b]	952 ± 617	386 ± 311*
MPAG Cl_R (mL/minute)[a]	19.3 ± 18.4	48.8 ± 46.8*

[a]Scaled by weight.
[b]Dose normalized.
*$p<0.05$ between GFR groups.
Cl/f = apparent total clearance.

Regarding genotyping, adequate frequencies of SNPs were found in UGT1A7 (T622C) and 2B7 (C802T) for comparisons. Presence of one or two UGT1A7 SNPs had reduced C_{max} (14.5 ± 9.92 vs. 28.7 ± 22.4 µg/mL; p=0.0106), area under the curve from 0 to 12 ($AUC_{0–12}$) (48.9 ± 20.2 vs. 82.9 ± 56.2 mg hour/L; p=0.0148), and $AUC_{6–12}$ (17.4 ± 10.6 vs. 31.1 ± 26.0 mg hour/L; p=0.0412) and increased renal clearance (Cl_R) (5.1 ± 4.3 vs. 3.2 ± 5.4 mL/minute; p=0.0255) versus wild types. Patients with a UGT2B7 (C802T) had increased T_{max} (1.7 ± 1.3 vs. 1.3 ± 1.8 hours; p=0.0554) versus wild types.
CONCLUSIONS: Alterations in GFR and SNPs in UGTs are responsible for differences in MPA disposition. Further evaluation is required to assess the contribution of other clinical parameters to enable an individualized approach to the treatment of glomerulonephritis.

Nutrition

154E. Hyperbilirubinemia Is More Common in Chronic Home Parenteral Nutrition Patients with Catheter Related Infections. *John K. Siepler, Pharm.D.*, Marianne Opilla, R.N., Thomas Diamantidis, Pharm.D., Reid A. Nishikiawa, Pharm.D., Rod Okamoto, B.S., R.Ph.; Nutrishare, Inc., Elk Grove, CA
PURPOSE: The cause of liver disease in chronic home parenteral nutrition (HPN) patients is multifactorial. Potential causes are excessive calorie delivery, deficiency of nutrients such as choline, and infections. Catheter infections (CRBSI) and exit site infections (EI) are common in HPN patients. We evaluated HPN patients to determine if abnormal bilirubin (BILI) was associated with CRBSI and EI.

METHODS: We examined the records of HPN patients from a home care provider for 2 years. We collected patient demographics and all BILI results as well as all CRBSI and EI. The patients were divided into those who had a CRBSI and/or EI (group 1) and those who did not (group 2). Mean maximum BILI and BILIs greater than 1.5, greater than 2, greater than 3, and greater than 5 were recorded in the two groups. Statistics were performed using a t-test and a chi-square test, with $p<0.05$ considered significant.
RESULTS: There were 136 patients; of those, 66 (48%) were in group 1. Patient demographics were similar in the groups. Mean maximum BILI was significantly higher in group 1 (1.89 ± 2.5 vs. 1.14 ± 1.4; p=0.02). Nineteen patients (29%) in group 1 and 10 (14%) in group 2 had a BILI greater than 1.5 (p=0.04). Eighteen (27%) in group 1 and seven (10%) in group 2 had a BILI greater than 2 (p=0.004). Ten (15%) in group 1 and three (4%) in group 2 had a BILI greater than 3 (p=0.02). Seven (11%) in group 1 and two (3%) in group 2 had a BILI greater than 5 (p=0.07). Using logistic regression, group 1 was more likely to have an abnormal BILI (OR = 1.5, 95% CI: 1.01–2.1; p=0.047).
CONCLUSIONS: We examined BILIs in 136 HPN patients, finding that abnormal BILI was more common in patients who had CRBSI and/or EI. Mean maximum BILI and number of patients who had BILI greater than 1.5, 2, and 3 were more common in those who had CRBSI and/or EI. The causes of BILI elevations in HPN patients are multifactorial, but age, gender, duration of HPN, arachidonic acid, choline, and fat provisions were similar in the two groups.
To be presented at the European Society of Parenteral and Enteral Nutrition Annual Meeting in Florence, Italy, September 2008.

Obesity

155. Incidence of Vitamin D Deficiency After Gastric Bypass Surgery. *Margaret Malone, Ph.D., FCCP,*[1] Sharon Alger-Mayer, M.D.[2]; (1) Albany College of Pharmacy, Albany, NY; (2) Albany Medical College, Albany, NY

PURPOSE: Patients undergoing gastric bypass surgery are at particular risk of calcium and vitamin D deficiency because the most active site of calcium absorption, the proximal duodenum, is bypassed as part of this procedure. In this retrospective study, we evaluated the 25-OH vitamin D and parathyroid hormone (PTH) levels of patients who had undergone gastric bypass surgery supplemented with usual care daily calcium (1200 mg) and vitamin D (800 units) daily.
METHODS: Medical charts from patients who had undergone gastric bypass surgery for weight loss were examined to collect their vitamin D and PTH levels after surgery. Data were stratified by the time (months) after surgery, n = number of samples during the period. Data are reported as the percentage of blood samples in which 25-OH vitamin D was more than 30 ng/mL or PTH was more than 69 mg/dL for each time interval.
RESULTS: One hundred sixty-four patients were included (135 females). The number of blood samples taken after surgery varied for each patient. Before surgery, 30%, n=4 of 13 of the 25-OH vitamin D level were more than 30 ng/mL; no PTH data were available. After surgery, the percentage of samples with 25-OH vitamin D more than 30 ng/mL per period was as follows: 1–3 months, 27% n=28 of 105; 4–6 months, 34%, n=34 of 97; 7–12 months, 40%, n=40 of 205; 13–24 months, 30%, n=17 of 56; 25–36 months, 34%, n=34 of 44; 37–48 months, 25%, n=5 of 20; 49–72 months, 26%, n=8 of 31; and 7–127 months, 48%, n=20 of 42. The percentage of samples with PTH more than 69 mg/dL was as follows: 1–3 months, 10%, n=4 of 40; 4–6 months, 19%, n=8 of 42; 7–12 months, 17%, n=12 of 71; 13–24 months, 27%, n=8 of 30; 25–36 months, 18%, n=5 of 27; 37–48 months, 21%, n=3 of 14; 49–72 months, 29%, n=5 of 17; and 73–127 months, 19%, n=6 of 31.
CONCLUSIONS: Most of these patients after gastric bypass had inadequate vitamin D concentrations in spite of supplementation. This may have been because of non-adherence with supplement recommendations, which we could not assess; inadequate intake; or both; this is an issue that warrants further investigation.

Oncology

156. Evaluation of a Change in Prescribing Patterns of Darbepoetin Alfa on Red Blood Cell Transfusion Requirements in Patients with Chemotherapy-Induced Anemia. *David M. Baribeault, B.S., BCOP*; Boston Medical Center, Boston, MA

PURPOSE: In July 2007, the Center for Medicare and Medicaid Services released new reimbursement requirements for the administration of erythropoietin-stimulating agents (ESAs). Pursuant to that release, our collaboratively developed treatment algorithm for chemotherapy-induced anemia was amended to reflect those changes. Because ESAs were approved by the U.S. Food and Drug Administration to decrease the reliance on packed red blood cell (PRBC) transfusion rates, and not to maintain any arbitrary hemoglobin concentration, an evaluation of the rates of PRBC transfusion before and after the change in treatment algorithm was conducted.
METHODS: Retrospective chart reviews for all patients with chemotherapy-induced anemia were conducted to evaluate transfusion rates. Patients were excluded if they had received a stem cell transplant (SCT) or who had a diagnosis of chronic lymphocytic leukemia. The two periods selected for this review were the 6 months immediately before the change in treatment algorithm and the 6 months immediately after the change, allowing a 28-day washout period. Additional data collected and analyzed included length of ESA treatment and ESA doses used.
RESULTS: The rate of PRBC transfusion increased by more than 36% after the change in practice. The duration of ESA therapy decreased in the second observation period by almost 25%. The cumulative dose of ESA decreased in the second observation period by 10%, and the average dose of ESA administered per treatment increased by around 20%.
CONCLUSIONS: After a change in practice related to the use of ESAs, the rate of PRBC transfusion at our center increased. Although the average length of therapy and the cumulative dose of ESA decreased in the 6 months after the change in practice, much higher individual doses of ESA were necessary to maintain the hemoglobin concentrations at 10 g/dL. Further investigation is warranted.

157E. Comparison of Erythroid Response (ER) Rates to Epoetin Alfa (EPO) Alone or in Combination vs Non-Erythropoiesis-Stimulating Agents (non-ESAs) in Treatment-Naïve Anemic MDS Patients – A Meta-analysis Approach. Victor Moyo, M.D.,[1] Patrick Lefebvre, M.A.,[2] Francis Vekeman, M.A.,[2] Mei-Sheng Duh, MPH, Sc.D.,[3] Behin Yektashenas, Pharm.D.,[1] *Suneel Mundle, Ph.D.*[1]; (1) Centocor Ortho Biotech Services, LLC, Bridgewater, NJ; (2) Groupe d'Analyse, Ltée., Montreal, QC, Canada; (3) Analysis Group, Inc., Boston, MA

PURPOSE: The combination of epoetin alfa (EPO) and granulocyte-macrophage colony stimulating factor (G/GM-CSF) has been associated with higher erythroid response (ER) rates versus EPO alone. Several non–erythropoiesis-stimulating agents (non-ESAs) have also been studied as single agents or in combination without growth factor. This meta-analysis compared ER rates achieved with EPO either as a single agent or in combination with G/GM-CSF or other agents versus non-ESA therapies (including thalidomide, azacytidine, all-*trans*-retinoic acid, and As_2O_3).
METHODS: Data were extracted from studies in PubMed, ASCO/ASH proceedings in myeloid dysplastic syndrome (MDS) patients treated with EPO±G/GM-CSF or other non-ESAs (cutoff September 30, 2007). For cross-comparison, only studies using International Working Group (IWG) or IWG-like ER criteria and treatment-naïve patients were selected. Pooled estimates of ER rates were calculated using random-effect (R-E) meta-analysis methods and were stratified by (1) EPO monotherapy (monotx), (2) EPO+G/GM-CSF, (3) EPO+non-ESAs, (4) non-ESA monotx, and (5) non-ESA combinations.
RESULTS: A total of 790 studies were identified; 35 were included. Most patients (more than 59%) had RA/RARS, except for patients receiving other non-ESAs in combination (45%). EPO monotx studies had lower transfusion dependency rates at baseline versus studies using EPO combinations or non-ESAs. EPO monotx studies

had comparable ER rates with studies using EPO+G/GM-CSF (p=0.371) or EPO + non-ESAs (p=0.642). However, EPO monotx studies had higher ER rates than non-ESA studies whether monotx (p=0.001) or combination regimens were used (p<0.001). Higher ER rates were also observed for studies using EPO+G/GM-CSF or EPO + non-ESAs versus studies using only non-ESAs in monotx or combination regimens.
CONCLUSIONS: These results suggest that in appropriately selected treatment-naïve patients, except for lenalidomide in del 5q patients, non-ESA therapies yield lower ER rates versus EPO monotx or EPO combination regimens. The benefit of adding non-ESAs to EPO warrants further evaluation.

Study Group	EPO Monotx	EPO+G/ GM-CSF	EPO + Non-ESAs	Non-ESA Monotx	Combination Regimens
No. of studies	9	6	4	11	5
No. of evaluable patients	589	152	108	413	91
Overall ER					
R-E %s (95% CI)					
Crude %s (95% CI)	57.6	53.0	50.7	50.7	62.9
	(45–70)	(49–57)	(42–59)	(43–59)	(44–81)
	64.8	30.9	33.2	25.3	26.4
	(56–74)	(21–41)	(29–38)	(17–34)	(17–35)

Presented at the 44th Annual American Society of Clinical Oncology (ASCO) Meeting, Chicago, IL, May 30–June 3, 2008.

158E. A Phase II Study of Intravenous REOLYSIN (Wild-type Reovirus) in the Treatment of Patients with Bone and Soft Tissue Sarcomas Metastatic to the Lung. *Scott A. Soefje, Pharm.D.,*[1] John Sarantopoulos, M.D.,[1] Kamalesh Sankhala, M.D.,[1] Catalain C. Mita, M.D.[1], J.J. Mahany, PA-C,[1] Tony Carmona, CCRC, CCRP,[1] Matt Coffey, Ph.D.,[2] George M. Gill, M.D.,[2] Karl Mettinger, M.D., Ph.D.,[2] Monica Mita, M.D.[1]; (1) University of Texas Health Science Center at San Antonio Cancer Therapy & Research Center, San Antonio, TX; (2) Oncolytics Biotech, Inc., Calgary, AB, Canada
PURPOSE: Reolysin (reovirus serotype 3) is a Dearing strain, naturally occurring, ubiquitous, human reovirus that replicates specifically in transformed cells possessing an activated Ras pathway producing cell lysis. The community-acquired infection is mild and limited to the upper respiratory and gastrointestinal tract. In vitro and in vivo studies in sarcoma cell lines showed significant antitumor activity.
METHODS: This phase II study was designed to characterize the efficacy and safety of Reolysin given intravenously every 28 days in patients with bone or soft tissue sarcoma with lung metastasis using a Simon two-stage design. Thirty-eight patients were be enrolled in the first stage, and up to 52 patients were enrolled in the second stage if at least one patient in the first stage experienced partial response or stable disease for at least 6 months.
RESULTS: Since July 2007, 21 patients (13 women), age 22–70 (median 51) were enrolled. Tumor types included malignant fibrous histiocytoma (5), osteosarcoma (5), leiomyosarcoma (4), synovial sarcoma (4), liposarcoma (1), Ewing's sarcoma (1), and undifferentiated round cell sarcoma (1). All patients had ECOG performance status 0 (10) or 1 (11). Eighteen patients had received prior chemotherapy, radiotherapy, biologic agents, or combinations for their metastatic disease. Side effects were mild to moderate (grade 1 or 2) and included mainly constitutional symptoms: fever, chills, arthralgia, and fatigue in all patients. Two patients experienced respiratory side effects such as cough and shortness of breath, and two patients had diarrhea. Hematologic side effects were rare and included neutropenia, with grade 2 or 3 (5) and grade 4 (1), and thrombocytopenia, with grade 2 (2). One patient experienced grade 2 aspartate aminotransferase elevation. Sixteen patients were evaluable for response to date: 3 patients had SD (10+, 4, and 2+ months), and 13 patients had PD.
CONCLUSIONS: Reolysin is well tolerated and shows promise for the treatment of metastatic sarcoma. Accrual is ongoing.
Published in J Clin Oncol 2008;26:A10568.

159. Pharmacokinetics of High-Dose Etoposide in Children Undergoing Autologous Stem Cell Transplantation for Various Solid Tumors: Relationship Between Age and Clearance. *Timothy R. McGuire, Pharm.D.,*[1] Konstantine Manouilov, Ph.D.,[2] Jasmine P. Davda, Ph.D.,[3] Bruce Gordon, M.D.[4]; (1) UNMC College of Pharmacy, Omaha, NE; (2) Quintiles, Inc., Overland Park, KS; (3) UNMC, Omaha, NE; (4) UNMC College of Medicine, Omaha, NE
PURPOSE: The goals of this study were to characterize the pharmacokinetics of high-dose etoposide in a pediatric population and to determine the relationship between pharmacokinetic values and patient characteristics, particularly age.
METHODS: Twenty-six children with solid tumors received high-dose etoposide at 1500 mg/m^2 as a continuous infusion for 24 hours. Blood samples were collected before dosing and then at 6, 12, 24, 30, 36, and 42 hours after the start of the infusion. The pharmacokinetics of etoposide was described by noncompartmental analysis. Clearance values normalized for body surface area (BSA) were compared between patients younger than 10 years and 10 years and older using the Mann-Whitney Rank Sum. A one-compartment model was also used to describe the population pharmacokinetics of etoposide by NONMEM. The effects of age, weight, BSA, and gender were tested to explain the intersubject variability of apparent clearance and volume of distribution.
RESULTS: BSA-normalized clearance was significantly higher in patients younger than 10 years compared with older children (p=0.02). NONMEM analysis demonstrated a significant influence of age (p<0.05) and body weight (p<0.05) on clearance, as well as age (p<0.01), body weight (p<0.01), and BSA (p<0.05) on volume of distribution. The model indicated that the patient's age had the most prominent effect on clearance and volume of distribution.
CONCLUSIONS: Consistent with some, but not all, previous reports, this study suggests an age-related effect on etoposide clearance.

160. Impact of Calcium and Magnesium Infusions on Response Rates in Metastatic Colorectal Cancer Patients Treated with Oxaliplatin. *Emily B. Borders, Pharm.D.*, Val R. Adams, Pharm.D., BCOP, FCCP; University of Kentucky, Lexington, KY
PURPOSE: Calcium gluconate and magnesium sulfate infusions are routinely used for the prevention of oxaliplatin-induced neuropathy. These infusions have recently been linked to lower response rates in metastatic colorectal cancer (mCRC) patients. The primary objective of this study was to compare response rates in mCRC patients treated with oxaliplatin-containing regimens alone versus patients treated with oxaliplatin-containing regimens plus calcium and magnesium infusions. The secondary objective was to compare the incidence of neuropathy between the two patient populations.
METHODS: The current study was a retrospective review of colorectal cancer patients treated with oxaliplatin at the Markey Cancer Center and the VA Hospital in Lexington, Kentucky. All mCRC patients treated with an oxaliplatin-containing chemotherapy regimen from August 2002 through August 2007 were included. Data collected included age, gender, diagnosis, presence of calcium and magnesium infusions, best response to therapy, chemotherapy regimen, and total oxaliplatin dose. The data will be evaluated using descriptive statistics.
RESULTS: More than 140 patients have been identified for inclusion in the study. Twenty-eight patients have been evaluated to date. The overall response rate was 41% (44 of 68) for patients who received calcium and magnesium infusions versus 50% (2 of 4) for patients who did not receive calcium and magnesium. The incidence of neuropathy was 36% (17 of 47) versus 50% (2 of 4) (with calcium and magnesium vs. without).
CONCLUSIONS: Research is in progress, and no final conclusions can be made; however, calcium and magnesium do not appear to lower response rates, but they do decrease neuropathy. Updated information will be presented.

161E. Vaccination of Renal Cell Cancer Patients with Modified Vaccinia Ankara Delivering Tumor Antigen 5T4 (TroVax) Administered with IL-2: A Phase II Trial. *Jose R. Murillo Jr., Pharm.D.,*[1] Joan Hernandez-McClain, MPH,[2] Robert J. Amato, M.D.,[2] Valerie C. Vance, B.S.,[2] Jaroslaw Jac, M.D.,[2] James P. Willis, M.D.,[2] Somyata X. Saxena, B.S.,[2] William Shingler, Ph.D.,[3] Stuart Naylor, Ph.D.,[3] Richard Harrop, Ph.D.[3]; (1) The Methodist Hospital,

Houston, TX; (2) The Methodist Hospital Research Institute, Houston, TX; (3) Oxford BioMedica, Oxford, UK

PURPOSE: The attenuated vaccinia virus MVA delivers the tumor antigen 5T4 (TroVax). More than 90% of renal tumors overexpress 5T4. TroVax has been evaluated in combination with low-dose IL-2 in an open-label phase II trial in metastatic renal cell cancer (RCC) patients. The safety and immunologic potency of TroVax in combination with IL-2 was determined.

METHODS: Eligibility: pathologic diagnosis of clear cell or papillary RCC, progressive measurable metastases, any prior therapy, adequate physiologic parameters, Karnofsky PS more than 80%, no active central nervous system involvement. IL-2 was administered subcutaneously in 8-week cycles at a dose of 250,000 µ/kg in week 1 (days 1–5) and 125,000 µ/kg in weeks 2–6 (days 1–5), followed by 2 weeks off. Up to six cycles of IL-2 were administered during a 48-week period. TroVax was administered by intramuscular injection every 3–4 weeks for the first four injections and every 8–12 weeks thereafter. Twenty-five patients with metastatic RCC were treated with TroVax plus IL-2. 5T4-specific cellular and humoral responses were followed, and clinical responses were assessed using RECIST criteria.

RESULTS: TroVax was well tolerated with no serious adverse events attributed to vaccination. Of 25 intent-to-treat patients, 21 mounted 5T4-specific antibody responses. Two patients showed a complete response (2 for 24+ months), 1 patient had a partial response (12+ months), and 6 patients had disease stabilization (6–21+ months). Median progression-free survival (PFS) and overall survival (OS) were 3.4+ months (1.5–24.8+) and 12.9+ months (1.9–24.8+), respectively. A statistically significant correlation was detected between the magnitude of 5T4-specific antibody responses and PFS and OS.

CONCLUSIONS: TroVax plus IL-2 was safe and well tolerated in all patients. The high frequency of 5T4-specific immune responses, number of complete responses, and correlation with clinical benefit are encouraging and warrant further investigation. A phase III study with TroVax (TRIST; TroVax Renal Immunotherapy Survival Trial) has completed accural.

Presented at the 2008 American Society of Clinical Oncology Annual Meeting, Chicago, IL, May 30–June 3, 2008.

Ophthalmology

162E. Effects of Bromfenac Sodium on Acute and Chronic Uveitis in Rabbits. Takahiro Ogawa, Ph.D.,[1] Tetsuo Kida, M.Sc.,[2] John J. Han, Pharm.D.,[3] *Clara K. Song, Pharm.D.,*[3] Timothy R. McNamara, Pharm.D.[3]; (1) Senju USA Inc., Woodland Hills, CA; (2) Preclinical Laboratories, Senju Pharmaceutical Co., Ltd., Kobe, Japan; (3) ISTA Pharmaceuticals, Inc., Irvine, CA

PURPOSE: Evaluate bromfenac sodium (BF) 0.1% ophthalmic solution in treatment of acute and chronic uveitis in several rabbit models.

METHODS: BF was tested on Dutch belted and white rabbits. *Acute anterior uveitis:* (a) Lipopolysaccharide (LPS) was injected intravenously into a marginal ear vein. One drop of BF was instilled at 1 hour before injection or 1 hour before and then every hour for 8 hours. Aqueous flare was continuously measured with a flare cell meter for 8 hours. (b) LPS was injected intravitreously. BF was instilled every 2 hours for 24 hours. Anterior inflammation was observed using slit lamp, and aqueous cells were measured at 24 hours. *Chronic uveitis:* BSA was injected intravitreously. BF or dexamethasone (DM) instilled 2 times/day. Anterior and posterior inflammations were observed for 25 days.

RESULTS: *Acute anterior uveitis:* Intravenous LPS increased aqueous flare, with peak level occurring at 1 hour. Single-drop instillation of BF completely inhibited increase in aqueous protein production, whereas pranoprofen demonstrated only 70% inhibition even with 8 times the dosing frequency. Intravitreous LPS gradually increased aqueous protein until 24 hours. BF demonstrated complete inhibition in anterior inflammatory signs and significant inhibition in polymorphonuclear leukocyte infiltration in anterior chamber. DM inhibited inflammatory signs by 50% and strongly inhibited elevation of leukocytes. *Chronic uveitis:* Ocular inflammatory signs induced by BSA reached peak levels between days 10 and 12. BF decreased anterior and posterior inflammations by 70 and 50%, respectively. DM inhibited anterior and posterior inflammation by 70 and 80%, respectively.

CONCLUSIONS: These studies suggest that COX enzyme is strongly involved in uveitis and that endogenously released eicosanoids induce signs of anterior and posterior inflammation observed in uveitis. BF was as efficacious in inhibiting both acute and chronic uveitis in rabbits as DM. These results confirm the efficacy seen in humans for anterior uveitis and suggest the possibility of its application and effectiveness in posterior uveitis.

Presented at the 80th Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, Ft. Lauderdale, FL, April 27–May 2, 2008. 4742/A548.

163E. Effect of Topical Bromfenac Sodium 0.1% Ophthalmic Solution on Laser-Induced Choroidal Neovascularization in Mice. Tetsuo Kida, M.Sc.,[1] Takahiro Ogawa, Ph.D.,[2] Hideyuki Sakaki, Ph.D.,[1] John J. Han, Pharm.D.,[3] *Clara K. Song, Pharm.D.,*[3] Tim R. McNamara, Pharm.D.[3]; (1) Preclinical Laboratories, Senju Pharmaceutical Co., Ltd., Kobe, Japan; (2) Senju USA Inc., Woodland Hills, CA; (3) ISTA Pharmaceuticals, Inc., Irvine, CA

PURPOSE: To evaluate the inhibitory effect of topically applied bromfenac sodium (BF) 0.1% ophthalmic solution, a nonsteroidal anti-inflammatory drug possessing potent cyclooxygenase (COX)-1and COX-2 inhibitory activity, in mice with choroidal neovascularization (CNV) induced by laser photo coagulation, and to compare the effect of BF 0.1% with vascular endothelial growth factor (VEGF)-neutralizing protein, recombinant murine soluble VEGF receptor 1/Fc chimeric protein (sVEGFR-1/Fc), in this model.

METHODS: Six-week-old female C57BL/6J mice were used. Laser burns with a 514-nm algon laser were performed at the posterior retina of anesthetized mice. Nineteen mice with successful laser burn were randomly assigned to receive one of three treatments: BF 0.1% or saline with or without an intravitreous injection of 250 ng of sVEGFR-1/Fc immediately after the laser burn. Mice were topically treated with 4 µL of BF 0.1% or saline 4 times/day for 2 weeks. Then, deeply anesthetized mice were perfused with 50 mg/mL fluorescein-labeled dextran. Eyes were enucleated and fixed in buffered formalin. The flat mounts of the retinal pigment epithelium–choroid–sclera were observed by fluorescence microscope. The total area of hyperfluorescent neovasculature was measured by image analysis software.

RESULTS: Measurement of the CNV area demonstrated that treatment with either topical BF 0.1% or intravitreous sVEGFR-1/Fc for 2 weeks resulted in significantly smaller CNV lesions than with saline. BF 0.1% and sVEGFR-1/Fc inhibited CNV at the rate of 71 and 51%, respectively.

CONCLUSIONS: Topical BF 0.1% ophthalmic solution significantly inhibited laser-induced CNV in mice. The degree of inhibition was similar to intravitreously administered sVEGFR-1/Fc. This study suggests that the COX enzyme is strongly involved in the promotion of CNV and that BF may be a useful drug in the treatment of posterior ocular diseases associated with neovascularization.

Presented at the World Ophthalmology Congress (WOC) Meeting, Hong Kong, June 28–July 2, 2008. Abstract 006675.

Pain Management/Analgesia

164E. Pharmacokinetics of Oxymorphone Extended-Release Tablets Following Consumption of Food or Alcohol. William D. Fiske, Ph.D., Irma H. Benedek, Ph.D., Harry Ahdieh, Ph.D., *Nancy Alvarez, Pharm.D.*; Endo Pharmaceuticals Inc., Chadds Ford, PA

PURPOSE: Two studies assessed the in vivo bioavailability of oral oxymorphone extended-release (ER) tablets under fed and fasted conditions (study 1) or after alcohol consumption (study 2).

METHODS: Both studies used a four-period crossover design wherein healthy volunteers were randomized to receive a single oral dose of oxymorphone ER (40 mg) under fasting conditions and

after a high-fat meal (oxymorphone immediate release was the study drug in the other two periods) or with each of four aqueous ethanol solutions (0, 4, 20, or 40%). All subjects received naltrexone (50 mg) to minimize opioid-related adverse events, and each treatment was separated by a 7-day washout. Serial blood samples for oxymorphone pharmacokinetics were obtained through 72 (study 1) or 48 (study 2) hours postdose.
RESULTS: Neither food nor ethanol significantly altered area under the curve or other pharmacokinetic parameters, aside from maximum concentration (C_{max}). In study 1, C_{max} was increased by 51% (geometric mean ratio for C_{max} = 1.51; 90% CI: 1.34–1.70) in fed subjects versus fasted subjects. In study 2, concentration-related increases in C_{max} (7, 31, or 70%) were observed when oxymorphone ER was administered with ethanol 4, 20, or 40%, respectively, relative to administration with water. Alterations in C_{max} appear unrelated to direct effects of alcohol on the oxymorphone ER tablet because the rate of oxymorphone release in vitro is unaffected by alcohol concentrations up to 40%.
CONCLUSIONS: Increases in the C_{max} of oxymorphone ER with a high-fat meal or alcohol were similar and unrelated to ER matrix degradation, suggesting that the increases occur by a similar mechanism (e.g., gastric emptying, increased splanchnic blood flow). Although the clinical impact of these C_{max} elevations is unknown, patients are advised not to take oxymorphone ER on a full stomach or with alcohol.
This research was funded by Endo Pharmaceuticals Inc. Published in J Pain 2008;9(suppl):36.

165E. Single-Dose Pharmacokinetic Comparison of ProSorb® Diclofenac Potassium Formulations. *Keith A. Moore, Pharm.D.,*[1] Dwight Stiff, Ph.D.,[2] Michael Lissy, M.D.,[2] Stephen E. Boesing, M.S.[1]; (1) Xanodyne Pharmaceuticals, Inc., Newport, KY; (2) AAIPharma Inc., Neu-Ulm, Germany
PURPOSE: The clinical utility of diclofenac potassium, a commonly prescribed analgesic, for mild to moderate pain relief may be hindered by its delayed, depressed, and/or inconsistent absorption characteristics. A diclofenac potassium formulation using ProSorb dispersion technology was developed to overcome these limitations. We evaluated and compared the pharmacokinetics of two investigational diclofenac potassium soft gelatin capsule (DPSGC) preparations and one investigational diclofenac liquid formulation, each incorporating ProSorb dispersion technology, to identify a formulation for further clinical study.
METHODS: In an open-label, single-dose, three-way crossover, relative bioavailability study, 24 healthy volunteers were randomized to receive each of the 25-mg DPSGC solid formulations prepared by different development processes (process A and process B) and a 1-mL (25 mg) liquid diclofenac formulation (similar to the fill liquid used to formulate the DPSGC products) during three inpatient visits, each separated by 3 days. Plasma samples were collected at selected time points through 6 hours after each dose. Diclofenac concentrations were determined using a validated high-pressure liquid chromatography method. Safety and tolerability were monitored throughout.
RESULTS: Area under the plasma concentration-time curve (AUC_{0-t}) for the three formulations was between 577 and 583 ng·hour/mL, and peak plasma concentrations (C_{max}) were between 958 and 1087 ng/mL, with the DPSGC process B group having the highest C_{max}. The times to C_{max} (t_{max}) were all less than 30 minutes, with the liquid formulation producing the shortest t_{max} (15 minutes). Plasma concentration-time course profiles showed consistent absorption characteristics for all three ProSorb diclofenac potassium formulations. One mild adverse event was observed (lingual paresthesia), and one participant discontinued because of an unrelated event (acute tonsillitis).
CONCLUSIONS: These data show that diclofenac potassium formulations using ProSorb dispersion technology are rapidly and consistently absorbed. These characteristics may be beneficial in settings where rapid and consistent drug absorption is desirable.
Supported by Xanodyne Pharmaceuticals, Inc.
Presented at ***ACCP: Please note, this poster has not been accepted at PAINWeek yet. If rejected, it will NOT be an encore presentation. Therefore, status to be determined. If accepted, citation is: "To be presented at PAINWeek 2008, Las Vegas, NV, September 4, 2008."

166. Complications Associated with Postoperative Intravenous Analgesia in Hospitals in the United States. *Winnie W. Nelson, Pharm.D., M.S.,*[1] Joris Diels, M.Sc.,[2] Shane Kavanagh, M.Sc.[2]; (1) Johnson & Johnson Pharmaceutical Services, Raritan, NJ; (2) Janssen Pharmaceutica, Beerse, Belgium
PURPOSE: To determine the incidence of complications associated with duration of exposure to postoperative intravenous analgesia.
METHODS: Of the 5 million discharges in the 2003 U.S. Premier Hospital Database, inclusion criteria were applied to define a patient population 18 years and older who underwent moderate to severe surgical procedures with likely significant postoperative pain. ICD-9-CM codes were used to identify complications caused by intravenous analgesic modalities. The incidence of complications caused by catheter/needle-related infections, complications associated with immobility (deep vein thrombosis [DVT] and pulmonary embolism [PE]), and complications associated with anticoagulants was assessed at different exposure intervals: no exposure, 1 day, 2 days, 3 days, and 4 or more days of exposure.
RESULTS: Of the 681,487 hospitalizations examined, the incidence of complications increased with the length of exposure to intravenous analgesic modalities. After adjusting for background covariates, the odds ratios of developing a catheter/needle-related infection, DVT, PE, and complications associated with anticoagulants were 2.18 (95% CI: 1.91–2.48), 1.88 (1.49–2.37), 1.39 (1.19–1.62), and 1.62 (1.52–1.74), respectively, comparing patients with 4 or more days of intravenous exposure with patients with no exposure ($p<0.0001$ for all four comparisons). Shorter exposures (1, 2, and 3 days) were also associated with increased odds of a complication compared with patients with no exposure. Increased duration of exposure was associated with increasing magnitude of the complication risk, supporting a trend similar to a dose-response relationship.
CONCLUSIONS: A retrospective analysis of hospital data indicated that increased duration of postoperative intravenous analgesia is associated with increased incidence of complications.

167E. Open-Label, Long-Term Assessment of Tolerability, Safety, and Effectiveness of Oxymorphone Extended Release for Chronic Low Back Pain. *Nancy Alvarez, Pharm.D.,*[1] Martin E. Hale, M.D.,[2] Marvin Tark, M.D.,[3] Harry Ahdieh, M.D.[1]; (1) Endo Pharmaceuticals Inc., Chadds Ford, PA; (2) Gold Coast Research LLC, Weston, FL; (3) Georgia Pain Clinic, Marietta, GA
PURPOSE: Chronic low back pain (CLBP) is among the leading causes of disability in the United States. Although opioid use for acute pain has been accepted for decades, CLBP management remains suboptimal because physicians are often reluctant to prescribe opioids for long-term use. We examined the long-term safety and effectiveness of oxymorphone extended release (ER) in patients with CLBP.
METHODS: This phase III, multicenter, open-label, 1-year study included men and women (age 18–75 years) with moderate to severe CLBP who had completed a previous double-blind trial of oxymorphone ER. Patients continued oxymorphone ER based on their dose in the previous study or were switched to oxymorphone ER from placebo and titrated to an optimal dose. Oxymorphone immediate release (IR) was available as rescue medication. Outcome measures included the 11-point Brief Pain Inventory (BPI; 0 = no pain, 10 = worst pain imaginable), Recall of Average Pain Relief (0% = no relief; 100% = complete relief), rescue medication use, and adverse events (AEs).
RESULTS: The safety population included 203 patients. The intent-to-treat population included 195 patients, of whom 73 (36%) completed the study. The mean dose of oxymorphone ER (115.5 ± 5.6 mg/day for the entire year) increased modestly during the study. The mean rescue medication dose of oxymorphone IR (17.6 ± 0.6 mg/day) remained stable throughout the year. The BPI scores (range 4.5–4.8) remained consistently lower than pretreatment levels. Pain relief was consistently rated at 60–70%. Adverse events

were reported by 147 (72.4%) patients, of whom 61 (30.1%) experienced AEs that were considered possibly or probably related to treatment. Eight patients experienced serious AEs. Twenty-eight (13.8%) discontinued treatment because of AEs.
CONCLUSIONS: In patients with moderate to severe CLBP, oxymorphone ER provided effective analgesia and was generally well tolerated. Little dose escalation was required.
Presented at the American Academy of Pain Medicine, Orlando, FL, May 4–7, 2004.

Pediatrics

168. Effectiveness of Recombinant Human Hyaluronidase-Augmented Subcutaneous Hydration in Children. *Coburn H. Allen, M.D.*, Andrea T. Cruz, M.D., Binita Patel, M.D., Erin E. Endom, M.D., Troy Bush, B.S., CCRP; Baylor College of Medicine and Texas Children's Hospital, Houston, TX
PURPOSE: Intravenous fluid therapy is challenging in dehydrated children with difficult venous access because of small, delicate veins or hypovolemia. Instead, fluid can be given by subcutaneous (SC) administration using recombinant human hyaluronidase (rHuPH20), a spreading agent that increases absorption. The Increased Flow Utilizing Subcutaneously Enabled–Pediatric Rehydration (INFUSE–Pediatric Rehydration) Study is designed to assess the utility, safety, and effectiveness of rHuPH20-augmented SC hydration.
METHODS: This is an ongoing multicenter, open-label, single-arm, phase IV proof-of-concept trial in patients age 2 months to 10 years with mild to moderate dehydration (Gorelick score 1–5) needing parenteral therapy. They receive 1 mL (150 U) SC rHuPH20, followed by 20 mL/kg of SC isotonic fluid during the first hour. SC maintenance hydration is continued as needed for up to 72 hours. Rehydration is deemed successful if the investigator attributes it primarily to rHuPH20-augmented SC fluid infusion and if the child is discharged from the emergency department without needing alternative fluid therapy. Target enrollment (50) should be completed by July 2008.
RESULTS: In the first 17 patients treated, mean age and weight were 2.0 years and 11.7 kg, respectively. Rehydration was successful in 14 (82%) patients. In the 14 patients who received the initial bolus (18 mL/kg or greater within the first 70 minutes), mean volume given the first hour was 19.5 mL/kg. Among all 17 patients, mean improvement in Gorelick score was -2.8 points. Mean total volume infused was 33.6 mL/kg (range 1.4–85.0 mL/kg). Infusions lasted 0.2–18.1 hours. Median time to first urine output was 1.5 hours (n=14), and median time to emergency department discharge was 3.4 hours. All patients had typical infusion site reactions, but none had serious adverse effects.
CONCLUSIONS: rHuPH20-augmented SC hydration appears to be a safe and effective way to provide clinically indicated fluid volumes in young children with mild to moderate dehydration.

169. Safety of Recombinant Human Hyaluronidase-Augmented Subcutaneous Hydration in Children. *Coburn H. Allen, M.D.*, Andrea T. Cruz, M.D., Binita Patel, M.D., Erin E. Endom, M.D., Troy Bush, B.S., CCRP; Baylor College of Medicine and Texas Children's Hospital, Houston, TX
PURPOSE: Multiple attempts to insert intravenous lines are painful and frightening for children and can delay treatment. An alternative route for parenteral fluids is subcutaneous (SC) administration with the spreading agent hyaluronidase. The Increased Flow Utilizing Subcutaneously Enabled–Pediatric Rehydration (INFUSE–Pediatric Rehydration) Study is designed to assess the utility, safety, and effectiveness of recombinant human hyaluronidase (rHuPH20)-augmented SC hydration in children.
METHODS: This is an ongoing multicenter, open-label, single-arm, phase IV, proof-of-concept trial in patients 2 months to 10 years old with mild to moderate dehydration (Gorelick score 1–5) needing parenteral therapy. They receive 1 mL (150 units) of SC rHuPH20, followed by a 20-mL/kg SC infusion of isotonic fluid for the first hour. SC hydration is continued as needed for up to 72 hours. Rehydration is deemed successful if the investigator attributes it primarily to rHuPH20-augmented SC fluid infusion and if the child is discharged from the emergency department to home without alternative fluid therapy. Assessments include infusion site reactions, adverse events (AEs), ease of use, and parent satisfaction. Target sample size (50) should be reached by July 2008.
RESULTS: In the first 17 patients receiving treatment, mean age and weight were 2.0 years (range 0.4–8.6 years) and 11.7 kg (range 5.1–29.6 kg), respectively. SC access was achieved with one attempt in 15 patients and two attempts in 2 patients. Three patients had infusion rate reductions and/or interruptions. All patients had typical infusion site reactions, consisting of swelling (n=17), erythema (n=15), pain (n=15), tenderness (n=8), and rash (n=1). No serious AEs occurred. Physicians rated the procedure as easy to perform in 16 of 17 cases, and 11 of 13 parents were satisfied or very satisfied.
CONCLUSIONS: rHuPH20-augmented SC hydration appears to be safe in young children with mild to moderate dehydration. SC access can usually be achieved immediately, on the first attempt.

170. Influence of Home Asthma Maintenance Therapy on Frequency of Pediatric Hospital Admissions. *Shirley M. Hogan, Pharm.D.,*[1] Kim G. Adcock, Pharm.D.,[1] Sunil Mathur, Ph.D.[2]; (1) University of Mississippi, Jackson, MS; (2) University of Mississippi, University, MS
PURPOSE: Asthma is a chronic inflammatory disease characterized by wheezing, cough, and shortness of breath. According to the 2007 Guidelines for the Diagnosis and Management of Asthma: Expert Panel Report 3 (EPR3), about 6 million children in the United States younger than 18 years are affected with asthma. Asthma is considered "controlled" when symptoms are infrequent. In addition, adequate control reduces emergency department visits and hospitalizations and prevents reduced lung growth in children and progressive loss of lung function. The ERP3, the 2007 update of the EPR2, continued to list inhaled corticosteroids (ICS) as the preferred maintenance treatment of asthma. Newer medications such as the leukotriene agonists (LTA) and cromolyn/nedocromil are considered alternatives to low-dose ICS in mild-persistent asthma only. When asthma symptoms are not adequately controlled on ICS, LTA may be used in combination with ICS, or long-acting b-agonists may be added to ICS instead of increasing to high-dose ICS. The purpose of this study was to determine if a relationship exists between asthma maintenance treatment and hospitalizations for asthma in pediatric patients.
METHODS: Charts from patients admitted to the Batson Children's Hospital for asthma exacerbations were reviewed. Data collected included demographic information, home maintenance therapy, and prescriber specialty.
RESULTS: A total of 269 admissions were reviewed. Of those, 193 were eligible for analysis. Demographic data included 86 (45%) females and 149 African Americans (77%). Average age at admission was 5 years. Fifty-five percent of children admitted were on inhaled steroid therapy; 33% were on montelukast therapy; and only 6% were receiving montelukast as monotherapy. Thirty-nine percent were not on any maintenance therapy, however.
CONCLUSIONS: These data indicate that the guidelines are not being followed for maintenance therapy, thus contributing to asthma exacerbations leading to hospital admissions. Therefore, education is needed for both parents and physicians.

171E. Cognitive and Sedative Effects of Guanfacine Extended Release in Children and Adolescents Aged 6 to 17 Years with Attention-Deficit/Hyperactivity Disorder. *John Renna, Pharm.D., M.S., R.Ph.,*[1] Scott H. Kollins, Ph.D.,[2] Timothy Wigal, Ph.D.,[3] Bradley Vince, D.O.,[4] Andrew Lyne, MSC, CStat,[5] Kimberly Farrand, MPH,[1] Thomas Roth, Ph.D.[6]; (1) Shire Development Inc., Wayne, PA; (2) Duke University Medical School, Durham, NC; (3) University of California, Irvine, CA; (4) Vince and Associates Clinical Research, Overland Park, KS; (5) Shire Pharmaceutical Development LTD., Basingstoke, UK; (6) Henry Ford Hospital Sleep Disorders Center, Northville, MI
PURPOSE: Guanfacine extended release (GXR), a selective a_{2A}-adrenoceptor agonist, has demonstrated efficacy in attention-

deficit/hyperactivity disorder (ADHD) in previous studies. This study assessed the effects of GXR on cognitive tasks in subjects 6–17 years old with ADHD. The secondary objective was to evaluate the potential sedative effects of GXR.
METHODS: In this double-blind, dose-optimization, noninferiority study, 121 subjects were randomized to GXR, and 57 subjects were randomized to placebo for 6.5 weeks. Cognitive assessments included the Choice Reaction Time (CRT) and Spatial Working Memory (SWM) tests (both from the Cambridge Neuropsychological Test Automated Battery), the Digit Symbol Substitution Task/Coding test (DSST/Coding), and the Permanent Product Measure of Performance. The Pictorial Sleepiness Scale (PSS) measured both daytime and evening sleepiness, and the Pediatric Daytime Sleepiness Scale (PDSS) measured only daytime sleepiness.
RESULTS: GXR did not impair reaction time as measured by the CRT: mean change from baseline to end point was 20.7 ± 63.1 milliseconds for GXR versus 21.9 ± 64.0 milliseconds for placebo (p=0.84). Changes in other CRT parameters also showed no significant differences between GXR and placebo at end point (p=0.30 for movement time, p=0.72 for total time, and p=0.98 for accuracy). GXR did not impair any aspect of SWM (p>0.05 for all). PDSS showed that GXR slightly decreased daytime sleepiness (p=0.02), whereas PSS subject and observer assessments showed no change in daytime sleepiness with GXR. Evaluations at 10 and 12 hours postdose showed greater evening sleepiness with GXR versus placebo.
CONCLUSIONS: GXR did not impair cognitive function or affect daytime sleepiness, but it did increase evening sleepiness in children and adolescents with ADHD.
Presented at the 63rd Annual Meeting of the Society of Biological Psychiatry, Washington, DC, May 1–3, 2008.

172. Evaluation of Dosage Form Information Provided in Pediatric Drug Trials. *Mark R. Haase, Pharm.D.,*[1] Sherry A. Luedtke, Pharm.D.,[1] Janie Robles, Pharm.D.,[2] Thomas M. Parker, Pharm.D.,[1] Richard D. Leff, Pharm.D.,[3] George P. Giacoia, M.D.[4]; (1) Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX; (2) Texas Tech University Health Sciences Center School of Pharmacy, Lubbock, TX; (3) Texas Tech University Health Sciences Center School of Pharmacy, Building 7, Room 119A, Dallas, TX; (4) National Institute of Child Health and Human Development, Bethesda, MD
PURPOSE: The International Conference on Harmonisation has provided recommendations for dosage forms to be used in pediatric trials. Because of a paucity of such dosage forms for many drugs used and studied in children, these recommendations are often not followed. A recent study of 10 highly powered journals (five pediatric and five general medicine) showed that many of the published pediatric studies in these journals did not provide adequate information about the dosage form, thus decreasing their reliability and validity. The purpose of this study was to determine whether a broader analysis of studies of oral medications in children 12 years and younger in high- and low-powered journals would yield similar results.
METHODS: A literature search was performed to identify trials using oral medications in children age 0–12 years. Trials were evaluated and classified as providing adequate, some, or no information regarding drug formulation. Further analysis of the data was performed, with some of the results listed below.
RESULTS: Three hundred five citations were identified, all published between 2003 and 2006. Of the studies published in pediatric journals, 31, 46, and 23% provided adequate, some, and no information, respectively, on the dosage form used. Nonpediatric journals provided adequate information in 33% of cases while providing some and no information in 45 and 23%, respectively. Of note, the Journal Citation Reports' impact factor had little correlation with the level of information about the dosage form provided. In addition, only 39% of studies documented administration procedure; formulation was not provided in 27%; less than half provided the manufacturer; and 9% documented palatability and tolerability of the medication.
CONCLUSIONS: Consistent with a previous report, in journals published between 2003 and 2006, a minority provide adequate information on dosage forms used in pediatric trials to allow reproduction of the study or incorporation into clinical practice.

173E. Long-Term Safety and Efficacy of Guanfacine Extended Release in Children and Adolescents Aged 6 to 17 Years with Attention-Deficit/Hyperactivity Disorder. *Floyd R. Sallee, M.D., Ph.D.,*[1] James J. McGough, M.D.,[2] Timothy Wigal, Ph.D.,[3] Daniel Sea, B.A.,[4] Andrew Lyne, MSC, CStat,[5] Joseph Biederman, M.D.[6]; (1) University of Cincinnati, Cincinnati, OH; (2) Neuropsychiatric Institute and David Geffen School of Medicine of UCLA, Los Angeles, CA; (3) University of California, Irvine, CA; (4) Shire Development, Inc., Wayne, PA; (5) Shire Pharmaceutical Development LTD., Basingstoke, UK; (6) Clinical and Research Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Harvard Medical School, Boston, MA
PURPOSE: Guanfacine extended release (GXR), a selective a_{2A}-adrenoceptor agonist, has demonstrated efficacy as monotherapy for attention-deficit/hyperactivity disorder (ADHD) in previous studies. The objectives of this study were to assess the long-term safety and efficacy of GXR in patients aged 6–17 years with ADHD.
METHODS: This study was an open-label extension of a placebo-controlled phase 3 monotherapy trial and an open-label phase 2 safety study of GXR and psychostimulant coadministration. Patients from the phase 2 trial receiving coadministered psychostimulants had the option to continue their psychostimulant treatment. Of the 259 patients who received GXR, 53 were coadministered psychostimulants. Optimal dose was achieved by upward titration to a maximum of 4 mg/day and maintained for up to 24 months. Safety assessments included adverse events (AEs), laboratory tests, and electrocardiograms. The main efficacy measure was ADHD Rating Scale IV (ADHD-RS-IV) total score change from baseline of the antecedent study to end point of the present study.
RESULTS: AEs were generally mild to moderate. The most common treatment-emergent AEs (TEAEs) included somnolence (30.5%), headache (24.3%), and upper respiratory tract infection (17.8%). The incidence of TEAEs was 87.3% overall. Thirty-one (12.0%) patients discontinued because of TEAEs (13.6% in the monotherapy group and 5.7% in the coadministration group). Small changes in blood pressure and pulse were noted. No electrocardiogram abnormality was reported as a serious AE. At end point, mean changes in ADHD-RS-IV total score were significant overall and for all weight-adjusted dose groups (p<0.001 for all).
CONCLUSIONS: In this long-term treatment study, GXR up to 4 mg/day was generally safe and effective in children and adolescents with ADHD.
Presented at the 63rd Annual Meeting of the Society of Biological Psychiatry, Washington, DC, May 1–3, 2008.

174E. Guanfacine Extended Release: Duration of Effect in Children and Adolescents Aged 6 to 17 Years with Attention-Deficit/Hyperactivity Disorder. *Floyd R. Sallee, M.D., Ph.D.,*[1] Andrew Lyne, MSC, CStat,[2] Joseph Biederman, M.D.[3]; (1) University of Cincinnati, Cincinnati, OH; (2) Shire Pharmaceutical Development LTD., Basingstoke, UK; (3) Clinical and Research Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Harvard Medical School, Boston, MA
PURPOSE: Guanfacine extended release (GXR), a selective a_{2A}-adrenoceptor agonist, has demonstrated efficacy as monotherapy in attention-deficit/hyperactivity disorder (ADHD). This analysis pooled data from two pivotal studies of subjects aged 6–17 years.
METHODS: In one trial, subjects were randomized to 2, 3, or 4 mg/day of GXR or placebo starting at 1 mg/day. Dose was escalated weekly by 1 mg/day with 2 or more weeks at maximum dose. In a second trial, subjects were randomized to 1, 2, 3, or 4 mg/day of GXR or placebo (similar dose-escalation schedule; 3 weeks at maximum dose). The primary efficacy measure in both trials was change in ADHD Rating Scale IV (ADHD-RS-IV) score from baseline. Duration of effect, a secondary measure, was evaluated with the Conners' Parent Rating Scale (CPRS) at 12, 14, and 24 hours postdose.
RESULTS: From baseline to end point, all GXR treatment groups showed significant improvement in ADHD-RS-IV versus placebo (p<0.001). Changes from baseline to end point in CPRS (±SD) were

significantly greater in each weight-adjusted actual dose versus placebo throughout the day. Change from baseline to end point at 12 hours for placebo (n=140) was -9.9 (18.4); for 0.01–0.04 mg/kg (n=146), -16.6 (20.8); for 0.05–0.08 mg/kg (n=200), -16.7 (19.7); for 0.09–0.12 mg/kg (n=102), -22.1 (17.2); and for 0.13–0.17 mg/kg (n=41), -25.9 (24.1); p<0.001, for all active groups versus placebo. At 14 hours, changes from baseline to end point were -9.9 (20.6), -15.8 (21.1), -15.3 (21.5), -17.8 (20.1), and -23.7 (24.4), respectively, p<0.001 for all active groups versus placebo. At 24 hours, these values were -5.7 (22.0), -11.4 (21.6), -11.4 (20.2), -16.7 (18.0), and -17.2 (20.3), respectively, p=0.003, for all active groups versus placebo.

CONCLUSIONS: When analyzed by weight-adjusted actual dose, results of GXR treatment show efficacy in reducing ADHD symptoms at all time points measured throughout 24 hours in subjects aged 6–17 years, as rated on the CPRS.

Presented at the 161st Annual Meeting of the American Psychiatric Association, Washington, DC, May 3–8, 2008.

175. Caffeine for Prevention or Treatment of Alprostadil-Induced Apnea in Infants with Congenital Heart Disease. *Marcia L. Buck, Pharm.D.*, D. Scott Lim, M.D., Joshua Attridge, M.D.; University of Virginia Children's Hospital, Charlottesville, VA

PURPOSE: Apnea occurs in 10–20% of infants receiving alprostadil. In a previous study, aminophylline reduced the incidence of alprostadil-induced apnea and lessened the need for mechanical ventilation. Caffeine may produce similar benefits with once-daily dosing and less risk of toxicity. The purpose of this study was to provide preliminary information on the utility of caffeine in preventing or treating alprostadil-induced apnea.

METHODS: A single-center retrospective cohort analysis was conducted of infants receiving alprostadil between June 1, 2006, and June 1, 2008. Patients were divided into those receiving caffeine and controls. Primary outcomes were development of apnea and intubation. Data were analyzed with unpaired *t*-tests.

RESULTS: Eighty-three infants were evaluated. Average (±SD) weight and gestational age were 3.0 ± 0.7 kg and 37.8 ± 2.2 weeks. The most common diagnoses were hypoplastic left heart syndrome and transposition of the great arteries. Alprostadil was initiated at 0.05 ± 0.03 µg/kg/minute, with a maximum of 0.06 ± 0.04 µg/kg/minute. Average treatment duration was 7.7 ± 9.7 days. Twenty-nine (35%) patients received caffeine. There were no statistically significant differences between caffeine and control patients in birthweight, gestational age, or alprostadil dose. A caffeine loading dose of 19.2 ± 4.8 mg/kg was followed by 4.8 ± 0.4 mg/kg/day for 7.5 ± 13.8 days (range 1–71 days). The average trough concentration was 13.3 ± 3.7 µg/mL. In nine patients, caffeine was initiated as prophylaxis when alprostadil was started. None developed apnea. Caffeine was started as treatment of apnea in 20 infants, with complete resolution in 16 (80%). Excluding temporary intubation for transport, 6 caffeine patients (7%) and 29 controls (54%) required mechanical ventilation. Only two caffeine patients (7%) were intubated for apnea, compared with eight controls (15%). Duration of mechanical ventilation was not different (3.6 ± 6.6 vs. 3.3 ± 5.4 days; p=0.87). Four controls developed apnea but did not require intubation.

CONCLUSIONS: In this sample, caffeine was effective in preventing or treating alprostadil-induced apnea. Prospective studies are warranted.

176E. Evaluation of Zolpidem Exposures in the Pediatric Population. Jill Griffith, Pharm.D.,[1] *Hanna Phan, Pharm.D.*,[2] Marcel J. Casavant, M.D.,[3] Milap C. Nahata, Pharm.D., FCCP,[4] S. David Baker, Pharm.D.[1]; (1) The Ohio State University College of Pharmacy; Nationwide Children's Hospital, Central Ohio Poison Control Center, Columbus, OH; (2) The Ohio State University, College of Pharmacy; The Research Institute at Nationwide Children's Hospital, Columbus, OH; (3) The Ohio State University, Colleges of Medicine and Pharmacy; The Research Institute at Nationwide Children's Hospital, Columbus, OH; (4) The Ohio State University, Colleges of Pharmacy and Medicine; The Research Institute at Nationwide Children's Hospital, Columbus, OH

PURPOSE: To evaluate potential adverse effects and the relationship between dose and severity of clinical outcome after single exposure of zolpidem (ZPM) in pediatric patients.

METHODS: The data from the American Association of Poison Control Centers on ZPM exposures reported to U.S. Poison Control Centers between January 2000 and December 2005 were retrospectively reviewed. Inclusion criteria were defined as age younger than 18 years, oral single-drug ingestion of ZPM 5- or 10-mg tablet, known quantity ingested, documented body weight, and follow-up of clinical outcome. Exclusion criteria included use of more than one substance ingested, the controlled-release formulation of ZPM, unknown quantity ingested, aged 18 years and older, numerically indefinable age, routes of exposure other than oral ingestion, weight not available, and pregnancy. Data were analyzed using descriptive statistics and Spearman correlation coefficient.

RESULTS: A total of 1343 ZPM exposures were reviewed and grouped on the basis of age (younger than 2, 2–5, 6–12, and 13–17 years). The median amount of ZPM ingested was 0.49 mg/kg (range 0.04–22.7 mg/kg). Most (60%) cases were accidental. Most (97%) cases involved home exposures. Major, moderate, minor, and no effect were noted in 0.2, 13.9, 47.7, and 36.9% of exposures, respectively. Clinically significant adverse effects included drowsiness (42%), ataxia (11%), vomiting (8%), dizziness (7.4%), and hallucinations (7.1%). Almost 43% of patients with exposures were treated and released from a health care facility, 7.7% (n=104) were admitted to a noncritical care or psychiatric floor, 1.7% were admitted to an intensive care unit, and 4.2% refused referral or left the facility against medical advice. No association was found between weight-based dose and clinical outcome severity.

CONCLUSIONS: Most adverse effects from ZPM ingestion were considered minor and neurologic in pediatric patients. No relationship between ZPM dose and outcome severity was found.

To be presented at the North American Congress of Clinical Toxicology (NACCT) Annual Meeting, Toronto, ON, Canada, September 2008.

177. Off-Label Medication Use and Associated Adverse Drug Events in a Pediatric Emergency Department. *Hanna Phan, Pharm.D.*,[1] Marc S. Leder, M.D.,[2] Matthew Fishley, B.S.,[3] Matthew Moeller, B.S.,[4] Milap C. Nahata, Pharm.D., FCCP[5]; (1) The Ohio State University, College of Pharmacy; The Research Institute at Nationwide Children's Hospital, Columbus, OH; (2) The Ohio State University, Department of Pediatric Emergency Medicine, College of Medicine; Nationwide Children's Hospital, Columbus, OH; (3) The Ohio State University, College of Pharmacy, Columbus, OH; (4) University of Cincinnati, The James L. Winkle College of Pharmacy, Cincinnati, OH; (5) The Ohio State University, College of Pharmacy and Medicine; The Research Institute at Nationwide Children's Hospital, Columbus, OH

PURPOSE: To determine the (1) frequency and type of off-label (OL) medication use in a pediatric emergency department (PED) and (2) the causality of adverse drug events (ADEs) associated with OL medication use.

METHODS: Medical records of patients (18 years or younger) admitted to the PED from January 10, 2007, to May 29, 2007, were retrospectively reviewed. OL use of a medication was determined based on U.S. Food and Drug Association–approved labeling. Medications before admission and medications ordered in the PED were evaluated. The Adverse Drug Reaction Probability Scale by Naranjo et al was used to evaluate reported ADEs to determine causality. Data were analyzed using descriptive statistics.

RESULTS: A total of 2191 patients with 6672 medication orders were evaluated; 26% (n=1707) of the medication orders were considered OL use; 70% (n=1201) and 30% (n=506) of these were medications ordered in the PED and before evaluation in the PED, respectively. Inhaled bronchodilators, including b-agonists and anticholinergics (28.9%), antimicrobials (14.1%), antihistamines/antiemetics (8.6%), analgesic/antipyretics (8.4%), and corticocorticoids/glucocorticoids (6.3%) were the most common medication classes used OL. Reported overall ADE incidence was less than 1% (n=39). Of these 39 ADEs, 5 resulted from the use of an OL medication. One patient was evaluated in the PED and then

admitted to the hospital because of the ADR (seizure) resulting from intentional ingestion, with "probable" causality. The remaining four patients experienced ADEs while in the PED. None of the remaining patients was admitted to the hospital because of the ADE (rash, dizziness, tachycardia, and gastrointestinal upset), with "possible" causalities.
CONCLUSIONS: OL medication use accounted for about one-fourth of prescriptions; it was most common for inhaled bronchodilators. Reported frequency of associated ADEs from OL medication use was less than 1%.

178. Effectiveness of Lactobacillus GG for Prevention of Antibiotic-Associated Diarrhea in the Pediatric Intensive Care Unit. *Allison M. Chung, Pharm.D., BCPS, AE-C,*[1] Stephen Davis, Pharm.D.[2]; (1) Auburn University, Department of Pharmacy Practice; University of South Alabama, Department of Pediatrics, Mobile, AL; (2) The University of Pittsburgh Medical Center, Pittsburgh, PA
PURPOSE: The primary objective of this study was to assess the efficacy of lactobacillus for preventing antibiotic-associated diarrhea (AAD) in the pediatric intensive care unit (PICU). A secondary outcome was to assess the safety and tolerability of lactobacillus in the PICU.
METHODS: This was a retrospective chart review. Medical records for 1 year were reviewed. Patients were included if they were admitted to the PICU, were between 0 and 18 years old, were on antimicrobials during the length of their PICU stay, and had been on lactobacillus therapy. Patients were excluded from the study if there was antimicrobial use in the previous 4 weeks before initiation of lactobacillus or if they had underlying gastrointestinal or bowel pathologies.
RESULTS: Two hundred seven patients were identified for inclusion in the study. Fifty-one patients met the inclusion criteria. The average age and weight of the patients were 3.57 ± 4.67 years and 17.20 ± 18.70 kg. The lactobacillus dose ranged from ½ capsule to 2 capsules/day. The average number of stools per day was 2.544 ± 1.7391. The average number of antibiotics per patient was 2.08 ± 1.045, and the most common antibiotics used were cephalosporins and clindamycin. The average number of antibiotic days per patient was 7.12 ± 3.653 days. Six (11%) of 51 patients had five or more stools. The remaining 45 patients (88%) were controlled with lactobacillus. There was a statistically significant positive relationship between the average stools per day and days in the PICU. There was also a statistically significant positive relationship between the average stools per day and days on lactobacillus. There were no adverse events associated with lactobacillus.
CONCLUSIONS: The observed data indicate that lactobacillus is tolerable and has benefit in preventing AAD in PICU patients.

179. Prematures with Respiratory Distress Syndrome Do Not Have Increased Chance of Patent Ductus Arteriosus Requiring Indomethacin Therapy Thereafter. *Zon-Min Lee Sr., Master*; Chang Gung Memorial Hospital, Taiwan, Taiwan
PURPOSE: Patent ductus arteriosus (PDA) is a common problem in very premature neonates, resulting in a significant left-to-right shunt and an increase in left ventricular output.[1, 2] PDA is also a common complication in neonates ventilated for respiratory distress syndrome (RDS)[3]; however, there are few published reports in the literature describing the correlation between Chinese neonates born with or without RDS and PDA with indomethacin therapy thereafter.
METHODS: In total, 664 neonates admitted to our neonatal intensive care unit (NICU) from January 1, 2006, to December 31, 2007, were enrolled in this study. The gestational age (GA) ranges from 24 to 42 weeks. Birth date, gestational age, RDS or not, radiographic image, finding of cardiac sonography, indomethacin use or not, and starting day of using indomethacin were all recorded.
RESULTS: Thirty-three (4.97%) of 664 included neonates received indomethacin. Nine (10.0%) of the 90 neonates with RDS received indomethacin, and 24 (4.18%) of the 574 neonates without RDS received indomethacin thereafter. Neonates born with RDS seemed to have higher probability of developing PDA, which prompts the use of indomethacin. However, in the group of 353 premature infants with GA of about 34 weeks, 8 (9.52%) of the 84 neonates with RDS received indomethacin, and 24 (8.92%) of the 269 neonates without RDS received indomethacin thereafter. The difference (p=0.867) was not significant.
CONCLUSIONS: There was no correlation between RDS and PDA with indomethacin therapy thereafter in the premature infants with GA of about 34 weeks, suggesting that prophylactic indomethacin therapy in the first 24 hours of life for the prevention of PDA in preterm infants with RDS is not necessary.

Pharmacoeconomics/Outcomes

180. A Cost Effectiveness Analysis of Computerized Clinical Decision Support Systems on Bacteremia. *Marc H. Scheetz, Pharm.D., M.Sc.,*[1] Maureen K. Bolon, M.D., M.S.,[2] Michael J. Postelnick, R.Ph., BCPS,[3] Todd A. Lee, Pharm.D., Ph.D.[4]; (1) Midwestern University, Department of Pharmacy Practice, Chicago, IL; (2) Northwestern University, Division of Infectious Diseases, Chicago, IL; (3) Northwestern Memorial Hospital, Department of Pharmacy, Chicago, IL; (4) Institute for Healthcare Studies; Division of General Internal Medicine – Northwestern University Feinberg School of Medicine, Chicago, IL
PURPOSE: Computerized clinical decision support systems (CDSS) have improved the breadth and scope of Antimicrobial Stewardship Teams (ASTs). The cost-effectiveness of ASTs using CDSS to optimize treatment for clinically significant bacteremias was explored.
METHODS: A model was constructed to compare the costs and outcomes of bacteremic patients receiving standard treatment versus standard treatment plus an AST consult using CDSS. Patients were monitored during the hospital admission of the bacteremic event, and quality-adjusted life-years (QALYs) were estimated for total patient life using national life expectancy data. Model parameters and costs, together with their distributions, were obtained from the literature and were estimated by experts when unavailable. Incremental cost-effectiveness ratios (ICER) were calculated to estimate the cost per QALY gained from the hospital perspective. Probabilistic sensitivity analyses were conducted using Monte Carlo simulations to estimate the uncertainty associated with the ICER.
RESULTS: The cost of the AST/CDSS intervention for bacteremia was $40,018 (95% CI: $27,591–$53,697), and the cost of standard treatment was $39,660 (95% CI: $27,290–$53,426). The difference in effectiveness between the two strategies was 0.08 QALYs (AST 8.00 QALYs, no AST 7.92 QALYs). Therefore, the base case ICER was $7368 per QALY gained (95% CI: $481–$36,319). Results from the probabilistic sensitivity analysis demonstrated more than a 90% likelihood that AST/CDSS would be cost-effective at a level of $20,000 per QALY.
CONCLUSIONS: Maintaining an AST with CDSS to improve efficacy for bacteremia is cost-effective from the hospital perspective. The estimate of $7368 per QALY gained for the AST/CDSS intervention compared with usual care is well within the cost-effectiveness estimates of many currently funded health care interventions and programs.

181. Cost-Effectiveness Analysis of Anticoagulation Strategies in Non–ST-Elevation Acute Coronary Syndromes. *Carleton B. Maxwell, Pharm.D.,*[1] David A. Holdford, Ph.D.,[2] Michael A. Crouch, Pharm.D.[3]; (1) VCU Health Systems, Richmond, VA; (2) VCU Medical College of Virginia, Richmond, VA; (3) South University School of Pharmacy, Savannah, GA
PURPOSE: To perform a cost-effectiveness analysis (CEA) comparing four anticoagulant strategies in the treatment of non–ST-elevation acute coronary syndrome (NSTE-ACS).
METHODS: This was a literature-based decision model from an institutional perspective. Data sources included the SYNERGY, ACUITY, and OASIS-5 trials, with consideration given to two subgroup analyses (SYNERGY and OASIS-5). Using these data, we created a decision tree model incorporating the outcomes associated with four antithrombotic regimens: unfractionated heparin (UFH)

plus eptifibatide, enoxaparin plus eptifibatide, bivalirudin alone, and fondaparinux plus eptifibatide. Percentage of eptifibatide use was consistent with glycoprotein IIb/IIIa blocker use in these clinical trials. Probabilities of success or complications (myocardial infarction, revascularization, and major/minor hemorrhage at 30 days) were calculated. Costs were assigned to each outcome incorporating the cost associated with diagnosis-related group and/or current procedural terminology codes, drug acquisition, and red blood cell infusions. Multiple sensitivity analyses were performed to assess alternative situations and to test the robustness of the model.

RESULTS: Base case analysis showed bivalirudin alone to be the least costly regimen ($1131 per average course) and dominating both in cost and effectiveness compared with enoxaparin plus eptifibatide ($1609) and UFH plus eptifibatide ($1739). Total average cost of fondaparinux and eptifibatide ($1184) was higher than bivalirudin alone and resulted in a higher incremental cost per each additional patient successfully treated ($2569) despite being slightly more effective than bivalirudin. Sensitivity analyses demonstrated that drug acquisition cost and probability of success assumed from these studies were key sensitivity variables. Bivalirudin lost its cost-effectiveness when two or more vials were necessary to complete a treatment course.

CONCLUSIONS: This CEA demonstrates that bivalirudin alone is the most cost-effective antithrombotic regimen in NSTE-ACS when its use is consistent with the ACUITY trial. Fondaparinux appears to be the most cost-effective regimen in those undergoing a conservative strategy.

182. Cost Effectiveness of Valsartan vs. Losartan to Delay Nephropathy Progression in Patients with Type 2 Diabetes and Hypertension. *Hsing-Ting Yu, MPH,*[1] Zhimei Liu, Ph.D.,[1] Homa Dastani, Ph.D.,[2] Quan V. Doan, Pharm.D., Ph.D.,[3] Suellen Curkendall, Ph.D.[4]; (1) Cerner LifeSciences, Beverly Hills, CA; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) Cerner LifeSciences; Outcomes Insights, Inc., Beverly Hills, CA; (4) Cerner LifeSciences, Vienna, VA

PURPOSE: Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD). Angiotensin II receptor blockers reduce nephropathy progression. We evaluated the costs: life-years (LYs) and quality-adjusted life-years (QALYs) associated with delaying nephropathy progression for 10 years for valsartan 320 mg (VAL320) and 160 mg (VAL160) and losartan 100 mg (LOS100).

METHODS: A Markov model was constructed from a payer's perspective to simulate nephropathy progression from microalbuminuria (microA) to macroalbuminuria (macroA) and then to ESRD for patients at age 57. The relative risk (RR) of transitioning from microA to macroA for VAL320 versus VAL160 (RR = 0.499) was drawn from the DROP head-to-head clinical trial, and the absolute risk reduction (ARR) comparing VAL160 and LOS100 (ARR = 0.0075) was computed indirectly from the VAL160 placebo and LOS100 placebo studies. The transition probability from macroA to ESRD (0.0172) was assumed to be the same across groups. Risk of myocardial infarction, risk of stroke, and annual direct medical costs were assumed to increase as nephropathy worsened. Probabilities, direct medical costs, and health utilities for the model were obtained from published literature. Costs and outcomes were discounted at 3%/year.

RESULTS: Estimated per-patient costs and outcomes were $104,375, 7.28 LYs, and 6.30 QALYs for VAL320; $116,498, 7.08 LYs, and 6.06 QALYs for VAL160; and $120,459, 7.04 LYs, and 6.01 QALYs for LOS100. In all sensitivity analyses, VAL320 had lower costs and greater QALYs than LOS100. VAL160 also dominated LOS100 unless the price of LOS100 was dropped to 60% below the current average wholesale price or unless the risk of transition to macroA was assumed to be lower for LOS100 than for VAL160.

CONCLUSIONS: The model suggests that, compared with LOS100 during a 10-year period, VAL320 produces greater life expectancy (0.29 QALY) at a savings of $16,084/patient, and VAL160 produces a greater life expectancy (0.05 QALY) at a savings of $3961/patient.

183E. Cost-Effectiveness of Aliskiren Added to Losartan and Optimal Antihypertensive Therapy in Type-2 Diabetic Patients with Albuminuria and Hypertension. Tom Delea, MSIA,[1] Oleg Sofrygin, M.S.,[1] *Helen Lau, M.S.,*[2] Veronica C. Munk, Ph.D.,[3] Sean Sullivan, Ph.D.[4]; (1) PAI, Brookline, MA; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) Novartis Pharma AG, Basel, Switzerland; (4) University of Washington, Seattle, WA

PURPOSE: A Markov model was developed to evaluate the cost-effectiveness of adding aliskiren to standard therapy from a U.S. health care system perspective.

METHODS: Aliskiren in the Evaluation of Proteinuria in Diabetes (AVOID) was a randomized, double-blind, 6-month study in which 300 mg of aliskiren was added to losartan and optimal antihypertensive therapy in patients with type 2 diabetes with albuminuria and hypertension (mean age = 60.8 years). Aliskiren significantly reduced mean urinary albumin creatinine ratio (UACR) by 20% (p=0.0009) and overnight urinary albumin excretion ratio by 18% versus placebo (p=0.009). Probabilities of progression from microalbuminuria (UACR 29–287 mg/g) to early overt nephropathy (UACR 288–1900) to advanced overt nephropathy (AON) (UACR more than 1900) were obtained from AVOID. Data from the Irbesartan in Diabetic Nephropathy Trial were used to estimate progression from AON to end-stage renal disease (ESRD); U.S. Renal Data System (USRDS) for probability of renal transplant; and U.S. vital statistics and published studies for estimates of disease-related mortality. Costs of aliskiren and losartan were based on wholesale acquisition costs; ESRD and transplantation costs were obtained from USRDS. Other costs were assumed to be similar across treatments. Utilities were based on published studies. Costs, life-years, and quality-adjusted life-years (QALYs) were evaluated for 20 years and discounted at 3% annually.

RESULTS: Adding 300 mg of aliskiren to losartan yields an additional 0.18 life-years free of ESRD (7.62 vs. 7.44), 0.10 total life-years (8.12 vs. 8.02), and 0.10 QALYs (5.98 vs. 5.88). Total costs are increased by $3135 ($63,652 vs. $60,517), reflecting increased costs of aliskiren and losartan of $7769 ($14,737 vs. $6,968), partially offset by $4860 in savings of ESRD and transplantation ($32,647 vs. $37,507). Cost per QALY gained with aliskiren is $32,420, which is below the generally acceptable range in the United States ($50,000–$100,000 per QALY).

CONCLUSIONS: The added renoprotective effects of 300 mg/day of aliskiren in patients with type 2 diabetes with albuminuria and hypertension may be cost-effective within a U.S. health care system.

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184. Persistence and Compliance for Patients Prescribed Fixed-Dose Valsartan/Hydrochlorothiazide as Compared to Free Combination Angiotensin Receptor Blocker and Hydrochlorothiazide. Gregory Hess, M.D., M.B.A.,[1] Jerrold Hill, Ph.D.,[1] Craig Plauschinat, Pharm.D., MPH,[2] *Homa Dastani, Ph.D.*[2]; (1) Surveillance Data Inc., Plymouth Meeting, PA; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ

PURPOSE: To evaluate medication compliance and persistence with fixed-dose combination (FDC) valsartan/hydrochlorothiazide (HCTZ) therapy compared with free combination angiotensin receptor blocker (ARB) and HCTZ, prescribed as two separate agents.

METHODS: A retrospective cohort study using an integrated medical and pharmacy claims database (Medstat Marketscan) for Medicare and commercially insured patients was conducted. Medication use for patients switching from fixed-dose combination ARB/HCTZ regimens to free combinations (FC) of the same compounds were compared with patients who remained on valsartan/HCTZ. Patients were matched 1:1 using propensity scoring to ensure comparable cohorts with respect to demographic and comorbid risk factors. Patients were monitored for 12 months postindex date. Compliance was measured using the medication possession ratio (sum of days' supply for all index prescriptions during the 12-month follow-up period, divided by 365 days).

Persistence was defined as the percentage of patients remaining on therapy at 12 months postindex date, with no gaps in therapy of more than 30 days.
RESULTS: A total of 1214 patients who received FDC valsartan/HCTZ and 1216 patients who received FC ARB+HCTZ were included (n=2430). Mean patient age was 62.1 years, and 60% were women. Mean compliance rate with valsartan/HCTZ FDC was 75.4% (SD ± 0.7%) compared with 53.6% (SD ± 0.9) with FC ARB + HCTZ patients (p<0.0001). Overall, 56.5% FDC valsartan/HCTZ patients were persistent compared with 13.4% FC ARB+HCTZ patients. Valsartan/HCTZ patients had an average of 271.5 days (SD ± 2.6) of drug supply during the 12-month study follow-up period compared with 192.9 days (SD ± 3.4) for ARB+HCTZ patients (p<0.0001).
CONCLUSIONS: Persistence and compliance with an FDC regimen of valsartan/HCTZ were significantly higher compared with the FC regimen. Improved adherence may lead to better blood pressure control and improved cardiovascular outcomes.

185. A Cost-Efficacy Analysis of Infused Biologic Therapies in the Treatment of Rheumatoid Arthritis Using Radiologic Outcomes. *Boxiong Tang, M.D., Ph.D.*, Heidi Waters, M.B.A., Scott McKenzie, M.D., Catherine T. Piech, M.B.A.; Centocor Ortho Biotech Services, LLC, Horsham, PA
PURPOSE: To estimate the cost-efficacy of two infused biologic therapies, infliximab (IFX) plus methotrexate (MTX) and abatacept (ABA)+MTX, compared with control (MTX) in rheumatoid arthritis (RA) patients using 1-year radiologic outcomes.
METHODS: The cost-efficacy analysis was based on incremental benefit versus control using data from IFX and ABA pivotal trials in RA patients. Drug cost was based on January 2008 wholesale acquisition cost and administration fees (IFX 100-mg vial $581, 2-hour infusion $203; ABA 250-mg vial $450, and 30- to 60-minute infusion $166). Annual dose was based on a 70-kg patient with induction and maintenance doses (3 mg/kg per infusion with nine infusions per year for IFX and 750 mg per infusion with 15 infusions per year for ABA). The cost of adverse events was not included in this analysis. The mean changes in erosion score (ES), joint space narrowing (JSN) score, and total Sharp score (TSS) between baseline and 12 months were used to measure efficacy. The cost-efficacy ratio (CER) is defined as the treatment costs divided by efficacy, indicating that the cost per unit end point improved.
RESULTS: The annual treatment costs (drug costs plus infusion costs) were $17,512 for IFX and $22,740 for ABA. The 52- to 54-week control-adjusted efficacy measures of ES, JSN, and TSS were -3.80, -1.80, and -5.70 for IFX and -0.86, -0.51, and -1.36 for ABA, respectively. The CERs were $4608 (ES), $9729 (JSN), and $3072 (TSS) for IFX compared with $26,442 (ES), $44,588 (JSN), and $16,721 (TSS) for ABA. IFX had lower cost and higher efficacy; the incremental cost-efficacy ratio indicated that IFX dominates ABA.
CONCLUSIONS: In this analysis, based on radiologic outcomes, IFX/MTX was cost-effective compared with ABA/MTX for the treatment of RA. The cost-effectiveness of these agents in clinical practice will depend on observational admininistered doses and reported effectiveness.

186. Immunosuppressant-Adherence and Willingness to Give Time for Self-Management Education in Community-Dwelling Adult Transplant Recipients at a U.S. Transplant Center. Jayashri Sankaranarayanan, M.Pharm., Ph.D., *Dean Collier, Pharm.D., BCPS*, Anne Reisdorff, Pharm.D. Candidate; University of Nebraska Medical Center, 986045 Nebraska Medical Center, Omaha, NE
PURPOSE: An understanding of immunosuppressant adherence and the demand for self-management education services (SMES) can inform policy-makers on the future model of care delivery. We evaluated the relationship of immunosuppressant adherence with the willingness to give time for receiving self-management education services (WTGT-SMES) in solid organ transplant (SOT) recipients.
METHODS: We designed a survey to collect demographics, self-reports of and barriers to immunosuppressant adherence, and WTGT-SMES. We analyzed survey responses of 567 community-dwelling adult SOT recipients, 19 years and older, from a leading Transplant Center in the United States from October 2007 to May 2008.
RESULTS: The survey response rate was 32%. Details are summarized below.

Characteristics	% Respondents or Mean ± SD[a]
Liver transplant	50%
Kidney or pancreas transplant	50%
Age (years)	56.05 ± 12.52[a]
Gender, male	55%
Education, above high school	68%
Married	70%
White race	90%
Insurance	Private, 60%; Medicare, 49%; Medicaid, 10%
Health status, good to excellent	77%
Duration from last transplant (years)	7.69 ± 5.96[a]
Immunosuppressant non-adherence, 1–20% of the time in the past 3 months because of:	Forgetting (30%), any reason (29%), carelessness (20%)
Immunosuppressant adherence barriers	"Cannot tell if it is working" (17%) "Missing when out of routine" (17%) "Too many capsules or tablets at one time" (8%) "Too many times a day" (6%) "Confused about payment for medication" (6%)
Time spent on transplant-related self-management (hours each week)	5.71 ± 9.63[a]
Perceived importance of SMES	77%
WTGT-SMES (yes)	72%
WTGT-SMES (minutes per month)	35.67 ± 18.61[a]

[a]After adjusting for transplant duration and time spent on transplant-related self-management, SOT recipients' WTGT-SMES was not associated with self-reports of or barriers to immunosuppressant adherence (p>0.05) but was positively associated with "perceived SMES importance" (p<0.001).

CONCLUSIONS: SOT respondents to our survey felt an SMES was important and were willing to give time to it. Policy-makers and pharmacy service providers need to consider this demand in this target population.

187. Cost Analysis of Direct Thrombin Inhibitor Use in Heparin Induced Thrombocytopenia at a Single Institution. *Shazia Raheem, Pharm.D.*, Andrew Eisenberger, M.D., David Diuguid, M.D., Jeffrey Jhang, M.D., Amy Dzierba, Pharm.D.; NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, NY
PURPOSE: When clinical suspicion arises, antibody tests may be used as a diagnostic tool for type II heparin-induced thrombocytopenia (HIT). At New York-Presbyterian Hospital, an enzyme-linked immunosorbent assay for HIT is determined by an outside laboratory. While awaiting antibody results, patients thought to have HIT are initiated on anticoagulant therapy with a direct thrombin inhibitor (DTI). Potential cost savings include in-hospital testing of HIT antibody and use of alternative agents such as fondaparinux.
METHODS: Retrospective cost analysis of DTI use in patients having a HIT antibody ordered in 2006. Test turnaround time, length of treatment with DTIs, anticoagulant complications, and potential pharmacy cost savings were assessed. Hospital acquisition costs were used to calculate DTI expense.
RESULTS: In 2006, HIT antibody tests were positive, negative, and indeterminant in 186, 535, and 16 patients, respectively. Sixty-two (33%) HIT-positive and 499 (93%) HIT-negative results were reported within a mean of 3.2 ± 1.7 days and were analyzed for cost analysis. Twenty-seven (44%) HIT-positive patients received DTIs for 490 patient-days, and 80 (16%) HIT-negative patients received DTIs for 747 patient-days, generating an estimated DTI cost of $1,200,000. Despite negative antibody results, 53 (66%) patients continued DTI treatment for 356 patient-days with an estimated drug cost of $361,000. Implementation of in-hospital testing and appropriate discontinuation of DTI therapy would yield a potential cost savings of $465,000. Eight (13%) bleeding complications were noted in the 62 patients who were HIT positive. Seven (26%) HIT-positive patients and 34 (43%) HIT-negative patients were eligible to receive fondaparinux, offering an additional cost savings of $440,000.

CONCLUSIONS: Reducing HIT antibody test result turnaround time and ensuring appropriate discontinuation of DTI therapy would potentially lead to substantial decreased drug expenditure and potentially prevent bleeding complications from unnecessary anticoagulation.

Pharmacoepidemiology

188. Point Prevalence of Parkinson's Disease (PD) Induced Psychosis (PDP) in a Large Managed Care Plan. *Robert J. Holt, Pharm.D., M.B.A.,*[1] Ami R. Sklar, MPH,[2] George A. Goldberg, M.D., FACP,[2] Carolyn R. Harley, Ph.D.,[2] Jonathan C. Johnson, M.S. Candidate,[2] Theodore Darkow, Pharm.D.[2]; (1) Ovation Pharmaceuticals and University of Illinois, Deerfield, IL; (2) Innovus, Eden Prairie, MN

PURPOSE: To determine point prevalence of Parkinson's disease (PD)-induced psychosis (PDP) by applying criteria from an expert working group (Mov Disord 2007;22:1061) to medical claims data from a large managed care plan with 10.7 million patients.

METHODS: Patients enrolled continuously for up to 10 years with a history of two or more diagnoses for non–drug-induced PD (ICD-9-CM: 332.0) were identified in September 2007. Patients with secondary/drug-induced PD, dementia with Lewy bodies, primary psychiatric disorders, or delusional disorders were excluded. Prevalence of PDP was estimated using three different criteria: (1) standard definition—one or more claim with a diagnosis of psychosis (ICD-9-CM: 298.0, 298.1, 298.4–298.9), hallucinations (ICD-9-CM: 293.82, 368.16, 780.1), or delusions (ICD-9-CM: 293.81, 297.1); (2) strict definition—one or more medical claim with a diagnosis of psychosis and one or more claim with a diagnosis of hallucinations or delusions; and (3) time-dependent definition—two or more psychosis, hallucinations, or delusions claims separated by at least 30 days (closest criteria to the working group definition).

RESULTS: A total of 4490 PD patients were identified in this cohort study (mean age = 69.3 years, more men than women, $p<0.00001$). Prevalence of PDP was estimated at 45 in 1000 (standard), 4 in 1000 (strict), and 11 in 1000 (time-dependent). PDP patients (standard definition) were older (77.5 years, $p<0.0001$; more than 99% were 50 years or older), and PD was equally prevalent in men and women ($p>0.05$). PDP patients more commonly had evidence of dementia (51% vs. 13%; $p<0.0001$) and use of atypical antipsychotics (28% vs. 5%; $p<0.0001$).

CONCLUSIONS: Data are lacking on the prevalence of PDP in the United States. Results indicate PDP is rare (4–45 per 1000 managed care PD patients) and represents a neuropsychiatric finding distinct from other psychoses, with important treatment implications (increased atypical neuroleptic use). Applying our rates to the estimated U.S. PD population of 1 million; PDP in the United States ranges from 4000 to 45,000. Further research is required to document the presumed efficacy of atypical neuroleptics in the treatment of this unique psychosis.

189. Prevalence of Cardiovascular Risk Factors and Medication Adherence Among Ethnic Groups Living in the Omaha Metropolitan Area. *Robyn M. Kondrack, Pharm.D.*, Stephanie R. Maciejewski, Pharm.D., Daniel E. Hilleman, Pharm.D., Syed M. Mohiuddin, M.D.; The Cardiac Center of Creighton University Medical Center, Omaha, NE

PURPOSE: Creighton University's Community Health Center is focused on engaging the local underserved community to promote healthy lifestyle choices that reduce adverse health outcomes in all ethnic groups. Health fairs and mobile education screening unit events identified differences in cardiovascular (CV) risk factors, medication use, and compliance among an ethnically heterogeneous patient population. The purpose of this analysis was to identify health disparities and medication compliance among different ethnic groups in the Omaha metropolitan area.

METHODS: Individuals attending health fairs and mobile health education screening events answered questions regarding family and personal medical history. Major CV risk factors were evaluated including hypertension (HTN), dyslipidemia (LIP), sedentary lifestyle (SL), smoking (SMO), and diabetes mellitus (DM). Laboratory testing included blood glucose and lipid profile. Self-reported medication use and compliance were also evaluated.

RESULTS: Characteristics of the 2530 participating individuals were as follows: 53 years old; 68% women; 57% black, 22% white, 7% Hispanic, and 14% other. Frequency of CV risk factors in our patients is shown in the following Table:

Ethnic Group	HTN (%)	LIP (%)	DM (%)	SMO (%)	SL (%)
Black	43	27	15	11	44
White	26	29	7	12	49
Hispanic	20	36	6	8	60
Participant average	34	25	12	10	47

Compliance with HTN medications was as follows: blacks 50%, whites 62%, and Hispanics 29%. Compliance with DM medications was as follows: blacks 33%, whites 63%, and Hispanics 50%. Compliance with LIP medications was as follows: blacks 27%, whites 28%, and Hispanics 36%.

CONCLUSIONS: Disparities exist between the different ethnic groups in both the prevalence of CV risk factors and in medication compliance for HTN, LIP, and DM. Further research is necessary to identify ways to reduce these health disparities.

Pharmacogenomics/Pharmacogenetics

190E. Additive Effects of β1 389 Arg/Gly α2c 322–325 Wt/Del Adrenergic Receptor Genotype Combinations on Adjudicated Hospitalizations and Death in the BEST Trial. *Mona Fiuzat, Pharm.D.,*[1] Christopher M. O'Connor, M.D.,[2] Peter E. Carson, M.D.,[3] Inder S. Anand, M.D., Ph.D.,[4] Jonathan Plehn, M.D.,[5] Stephen S. Gottlieb, M.D.,[6] Marc A. Silver, M.D.,[7] JoAnn Lindenfeld, M.D.,[8] Alan Miller, M.D.,[9] Michel White, M.D.,[10] Stephen S. Liggett, M.D.,[6] Alastair D. Robertson, Ph.D.,[8] Michael R. Bristow, M.D., Ph.D.[11]; (1) ARCA Biopharma, Denver, CO; (2) Duke University Medical Center, Durham, NC; (3) Department of Veterans Affairs, Washington, DC; (4) Department of Veterans Affairs, Minneapolis, MN; (5) National Heart, Lung and Blood Institute, Bethesda, MD; (6) University of Maryland, School of Medicine, Baltimore, MD; (7) Advocate Christ Medical Center, Oak Lawn, IL; (8) University of Colorado Health Sciences Center, Denver, CO; (9) University of Florida, School of Medicine, Jacksonville, FL; (10) Montreal Heart Institute, Montreal, QC, Canada; (11) ARCA Biopharma, University of Colorado Health Sciences Center, Denver, CO

PURPOSE: The 2708-patient Beta Blocker Evaluation of Survival Trial (BEST) contained a 1040-patient DNA substudy, testing the hypothesis that polymorphisms in the β_1- (codon 389 Arg→ Gly) and α_{2c}- (322-325 wild type→ deletion) adrenergic receptors influence the treatment effects of bucindolol. Treatment effects of bucindolol are further enhanced by the β_1-389Arg/Arg α2c-wild type (Wt)/deletion (Del) genotype combinations, exhibiting additive efficacy.

METHODS: The BEST end points committee adjudicated (Adj) all 5086 hospitalizations (H) in BEST and classified them into cardiovascular (CV), non-CV, and other subcategories including CVH due to worsening heart failure (HFH). The end points committee had previously adjudicated mortality type.

RESULTS: These data are presented as bucindolol/placebo time to event (TTE) hazard ratios (95% confidence intervals) analyzed in a covariate-adjusted Cox model and are reported for the entire cohort, as well as in the 1040 DNA substudy by β_1 389/α_{2c} genotype combination:

End Point	Entire Cohort (n=2708)	β1 389 Arg/Arg + α2c Wt/Wt or Del Carrier (n=493) ("Very Favorable")	β1 389 Gly Carrier + α2c Wt/Wt (n=413) ("Favorable")	β1 389 Gly Carrier + α2c Del Carrier ("Unfavorable") (n = 134)
MTTE/Adj	0.87**	0.62*	0.75	1.04
	(0.76, 1.00)	(0.39, 0.99)	(0.48, 1.17)	(0.43, 2.54)
	841 E	80 E	85 E	24 E
MTTE/Adj or TxTTE/Adj	0.86*	0.57*	0.76	1.04
	(0.75, 0.98)	(0.36, 0.89)	(0.50, 1.16)	(0.43, 2.54)
	911 E	88 E	94 E	25 E
CVMTTE/Adj	0.84*	0.52*	0.60*	1.11
	(0.72, 0.97)	(0.31, 0.88)	(0.36, 0.97)	(0.45, 2.78)
	714 E	64 E	73 E	22 E
HFHTTE/Adj	0.76****	0.56***	0.77	0.73
	(0.66, 0.87)	(0.39, 0.82)	(0.53, 1.13)	(0.35, 1.53)
	829 E	121 E	115 E	38 E
CVHTTE/Adj	0.82****	0.64***	0.91	0.96
	(0.73, 0.91)	(0.48, 0.86)	(0.68, 1.22)	(0.53, 1.76)
	1267 E	204 E	190 E	53 E
Non-CVHTTE/Adj	0.94	0.94	1.11	0.99
	(0.83, 1.07)	(0.69, 1.28)	(0.8, 1.55)	(0.48, 2.01)
	992 E	167 E	149 E	39 E

B = bucindolol; E = no. of events; H = hospitalization; M = all-cause mortality; P = placebo; Tx = transplant.
*p<0.05; **p=0.053; ***p<0.01; ****p<0.001.

CONCLUSIONS: The β_1 389 Arg/Gly α_{2c} 322-325 Wt/Del polymorphism substantially influenced bucindolol treatment effects on clinical end points, and the β_1-389 Arg/Arg α_{2c}-Wt/Del genotype combinations showed additive bucindolol efficacy. The therapeutic effects of bucindolol can be improved by pharmacogenetic targeting.
To be presented at the Heart Failure Society of America Annual Meeting in Toronto, ON, Canada, September 21–24, 2008.

191. Pharmacogenetic vs. Clinical Adjustments During Warfarin Initiation. *Gloria R. Grice, Pharm.D.,*[1] Petra A. Lenzini, MSC,[2] Paul E. Milligan, Pharm.D.,[2] Mary B. Dowd, Pharm.D.,[3] Sumeet Subherwal, M.D.,[2] Elena Deych, M.S.,[2] Charles Eby, M.D.,[2] Cristi R. King, B.S.,[2] Rhonda M. Porche-Sorbet, M.S.,[2] Claire V. Murphy, Pharm.D.,[4] Renee M. Marchand, Student,[2] Eric A. Millican, B.S.,[2] Robert L. Barrack, M.D.,[2] John C. Clohisy, M.D.,[2] Kathryn E. Kronquist, Ph.D.,[3] Susan K. Gatchel, CCRC,[2] Brian F. Gage, M.D.[2]; (1) St. Louis College of Pharmacy, St. Louis, MO; (2) Washington University, St. Louis, MO; (3) Kaiser Permanente Colorado, Lafayette, CO; (4) Barnes-Jewish Hospital, St. Louis, MO

PURPOSE: (1) Retrospectively, to develop pharmacogenetic and clinical dose-refinement algorithms to predict the therapeutic warfarin dose after 4 days of therapy and (2) prospectively, to compare the 30-day laboratory and clinical outcomes of these two algorithms.
METHODS: In orthopedic patients beginning warfarin therapy, we used stepwise regression to develop pharmacogenetic and clinical dose-refinement algorithms and prospectively validated the accuracy and safety of these algorithms.
RESULTS: The pharmacogenetic algorithm used *CYP2C9* genotype, smoking status, perioperative blood loss, liver disease, international normalized ratio (INR) values, and initial warfarin doses to predict the therapeutic dose (*VKORC1* did not appear to be as useful in dose-refinement because it was in dose-initiation algorithms). The R^2 was 82% in a derivation cohort (n=86) and 70% when used prospectively (n=146). The R^2 of the clinical algorithm that used INR values and initial warfarin doses to predict the therapeutic dose was 57% in a derivation cohort (n=179) and 48% in a prospective validation cohort (n=146). After 30 days, the percent time spent in the therapeutic range was 7% higher (95% CI: 2.7–11.7%) in the pharmacogenetic cohort. The risk of laboratory or clinical adverse events was also significantly reduced in the pharmacogenetic cohort (hazard ratio 0.54; 95% CI: 0.29–0.97).
CONCLUSIONS: In this nonrandomized study of orthopedic patients, pharmacogenetic dose refinements were associated with more time spent in the therapeutic range and fewer laboratory or clinical adverse events; these dose refinements also correlated more closely with therapeutic dose. To facilitate gene-guided warfarin dosing, we created www.WarfarinDosing.org.

192. Vitamin K Epoxide Reductase Genotype Is Associated with Warfarin Dose Requirements in Hispanics. *Larisa H. Cavallari, Pharm.D.*, Kathryn M. Momary, Pharm.D., Nancy L. Shapiro, Pharm.D., Edith A. Nutescu, Pharm.D., Shitalben R. Patel, M.S., Marlos A.G. Viana, Ph.D.; University of Illinois at Chicago, Chicago, IL

PURPOSE: Vitamin K epoxide reductase complex 1 (*VKORC1*) genotype has been associated with warfarin dose requirements in European whites, Asians, and African Americans. However, Hispanics, who constitute the largest minority population in the United States, are underrepresented in pharmacogenomics studies with warfarin. We sought to determine whether *VKORC1* genotype influences warfarin dose requirements in patients of Hispanic ethnicity.
METHODS: Genetic samples were collected from 31 Hispanics, by self-report (97% of Mexican origin), who were on a stable dose of warfarin, defined as the same dose for three or more consecutive clinic visits during at least a 6-week period. Demographic characteristics and clinical data, including the INR during stable dosing, were recorded. The *VKORC1* G-1639A and cytochrome P450 (CYP) 2C9 genotypes were determined by polymerase chain reaction and pyrosequencing methods. Warfarin dose was logarithmically transformed to enhance normality. Warfarin dose, clinical characteristics, and *CYP2C9* genotype distribution were compared between *VKORC1* genotype groups.
RESULTS: Allele frequencies were 0.34 for *VKORC1* -1639A, 0.08 for *CYP2C9*2*, and 0.06 for *CYP2C9*3*. Genotypes were in Hardy-Weinberg equilibrium. Age, sex, INR, use of potentially interacting drugs, and *CYP2C9* genotypes were similarly distributed among the *VKORC1* AA (n=5), AG (n=11), and GG (n=15) genotype groups, whereas body mass index was higher in the GG group (p=0.04). The mean ± SD log-transformed warfarin doses in the AA, AG, and GG genotype groups were 1.2 ± 0.2, 1.4 ± 0.2, and 1.6 ± 0.2 mg/week, respectively (p=0.002 by analysis of variance). The difference in dose between *VKORC1* genotype groups remained when body mass index was included as a covariate in the analysis of variance (p=0.016).
CONCLUSIONS: Our data suggest that the *VKORC1* genotype is a significant contributor to warfarin dose requirements in patients of Hispanic ethnicity.

193E. Leukocyte Expression of Atherosclerosis-Related Genes in Response to Atorvastatin Differs by CYP3A5 Genotype. *Julio D. Duarte, Pharm.D.*, Gregory J. Welder, AA, Issam Zineh, Pharm.D.; University of Florida College of Pharmacy, Gainesville, FL

PURPOSE: HMG CoA (3-hydroxy-3-methylglutaryl coenzyme A) reductase inhibitors (statins) are standard of care in cardiovascular disease, in part because of their anti-inflammatory effects. However, variability in response exists, and polymorphic drug metabolism may contribute. Atorvastatin is metabolized by cytochrome P450 (CYP) 3A5. Polymorphisms in the *CYP3A5* gene may contribute to variability in the systemic anti-inflammatory effects of statins. Thus, in a pilot experiment, we investigated whether changes in in vivo leukocyte expression of atherosclerosis-related genes after atorvastatin treatment differed by CYP3A5 genotype.
METHODS: Circulating leukocytes were collected from two healthy women selected on CYP3A5 genotype and matched on age before and after treatment with atorvastatin 80 mg/day for 8 weeks. One participant was a CYP3A5 expressor (CYP3A5*1 carrier), and one was a nonexpressor (CYP3A5*3/*3 genotype). Leukocyte gene expression analysis was performed using an RT-PCR (reverse transcriptase-polymerase chain reaction) array for genes involved in atherosclerosis (SuperArray Bioscience Corp., Frederick, MD). Fold changes in expression in response to atorvastatin were calculated by the $2^{-\Delta\Delta Ct}$ method.
RESULTS: Atorvastatin effects on gene expression differed by CYP3A5 genotype. Atorvastatin caused a 2-fold or greater change in 22 genes in the CYP3A5 nonexpressor and 25 genes in the expressor. The ratio of down- to up-regulated genes was high in the CYP3A5 nonexpressor (60:40), whereas the converse was true for

the CYP3A5 expressor (40:60). For genes commonly modulated in both patients, there was a stark difference in the magnitude and/or direction of the change.
CONCLUSIONS: CYP3A5 genotype may influence the anti-inflammatory effect of atorvastatin in humans. These preliminary findings indicate the need for further investigation into the clinical effect of CYP3A5 on atorvastatin therapy using various phenotypes.
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194. Rapid Phenotyping of Ganciclovir Resistance Mutations from Human Cytomegalovirus Infections in Liver Transplant Recipients. *Gregory Smallwood, B.S.Phr., Pharm.D.,*[1] Tim Barnett, Ph.D.,[2] Katie Casper, M.S.,[2] Thomas Heffron, M.D.[1]; (1) Emory University School of Medicine, Atlanta, GA; (2) Children's Healthcare of Atlanta, Atlanta, GA
PURPOSE: Reduced susceptibility to the antiviral drug ganciclovir is increasingly observed in cytomegalovirus infections of liver transplant patients, greatly complicating treatment protocols and reducing the prognosis. As we previously reported, we have identified numerous mutations of the cytomegalovirus (CMV) from clinical isolates obtained from liver transplant recipients. Clinical outcomes associated with these isolates have been associated with "clinical resistance" to ganciclovir. Most research aimed at identifying ganciclovir-resistant CMV has centered on the identification of mutations in two genes, *UL97* and *UL54*, and characterization of these mutations by a process called "recombinant phenotyping." In this study, we developed an improved recombinant phenotyping method for CMV.
METHODS: Using a reporter strain (Towne-SEAP) that is propagated in *Escherichia coli* as a bacterial artificial chromosome, an individual mutation can be introduced into the *UL97* gene in 1–2 weeks using rapid *E. coli* genetic techniques. After transfection into host cells, recombinant virus particles are produced that contain two different reporter genes, green fluorescent protein (GFP) and secreted alkaline phosphatase (SEAP). Growth of recombinant virus in different concentrations of ganciclovir is monitored visually (by GFP), and antiviral susceptibility levels are calculated by measuring SEAP activity in culture supernatants, which will be shown.
RESULTS: With the introduction of three mutations from clinical isolates from liver transplant patients, a system has been developed that measures the degree of "clinical resistance" together with dose-appropriate recommendations for clinical use. With the incorporation of known (A594V) and novel (N510S and N597Y) mutations into *UL97*, dose concentration curves required for viral kill are produced.
CONCLUSIONS: With the use of this engineered reporter virus for antiviral resistance, quick identifications of resistant CMV with dose recommendations are now possible. The reporter virus, Towne-SEAP, represents a dramatic improvement on existing methods, with its ability to deliver a more comprehensive analysis of mutations affecting drug susceptibility of CMV.

195. A Pharmacogenetic-Directed Treatment Strategy Reduces Cost of Hospitalizations in Patients with Moderate to Severe Heart Failure (HF) Treated with Bucindolol. *Bruce R. Koch II, Pharm.D.*; ARCA Biopharma, Inc., Denver, CO
PURPOSE: Bucindolol is a next-generation, nonselective β-adrenoceptor (AR) antagonist with mild vasodilating properties and α_1-AR antagonism. The Beta Blocker Evaluation of Survival Trial (BEST) evaluated bucindolol in 2708 patients with moderate to severe heart failure (HF). A prospective pharmacogenetic analysis collected information on 1040 patients in BEST. Analyses of these data revealed a differential clinical benefit of bucindolol in patients with polymorphisms in either the β_1- or α_{2c}-AR. The present study evaluates the hospitalization costs associated with these differential clinical benefits among genotypes.
METHODS: The BEST economic substudy compared the costs, by genotype, of all-cause and HF hospitalization in patients treated with bucindolol or placebo. Genotypes were defined, according to clinical benefit of polymorphisms of the β_1-AR (389Arg/Gly) and α_{2c}-AR (322-325 wild type/deletion), as very favorable, favorable, and unfavorable. Patients with the Arg/Arg homozygous variant of the β_1-AR, irrespective of α_{2c}-AR polymorphism status, were classified as having the very favorable genotype (47% of BEST population). A favorable genotype was defined as a β_1-AR Gly carrier (i.e., heterozygous or homozygous) with no 322-325 deletion polymorphism of the α_{2c}-AR (40% of BEST). The unfavorable genotype was defined as being both a β_1-AR Gly carrier and a 322-325 deletion carrier of the α_{2c}-AR (13% of BEST).
RESULTS: For patients with the very favorable genotype, all-cause hospitalization costs were $6717 lower and HF hospitalization costs were $4667 lower for bucindolol than for placebo. All-cause and HF hospitalization costs for patients with the favorable genotype were $265 lower and $933 higher, respectively, for bucindolol versus placebo. All-cause and HF hospitalization costs for patients with the unfavorable genotype were higher with bucindolol versus placebo ($7947 and $5760, respectively).
CONCLUSIONS: These results suggest that individualization of β-blocker treatment in HF patients based on genetic information has the potential to greatly decrease associated hospitalization costs.

Association of CYP3A5 and VEGF Gene Polymorphisms with Hypertensive Nephropathy

196. Association of CYP3A5 and VEGF Gene Polymorphisms with Hypertensive Nephropathy. *Jae-Wook Yang, Ph.D., Pharm.D.,*[1] Ian V. Hutchinson, Ph.D., D.Sc.,[2] Vera Pravica, M.D., Ph.D.,[3] Tariq Shah, M.D.,[4] Deborah Maurer, R.N., M.B.A.,[5] David I. Min, Pharm.D.[1]; (1) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Los Angeles, CA; (2) USC School of Pharmacy, Los Angeles, CA; (3) USC/National Institute of Transplantation, Los Angeles, CA; (4) St. Vincent Medical Center and National Institute of Transplantation, Los Angeles, CA; (5) St. Vincent Medical Center, Los Angeles, CA
Background: Hypertensive nephropathy (HTN) is the second most common cause of end-stage renal disease leading to kidney transplantation.
Objective: This study investigated the association between genetic polymorphisms of CYP3A5 (cytochrome P450 3A5) and VEGF (vascular endothelial growth factor) in transplant recipients with hypertensive nephropathy compared with a selected nonhypertensive control group.
METHODS: The cause of end-stage renal disease was determined in kidney recipients receiving transplantations at St. Vincent Medical Center, Los Angeles, between 2000 and 2006. A total of 197 patients were identified whose cause of renal failure was hypertensive nephropathy. As a control group, 70 kidney donors (60 live donors) were selected who were screened and showed no evidence of risk of hypertension or other cerebrovascular disease. Patients and controls were genotyped for cytochrome P450 (CYP) 3A5 (rs776746) or vascular endothelial growth factor (VEGF) (rs1570360) polymorphisms using an Applied Biosystems allelic discrimination assay. Allele and genotype distributions and Hardy-Weinberg equilibrium were analyzed using the χ^2 test.
RESULTS: The allele and genotype distributions for CYP3A5 and VEGF are shown in the Table. All genotypes were in Hardy-Weinberg equilibrium.

	Allele or Genotype	Control (n=70)	HTN (n=197)	p-value
CYP3A5	G	78.6	64.7	
	A	21.4	35.3	0.0024
	G/G	62.9	46.7	
	G/A	31.4	36.0	
	A/A	5.7	17.3	0.02
VEGF	G	33.0	81.0	
	A	67.0	19.0	0.0007
	G/G	45.7	67.0	
	G/A	42.9	27.9	
	A/A	11.4	5.1	0.005

CONCLUSION: The G allele and the G/G genotypes for both CYP3A5 and VEGF are significantly associated with HTN. These associations may reflect the pathogenesis of hypertension per se or the development of nephropathy leading to end-stage renal disease.

197E. Liver X Receptor Alpha (LXRA) Gene Polymorphism Associates with Baseline Cholesterol But Not Statin Response in Healthy Volunteers. *Elvin T. Price, Pharm.D.,*[1] Richard S. Schofield, M.D.,[2] Issam Zineh, Pharm.D.[1]; (1) University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, FL; (2) Division of Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, FL

PURPOSE: Elevated plasma cholesterol is a well-known risk factor for cardiovascular disease (CVD). Genetic factors have been linked to interindividual variability in cholesterol concentrations. The liver X receptor-a (LXRA) is a transcription factor involved in cholesterol homeostasis. LXRA has commonly inherited single nucleotide polymorphisms (SNPs) that associate with variable lipid profiles and metabolic phenotypes. Furthermore, statin drugs work in part through LXRA-dependent mechanisms. We thus tested whether the LXRA SNP rs2279238 (C>T) was associated with baseline or end-of-treatment cholesterol concentrations in a population of healthy volunteers taking atorvastatin 80 mg/day.

METHODS: Subjects were eligible if they were at least 18 years old without CVD or diabetes. Subjects received atorvastatin 80 mg/day until end of study. Baseline and 8-week low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), triglycerides, and total cholesterol (TC) concentrations were measured. Genotype determination was performed by TaqMan. Baseline lipids and changes after 8 weeks of atorvastatin were assessed using independent *t*-tests stratified by genotype group.

RESULTS: A total of 80 subjects (63% women; 79% white) were analyzed. Baseline age, TC, LDL-c, HDL-c, and triglycerides were 32 ± 13 years, 184 ± 42 mg/dL, 100 ± 33 mg/dL, 62 ± 17 mg/dL, and 107 ± 70 mg/dL, respectively. The variant T-allele frequency was 16%. Variant T-allele carriers showed higher baseline TC and LDL-c compared with wild-type CC (TC: 202 ± 46 vs. 176 ± 37 mg/dL; LDL-c: 114 ± 35 vs. 93 ± 32 mg/dL; p<0.03 for comparisons). There were no significant differences in response to 8 weeks of atorvastatin for any of the biomarkers measured (data not shown).

CONCLUSIONS: LXRA T carriers for the above SNP showed about 15–20% higher baseline TC and LDL-c compared with wild-type homozygotes. This SNP did not associate with variable lipid lowering in response to atorvastatin. These findings support data from previous studies, which have identified LXRA as a contributor to the genetic variability associated with dyslipidemia.

To be presented at the 4th Biologie Perspective Santorini Conference "Functional Genomics Towards Personalized Health Care," Santorini, Greece, September 21–23, 2008.

198. Influence of Serotonin Transporter Genotype on Aspirin Response. *Kathryn M. Momary, Pharm.D., BCPS,*[1] Jeffrey R. Bishop, Pharm.D., M.S.,[1] Nancy L. Shapiro, Pharm.D.,[1] Edith Nutescu, Pharm.D.,[1] Larry Brace, Ph.D.[2], Stacy Shord, Pharm.D., BCOP,[1] Cathy M. Helgason, M.D.,[2] Larisa H. Cavallari, Pharm.D.[1]; (1) University of Illinois at Chicago College of Pharmacy, Chicago, IL; (2) University of Illinois at Chicago College of Medicine, Chicago, IL

PURPOSE: There is substantial interpatient variability in the inhibitory effects of aspirin on platelet aggregation. Serotonin promotes platelet aggregation, and serotonin transporter genotype (*SLC6A4*) has been associated with risk of myocardial infarction. There are no data on whether genetic variation in *SLC6A4* influences aspirin response. We sought to determine whether the *SLC6A4* long/short promoter variant is associated with aspirin's effects on platelets.

METHODS: In this prospective cohort study, blood was collected from 59 subjects of various races who were taking single antiplatelet therapy with aspirin. Blood was used to determine *SLC6A4* genotype (by fragment analysis), ex vivo platelet aggregation (by the method of Born), fasting lipid profile, and salicylate concentrations (by high-pressure liquid chromatography). Response to aspirin was classified as complete or partial based on ex vivo platelet aggregation response to arachidonic acid, epinephrine, collagen, and adenosine diphosphate. Aspirin response, salicylate and lipid levels, and other clinical data were compared between the *SLC6A4* long/long, long/short, and short/short genotype groups.

RESULTS: The frequency of the variant *SLC6A4* short allele was 0.37. Genotype distributions were in Hardy-Weinberg equilibrium within each racial group included in the study. Thirty (51%) subjects were classified as partial responders to aspirin. Subject characteristics, serotonin reuptake inhibitor use, aspirin dose, lipid levels, and salicylate levels were similar in subjects with the *SLC6A4* long/long (n=27), long/short (n=20), and short/short (n=12) genotype. There was also no significant difference in the frequency of partial responders to aspirin in the long/long (52%), long/short (60%), and short/short (33%) genotype groups (p=0.30).

CONCLUSIONS: Our data do not provide evidence to support a relationship between genetic variation in the *SLC6A4* promoter region and aspirin response as measured by ex vivo platelet aggregation.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

199. A Pharmacokinetic Study of Adjuvant Chemotherapy in Overweight and Obese Women. *Lisa Garrity, Pharm.D.,*[1] Robert DiCenzo, Pharm.D.,[2] Alan Forrest, Pharm.D.,[1] Jennifer J. Griggs, M.D., MPH[3]; (1) University at Buffalo, Buffalo, NY; (2) St. John Fischer College, Rochester, NY; (3) University of Rochester, Rochester, NY

PURPOSE: Dosing of adjuvant chemotherapy in overweight and obese women remains controversial, with many practitioners imposing a maximum dose limit on this population. These lowered doses are associated with decreased rates of survival. The purpose of this project was to correlate variability in pharmacokinetic parameters for cyclophosphamide, doxorubicin, and doxorubicinol with measures of body composition including bioelectrical impedance (BIA) and dual-energy x-ray absorptiometry (DEXA) scans.

METHODS: Two-compartment pharmacokinetic models were fit to data from 29 women receiving their first course of adjuvant chemotherapy (60 mg/m^2 of doxorubicin given as an intravenous bolus, followed by a 600-mg/m^2 cyclophosphamide intravenous infusion). No dose limits were imposed. Plasma concentrations of cyclophosphamide, doxorubicin, and doxorubicinol were measured by high-pressure liquid chromatographic assay of venous blood samples collected at 1, 1.5, 2, 3, 4, 6, 8, 24, and 48 hours after starting the cyclophosphamide infusion. Resulting pharmacokinetic parameters were screened against variables including measures of body composition (height, weight, and BIA and DEXA scans), followed by stepwise regression to determine which variables best described pharmacokinetic parameter variability.

RESULTS: Lean mass best predicted variability in apparent volume of distribution of cyclophosphamide (R^2=0.498, p<0.001) and clearance of doxorubicin (R^2=0.347, p=0.001). Body surface area was best correlated to variability in clearance of cyclophosphamide (R^2=0.193, p=0.019). Variability in the conversion of doxorubicin to doxorubicinol was best predicted by percent body fat (R^2=0.491, p<0.001), as was variability in doxorubicinol aura under the curve normalized to doxorubicin dose (R^2=0.362, p=0.001).

CONCLUSIONS: Measures of body composition derived from DEXA scans had improved correlation to pharmacokinetic parameters. However, body composition only partially explains variability in pharmacokinetic parameters for these agents.

200. Population Pharmacokinetics of Oritavancin. *Christopher M. Rubino, Pharm.D., BCPS,*[1] Scott A. Van Wart, M.S.,[1] Sujata M. Bhavnani, Pharm.D., M.S.,[1] Jill S. McCollam, Pharm.D.,[2] Paul G. Ambrose, Pharm.D., FIDSA[1]; (1) ICPD/Ordway Research Institute, Albany, NY; (2) Targanta Therapeutics Corporation, Indianapolis, IN

PURPOSE: Oritavancin (ORI) is a novel lipoglycopeptide currently in late-stage development for the treatment of complicated skin and skin structure infection. Data from 12 studies (nine phase 1 studies, two phase 2 studies, and one phase 3 study) were pooled to conduct a population pharmacokinetics (PK) analysis, including an evaluation of factors predictive of ORI PK.

METHODS: ORI was administered as both single- and multiple-

dose intravenous infusions in fixed doses ranging from 100 to 800 mg or weight-based doses ranging from 0.02 to 10 mg/kg. PK sampling schemes varied by study. Candidate PK models were fit to plasma data using Monte Carlo parametric expectation maximization with SADAPT. Using population covariate analysis, several demographic and disease characteristics (e.g., age, sex, body size, diagnosis, concomitant diseases) were evaluated for their impact on the PK parameters.
RESULTS: A total of 6290 plasma concentrations from 560 subjects were analyzed. The most robust fit to the data was obtained using a three-compartment model (one central, two peripheral) with zero-order intravenous infusion and first-order elimination. Overall, excellent fits were obtained; the equation of the regression fit line through the observed versus individual fitted concentrations showed a low intercept (0.28 µg/mL), a slope near unity (1.01), and an r^2=0.951. Covariate analysis indicated a statistically significant relationship between ORI clearance and both total body weight (most pronounced above 110 kg) and study phase, suggesting that dose modifications may be required for patients weighing 110 kg and more. A statistically significant relationship between ORI volume of the central compartment and both body surface area and age was identified. The mild nature of this relationship suggests that dosing adjustments are not necessary for elderly patients.
CONCLUSIONS: These results were used to support the new drug application for ORI. The population PK model described will allow estimation of ORI exposure for future PK-pharmacodynamics analyses for efficacy and safety.

201. Linear Dose Proportionality, Low Inter- and Intrasubject Variability, and Safety of Lisdexamfetamine Dimesylate in an Open-Label Single-Dose Pharmacokinetic Study in Healthy Adult Volunteers. *James Ermer, M.S.,*[1] Robert Homolka, M.S.,[1] Patrick Martin, M.D.,[1] Mary Buckwalter, M.S.,[1] Jaideep Purkayastha, M.S.,[1] Benno G. Roesch, M.D.[2]; (1) Shire Development Inc., Wayne, PA; (2) Advanced Biomedical Research, Inc., Hackensack, NJ
PURPOSE: D-Amphetamine is the active moiety of the prodrug lisdexamfetamine dimesylate (LDX). The safety, tolerability, dose proportionality, and variability in pharmacokinetic (PK) parameters of D-amphetamine and LDX were described across a range of doses from 50 to 250 mg.
METHODS: In this dose-escalation study of LDX in healthy adults aged 18–55 years, subjects received a single LDX dose on day 1 of five dosing periods (sequentially 50, 100, 150, 200, and 250 mg). Subjects did not receive the next scheduled dose if two consecutive blood pressure readings were more than 160 systolic blood pressure or more than 100 diastolic blood pressure in 1 hour. Plasma D-amphetamine concentrations were measured predose and 0.25–96 hours postdose. Descriptive statistics were used. Dose proportionality of C_{max} and $AUC_{0-\infty}$ was determined using regression analysis. Safety assessments included adverse events (AEs), vital signs, and physical examination.
RESULTS: Twenty, 20, 18, 12, and 9 subjects received 50, 100, 150, 200, and 250 mg of single LDX doses, respectively. Mean D-amphetamine PK values increased in a linear, dose-dependent manner for C_{max} (44.6, 84.6, 126.6, 168.8, and 246.3 ng/mL, respectively) and $AUC_{0-\infty}$ (818.1, 1548.2, 2503.4, 3336.2, and 5132.5 ng·hour/mL, respectively). Median T_{max} ranged from 4 to 6 hours, and median $t_{1/2}$ ranged from 10.6 to 11.7 hours. There was low inter- and intrasubject variability (less than 20%) between 50- and 150-mg doses in both C_{max} and $AUC_{0-\infty}$. Common AEs (more than 15%) were nausea, dizziness, headache, psychomotor hyperactivity, and dysuria. Dose-dependent increases in mean blood pressure and pulse peaked at 2 hours and 8–12 hours, respectively (systolic blood pressure 124–153 mm Hg; diastolic blood pressure 79–92 mm Hg; and pulse 75–87 beats/minute). Ten subjects were discontinued per prespecified blood pressure stopping rules.
CONCLUSIONS: The PK of D-amphetamine was dose proportional over the doses of 50–250 mg of LDX. Low variability in PK parameters was observed, both within and between subjects. There were no unexpected adverse events.
Supported by funding from Shire Development Inc.

202. Plasma Protein Binding of Anidulafungin Is Similar to Other Major Echinocandins. *Philip Inskeep, Ph.D.*, Jian Lin, M.S.; Pfizer Global Research and Development, Groton, CT
PURPOSE: Anidulafungin is one of three echinocandins approved in the United States for the intravenous treatment of systemic fungal infections. Early reports, using ultracentrifugation methods relying on total radioactivity, indicated that protein binding of anidulafungin in human plasma (84%) was substantially lower than independently determined values of protein binding for caspofungin (97%) or micafungin (99%). Similar differences were observed for rat and dog plasma. Subsequent to the initial protein binding study with anidulafungin, a nonenzymatic intramolecular rearrangement of anidulafungin when incubated in plasma was observed. This product retains the radiolabel and thus would not be distinguishable from anidulafungin when total radioactivity is measured in the protein-free fraction from ultracentrifugation. Therefore, this study further assessed plasma protein binding using an alternative method.
METHODS: Protein binding of unlabeled anidulafungin in rat, dog, monkey, and human plasma at 37ºC was determined using dialysis and a liquid chromatographic mass spectrometric (LC/MS/MS) method specific for parent.
RESULTS: Using dialysis and the specific LC/MS/MS assay, more than 99% of plasma anidulafungin was observed to bind to protein across the initial concentration range of 1.0–10 µg/mL for all four species (and 100 µg/mL in monkey plasma). In addition, the amount of parent anidulafungin decreased during the incubation period. This observation is consistent with the hypothesis that nonbinding degradation products of radiolabeled anidulafungin were formed in the previous studies, resulting in lower estimations of protein binding.
CONCLUSIONS: Plasma protein binding of anidulafungin is similar to other major echinocandins. These studies underscore the importance of using specific analytic methods, rather than total radioactivity, to assess the protein binding of macromolecules having the potential for nonenzymatic rearrangements.

203. Pharmacokinetics of Small and Large Molecules in a Nephrotic Model of Glomerular Disease. *Melanie S. Joy, Pharm.D.,*[1] Debbie Gipson, M.D., MPH,[2] Howard Trachtman, M.D.[3]; (1) University of North Carolina, Schools of Medicine and Pharmacy, UNC Kidney Center, Chapel Hill, NC; (2) University of North Carolina, School of Medicine, Chapel Hill, NC; (3) Schneider Children's Hospital, New Hyde Park, PA
INTRODUCTION: Patients with nephrotic syndrome have modifications in glomerular filtration rate and proteinuria and concomitant reductions in serum albumin. The influence of the nephrotic syndrome on the pharmacokinetics (PK) of drugs is warranted.
PURPOSE: To evaluate the effects of the nephrotic syndrome on the PK of a small (mw = 473 daltons), highly bound (99%) molecule and a large (mw = 145 kilodalton) molecule.
METHODS: Nephrotic patients with focal segmental glomerulosclerosis (FSGS) participated in a single- and multiple-dose PK study with rosiglitazone 3 mg/m^2 orally divided twice daily and adalimumab 24 mg/m^2 subcutaneously every 2 weeks. Blood was collected at 0, 0.5, 1, 2, 4, 6, 8, 12, 18, 30, and 48 hours for rosiglitazone and at 0, 2, 8, 12, 30, and 42, 168, and 336 hours for adalimumab. Because rosiglitazone and adalimumab exhibit stationary PK, a noncompartmental PK approach (WinNonlin v. 4.1) was used for initial estimates to enable comparison with control populations. A Student's *t*-test or Wilcoxon signed rank test was used to determine differences in PK.
RESULTS: Eleven and 10 patients from 4 to 36 years old received rosiglitazone and adalimumab, respectively. Patient demographics were aged 16 ± 7.5 years, 52% white, 57% male, body surface area 1.5 ± 0.42 m^2, and 57% postpubertal. Baseline laboratory test values were glomerular filtration rate (GFR) 122 ± 63 mL/minute, urine protein-to-creatinine ratio 9.9 ± 8.6, and serum albumin 2.2 ± 0.99 g/dL.

Table[a]

	Adalimumab		Rosiglitazone	
	FSGS (n=10)	*RA* (n=9)	*FSGS* (n=11)	*StageI/II CKD* (n=15)
T_{max} (hours) 55 ± 62*	131 ± 56	1.8 ± 0.9	2.0 (1.0–4.0)	
C_{max} (µg/mL)[b]	9.2 ± 4.1*	13.7 ± 2.7	0.11 ± 0.09	0.12 ± 0.03
$T_{1/2}$ (hours)	159 ± 155*	389 ± 71	2.6 ± 0.7	4.5 ± 1.9
AUC (µg hour/mL)[b]	1646 ± 1202*	3622 ± 587	0.34 ± 0.21*	0.78 ± 0.31
Cl/F (mL/minute)[c]	20.2 ± 8.4*	12.6 ± 2.3	159 ± 170*	48.0 ± 16.0

[a]Single-dose pk data.
[b]Number of doses corrected.
[c]Weight scaled to 0.75 power.
*p<0.05 between FSGS and comparison group.
CKD = chronic kidney disease.

CONCLUSIONS: Patients with nephrotic syndrome receiving representative small and large molecular therapeutic entities have enhanced apparent total clearance (Cl/F) and reduced area under the curve (AUC) compared with nonnephrotic control populations.

204. Evaluation of Vancomycin Dosing Protocol for Cardiothoracic Surgery Prophylaxis. *Mannhu N. Ton, Pharm.D.*, Helen S. Lee, Pharm.D., Lauri Thrupp, M.D., Jeffrey Milliken, M.D., Patria Fopiano, BSN; UC Irvine Medical Center, Orange, CA

PURPOSE: In cardiothoracic surgery (CTS), the use of cardiopulmonary bypass (CPB) can affect the pharmacokinetics of prophylactic antibiotics such as vancomycin. In 2006, to further optimize surgical antibiotic prophylaxis, our institution implemented a weight-based vancomycin dosing protocol for CTS using 15 mg/kg up to 1.5 g. The objectives of this study were to evaluate adherence to the vancomycin dosing protocol, to assess vancomycin levels achieved about 12 hours after the preoperative dose (VL12), and to evaluate the possible need for administration of intraoperative dose of vancomycin for CTS.
METHODS: This retrospective review included 30 adult patients who underwent CTS from April 2006 to February 2007, received vancomycin prophylaxis, and had VL12 drawn. Other data collected include baseline demographics, comorbidities, type of CTS, duration of surgery, duration of CPB, intraoperative blood transfusions, baseline serum creatinine, vancomycin dosage, and VL12.
RESULTS: The weight-based vancomycin dosing protocol was adhered to in 17 of 30 patients. The non–weight-based group received a vancomycin dose of 1 g. Differences in level sampling time among patients led to the use of extrapolated vancomycin concentrations. Vancomycin concentrations greater than 4 µg/mL were achieved in 9 (69%) and 13 (88%) patients in non–weight-based and weight-based groups, respectively. Six patients had levels equal to 4 µg/mL or less; possible factors contributing to the lower levels were vancomycin dosage less than 15 mg/kg, high creatinine clearance, and longer duration of CPB. A trend toward decreased vancomycin levels with a longer duration of CPB was observed.
CONCLUSIONS: The weight-based vancomycin dosing of 15 mg/kg was more consistent in achieving concentrations greater than 4 µg/mL at about 12 hours after the preoperative dose compared with the standard 1-g dose.

Psychiatry

205E. A Characterization of Polypharmacy in an Inpatient Bipolar Population. *Kali M. Schulz, Pharm.D.*, Kevin Furmaga, Pharm.D., BCPP, G. Robert DeYoung, Pharm.D., BCPS; Saint Mary's Health Care, Grand Rapids, MI

PURPOSE: The purpose of this study was to characterize pharmacotherapy regimens used to manage acute bipolar symptoms in hospitalized patients. Opportunities to improve inpatient treatment of acute mania were identified by comparing polypharmacy regimens on hospital admission and discharge with current treatment guidelines for bipolar mania.
METHODS: Charts of 100 randomly selected adult inpatients discharged between December 31, 2006, and July 1, 2007, with a diagnosis of bipolar disorder were reviewed. Data were categorized according to diagnosis and medication regimen at both admission and discharge. Adherence to current guidelines was assessed by comparing medication regimens before admission and at discharge with the guideline algorithm. Secondary outcomes included (1) the occurrence of polypharmacy before admission compared with the occurrence at discharge and (2) the impact of an axis II diagnosis on adherence.
RESULTS: A total of 100 charts were reviewed. Seventy-three patients were included in the analysis of medication at admission, and 96 patients were included in the analysis of medications at discharge. On admission, 28.8% of patients had pharmacotherapy regimens consistent with guideline recommendations. This improved to 51% at discharge (p=0.005). The mean number of medications used to manage bipolar symptoms on admission and at discharge did not change (2.85 vs. 2.71, respectively; p=0.49). The most common reasons for non-adherence to treatment guidelines included the use of topirimate as a mood stabilizer and the use of antidepressants or stimulants in patients with manic symptoms. Patients with both a bipolar disorder diagnosis and an axis II diagnosis did not differ from the overall study population with respect to adherence to current guidelines.
CONCLUSIONS: Adherence to current guidelines improved during admission largely through the elimination of antidepressants and stimulants from treatment regimens. The presence of an axis II diagnosis did not increase the risk of non-adherence to treatment guidelines.
Presented at the Great Lakes Pharmacy Resident Conference, West Lafayette, IN, April 23–25, 2008.

206E. Improvement in Attention-Deficit/Hyperactivity Disorder Symptoms in Children with Lisdexamfetamine Dimesylate Versus Extended-Release Mixed Amphetamine Salts and Placebo in an Analog Classroom. Frank Lopez, M.D.,[1] Ann C. Childress, M.D.,[2] *Stacey Curtiss, Pharm.D.*[3]; (1) Children's Developmental Center, Winter Park, FL; (2) Center for Psychiatry and Behavioral Medicine, Inc., Las Vegas, NV; (3) Shire Development Inc., Wayne, PA

PURPOSE: Lisdexamfetamine dimesylate (LDX) is a prodrug stimulant indicated for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children aged 6–12 years and in adults. This post hoc analysis compared the efficacy and safety of LDX and mixed amphetamine salts extended release (MAS XR) with placebo in children with ADHD.
METHODS: This was a multicenter analog classroom study of LDX (30, 50, and 70 mg/day), MAS XR (10, 20, and 30 mg/day; about equivalent in amphetamine content to the three LDX doses, respectively), and placebo in children with ADHD. After a 1-week screening and 3-week dose optimization with MAS XR, children received 1 week each of LDX, MAS XR, and placebo in a randomized, double-blind, three-way crossover protocol. Efficacy in this post hoc analysis was change from first measurement on the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale and the Permanent Product Measure of Performance (PERMP). Both SKAMP and PERMP were measured at 1, 2, 3, 4.5, 6, 8, 10, and 12 hours postdose in an analog classroom. Safety parameters included adverse events, vital signs, and electrocardio-grams.
RESULTS: Fifty of 52 children completed the study. After 2 hours postdose, LDX and MAS XR produced significant improvements at all time points compared with placebo, based on least-square mean changes on SKAMP-Deportment (p<0.01), SKAMP-Attention (p<0.05, except at 2 hours postdose for MAS XR), PERMP-Attempted, and PERMP-Correct (both p<0.0001). LDX produced significantly greater improvement compared with MAS XR at 12 hours postdose on the PERMP-Attempted and PERMP-Correct (both p<0.05) but not on the SKAMP measures. During the double-blind period, treatment-emergent adverse events (mild to moderate) occurred in 16, 18, and 15% of subjects taking LDX, MAS XR, and placebo, respectively.
CONCLUSIONS: LDX is an effective, generally well-tolerated treatment for ADHD in 6- to 12-year-old children.
Supported by funding from Shire Development Inc.
Presented at the 2007 College of Psychiatric and Neurologic Pharmacists, Colorado Springs, CO, April 15–18, 2007.

Substance Abuse/Toxicology

207. Characterization of Alcohol-Related Knowledge, Behavior, and Attitudes of First-Year Doctor of Pharmacy Students. Laurel L. Andrews, Pharm.D., Scott A. Baggarly, Ph.D., Darren A. LeBlanc, Pharm.D. Candidate, Edwin H. Adams, Pharm.D., Connie L. Smith, Pharm.D., Ann M. Wicker, Pharm.D., *W. Greg Leader, Pharm.D.*; University of Louisiana at Monroe College of Pharmacy, Monroe, LA

PURPOSE: The purpose of this study was to characterize the knowledge, behavior, and attitudes of first-year pharmacy students with respect to alcohol use.

METHODS: Using a validated survey, alcohol-related knowledge, behavior, and attitudes of 87 first-year pharmacy students were measured. After obtaining informed consent, surveys were administered to first-year pharmacy students in the ULM College of Pharmacy. Researchers were blinded to study participants. Student drinking behaviors were categorized on the basis of the quantity and frequency of alcohol use. Alcohol problem (past-year and lifetime), attitude, and knowledge scores were calculated. Potential interactions between alcohol-related knowledge, behavior, and attitudes were evaluated.

RESULTS: A quantity-frequency index (QFI) was used to classify student drinking behaviors into six categories: abstainers (23%), infrequent (9.2%), light (24.1%), moderate (16.1%), moderate-heavy (17.2%), and heavy (10.3%). Attitude scores for abstainers were significantly greater than for students classified as moderate-heavy ($p<0.0001$) or heavy drinkers ($p<0.0001$). Attitude scores of women were greater than men ($p=0.0136$), indicating a more responsible attitude toward drinking. Attitude scores for students reporting no alcohol-related problems were significantly higher than for students who reported five or six problems ($p=0.0004$). Knowledge scores ranged from 25 to 90, with a mean score of 60.69, comparable with the validation sample score of 63.07. There was no significant difference in knowledge scores by age ($p=0.1594$) or by QFI category ($p=0.9544$), but women had higher knowledge scores than men ($p=0.0238$). Attitude scores and knowledge scores were relatively independent. ($r=0.2953$).

CONCLUSIONS: Slightly less than half of surveyed students were classified as moderate to heavy drinkers. Female students tended to have attitude scores indicating more responsible use and greater knowledge concerning alcohol and its effects. The next step is to determine whether a Web-based educational intervention would affect alcohol-related knowledge, behavior, and attitudes.

208. A Randomized Trial Assessing the Effectiveness of a Pharmacist-Delivered Program for Smoking. *Larry A. Dent, Pharm.D., BCPS,*[1] Kari J. Harris, Ph.D., MPH,[2] Curtis W. Noonan, Ph.D.[3]; (1) University of Montana, Skaggs School of Pharmacy, Department of Pharmacy Practice, Missoula, MT; (2) University of Montana, School of Public and Community Health Sciences, Missoula, MT; (3) University of Montana, Skaggs School of Pharmacy, Department off Biomedical Sciences, Missoula, MT

PURPOSE: As trained and accessible health care professionals, pharmacists are in an ideal position to provide tobacco cessation interventions. However, few published studies have assessed the efficacy of tobacco cessation services by pharmacists. This is the first randomized controlled trial in the United States to assess the effectiveness of a pharmacist-delivered group program for tobacco smoking cessation compared with standard care in a community setting.

METHODS: Design of the study was an open-label randomized controlled trial. The study was conducted at a Montana Veterans Health Administration, Community-Based Outpatient Clinic, in Missoula, Montana. Patients included 101 smokers who were randomized from October 3, 2005, to March 30, 2007, with the last 6-month follow-up survey completed on November 6, 2007. Participants assigned to the treatment group (n=50) participated in a three-session pharmacist-delivered group program, and those assigned to the control group (n=51) received one 3- to 5-minute standard care session over the telephone. Participants in both groups were offered either bupropion immediate-release tablets or a nicotine patch at no cost.

RESULTS: The main outcome measure was biochemically confirmed 7-day point prevalence abstinence at 6 months after quit date. Using intention-to-treat procedures, confirmed abstinence rates at the end of 6 months were 28% in the pharmacist-delivered treatment group and 11.8% in the standard care control group ($p<0.048$).

CONCLUSIONS: This study demonstrates that pharmacists are effective providers of tobacco cessation interventions. This is the first randomized controlled trial of a pharmacist-delivered smoking cessation intervention conducted in the United States. Greater use of pharmacists in tobacco cessation efforts could have a significant impact on smoking rates, prevention of tobacco-related disease, and improvement in public health across the United States.

Transplant/Immunology

209. The Evaluation of Renal Clearance Calculations for Hepatic Failure Patients Awaiting Liver Transplantation. *Gregory Smallwood, B.S.Phr., Pharm.D.,*[1] Candace Stearns, Pharm.D.,[2] Thomas Heffron, M.D.[1]; (1) Emory University School of Medicine, Atlanta, GA; (2) Emory University Healthcare, Atlanta, GA

BACKGROUND: Estimation of renal clearance in patients with hepatic dysfunction is difficult to obtain by mathematic equation. Currently, several methods are used to estimate creatinine clearance (CrCl); these include the Cockroft-Gault (CG) equation, the modification-of-diet-in-renal-disease (MDRD-6) equation, and a newly described Nix formula in patients with hepatic failure.

PURPOSE: The aim of this study was to compare three methods of renal clearance estimation to actual, measured, 24-hour CrCl in patients awaiting liver transplantation.

METHODS: This was an institutional review board–approved study that collected data on 24-hour CrCl from patients who were awaiting liver transplantation. The 24-hour CrCl was then compared with the CG and MDRD-6 as well as the newly described Nix formula. Strength of correlation between methods was then determined by the Pearson R method, with good strength of correlation set at 0.75.

RESULTS: A total of 120 patients had evaluable data points with a mean age of 53 years; 59.2% were men, and 13% were African American. Overall, the CG correlation was very similar to the Nix formula ($r=0.680$ vs. $r=0.683$) with respect to overall correlation. For patients with model of end-stage liver disease (MELD) scores greater than 15, the Nix formula appeared to better correlate CrCl compared with the other two methods ($r=0.841$ vs. 0.772 and 0.625). Based on type of liver disease, the MDRD-6 value had the highest correlation for immune-mediated diseases with Pearson $r=0.962$. For patients with CrCl less than 60 mL/minute who were at risk of renal accumulation of drugs, correlation was similar between all three methods, with r values of only 0.551, 0.512, and 0.525.

CONCLUSIONS: Good strength of correlation was seen in patients with MELD scores greater than 15 with the newly described Nix formula. Because of lower than expected Pearson r values in patients with renal insufficiency, additional studies should be undertaken to estimate clearance in this group of patients.

210E. AcMPAG Levels and UGT Genetic Variations Are Associated with Occurrence of Side Effects in Thoracic Transplant Recipients Treated with Mycophenolate Mofetil. *Lillian S.L. Ting, B.Sc., M.Sc.(Pharm.), Ph.D. Student,*[1] Marie-Odile Benoit-Biancamano, DMV, M.Sc., Ph.D. Candidate,[2] Olivier Bernard, B.Sc.(Pharm.), M.Sc.,[2] K. Wayne Riggs, B.Sc. (Pharm.), Ph.D.,[3] Chantal Guillemette, Ph.D.,[2] Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAH[4]; (1) University of British Columbia, Vancouver, BC; Canada (2) CHUL Research Centre, Laval University, Quebec City, QC, Canada; (3) University of British Columbia, Vancouver, BC, Canada; (4) University of British Columbia, BC Women's Hospital and Health Centre, Vancouver, BC, Canada

PURPOSE: Mycophenolate mofetil (MMF), a prodrug of mycophenolic acid (MPA), is a commonly used immunosuppressive

drug in solid organ transplantation. MPA is metabolized by UDP-glucuronosyltransferases (UGTs) to the major phenolic glucuronide (MPAG, 95%) and the minor acyl glucuronide (about 5%, AcMPAG), which is pharmacologically active and potentially toxic. We studied whether polymorphisms in the *UGT* genes and MPA and AcMPAG levels were associated with the occurrence of side effects related to MMF, namely rejection, infections, anemia, leucopenia, thrombocytopenia, and diarrhea.
METHODS: Twenty-five heart and 27 lung transplant recipients in British Columbia, Canada, were recruited, and blood samples were obtained at 0, 0.3, 0.6, 1, 1.5, 2, 4, 6, 8, 10, and 12 hours after MMF administration. Concentrations of MPA, MPAG, and AcMPAG were determined by a validated high-performance liquid chromatography method with ultraviolet detection. More than 40 genetic polymorphisms in the *UGT1A8, UGT1A9*, *UGT2B7*, and *ABCC2* genes were assessed by direct sequencing of polymerase chain reactions. Heterozygous and homozygous polymorphisms were pooled as one group. Association of side effects with variables (e.g., MPA and AcMPAG levels, polymorphisms, gender, comedication) was performed by Fisher's exact test.
RESULTS: Women had a higher occurrence of infections. AcMPAG levels greater than 50 µg·hour/mL and use of cyclosporine (vs. tacrolimus or sirolimus) as comedication were significantly associated with increased risk of rejection ($p<0.05$). *UGT2B7* -79G>A polymorphism correlated with an increased risk of occurrence of anemia ($n=4$, $p<0.05$). In addition, there was a trend for patients with infections to have increased AcMPAG levels, and anemic patients tended to have a higher MPA-free fraction (greater than 4%).
CONCLUSIONS: Results indicate that AcMPAG levels, gender, comedication, and certain *UGT* polymorphisms are associated with the occurrence of side effects. Findings warrant additional studies with larger sample size.

211. Pharmacokinetics of Mycophenolate and Its Glucuronidated Metabolites in Stable Islet-Cell Transplant Recipients. Mai Al-Khatib, B.Sc. (Pharm.), M.Sc. Student,[1] R. Jean Shapiro, M.D., FRCPC,[2] Nilufar Partovi, B.Sc. (Pharm.), Pharm.D.,[3] *Lillian S.L. Ting, B.Sc., M.Sc. (Pharm.), Ph.D. Student,*[1] Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAH[4]; (1) University of British Columbia, Vancouver, BC, Canada; (2) University of British Columbia, Vancouver General Hospital, Vancouver, Canada; (3) University of British Columbia and Vancouver General Hospital, Vancouver, BC, Canada; (4) University of British Columbia, BC Women's Hospital and Health Centre, Vancouver, BC, Canada
PURPOSE: The purpose of this pilot study was to characterize the pharmacokinetics of mycophenolic acid (MPA) and its glucuronidated metabolites, MPAG (phenolic-glucuronide) and AcMPAG (acylglucuronide), in stable islet-cell transplant recipients.
METHODS: Five subjects were entered in this open-label study after written informed consent. On administration of a steady-state morning mycophenolate mofetil (MMF) dose, blood samples were collected at 0, 0.3, 0.6, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 hours postdose. Total MPA, MPAG, and AcMPAG concentrations were measured by a validated high-performance liquid chromatography method with ultraviolet detection and pharmacokinetic parameters analyzed by noncompartmental modeling using WinNonlin 5.2.
RESULTS: (Data are in mean ± SD.) Subjects included four women and one man who had received 3.0 ± 0.7 islet transplants by the date of the study. Days after the last transplant ranged from 48 to 345. Age was 49.6 ± 8.0 years, and weight was 61.4 ± 7.23 kg. Serum albumin concentration was 4.1 ± 3.0 g/dL, and serum creatinine was 1.0 ± 0.4 mg%. All patients were also on tacrolimus but not steroids. MMF dosage was either 1.5 or 1.75 g/day (25.5 ± 3.0 mg/kg/day). Pharmacokinetic parameters for MPA were area under the curve (AUC) (0–12 hours) 75.44 ± 31.82 µg·hour/mL; dose-normalized AUC (0–12 hours) 74.09 ± 33.42 µg·hour/mL; maximal concentration (C_{max}) 21.00 ± 5.73 µg/mL; dose-normalized C_{max} 19.91 ± 6.02 µg/mL; time to C_{max} 3.20 ± 3.82 hours; minimum concentration (C_{min}) 1.83 ± 1.30 µg/mL; and dose-normalized C_{min} 1.77 ± 1.30 µg/mL. AUC ratios of MPAG:MPA and AcMPAG:MPA were 10.80 ± 4.29 and 0.14 ± 0.07, respectively.
CONCLUSIONS: To our knowledge, this is the first study to determine the pharmacokinetics of MPA and two of its glucuronidated metabolites in the islet transplant population. These preliminary data show wide interpatient pharmacokinetic variability and warrant further study in a larger group of patients. Further studies should also focus on determining if genetic variation in UDP-glucuronosyltransferase isoenzymes can explain the observed wide interpatient variability.

212. Disparate Effects of Immunosuppression on Influenza Vaccine Responses by Lung Transplant Patients. *Mary S. Hayney, Pharm.D., M.P.H.,*[1] Holly Thomas, B.A., MSSW,[2] Mary L. Francois, R.N., MSN,[2] Kelly L. Radford, R.N.,[2] John J.M. Moran, B.S.,[1] Keith C. Meyer, M.D.[3]; (1) University of Wisconsin School of Pharmacy, Madison, WI; (2) University of Wisconsin Hospital and Clinics, Madison, WI; (3) University of Wisconsin School of Medicine and Public Health, Madison, WI
PURPOSE: Lung transplant patients are at high risk of morbidity and mortality from influenza infection. Annual influenza immunization is recommended. The ability to mount an antibody response is limited by immunosuppressive medications and may vary with type of immunosuppressive medications used. We hypothesized that mycophenolic acid and cyclosporine would be associated with lower influenza vaccine response rates than azathioprine and tacrolimus.
METHODS: Inactivated influenza vaccine was administered to lung transplant patients in three seasons. Each individual had blood drawn before and 2–4 weeks after receiving the inactivated trivalent influenza vaccine. Influenza antibody concentrations were measured by hemagglutination inhibition assay. Cyclosporine versus tacrolimus and mycophenolic acid versus azathioprine vaccine response rates (at least 4-fold increase in antibody concentration to at least one vaccine virus) were compared by chi-square or Fisher's exact tests.
RESULTS: One hundred sixty-four influenza vaccine responses in 90 lung transplant patients (time posttransplant median 54 months; range 2–180 months) were measured during the 2004–2005, 2005–2006, and 2006–2007 influenza seasons. No difference in vaccine response rate was detected when the calcineurin inhibitors tacrolimus (56 [55%] of 102) and cyclosporine (27 [45%] of 60) were compared ($p=0.4$). Mycophenolic acid (55 [44%] of 126) was associated with lower influenza vaccine antibody response rates compared with azathioprine (16 [89%] of 18) ($p<0.001$).
CONCLUSIONS: The choice of calcineurin inhibitor may not affect protection conferred by influenza immunization. Influenza vaccine antibody response is influenced by administration of mycophenolic acid, possibly because of its profound effect on B-cell proliferation. Future studies should measure protection from influenza infection conferred by immunization and investigate alternative vaccination strategies for lung transplant patients.

213. Pediatric Renal Transplant Recipients' Characteristics Associated with IST Adherence. *Marie A. Chisholm-Burns, Pharm.D., MPH,*[1] Christina Spivey, Ph.D.,[1] Mona Zawaideh, M.D.,[2] Rick Rehfeld, B.A.[1]; (1) The University of Arizona College of Pharmacy, Tucson, AZ; (2) The University of Arizona Department of Pediatrics, Tucson, AZ
PURPOSE: To determine a profile of pediatric renal transplant recipients (RTRs) who are at high risk of immunosuppressant therapy (IST) non-adherence.
METHODS: Retrospective analyses were performed on follow-up data routinely reported by transplant centers to the United Network for Organ Sharing database in the U.S. Renal Data System (USRDS). The USRDS also consists of Medicare Part A and B claims. All RTRs (18 years or younger) who received their primary and only renal transplantation between January 1995 and December 2000, who had at least 36 months of data in the USRDS (or had data until date of graft failure or death, if occurring before the end of the 36-month period), and who were prescribed a calcineurin inhibitor (cyclosporine or tacrolimus) were included in the analyses. The primary dependent variable was IST adherence as measured by the medication possession ratio (MPR). Stepwise multiple regression

analysis was used to assess the relationship between MPR and the following independent variables: age at transplantation, race, ethnicity, gender, calcineurin inhibitor type, donor type, and time posttransplantation. Odds ratios were calculated.
RESULTS: A total of 978 individuals met the inclusion criteria. Mean age at time of transplantation was 12 years (SD = 5.4); 58% were male, 73% were white, 55% had living donors, and 65% used cyclosporine. The mean MPR was 0.50 (SD = 0.35). The stepwise regression model ($p<0.05$) indicated that the following factors contributed to higher MPRs: increased age at transplantation, decreased time posttransplantation, "other" race identification (e.g., Asian/Pacific Islander, American Indian), and no tacrolimus use. RTRs who were younger than 10 years or who used tacrolimus were more likely to have lower MPRs (OR = 2.47 and 1.88, respectively); "others" were less likely to have lower MPRs (OR = 0.41).
CONCLUSIONS: Adherence interventions should target younger RTRs, RTRs with non-other race identification, those on tacrolimus, and those with longer time posttransplantation.

214. Seroconversion Rates with an Accelerated Hepatitis A and/or B Vaccine Schedule in Heart Transplant Candidates. *Sharon Sam, Pharm.D.,*[1] Jodie M. Fink, Pharm.D., BCPS[2]; (1) Cleveland Clinic, River Forest, IL; (2) Cleveland Clinic, Cleveland, OH
PURPOSE: The monovalent hepatitis B and combination hepatitis A and B vaccines are conventionally administered at 0, 1, and 6 months. An accelerated schedule was U.S. Food and Drug Administration approved for both hepatitis vaccines at 0, 1, and 3 weeks and was implemented at Cleveland Clinic in patients awaiting heart transplantation. However, the success of this accelerated vaccine schedule in achieving sufficient hepatitis antibody titers in heart transplant candidates has yet to be established.
METHODS: The primary objective of this retrospective medical record review was to assess the rates of seroconversion at the time of transplantation with the accelerated hepatitis vaccine schedule in heart transplant candidates. Secondary objectives were to evaluate the number of administered vaccine doses on antibody response and length of time between the last vaccine dose and transplant date. Heart transplant candidates receiving the accelerated protocol between January 2005 and December 2007 were included. Patients were excluded if they were previously immunized to hepatitis A or B, required only the hepatitis A vaccine, received the standard vaccine protocol, or received less than two doses of the vaccination series.
RESULTS: Forty-four patients were enrolled. Seroconversion rates for hepatitis B and A were 16% (7 of 44) and 33% (11 of 33), respectively. Of the patients receiving three or more doses, the seroconversion rates were 21% (5 of 24) for hepatitis B and 53% (10 of 19) for hepatitis A. Average length of time between the last vaccine dose and transplant date increased with the number of doses (9, 14, and 78 days for two, three, and four doses, respectively). No differences in comorbidities were identified between the positive and negative seroconversion groups.
CONCLUSIONS: Seroconversion rates with the accelerated vaccination schedule in heart transplant candidates were low. With limited data, the results provide insight on the use of this accelerated schedule in the heart transplant population.

215E. A Survey of Immunosuppressive Strategies in Liver Transplant Patients with Hepatitis C Virus. *Timothy M. Clifford, Pharm.D., BCPS,*[1] Hoonbae Jeon, M.D.,[2] Thomas D. Johnston, M.D.,[2] Dinesh Ranjan, M.D.,[2] Roberto Gedaly, M.D.[2]; (1) University of Kentucky Healthcare, Lexington, KY; (2) University of Kentucky Department of Surgery, Section of Transplantation, Lexington, KY
PURPOSE: To determine current immunosuppression regimens and different strategies for the treatment of acute cellular rejection in patients with hepatitis C virus (HCV) after liver transplantation.
METHODS: A 14-question survey was sent to 264 liver transplant programs worldwide. An Access database was created, and results were analyzed by Stata v. 9.0 for Windows.
RESULTS: Responses were received from 81 programs. In 27 centers (33.8%), the immunosuppression protocol used in patients with HCV after transplantation was different compared with non-HCV patients. Tacrolimus-based immunosuppression was used in 70 centers (86.42%). Triple therapy using tacrolimus, mycophenolate mofetil, and steroids was the most common regimen (41%). Steroid-free protocols were used in six programs (7.4%). In nine other centers (11%), steroids were discontinued within 1 week. In 56% of centers, steroids were withdrawn within 3 months, and in 98%, steroids were discontinued by 1 year. Mild rejection was treated by increasing baseline immunosuppression in 75% of the centers. Moderate rejection was treated by increasing baseline immunosuppression in 38%, steroid bolus 44%, and either one in 16% of the centers. Severe rejection was treated with steroid bolus in 46% and antibodies in 16%. In 24% of the centers, the most common treatment for severe rejection was either increasing baseline immunosuppression or using steroid bolus. Thirty-six U.S. programs and 45 non-U.S. programs were scrutinized. Non-U.S. programs used more cyclosporine than U.S. programs in patients with HCV (35.6% vs. 2.8%; $p<0.001$). Duration of steroid therapy was shorter in U.S. programs versus non-U.S. programs (10.8 vs. 29.4 weeks; $p<0.001$).
CONCLUSIONS: Currently, there is a lack of consensus regarding the most appropriate immunosuppressive regimen and the best way to treat rejection in patients with HCV posttransplantation. This survey will allow transplant teams to know the most common practices in the management of this group of patients.
Presented at the American Transplant Congress, Toronto, ON, Canada, June 1–4, 2008.

216E. Statin Therapy and Corticosteroid Therapy in Kidney Transplantation: Effects on Cardiovascular Event and Death Rates. *Ruth-Ann M. Lee, Pharm.D.*, Adele H. Rike, Pharm.D., Rita R. Alloway, Pharm.D., Jason J. Everly, Pharm.D., Amit Govil, M.D., Janet Durbin, R.N., E. Steve Woodle, M.D.; University of Cincinnati, Cincinnati, OH
PURPOSE: Statin therapy has been shown to reduce acute rejection (AR) risk in cardiac transplantation (txp). Moreover, statin therapy reduces risk of cardiovascular events (CVEs) in the general population. The purpose of this study was to evaluate statin therapy on AR, CVEs, and patient (pt) survival in kidney txp recipients.
METHODS: Pts were categorized by the presence or absence of statin therapy post-txp. Univariate analysis (UVA) and multivariate analysis (MVA) were conducted by stepwise logistic regression (STATA v. 9.2) to determine significant risk factors for AR, CVEs, and pt survival. Kaplan-Meier analysis was conducted for pt survival and CVE rates.
RESULTS: A total of 638 renal txp pts were analyzed from 1997 to 2007 (46% statin vs. 54% no statin). Baseline characteristics and AR rates were similar between groups. Statin therapy post-txp was associated with increased pt survival (95% vs. 90%, $p<0.02$) and decreased incidence of CVE (15% vs. 21%, $p<0.05$). Individual factors for CVE evaluated by UVA and found to be insignificant included current percent reactive antibody more than 25%, high-density lipoprotein less than 40 mg/dL, African American recipient race, age, and gender. Significant factors for CVE on UVA included pre-txp diabetes (DM), statin therapy, repeat txp, deceased donor (DD), corticosteroid therapy (CS), and DR mismatch of more than zero. Significant factors on final MVA included DM (OR = 3.2, CI: 2.0–4.9) and CS (OR = 3.2, CI: 2.0–4.9). Significant factors for pt survival on UVA included pre-txp DM, statin therapy, DD, CS, delayed graft function, and DR mismatch more than zero. Significant factors on final MVA included DM, male gender, and CS. Statin therapy approaches significance in the MVA for decreasing risk of CVE ($p=0.07$) and death rates ($p=0.08$).
CONCLUSIONS: This analysis indicates that CS increases CVE and death rates. Statin therapy offers a means for reducing cardiovascular risk in pts receiving CS.
Presented at the American Transplant Congress, Toronto, ON, Canada, June 1–4, 2008.

Urology

217. Effects of Silodosin, a Uroselective α-Blocker, in Men with

Symptoms of Benign Prostatic Hyperplasia: Pooled Results of 2 Phase 3 Studies. Marc Gittelman, M.D.,[1] *Lawrence Hill, R.Ph., Pharm.D.,*[2] Weining Volinn, M.S.,[2] Gary Hoel, R.Ph., Ph.D.[2]; (1) South Florida Medical Research, Aventura, FL; (2) Watson Laboratories, Inc., Salt Lake City, UT

PURPOSE: The efficacy and safety of silodosin, an α-blocker with high a-1A– to a-1B–receptor selectivity, were evaluated in two phase 3 studies in men with symptoms of benign prostatic hyperplasia (BPH).

METHODS: In two identical, randomized, double-blind, parallel-group studies, men 50 years and older with International Prostate Symptom Scores (IPSS) of 13 or more and peak urinary flow rates (Q_{max}) of 4–15 mL/second received 8 mg of silodosin or placebo once daily for 12 weeks. The primary end point was change in IPSS from baseline to last observation carried forward (LOCF). Between-group statistical comparisons were based on least-squares mean difference (LSM) changes from baseline to LOCF using analysis of covariance.

RESULTS: Nine hundred twenty-three patients had one or more primary efficacy evaluations (silodosin, n=466; placebo, n=457). Almost half (45%) were 65 years or older. At LOCF, total IPSS (LSM difference between silodosin and placebo, -2.8) and irritative (LSM difference, -1.0) and obstructive (LSM difference, -1.9) IPSS subscores were significantly reduced in patients receiving silodosin versus placebo ($p<0.0001$). Total IPSS LSM difference changes from baseline between treatment groups were similar in each age group: younger than 65 years (-2.9), 65 years and older (-2.7), and 75 years and older (-2.9). Improvements in Q_{max} were significantly greater with silodosin than placebo (LSM difference, 1.0; $p=0.0007$). The only treatment-related serious adverse event was suspected syncope in a patient who had taken concomitant prazosin, an excluded medication. The most common treatment-related adverse events were (generally mild) retrograde ejaculation (28.1% vs. placebo, 0.9%), dizziness (2.4% vs. 0.7%), headache (1.3% vs. 0.2%), and diarrhea (1.1% vs. 0.2%). The number of patients with treatment-related orthostatic hypertension was similar for silodosin (9 [1.9%]) and placebo (7 [1.5%]).

CONCLUSIONS: Silodosin provided significant relief of BPH symptoms in older men. Silodosin was generally well tolerated and had a placebo-like cardiovascular safety profile. Selectivity of α-blockade for a-1A receptors may minimize cardiovascular effects.

218. Long-Term Effects of Silodosin, a Uroselective α-Blocker, in Men with Symptoms of Benign Prostatic Hyperplasia. Marc Gittelman, M.D.,[1] *Lawrence Hill, R.Ph., Pharm.D.,*[2] Weining Volinn, M.S.,[2] Gary Hoel, R.Ph., Ph.D.[2]; (1) South Florida Medical Research, Aventura, FL; (2) Watson Laboratories, Inc., Salt Lake City, UT

PURPOSE: In two identical double-blind, placebo-controlled, phase 3 studies (n=923), 12-week therapy with silodosin, a uroselective α-blocker, attenuated urinary symptoms associated with benign prostatic hyperplasia (BPH). This 40-week, open-label extension study was designed to determine the long-term efficacy and safety of silodosin in this patient population.

METHODS: Men 50 years and older with International Prostate Symptom Scores (IPSS) of 13 or higher and peak urinary flow rates of 4–15 mL/second were enrolled in the initial phase 3 studies. Those who completed either study were eligible to enroll in the open-label extension; all participants received 8 mg of silodosin once daily for 40 weeks. Data related to adverse events and changes in IPSS from baseline to last observation carried forward (LOCF) were summarized descriptively.

RESULTS: A total of 661 patients received one or more doses of open-label study medication. Many (46%) were 65 years and older. Slightly more had received placebo (n=347) versus silodosin (n=314) as double-blind treatment. Among patients who finished the study without a major protocol violation (n=429), reductions in IPSS total (mean ± SD) at LOCF were -4.5 ± 6.7 and -1.6 ± 6.0 for those previously receiving placebo and silodosin, respectively. Reductions in IPSS subscales were observed not only in the previous placebo (irritative, -1.7 ± 3.2; obstructive, -2.7 ± 4.2) but also in the previous silodosin group (irritative, -0.6 ± 2.7; obstructive, -1.0 ± 3.9). In the previous placebo group, IPSS total reductions were similar for patients younger than 65 (-4.3 ± 7.0) and 65 years and older (-4.6 ± 6.5). The most common treatment-related adverse events were retrograde ejaculation (20.3%), dizziness (1.8%), diarrhea (1.5%), orthostatic hypotension (1.4%), nasal congestion (1.4%), decreased libido (1.4%), and headache (1.1%). No treatment-related cardiac disorders occurred, and no patient experienced a treatment-related serious adverse event.

CONCLUSIONS: Nine-month treatment with silodosin resulted in maintained safety and enhanced efficacy compared with 12-week treatment in men with signs and symptoms of BPH.

219. Pharmacokinetics of Oxybutynin Topical Gel: Effects of Showering, Sunscreen Application, and Person-to-Person Transference. *Kim E. Caramelli, M.S.*, Stephanie Stanworth, M.S., Weining Volinn, M.S., Gary Hoel, R.Ph., Ph.D.; Watson Laboratories, Inc., Salt Lake City, UT

PURPOSE: We examined the pharmacokinetics of oxybutynin chloride topical gel (OTG; 10% w/w; 1 g/day delivers about 4 mg/day of oxybutynin), an investigational treatment for overactive bladder, under conditions simulating actual use.

METHODS: Healthy volunteers aged 18–45 years were enrolled in three randomized, open-label studies. In a showering study, subjects (n=15) received OTG daily for 35 days. After dosing on days 14, 21, 28, and 35, subjects did not shower, or else they showered 1, 2, or 6 hours later; serial blood samples were obtained for 24 hours after dosing. In a single-dose sunscreen study, subjects (n=14) applied OTG alone, 30 minutes after sunscreen or 30 minutes before sunscreen; blood was collected for 72 hours after dosing. In a single-dose transference study (n=52), one partner in each of 26 couples applied OTG to the abdomen. One hour after dosing, partners rubbed abdomens for 15 minutes. About half of the treated partners were randomized to wear a T-shirt during contact; other subjects had bare abdomens. Blood was drawn for 48 hours after contact.

RESULTS: Mean AUC_{0-24} of oxybutynin was similar with showering (113.5–147.2 ng·hour/mL) or without (134.4 ng·hour/mL). Median T_{max} was shorter with showering (3.0–6.5 hours) than without (12.0 hours). Mean AUC_{0-72} was 83.6–91.2 ng·hour/mL with sunscreen and 84.5 ng·hour/mL without; median T_{max} was 24.0 hours under all conditions. Transference to untreated partners occurred when treated partners had a bare abdomen, but mean C_{max} (0.94 ng/mL) was less than typically observed with direct treatment (about 4 ng/mL). When treated partners wore clothing during contact, transference was undetectable in most (12 of 14) subjects and negligible (C_{max} of 0.10 ng/mL or less) in the rest.

CONCLUSIONS: Showering and use of sunscreen did not induce clinically meaningful changes in the pharmacokinetics of OTG. Transference occurred but was blocked almost entirely when the treated partner wore a shirt.

220E. Steady-State Pharmacokinetics of an Investigational Oxybutynin Topical Gel in Comparison with Oxybutynin Transdermal System. *Kim E. Caramelli, M.S.,*[1] David R. Staskin, M.D.,[2] Weining Volinn, M.S.[1]; (1) Watson Laboratories, Inc., Salt Lake City, UT; (2) Weill Medical College of Cornell University, New York, NY

PURPOSE: Oxybutynin chloride topical gel (OTG) is a 10% w/w ethanolic gel formulation of oxybutynin hydrochloride that is designed as a once-daily product. OTG is expected to provide the same advantages as the oxybutynin patch (oxybutynin transdermal system [OXY-TDS]) over orally administered treatments for overactive bladder in convenience and anticholinergic adverse effects, with better skin tolerability. The steady-state pharmacokinetics of OTG and of OXY-TDS were compared in healthy adults.

METHODS: Male and female volunteers (n=22; aged 18–44 years) in this randomized, open-label, two-way crossover study received 18 days of OTG 1 g daily (about 4 mg/day of oxybutynin) or OXY-TDS (1 patch every 3.5 days for 2 weeks, followed by a 4-day application; 3.9 mg/day). Participants received the crossover formulation after a 14-day washout. Multiple blood samples were

taken during the final 4 days of dosing (last four daily applications of OTG or last application of OXY-TDS) for measurement of plasma concentrations of oxybutynin.
RESULTS: Steady-state treatment with OTG and OXY-TDS produced similar oxybutynin plasma concentrations throughout the 4-day dosing interval. Mean oxybutynin $AUC_{0–96}$ for OTG (321.7 ng·hour/mL) was 2.9% higher than that for OXY-TDS (312.5 ng·hour/mL). The mean paired difference in steady-state C_{avg} (mean ± SD) was not significant (0.10 ± 1.13; p=0.7098). No erythema was observed at any gel application site. No severe or serious adverse events occurred; no participant discontinued because of an adverse event.
CONCLUSIONS: OTG and OXY-TDS exhibited similar steady-state pharmacokinetics and are expected to produce comparable efficacy. The excellent skin tolerability of OTG may contribute to improved patient acceptability and use.
Presented at the American Urological Association Annual Meeting, Orlando, FL, Tuesday, May 20, 2008.

Women's Health

221. Kansas Pharmacists' Knowledge, Attitudes, and Beliefs Regarding Over-the-Counter Emergency Contraception. *LaDonna S. Hale, Pharm.D.,*[1] Julie S. Shrack, PA-S,[1] Erin K. Stump, PA-S,[1] Gina M. Berg-Copas, Ph.D.(C)[2]; (1) Wichita State University, Wichita, KS; (2) Kansas University School of Medicine, Wichita, KS
INTRODUCTION: In August 2006, the U.S. Food and Drug Administration approved the sale of emergency contraception (EC) without a prescription as levonorgestrel (Plan B®). EC efficacy is highest when used as soon as possible postcoitus; thus, over-the-counter sale is assumed to improve timely acquisition. Pharmacists' knowledge, attitudes, and beliefs regarding EC are important to evaluate because they may affect patient counseling and access and be a source of professional ethical stress.
PURPOSE: Measure knowledge, attitudes, and beliefs of Kansas pharmacists regarding EC.
METHODS: A survey with 46 items assessing respondent characteristics, knowledge, and attitudes/beliefs was mailed to all 2601 registered Kansas pharmacists. Knowledge question answer options were "true," "false," and "I don't know." Attitudes/beliefs were measured using a 5-point Likert scale. Data were analyzed using the Student's *t*-test, the χ^2 test, and an analysis of variance as appropriate. Statistical significance was set at $p \leq 0.05$.
RESULTS: Twenty-two percent of pharmacists responded (n=583). The overall mean knowledge score was 57% ± 20%; however, scores were higher in pharmacists working where EC was sold (46% ± 21% vs. 61% ± 18%; p<0.001). A majority of pharmacists surveyed stated they would dispense EC in cases of rape (80%), incest (79%), and regardless of the situation (62%). However, many expressed concerns including selling EC without the patient's medical history (60%), patient's emotional status (60%), EC's use as a regular form of birth control (44%), medical liability (41%), promoting unsafe sex (37%), and legal liability associated with checking age (36%). Differences in willingness to dispense "regardless of the situation" were associated with religious affiliation, political affiliation, and population of primary practice setting.
CONCLUSIONS: In this survey, the knowledge of Kansas pharmacists regarding EC was low. Although most pharmacists surveyed were willing to dispense EC, a significant number expressed concerns, indicating this may be causing some professional ethical stress deserving of further discussion.

222. Knowledge of Emergency Contraception Among Health Professions Students. *Deborah A. Sturpe, Pharm.D.*, Jorie A. Glick, Pharm.D., Francoise Pradel, Ph.D., Puckwipa Suwannaprom, M.A., Stuart T. Haines, Pharm.D.; University of Maryland School of Pharmacy, Baltimore, MD
PURPOSE: Emergency contraception (EC) may prevent unwanted pregnancies and abortions if used appropriately. Lack of knowledge about EC among health care practitioners may limit appropriate recommendation, prescribing, dispensing, or administration of EC. The purpose of this study was to identify factors associated with EC knowledge among health professions students.
METHODS: A cross-sectional Web-based survey of students enrolled in the BSN, DDS, DPT, M.D., MSW, and Pharm.D. programs at the University of Maryland–Baltimore inquired about knowledge, attitudes, and behaviors related to EC. Knowledge items assessed mechanism of action (MOA), efficacy, safety, timing of use, and pregnancy testing. Bivariate analyses compared students' characteristics across programs, and a multivariate logistic regression assessed the impact of various factors on knowledge.
RESULTS: Of 3313 students contacted, 514 (15.5%) responded. Sixty-eight percent of respondents possessed poor knowledge (0–2 correct answers/5 items), and 32% possessed fair to good knowledge (3–5 correct). A minority of students were knowledgeable about MOA (6%), contraindications (19%), and comparative safety between EC and routine hormonal contraception (5%). Students who answered questions about MOA incorrectly were significantly more likely to believe that EC causes abortions (p<0.03). Pharm.D. students were more likely to possess fair to good knowledge (48%) compared with students enrolled in other programs (adjusted OR = 3.40; CI: 1.73–6.71). Students reporting formal academic coursework about EC were more likely to possess fair to good knowledge compared with those reporting no formalized education and/or experiences (adjusted OR = 3.03; CI: 1.64–5.60).
CONCLUSIONS: Few health professions students are knowledgeable about EC, and misinformation is common. Lack of knowledge may result in less than optimal care of patients. Academic coursework, but not experiential rotations, is associated with significant improvements in knowledge. To optimize knowledge among health professions students, EC education should be included in the didactic curriculums of health professions programs.

223. Comparison of Exogenous Intravenous Immunoglobulin (IVIG) Exposure and Endogenous IgG in Pregnancy. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAH,*[1] Mai Al-Khatib, B.Sc. (Pharm.), M.Sc. Student,[2] Lillian S.L. Ting, B.Sc., M.Sc. (Pharm.), Ph.D. Student,[2] Patricia A. Schultz, R.N., MHA,[3] Edwina Houlihan, R.N.,[4] Mary D. Stephenson, M.D., M.Sc.[5]; (1) University of British Columbia, BC, Canada, Women's Hospital and Health Centre, Vancouver, BC, Canada; (2) University of British Columbia, Vancouver, BC, Canada; (3) University of Chicago, Chicago, IL; (4) Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada; (5) University of Chicago, University of British Columbia, and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada
PURPOSE: To characterize intravenous immunoglobulin (IVIG) pharmacokinetics in women with recurrent miscarriages and compare IVIG exposure to endogenous immunoglobulin G (IgG) concentrations before and during pregnancy.
METHODS: Thirty-four women participated at two centers (randomized placebo-controlled trial for idiopathic secondary recurrent miscarriage, n=24; open-label pharmacokinetic study for treatment of antiphospholipid syndrome, n=10); 22 received IVIG (Gamimune N 5%) 500–1000 mg/kg and 12 received placebo during a 2- to 10-hour period every 4 weeks, from prepregnancy until 18–20 weeks of gestation. Serum IgG concentrations were measured by rate nephelometry before and 0.5 hour and 1, 2, 3 and 4 weeks after each dose (prepregnancy and first and second trimesters).
RESULTS: Mean (±SD) age was 34.4 ± 4.3 years and 36.0 ± 5.6 years; number of prior miscarriages was 4.8 ± 1.6 and 3.8 ± 1.2 for IVIG and placebo groups, respectively. Pharmacokinetic parameters (mean ± SD) for IVIG versus placebo were as follows:

1. Prepregnancy (n=20, IVIG; n=12, placebo)
   Maximum concentration (C_{max}, g/L) 24.8 ± 4.5, 10.8 ± 2.5
   Minimum concentration (C_{min}, g/L) 11.8 ± 2.1, 9.2 ± 2.3
   Area under the curve ($AUC_{0–\tau}$, g·hour/L) 10,701.9 ± 2051.7, 5762.5 ± 1493.7
2. First trimester (n=12, IVIG; n=7, placebo)
   C_{max} (g/L) 28.8 ± 7.4, 10.5 ± 2.8
   C_{min} (g/L) 12.6 ± 2.3, 8.9 ± 2.2
   $AUC_{0–\tau}$ (g·hour/L) 11,589.7 ± 2265.1, 5643.9 ± 1981.2
3. Second trimester (n=10, IVIG; n=6, placebo)

C_{max} (g/L) 25.5 ± 4.3, 9.2 ± 2.1
C_{min} (g/L) 11.8 ± 2.4, 7.7 ± 2.3
$AUC_{0-\tau}$ (g·hour/L) 10287.3 ± 2945.6, 5617.4 ± 1628.6
(All parameters p>0.05; repeated-measures analysis of variance with Student-Newman-Keuls test)

Dosages (mg/kg) and AUCs did not differ significantly within the IVIG group between the three sampling periods. Roughly estimated contributions of exogenously administered IVIG to total $AUC_{0-\tau}$ [$AUC_{0-\tau}$(IVIG) minus $AUC_{0-\tau}$(placebo)] were 4939.4 g·hour/L (prepregnancy), 5945.8 g·hour/L (first trimester), and 4669.9 g·hour/L (second trimester).

CONCLUSIONS: Interpatient variability in IVIG pharmacokinetics was observed. Pregnancy did not have a significant effect on exposure to the same dosage of exogenously administered IVIG. The estimated contribution of exogenous IVIG (i.e., 5200 g·hour/L) to total $AUC_{0-\tau}$ was similar to endogenous IgG (i.e., about 5700 g·hour/L). These preliminary data provide the basis for future studies focused on individualized dosing and patient outcomes.

224. Adherence to Osteoporosis Treatment Guidelines in Postmenopausal Women at Two Family Medicine Clinics. *Cary R. Mountjoy, Pharm.D.*, Sarah Shrader, Pharm.D., BCPS, Kelly Ragucci, Pharm.D., FCCP, BCPS, CDE; South Carolina College of Pharmacy – MUSC Campus, Charleston, SC

INTRODUCTION: More than 1.5 million osteoporotic fractures occur annually in the United States, 300,000 of which are hip fractures, which is the most catastrophic osteoporosis outcome; however, it is largely preventable. Guideline adherence in individual practices should be evaluated to implement improvements in the care of patients with this disease state.
PURPOSE: Evaluate adherence to osteoporosis treatment guidelines by physicians and patients at two university-affiliated family medicine clinics.
METHODS: One hundred thirteen postmenopausal women with a diagnosis code for osteoporosis between July 2006 and 2007 were identified through the electronic medical record. Institutional review board approval was obtained. A retrospective chart review (n=113) was conducted, and a voluntary telephone survey (n=50) was administered to determine patient and physician adherence to the 2008 National Osteoporosis Foundation treatment guidelines. Descriptive statistics are provided.
RESULTS: Of the 113 women enrolled in the study, the mean age was 77, and 25% had a previous fracture. Fifty-eight percent of women were prescribed guideline-endorsed pharmacotherapy for osteoporosis. Of those on treatment, 97% were receiving a bisphosphonate. Eighty-three percent had baseline dual-energy x-ray absorptiometry (DEXA) scans, but only 15% had follow-up DEXA scans every 2 years thereafter. Seventy percent of telephone responders reported taking calcium regularly; however, 40% were taking an inappropriate calcium salt. Eighty-two percent recalled receiving non-pharmacological advice, and 26% self-reported fractures postdiagnosis.
CONCLUSIONS: Adherence to osteoporosis treatment guidelines is currently not optimal at these two clinics. Efforts should be made to maximize the number of patients receiving pharmacological treatment and appropriate calcium and vitamin D supplementation and to ensure appropriate DEXA scan follow-up. A pharmacy-based osteoporosis referral service is currently under development to help improve these osteoporosis outcomes.

CLINICAL PHARMACY FORUM

Adult Medicine

225. Implementation of a Prospective Pharmacist Review on a Hospitalist Unit. *Melissa M. Blair, Pharm.D., BCPS, FCCP, CDE*, Jennifer E. Reel, Pharm.D., Mark E. Allen, M.B.A.; New Hanover Regional Medical Center, Wilmington, NC

PURPOSE: To document the effect of a prospective pharmacist review service on a newly formed hospitalist unit in a level II trauma, community teaching hospital.
METHODS: With the implementation of a hospitalist unit during the first quarter of 2008, the decision was made to place a nonorder entry pharmacist on the unit during weekdays. Primary pharmacist responsibilities included a review of patients admitted in the previous 24 hours with a focus on identifying drug-related problems, medication reconciliation, antibiotic streamlining, Centers for Medicare and Medicaid Services indicators, and other common issues. Follow-up of previously identified issues was also stressed. Pharmacists intervened either through direct interaction with other health care professionals or the use of a recommendation sheet left in the patient's chart. Participating pharmacists were also asked to document interventions in CliniDoc, a Web-based documentation system by Gold Standard.
RESULTS: A total of 791 pharmacist interventions were recorded between March 1 and May 31, 2008. Most of these were chart reviews (35%), followed by medication reconciliation (25%). Twenty-two percent of interventions were classified as dosing issues, and 7% dealt with appropriate therapy recommendations. Although many interventions were not associated with dollar amounts in CliniDoc, a minimum of $20,000 was saved. Data were also limited because of reliance on pharmacist documentation in a separate system; therefore, these numbers are thought to underestimate the true impact. In addition, pharmacists cited being pulled away for other duties and a need for standardization of care as limitations.
CONCLUSIONS: Based on interventions recorded, the implementation of a pharmacist prospective review of patients on a hospitalist unit was successful. Challenges exist regarding how to expand the service to other areas of the hospital.

Ambulatory Care

226. Development and Implementation of an Interdisciplinary Mobile Wellness Clinic for a Medically Underserved Population. *Monica L. Skomo, B.S., Pharm.D.*, Holly Lassila, R.Ph., Dr.PH., Hildegarde J. Berdine, B.S., Pharm.D., Christine K. O'Neil, B.S., Pharm.D.; Duquesne University, Pittsburgh, PA

PURPOSE: (1) To describe the development and implementation of an interdisciplinary mobile wellness clinic for the medically underserved and (2) to describe the demographics and screening results of this population.
METHODS: The Spirit of Health Initiative is a unique collaboration between the Duquesne University Mylan School of Pharmacy, the Sisters of St. Francis, and the Mercy Parish Nurse Program. An RV named the *Spirit of Health*, staffed by pharmacist faculty, fellows, pharmacy students, and nurses, travels to food pantries in the Pittsburgh area to provide health promotion and screening services to medically underserved people.
RESULTS: From September 2005 through August 2007, the *Spirit of Health* visited four sites on a monthly basis and had 1087 patient visits; 69% of patients were women. The mean patient age was 67 years. A total of 876 blood pressures, 481 cholesterol screenings, 256 bone density screenings, and 125 body mass indexes and body fat analyses were conducted; 27.9% of patients had a systolic blood pressure of 140 mm Hg or more, and 8.9% had a diastolic blood pressure of 90 mm Hg or more; 24.6% had a T-score of -2.00 or less, and 55.5% had a T-score of -1.00 or less; 63.2% of body mass indexes were 25 or more, with 36% classified as overweight and 27.2% classified as obese; 62.5% of women and 71.4% of men exceeded the healthy body fat range for their age and gender; 44.3% of patients had a total cholesterol value of 200 mg/dL or higher, and 26.9% had an HDL less than 40 mg/dL.
CONCLUSIONS: The Spirit of Health Initiative is a successful interdisciplinary practice model that has brought health promotion and screening services to various medically underserved communities in the Pittsburgh area. According to the screening results, there are tremendous opportunities available for pharmacists, pharmacy students, and other members of the interdisciplinary team to make a positive impact on the overall health and well-being of these patients.

227. Outcomes and Perceptions of a Pharmacist-Managed Smoking Cessation Group Clinic. *Ann M. Philbrick, Pharm.D.,*[1]

Erin N. Newkirk, Pharm.D.,[2] Karen Farris, Ph.D.,[3] Kathleen E. Horner, Pharm.D.,[1] Deanna L. McDanel, Pharm.D.[1]; (1) University of Iowa Hospitals and Clinics, Iowa City, IA; (2) Froedtert & the Medical College of Wisconsin, Milwaukee, WI; (3) University of Iowa, Iowa City, IA

PURPOSE: In February 2007, the University of Iowa Hospitals and Clinics Department of Pharmaceutical Care established a pharmacist-managed Smoking Cessation Group Clinic. The purpose was to quantify quit rates at 3, 6, and 12 months after participation in the clinic and determine patients' perceptions at 3 months.

METHODS: Patients consented to follow-up. Fagerstrom score was determined at clinic enrollment, and other data were collected from patient records. At 3, 6, and 12 months, patients were contacted by telephone and asked about current smoking status. At 3 months, patients were asked to rate on a Likert scale their perceptions of individual aspects of the clinic (1 = least helpful and 5 = most helpful) and how they perceived their cessation aid (1 = least helpful and 10 = most helpful). Data are available for 18, 14, and 7 patients at 3, 6, and 12 months, respectively, and continue to be collected on the 21 consented patients.

RESULTS: At 3 months, 56% (10 of 18) of patients reported being smoke free. Patients with a lower Fagerstrom score were more likely to be successful in their quit attempt (p=0.044). Using nonnicotine prescription cessation aids, having more quit attempts, and setting a quit date were associated with cessation success at 3 months (p<0.1). At 6 and 12 months, 64% (9 of 14) and 57% (4 of 7) of patients, respectively, were smoke free. Patients who quit smoking rated their cessation aid higher than those who did not quit smoking (8.56 ± 0.88 vs. 6.71 ± 2.81, respectively; p=0.14). Aspects of the clinic most helpful were group interaction (4.61 ± 0.7), discussion of quit preparation (4.56 ± 0.78), cessation medications (4.5 ± 0.62), and withdrawal of nicotine (4.39 ± 0.85).

CONCLUSIONS: The pharmacist-managed Smoking Cessation Group Clinic had cessation rates greater than 50% at all data end points. A lower Fagerstrom score was associated with successful cessation. The group-based format of the clinic was perceived as helpful by patients.

228. Antiarrhythmic Medication Monitoring by Clinical Pharmacists in an Outpatient Setting. *Melissa J. Snider, Pharm.D., BCPS*, Steven Kalbfleisch, M.D., Cynthia Carnes, Pharm.D., Ph.D.; Ohio State University Medical Center, Columbus, OH

PURPOSE: To establish a standardized approach to monitoring chronic antiarrhythmic medications by clinical pharmacists in an outpatient setting and review interventions resulting from protocol implementation.

METHODS: A retrospective chart review was performed in outpatients enrolled in an antiarrhythmic medications monitoring clinic. Patients whose visits occurred between July 2007 and April 2008 were included. Compliance with protocols based on established guidelines and manufacturer recommendations was assessed, and the type and frequency of pharmacist interventions were determined.

RESULTS: A total of 132 patients were enrolled, with 33% of patients having at least one follow-up visit. Patients (n) were on amiodarone (58), sotalol (40), dofetilide (28), or propafenone (8). At enrollment, only 44.8% of patients had all recommended laboratory and objective testing. After the initial visit, 98.5% of patients were up-to-date on testing. After follow-up visits, 100% of patients were up-to-date on testing. Of the follow-up visits, 90.3% occurred within 10% of recommended date. Pharmacist interventions occurred during 54.5% of visits, including unrecognized adverse event detection (i.e., pulmonary function decline, QT prolongation, or laboratory abnormality) and significant drug interaction identification. Continuum of care was facilitated by the pharmacist either by coordination of referral to specialty clinics (n=7) (i.e., pacemaker clinic, anticoagulation clinic, or electrophysiology clinic) or pharmacist contact with outside physicians (n=30) (i.e., PCP, EP physicians, and other cardiologists). Amiodarone was associated with the highest rate of adverse reactions (23.0% of visits). For six patients, a change in antiarrhythmic medication was recommended, 50% of which resulted in discontinuation of therapy.

CONCLUSIONS: Pharmacist monitoring of outpatient antiarrhythmic medication therapy improved compliance with completion of recommended testing protocols and resulted in identification of adverse events and significant clinical interventions.

229. Patient Health Outcomes of a Pharmacist Medication and Disease Management Service in an Urban Physician Office Practice Using MTM Software. *Hildegarde J. Berdine, Pharm.D., BCPS*; Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA

PURPOSE: (1) Evaluate the impact of a pharmacist consultative service on clinical health outcomes in a referred patient population of an urban family practice and (2) standardize the collection of data and patient outcomes using clinical support pharmacist-specific software.

METHODS: Patients were referred to the pharmacist practice by two family practice physicians. Patients with diabetes who met with the pharmacist for a minimum of 6 months were included in the analysis. Fourth-year pharmacy students collected patient data, developed a pharmaceutical care plan, and documented all clinical data in the clinical support software, Medication Pathfinder. The delivery of care incorporated the core elements of medication therapy management (MTM). Outcomes measured included change in clinical data from baseline to most recent visit. Parameters measured included number of patient visits, number of drug therapy or disease management interventions, and number of core elements of MTM provided.

RESULTS: Twenty-seven patients with diabetes were seen by the pharmacist for a mean number of 4.5 visits from May 2007 through May 2008. Average age of the cohort was 56 ± 13.8 years, with 48% of the population women and 52% men. Changes in clinical data included (mean ± SD at baseline, follow-up) hemoglobin A1c 8.3 ± 1.9, 7.8 ± 1.5; systolic blood pressure 128.7 ± 14.4, 123.6 ± 11.8; and total cholesterol 197.4 ± 67.9, 176.2 ± 43.9 (NS paired t-test). More than 300 interventions and core elements of MTM were documented, and the three most commonly reported were patient consultation and education, patient care recommendations, and suboptimal drug regimen.

CONCLUSIONS: The pharmacist consultative services demonstrated a positive trend in managing risk factors for cardiovascular disease in a diabetes cohort. The clinical support software facilitated the collection of patient data, provided the pharmacist with an electronic patient chart, and enabled data extraction to support scholarly efforts and document outcomes.

230. Preliminary Assessment of Asthma Quality of Care Indicators at a Multi-disciplinary, Primary Care Clinic for Uninsured Patients. *Claresta L. Mohrman, Pharm.D.*, Theresa R. Prosser, Pharm.D.; St. Louis College of Pharmacy, St. Louis, MO

BACKGROUND: Asthma does not receive as much attention as other chronic diseases such as diabetes. The estimated annual 4000 deaths, 5000 hospitalizations, and 18,000 emergency department visits are largely preventable with proper treatment. Healthy People 2010 asthma goals include decreasing deaths and urgent care use, improving medication use, and increasing patient education.

PURPOSE: Compare current care to quality indicators based on the National Asthma Education and Prevention Program (NAEPP 2007) to identify methods for improvement.

METHODS: Charts were identified by pharmacy profiles (albuterol use), manual chart search, or ICD-9 codes and confirmed by chart documentation of diagnosis. Data were retrospectively collected on 11 quality indicators.

RESULTS: Of the 81 charts, 11% had spirometry within 2 years (NAEPP goal: 100% in 1–2 years), 30% had asthma assessed with subjective/objective data within 6 months (100% every 6 months), 22% had asthma education within 2 years (100% every visit), 100% had tobacco counseling at last visit (100% every visit), 72% had prescription for quick-relief inhaler (100%), and 16% overused (more than one canister/month) quick-relief inhalers. In the past year, 56% were prescribed an inhaled corticosteroid (of these, 10% were at least 70% adherent), and 28% of patients had an exacerbation.

CONCLUSIONS: Asthma control is not adequately assessed (clinically or by spirometry). A significant subset of patients has exacerbations requiring treatment. Overuse of quick-relief inhalers indicates risk of morbidity. Corticosteroids may be underprescribed and have poor patient adherence. Proposed changes include (1) providing office spirometry, (2) creating systematic methods to collect data at each visit to promote asthma assessment, (3) increasing frequency of asthma education, and (4) facilitating pharmacist-physician interoffice communication regarding non-adherence to corticosteroids and overuse/lack of quick-relief inhalers. Data on all indicators will be presented. Specific methods regarding changes 2 and 4 above will be shared that are likely applicable to other sites.

231. Effectiveness of a Collaborative Lipid Clinic Developed in an Academic Heart Hospital Ambulatory Care Clinic. *Margueritte Hevezi, Pharm.D.*, Melissa Snider, Pharm.D., Scott Merryman, M.D., Vasudevan Raghavan, M.D., MBBS, Trisha Jordan, Pharm.D., M.S., Noelle E. Daugherty, Pharm.D.; The Ohio State University Ross Heart Hospital, Columbus, OH

PURPOSE: To establish the effectiveness of a collaborative lipid clinic partnering clinical pharmacists with physicians in an outpatient setting by evaluating lipid panel changes and achievement of targeted goals.

METHODS: Electronic medical records of patients seen between March 2006 and May 2008, having 3 or more visits, and have been seen for a period of at least 3 months in The OSU Comprehensive Lipid Management Clinic were reviewed. Descriptive statistics were used to compare baseline and most recent lipid panels to each other and to targeted lipid goals.

RESULTS: A total of 168 patients were included. The proportion of patients at targeted ATP III lipid goals increased from 32% at baseline to 71% for LDL-c, and from 42% at baseline to 74% for total cholesterol (TC). The mean baseline LDL-c was 141 mg/dL compared with the most recent mean LDL-c of 100 mg/dL, an absolute reduction of 41 mg/dL. Mean baseline TC was 226 mg/dL compared with the most recent mean TC of 173 mg/dL, an absolute reduction of 53 mg/dL. Mean HDL-c increased by 5% from baseline. Targeted LDL-c goal was decreased for 71 patients (42%) because of physician assessment, 23 (32%) of these patients met their decreased LDL-c goal.

CONCLUSIONS: The collaboration of clinical pharmacists with physicians resulted in cardiovascular risk reduction by intensification of targeted LDL-c goal, and improving components of the lipid panel and proportions of patients at targeted goals.

Cardiovascular

232E. Impact of a Group Heart Failure Clinic on Patient Outcomes in a Veteran Population. *Adrienne Matson, Pharm.D., BCPS,*[1] Kate Schmoll, Pharm.D.,[1] Douglas T. Steinke, Ph.D.[2]; (1) Veterans Affairs Medical Center, Lexington, KY; (2) University of Kentucky College of Pharmacy, Lexington, KY

PURPOSE: To evaluate the impact of a group heart failure (HF) staffed by a clinical pharmacist, registered nurse, and dietician on patient outcomes in a veteran population. The primary objective of this study was to evaluate the impact of a multidisciplinary group (HF) clinic on quality of life. Secondary outcomes evaluated were medication optimization, medication adherence rates, patient knowledge, and HF-related medical visits.

METHODS: Baseline characteristics and other pertinent data were collected for analysis using electronic chart review. Quality of life and patient knowledge were evaluated using the Kansas City Cardiomyopathy Questionnaire at baseline and subsequent visits. Medication optimization was measured by initiation and titration of b-blockers and angiotensin-converting enzyme (ACE) inhibitors to national HF guidelines. Assessment of adherence to HF medications was measured using medication possession ratios (MPRs). HF-related medical visits to primary care and the emergency department were measured 1 year before and 1 year after the first group HF clinic visit. Paired Student's *t*-tests were used to assess changes in quality of life, hospital admissions, patient knowledge, and MPR. Medication optimization was measured using McNemar's test.

RESULTS: A total of 44 patients met criteria for chart review. Quality of life statistically improved after the fourth HF group clinic visit ($p=0.012$). Patient knowledge significantly improved after the second visit ($p=0.029$). HF-related primary care and emergency department visits showed a significant decrease ($p=0.001$). Medication optimization showed a significant increase from baseline for ACE inhibitors and β-blockers ($p<0.001$). The MPR measurements showed a positive trend.

CONCLUSIONS: A multidisciplinary group clinic can improve outcomes in a veteran HF population. This observation may be because of closer follow-up, education, and medication optimization.

Presented at the Great Lakes Pharmacy Resident Conference, West Lafayette, IN, April 23–25, 2008.

233. A Retrospective Review of Bivalirudin Versus Glycoprotein IIb/IIIa Inhibitors Plus Heparin for Percutaneous Coronary Intervention. *John P. Lindsley, Pharm.D.*, Kerry K. Pickworth, Pharm.D., Danielle M. Blais, Pharm.D.; The Ohio State University Medical Center, Columbus, OH

PURPOSE: In 2004, our institution performed a review of bivalirudin, which revealed a decreased incidence of bleeding and length of stay (LOS) compared with glycoprotein IIb/IIIa inhibitors (GPIIb/IIIa) plus heparin during percutaneous coronary intervention (PCI). As part of a quality initiative, this outcome was discussed with the interventional cardiology staff and prompted operational pharmacy changes, making bivalirudin readily accessible to the catheterization laboratory. The objective of this study was to reevaluate the bleeding and LOS previously seen at our institution with bivalirudin compared with GPIIb/IIIa plus heparin.

METHODS: A retrospective review was conducted in all patients admitted to a cardiology service who underwent PCI and received bivalirudin or a GPIIb/IIIa from December 2006 to May 2007. Patients with ST-elevation myocardial infarction, prisoners, and patients younger than 18 or older than 89 years were excluded. Demographic data, catheterization indication, thrombolysis in myocardial infarction (TIMI) risk score pertinent laboratory values, bleeding complications, blood transfusions, and LOS were collected. Institutional review board approval was obtained.

RESULTS: A total of 389 patients were identified to have received bivalirudin, abciximab, or eptifibatide. After exclusions, 103 patients received bivalirudin, and 145 patients received GPIIb/IIIa. The two treatment arms were similarly matched including TIMI score, bivalirudin 3.3, and GPIIb/IIIa 3.5 ($p=0.29$). Total bleeding was significantly lower with bivalirudin compared with GPIIb/IIIa, 2.9% versus 14.5% ($p<0.005$). LOS was also significantly lower with bivalirudin, 1.9 days versus 3.1 days ($p<0.005$). Compared with our previous data, both bivalirudin and GPIIb/IIIa showed a reduction in LOS by 50%. However, bivalirudin showed a greater reduction in bleeding incidence versus GPIIb/IIIa, 79% versus 46%.

CONCLUSIONS: Bivalirudin was associated with decreases in bleeding and LOS compared with GPIIb/IIIa plus heparin. Compared with previous data, bivalirudin had a greater reduction in bleeding incidence. This quality initiative continued to yield a decrease in the incidence of bleeding and LOS at our institution with both agents.

234. Comparison of a Warfarin Dosing Nomogram with Conventional Physician Dosing. *Paul Juang, Pharm.D.*,[1] Kelle Turner, Pharm.D.,[2] Dennis Bouselli, Pharm.D.[2]; (1) St. Louis College of Pharmacy, St. Louis, MO; (2) Missouri Baptist Medical Center, St. Louis, MO

PURPOSE: As part of the 2008 National Patient Safety Goals issued by Joint Commission, health systems must reduce the risk of patient harm associated with anticoagulation therapy through the use of approved protocols for the initiation and maintenance of anticoagulation therapy. The objective of this study was to develop and implement a warfarin dosing nomogram for inpatient medical patients and compare its effectiveness with physician-adjusted dosing.

METHODS: The health system's electronic medical record system

was used to identify the control population, which included patients admitted in May 2007 receiving doses of warfarin. The study population consisted of patients admitted to a cardiac telemetry floor during May 2008. Patients receiving warfarin before admission and patients admitted for orthopedic procedures were excluded. The dosing nomogram was developed by examining previously published data. The primary end point was the time to therapeutic international normalized ratio (INR). Secondary end points included the number of bleeding and thrombosis events, defined as the number of all documented events occurring during admission. Fisher's exact test, the χ^2 test, and the Student's *t*-test were used as appropriate.
RESULTS: Nine patients were started on the warfarin dosing nomogram, and 56 patients served as the control population. No significant differences were observed in the baseline demographics. No significant difference was observed in the time until therapeutic INR (study, 3.4 days, vs. control, 3.6 days) and the number of patients who achieved therapeutic INR before hospital discharge (study, 55.5%, vs. control, 58.9%). Similar rates of thrombosis (one in study group and three in control group) and bleeding (none in study group and two in control group) were observed between groups.
CONCLUSIONS: Use of a warfarin dosing nomogram appears to be as effective in achieving therapeutic INR as physician-adjusted dosing and was associated with similar rates of adverse events.

Chapter Poster

235. Canadian College of Clinical Pharmacy: Chapter Overview and Strategic Initiatives. *Christine A. Hughes, B.Sc.Pharm., Pharm.D.,*[1] Linda D. Dresser, Pharm.D.,[2] Lisa McCarthy, B.Sc.Phm., Pharm.D.,[3] Thomas E.R. Brown, Pharm.D.,[4] Suzanne C. Taylor, Pharm.D.,[5] Andrea Kent, Pharm.D.[6]; (1) Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada; (2) North York General Hospital, Toronto, ON, Canada; (3) McMaster Family Health Team, Hamilton, ON, Canada; (4) Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada; (5) Drug Use Optimization BC Ministry of Health, Pharmaceutical Services Division, New Westminster, BC, Canada; (6) Colchester East Hants Health Authority, Truro, NS, Canada
PURPOSE: To provide an overview of the Canadian College of Clinical Pharmacy (CCCP), which has been an active chapter of ACCP since 1992.
METHODS: We reviewed the current membership and strategic initiatives of CCCP.
RESULTS: CCCP has 106 active members, including 26 student/resident members. CCCP's mission is "to advance human health and quality of life by helping pharmacy practitioners, educators and researchers to expand, support and enhance direct patient care practice." To support this mission, CCCP has several key strategic initiatives: (1) Awards and Grants – CCCP supports several awards and grants each year including a research award, meritorious service award, education grant, mini-sabbatical grant, and best poster award. (2) Annual general meeting – The annual general meeting of CCCP is held in collaboration with the Canadian Association of Population Therapeutics (CAPT) and the Canadian Society of Clinical Pharmacology (CSCP) annual meetings in the forum known as the Canadian Therapeutics Congress (CTC). This collaboration supports one of the strategic goals of CCCP in providing a forum for collaboration and cooperation in the development of pharmacotherapeutical-related research in Canada. (3) Recruitment – Several recruitment initiatives have recently been implemented including ACCP bucks for referring new members and free membership for pharmacy residents/student members. (4) Web site – Improvements to the Web site including postings for career opportunities and a members-only section for specialty areas/networking.
CONCLUSIONS: Based on these and other strategic goals, CCCP continues to grow and strengthen its role in supporting advanced pharmacy practitioners in Canada.

Clinical Administration

236. National Patient Safety Goal 3E: The Utility of Benchmarking in the Realm of Optimizing Pharmacy Practice and Patient Safety. *Charlene A. Hope, Pharm.D., BCPS,*[1] Stacy Ramga, Pharm.D., M.S.,[1] Karen Miller, Pharm.D.,[1] Lisa Prather, Pharm.D., BCPS,[1] Bea Dys, Pharm.D.[2]; (1) Comprehensive Pharmacy Services, Memphis, TN; (2) Medication Management/Comprehensive Pharmacy Services, Dracut, MA
PURPOSE: This study evaluated the level of clinical pharmacy services with regard to anticoagulation and the progress toward implementation of the Joint Commission National Patient Safety Goal 3E standards. The secondary objective compared the drug cost of anticoagulants per pharmacy-adjusted patient days (PAPD) of several hospitals within a functional benchmarking group.
METHODS: The study was designed as a retrospective review for July 2007 through December 2007. Data were collected by two separate methods. The first data collection phase involved a retrospective survey administered to a group of hospitals with contracted pharmacy services. The second data collection phase involved obtaining hospital metrics, which included drug spend data from the designated hospital data intelligence tool, Hyperion.
RESULTS: The preliminary response rate for the survey was 46%. The survey revealed that most hospitals did not have dedicated pharmacy support for anticoagulation therapy but did use tools such as protocols, procedures, order forms, and order sets to establish safe practices with regard to anticoagulation therapy. Of respondents, 33% indicated about 8 hours/week of pharmacist time was dedicated to anticoagulation management. The average anticoagulant drug spend was $6.41/PAPD. In addition, 91% of respondents indicated pharmacist involvement in a multidisciplinary anticoagulation committee and tracking medication events related to anticoagulants. Although the responding departments seemed to have established policies and procedures for improving patient safety, the annual education of health care providers appeared to lack consistency and structure.
CONCLUSIONS: Even though 33% is a reasonable proportion of health care institutions that seem to be moving forward with the standards and deadlines established by National Patient Safety Goal 3E, progress is slow, and there are several challenges with implementation because of the multidisciplinary criteria of the goals. The overall impact of focused pharmacy practices on the cost of anticoagulants is dependent on the operational integrity of the department.

237. Clinical Quality Improvement (CQI) Process on the Use of Erythropoiesis Stimulating Agents (ESAs) Following the Updated Guideline of the Centers of Medicare & Medicaid Services (CMS) Started July 2007. *Tiffany H. Bach, Pharm.D.*, Vuong Green, Pharm.D., Siu-Fun Wong, Pharm.D., FASHP, FCSHP; Western University of Health Sciences, College of Pharmacy, Pomona, CA
PURPOSE: To assess the effectiveness of the newly developed Erythropoiesis-Stimulating Agents (ESAs) Order and Administration Form in reenforcing the compliance of the medical office staff on the use of ESA according to the 2007 updated guideline of the Centers of Medicare and Medicaid Services (CMS).
METHODS: A retrospective chart review was conducted using patients who followed the CMS guidelines before and after the implementation of the new clinical quality improvement (CQI) protocol. The CQI study included CQI implementation and quality assessment. Five main steps in the CQI process were as follows: (1) identify problem in the system through data collection, (2) identify root cause of the problem by analyzing data, (3) design intervention tool to correct or eliminate future problem, (4) implement the intervention tool, and (5) provide follow-up assessment for quality improvement.
RESULTS: A total of 29 patients were included in the review. Weight-based and dosing frequency accounted for the most common error in dosing. Five of 29 patients were evaluable to assess the impact of the before and after of the CQI protocol. A total of 11 dosing noncompliances were discovered in these five patients before CQI implementation versus only two dosing noncompliances after the implementation of the CQI. Cost-benefit analysis in these

five patients showed that about $6000 could be avoided if dosing administration complied with the CMS guidelines. A projected annual cost avoidance of $179,071 can be expected at the Hematology-Oncology Medical Group of Orange County, Inc.
CONCLUSIONS: Introducing the CQI process showed positive outcomes with regard to compliance with CMS guidelines, optimizing patient's care, and ensuring drug reimbursement. The CQI provided a guiding tool to staff members to prevent dosing administration and documentation and was confirmed to be well accepted, as indicated in the Staff Satisfaction Survey.

238. Evaluation of Antimicrobial Stewardship Programs and Their Relationship to Pharmaceutical Expenditures. *Lisa Prather, Pharm.D., BCPS,*[1] Charlene A. Hope, Pharm.D., BCPS,[1] Stacy Ramga, Pharm.D., M.S.,[1] Karen Miller, Pharm.D.,[1] Bea Dys, Pharm.D.[2]; (1) Comprehensive Pharmacy Services, Memphis, TN; (2) Medication Management/Comprehensive Pharmacy Services, Dracut, MA
PURPOSE: This study evaluated the level of clinical pharmacy services around antimicrobial stewardship within a cohort of hospital pharmacy departments. A secondary objective used comparative benchmarking tools to evaluate the impact of antimicrobial stewardship on pharmaceutical expenditures on cephalosporins, antifungals, penicillins, fluoroquinolones, and miscellaneous anti-infectives.
METHODS: This retrospective review included a survey of clinical pharmacy services and hospital pharmaceutical expenditure metrics data of select antimicrobials per pharmacy-adjusted patient day (PAPD). Data were collected from June through December 2007.
RESULTS: The survey produced a preliminary response rate of 24 (75%) of 32. Of the respondents, 81% of the pharmacists spent around 8 hours or less per week focused on antimicrobial management,and only 25% reported having a multidisciplinary antimicrobial stewardship team. The core strategy toward antimicrobial management practiced by 70% focused on formulary restrictions by the Pharmacy & Therapeutics Committee. Supplemental strategies implemented included intravenous to oral conversion (70%) and multidisciplinary development of practice guidelines (50%). Metrics data showed that the average antimicrobial expenditure was $55.22/PAPD. Drug classes contributing to the antimicrobial spend/PAPD were cephalosporins ($6.30), antifungals ($5.14), penicillins ($10.63), fluoroquinolones ($5.09), and miscellaneous anti-infectives ($28.06).
CONCLUSIONS: A deficiency of clinical pharmacy services in antimicrobial stewardship was seen; however, most institutions implemented at least one core strategy. Increasing antimicrobial resistance with a shift to broad-spectrum antimicrobial use without adequate management demands a focus on creative strategies for antimicrobial stewardship requiring fewer resources. Supplemental strategies, such as education on antimicrobial management in addition to collaboration with other health care providers, are required to optimize clinical outcomes and minimize antimicrobial resistance.

239E. Cost Benefit Analysis of a Novel Oncology Pharmacy Practice Model in a Private Medical Oncology Office. *Siu-Fun Wong, Pharm.D.*; Western University of Health Sciences, Pomona, CA
PURPOSE: In oncology practice, the success of a practice is highly dependent on providing efficient patient care operations, particularly with ongoing changes in Medicare reimbursements. Many oncology pharmacy practice models in hospital and ambulatory care settings have been described in the literature, but none can be identified in a physician-owned practice office. The purpose of this study was to conduct a cost-benefit analysis of a novel oncology pharmacy practice model in a medical oncology private practice.
METHODS: A clinical research program was initiated by an oncology pharmacist at a medium-sized medical oncology office in 2002 with 60% full-time employee effort. Responsibilities included serving as principal investigator, protocol selection/development/activation, regulatory documentation, contract negotiation, subject accrual/management, and data management. Additional clinical and administrative services were provided as needed. Cost-benefit analyses = [cost avoidance + research grants] – [pharmacist salary + indirect costs] per year were conducted.
RESULTS: From 2002 to 2006, 25 protocols were activated including five investigator-initiated trials with 117 subjects enrolled. The cumulative research grants funded amounted to 1.5 million. Additional accomplishments included initiation of a cofunded pharmacy research fellowship, standardization of chemotherapy orders to reduce medication errors and administration costs, administrative analyses leading to personnel justification for pharmacy technician and data managers, and medical economic analyses to optimize drug therapy for major cancer types. The pharmacist also provided pharmacotherapy consultation and education to patients and other health care providers. The medical office developed into a progressive practice environment for teaching/training activities. Cost analysis concluded net benefit gains of $8000K at year 2 and reaching $145,000 at year 5.
CONCLUSIONS: A trained oncology pharmacist in a private practice office is a cost benefit. Furthermore, pharmacist activities can reduce medication errors and costs, optimize drug therapy, and improve patient outcomes.
Presented at the HOPA/ISOPP 2008 Joint Annual Conference, Anaheim, CA, June 18–21, 2008.

Community Pharmacy Practice

240. On the Road to Improved Trucker's Health – Road to Opportunity for Pharmacists. *John T. Johnson, Pharm.D., CDE*, Amber Watts, Pharm.D., Josh Guffey, Pharm.D.; University of Georgia College of Pharmacy, Athens, GA
PURPOSE: To determine if providing health screenings and education at a trucking terminal would be a valuable service for truckers and their company and provide a viable avenue for pharmacist clinical services.
METHODS: From October 2007 through March 2008, we screened 232 truckers from Marten Trucking in Atlanta, GA, and provided health education related to diabetes, hypertension, high cholesterol, and obesity. Payment for these services was made by the company and was part of the new driver orientation.
RESULTS: Health statistics from this population were about the same as national averages; 78% of the truckers with blood pressure greater than 140/80 mmm Hg were not taking drugs, and 81% of men and 75% of women had waist circumferences greater than 40 and 35 inches, respectively. Other screening results showed high rates of physical inactivity, elevated cholesterol concentrations, and the need for health education.
CONCLUSIONS: Screening, education, and medical monitoring in this underserved population are necessary, and companies are willing to pay for this service to keep their trucks on the road.

241. Positive Impact of Pharmacist Intervention with Medicare Patients with Diabetes – Georgia Pharmacist Association and Center for Medicare and Medicaid Services Project Outcomes. *John T. Johnson, Pharm.D., CDE*; University of Georgia College of Pharmacy, Athens, GA
PURPOSE: To determine if Medicare patients with diabetes who receive quarterly monitoring and education, the intervention group, achieve better outcomes than those receiving basic pharmacy services.
METHODS: A total of 100 patients were enrolled from 10 different pharmacies across Georgia in a year-long study. Ten patients who were Medicare recipients with a diagnosis of diabetes were enrolled at each of the 10 pharmacies. Pharmacists in the control group were instructed to obtain a baseline A1c, fasting lipid panel, and blood pressure and another of these measurements at the end of the study. Pharmacists in the intervention group were asked to obtain these in addition to quarterly results in between the baseline and end-of-study results. None of the pharmacists was informed about the other pharmacist participants in the study.
RESULTS: A total of 88 patients completed the study, with 39 in

the standard care group and 47 in the intervention group. The average A1c in the control group went from a baseline of 7.5 to an end-of-study 7.6, whereas the A1c in the intervention group improved from 7.83 at baseline to 6.74 at the end of study.The percentage of patients who achieved an end-of-study A1c less than 7% was 52% in the control group and 67% in the intervention group. Average blood pressure and fasting low-density lipoprotein values improved in the intervention group, as did the number of patients receiving annual dilated eye examinations, foot care, dental examinations, and immunizations.
CONCLUSIONS: Pharmacists in community settings can improve the health and outcomes of patients with chronic conditions such as diabetes.

242. Cost-Benefit Analysis of Non-dispensing Patient Care Services in an Independent Community Pharmacy. Erin Harris, Pharm.D.,[1] *Brenna Button-Neumann, Pharm.D.,*[1] Timothy Mitchell, R.Ph.,[1] Peggy G. Kuehl, Pharm.D.[2]; (1) Advantage Health Care, Neosho, MO; (2) University of Missouri–Kansas City School of Pharmacy, Kansas City, MO
PURPOSE: Nondispensing patient care services (NDPCs), including medication therapy management (MTM), are becoming common activities in community settings. The purpose of this study was to determine the cost benefit of NDPCs provided by an independent community pharmacy in southwestern rural Missouri in 2006 and 2007.
METHODS: The study site was a licensed consulting pharmacy associated with three independent community pharmacies. NDPCs were implemented in August 2005 by a 0.5 FTE pharmacist and have expanded to a broad variety of programs and services provided by three pharmacists, a resident, pharmacy students, and support staff. Costs included supplies and personnel. Revenues were identified using insurance and prescription claims databases, patient documentation forms, and the pharmacy's accounting records. All costs and revenues were adjusted to U.S. $2007. Cost benefit was determined from the perspective of the pharmacy. Sensitivity analysis assessed the variations associated with type of pharmacist and time spent providing services.
RESULTS: Revenues for services (total [2006 and 2007, respectively]) were as follows: screenings $704.40 ($339.40, $365.00); MTM $14,770.38 ($2375.48, $12,394.90); disease state management: $1578.91 ($1043.91, $535.00); immunizations: $147,090.31 ($98,196.54, $48,893.77); specialty services: $19,703.99 ($7979.05, $11,724.94); and teaching/grants: $4642.72 ($1542.72, $3100.00). Total revenues were $188,490.71 ($111,477.10, $77,013.61). Total expenses were $162,123.49 ($82,390.00, $79,733.49). Cost-benefit ratios were 1:1.16 (1:1.35, 1:0.97). Sensitivity analysis indicates these results are robust when a resident's time is replaced by a pharmacist or when the time to provide services is increased by 12.5%.
CONCLUSIONS: During the 2 years of this study, a spectrum of NDPCs was provided at this independent community pharmacy at an overall profit. Immunizations accounted for most revenues; however, all activities generated revenue. Overall, $1.16 in revenues were generated for every $1 invested (expenses). These findings demonstrate that NDPCs can be viable in community pharmacies and can serve as a model for others seeking to provide these services.

Critical Care

243. Impact of a Severe Sepsis Order Set on Compliance with the Severe Sepsis Bundles and Subsequent Outcomes. *Kara W. Orwig, Pharm.D.*, Thomas C. Rushton, M.D.; Saint Mary's Medical Center, Huntington, WV
PURPOSE: The objective of this study was to measure the impact of a standardized order set on compliance with the Institute for Healthcare Improvement Severe Sepsis Bundle elements and subsequent outcomes among patients with severe sepsis or septic shock.
METHODS: Prospective identification of 191 patients with severe sepsis or septic shock using Society of Critical Care Medicine consensus definitions occurred between December 2006 and May 2008. Elements of the bundle evaluated included lactate measurement, adequate fluid bolus, blood cultures collected before antibiotics, central venous pressure (CVP) more than 8 mm Hg within 6 hours, central venous oxygen saturation (SVO_2) of 70% or more within 6 hours, and use of drotrecogin alfa. Outcome measures evaluated included intensive care unit (ICU) length of stay (LOS), hospital LOS, and in-hospital mortality.
RESULTS: The order set was used for the management of 63 (33%) of 191 patients. Compliance with all six elements occurred in only 1 (0.5%) of 191 patients. Compliance with five of the six elements significantly improved with use of the order set, which included lactate measurement, adequate fluid bolus, goal CVP achieved, goal SVO_2 achieved (all $p<0.0001$), and administration of drotrecogin alfa ($p=0.002$). Although hospital LOS did not change, ICU LOS was decreased by 1 day (11.1 days vs. 10.1 days). A significant 40% reduction in mortality occurred among patients managed with the order set (OR = 0.39; 95% CI: 0.27–0.75; $p=0.004$).
CONCLUSIONS: Use of an order set improved compliance with the severe sepsis bundles, but compliance with all six elements was rare. The order set resulted in a significant reduction in mortality; thus, efforts should be made to encourage and optimize use.

244. A Review of Recombinant Activated Factor VII (Novoseven®) Use in a Large Community Hospital. *Christy D. Burrows, Pharm.D.*, Vickie L. Bridges, Pharm.D., Carla A. Zeilmann, Pharm.D., BCPS; St. John's Hospital, Springfield, MO
PURPOSE: Recombinant factor VIIa (rFVIIa, Novoseven) has been increasingly used for off-label indications, including use as a hemostatic agent in massive bleeding. However, rFVIIa may cause significant thromboembolic complications. The purpose of this evaluation was 3-fold: first to assess the appropriateness of rFVIIa administration, second to evaluate possible adverse events related to rFVIIa administration, and finally to determine if a correlation between the amount of blood products given before rFVIIa and mortality exists.
METHODS: Medical records of 49 patients who received rFVIIa between October 2006 and October 2007 were reviewed. Reason for rFVIIa use and blood products (fresh frozen plasma, packed red blood cells, platelets, or cryoprecipitate) received before rFVIIa administration determined the appropriateness of rFVIIa. Possible adverse events related to rFVIIa were also documented for each patient.
RESULTS: All patients received rFVIIa for an off-label use, with trauma being the primary reason for use. Ten (22%) patients were administered the required amount of blood products before rFVIIa administration and were therefore considered appropriate recipients of rFVIIa. One patient developed deep venous thrombosis after receiving rFVIIa in the setting of septic shock. Twenty-one patients (47%) died; 12 (57%) of those patients received no prior blood products, compared with 5 (24%) who received an appropriate amount and 4 (19%) who received some amount of blood products before rFVIIa administration.
CONCLUSIONS: rFVIIa was used entirely for off-label indications during the study period. Patients who did not receive blood products before receiving rFVIIa seemingly had a higher risk of mortality. The results are being critically evaluated to develop guidelines for the use of rFVIIa within the institution.

Education/Training

245. Impact of Clinical Pharmacy Services Provided Through Advance Practice Pharmacy Rotations in a Rural Medical Center. *Kimberly L. Tackett, Pharm.D.,*[1] Felix S. Smith, Pharm.D.[2]; (1) South University, School of Pharmacy, Savannah, GA; (2) Coastal Carolina Medical Center, Hardeeville, SC
PURPOSE: To measure the impact on clinical interventions and cost savings after establishment of an advance practice rotation for pharmacy students at a rural community hospital.
METHODS: Coastal Carolina Medical Center is a for-profit 40-bed community hospital that currently employs one full-time director and two per diem pharmacists. In March 2007, a faculty member

from South University was assigned to this site to develop an advanced practice rotation for pharmacy interns. The interns, under the guidance of the preceptor, would perform clinical functions including intravenous to oral transition, renal dosing, kinetic dosing, review of antibiotic orders for appropriateness, medication reconciliation, patient counseling, and formulary reviews. In addition, the students would participate in the education of nurses, physicians, and patients.
RESULTS: After establishing the practice site, the students will now be able to participate in weekly meetings evaluating medication therapy for patients admitted to the rehabilitation unit and counsel patients in a local internal medicine clinic. Students participate in daily rounds with the hospitalist to provide a variety of clinical pharmacy services that were not available previously including medication reconciliation, patient counseling, and nursing education. The preceptor was not available for rounds but was available to review patient therapy with the students. When possible, interventions were documented in the patient chart and cosigned by the preceptor. To date, the average number of interventions per month has risen from 28 to 52, resulting in a cost savings of $7500 per month. Interventions documented by the students include discharge counseling, pharmacokinetic dosing, renal dosing, warfarin monitoring, and reporting of adverse drug reactions.
CONCLUSIONS: The development of an advanced practice rotation site at Coastal Carolina Medical Center may serve as a guide to other rural community hospitals with staffing restrictions because of its impact on clinical services leading to cost savings.

246. Descriptive Evaluation of a Collaborative Clinical Pharmacy Research Assistant Program for Pharmacy Students. *Flora G. Estes, Pharm.D.,*[1] Lincy S. Lal, Pharm.D., Ph.D.,[2] Barbara E. Hayes, Ph.D.[1]; (1) Texas Southern University College of Pharmacy and Health Sciences, Houston, TX; (2) UT M.D. Anderson Cancer Center, Houston, TX
PURPOSE: This program strives to expose pharmacy students to research methodologies and research questions in clinical pharmacy through didactic and interactive activities in collaboration with a college of pharmacy and a county hospital institution. The aim of the program is to increase student awareness of research/academic opportunities in clinical pharmacy.
METHODS: Students were selected on the basis of academic standing, professional year standing, and interest in research. An interview process was used for the final selection of the students. Selected candidates were subsequently assigned a research mentor in the department of pharmacy practice, in collaboration with clinical pharmacy specialists. They were required to assist in the development, data extraction, data analysis, and presentation of the project. All funding was made available through the college of pharmacy.
RESULTS: From 2004 to 2006, four students were involved in the program. The students selected were in their first professional year, and they participated in the research program until the end of their third year. The students participated in projects dealing with oral anticoagulation management; evaluating the use of palivizumab for prophylaxis of respiratory syncytial virus in children; medication use evaluation of pioglitazone; evaluation of the effects of atazanavir on the liver; and tenofovir on the kidney. Selected projects were presented at national meetings, and two have been published in peer-reviewed journals. Postgraduation, the students matriculated into further training programs and are continuing their professional development in a general residency, a 2-year fellowship, and medical school.
CONCLUSIONS: The collaborative program appears to be beneficial in increasing the students' motivation to pursue further training. Steps are being taken to increase the funding, the number of mentors, the didactic classes, and the number of students included in the program.

247. An Academician Preparation Program: Statewide Outreach to Pharmacy Residents. *Jean M. Nappi, Pharm.D., FCCP, BCPS*, Marlea Wellein, Pharm.D., Sandra Garner, Pharm.D.; Medical University of South Carolina, Charleston, SC
PURPOSE: The purpose of the Academician Preparation Program (APP) is to generate interest in academic careers after residency training. The program was created in 2005 after noting a decline in the number of residents seeking academic positions after their training.
METHODS: Teaching and research activities are part of the Medical University of South Carolina (MUSC) residency program. After reviewing descriptions of teaching certificate programs from other colleges of pharmacy, specific goals and objectives for the APP were created. This program was offered as an option to 2005–2006 MUSC residents. Requirements for the APP certificate include attendance at additional seminar sessions (#15) and participation in additional teaching/evaluating activities beyond what was outlined in the residency program. An abstract and manuscript suitable for peer review are required. Each resident is assigned a faculty mentor for the APP. Each resident maintains a teaching portfolio, which includes examples of handouts and copies of evaluations that residents perform on students. Residents meet with their mentor quarterly to review progress toward the APP requirements. Mentors also evaluate resident didactic lectures and small group teaching experiences. The program was expanded to include VA residents in Charleston in the 2006–2007 academic year and statewide in 2007–2008.
RESULTS: In 2006, 13 residents completed the program (5 assumed full-time academic positions). The next year, 10 residents completed (3 accepted full-time academic positions. This year (2007–2008), 28 residents throughout the state are participating.
CONCLUSIONS: An optional, organized APP is of interest to residents and fosters academic careers.

Emergency Medicine

248. Justification for Emergency Department Clinical Pharmacy Services in a Rural, Tertiary Medical Center. *Benjamin Miles, Pharm.D.*, Marybeth Boudreau, Pharm.D., Jamie L. Cronin, Pharm.D., James A. Cattin, R.Ph., M.S., Dan Moellentin, Pharm.D.; Eastern Maine Medical Center, Bangor, ME
PURPOSE: Pharmacists' interventions have been shown to positively affect cost avoidance in the emergency department (ED). The primary objective of this study was to determine the financial feasibility and return on investment of interventions performed by a clinical pharmacist in the ED, where 60,000 patients are seen annually.
METHODS: A prospective, 8-week evaluation of interventions (institutional review board exempt) in a 28-bed ED was undertaken. A dedicated ED pharmacist provided peak-hour services 8 hours/day. An electronic database was developed, and accepted interventions were documented and categorized. A system developed by Mutnick and colleagues was used to quantify cost savings and avoidance data. Cost savings was defined as a measurement of actual dollars saved by a particular intervention because of a potential increase in drug therapy or laboratory testing costs. Cost avoidance was the prevention of additional resources and/or drug-related complications that increased length of stay or resulted in admission. To validate the calculated cost savings and avoidance, 10% of all interventions were reviewed by a team consisting of two clinical pharmacists, a physician, and a revenue analyst. Cost savings and avoidance were annualized and extrapolated.
RESULTS: A total of 388 interventions were documented during the 8-week study period. Medication reconciliation interventions made up most interventions (217), followed by quality of care (61), pharmacotherapy review (43), and drug information (40). Other interventions included dose adjustments, pharmacokinetics, adverse drug reaction management, adverse drug event prevention, and patient education. Cost savings for the study period was $29,165, annualized to $174,990. Cost avoidance was $155,288, annualized to $931,728.
CONCLUSIONS: ED-based clinical pharmacist interventions demonstrated cost savings and avoidance, and dedicated clinical pharmacy services were determined to be financially feasible. Hospital administration has since approved continued ED pharmacy services.

249. Implementation of an Emergency Pharmacist. *Darrel W. Hughes, Pharm.D.,*[1] Pamela R. Maxwell, Pharm.D., BCPS,[1] Kay Green, R.Ph., BCPS,[2] James S. Lewis II, Pharm.D.,[1] Yolanda Laurel, R.Ph., M.B.A.[2]; (1) University Health System, University of Texas at Austin College of Pharmacy, University of Texas Health Science Center, San Antonio, TX; (2) University Health System, San Antonio, TX

PURPOSE: University Hospital (UH) is the leading Level I Trauma Center for a 22-county region of Texas. Although UH has been a leader in emergency medicine care for years, the emergency center (EC) has never had a full-time clinical pharmacist. Our purpose was to implement trial clinical EC pharmacy services to document and analyze intervention types and demonstrate value of an emergency pharmacist.

METHODS: A pharmacist resident spent 1 month in the EC under the supervision of the pharmacy residency director and the medical director of the EC. From November 1, 2007, to November 30, 2007, the pharmacy resident participated in code blues, traumas, and routine patient work-up. Interventions were recorded in a preexisting documentation system. Cost impact analyses were performed using dollar amounts tied to intervention types.

RESULTS: One hundred thirty-six clinical interventions were documented by the pharmacy resident. Breakdown of intervention type is presented in the Table. The most common intervention types were drug information 25% (n=35), code/trauma participation 14% (n=20), and therapeutic recommendation 11% (n=16). The total cost impact of these interventions was $66,783, resulting in an average cost impact per intervention of $491.

CONCLUSIONS: Interventions collected during this study were used to justify a full-time emergency pharmacist. Opportunities for intervention in an EC are similar to those in other areas of practice within a health system.

Table. EC Interventions by Type (n=136)

Intervention Type	No. of Inventions (%)
Drug information	35 (25)
Code blue/trauma	20 (15)
Therapeutic recommendation	16 (12)
Clarification of order	8 (6)
Dosage adjustment	6 (4)
Identification of drug allergy	6 (4)
Narrow antimicrobial coverage	6 (4)
Recommendation of formulary drug	6 (4)
Prevent potential drug interaction	5 (4)
Prevent potential adverse drug reaction	5 (4)
IV to PO switch	5 (4)
Prevent aminoglycoside toxicity	5 (4)
Others	13 (10)

IV = intravenous; PO = by mouth.

250. Development, Delivery, and Outcomes of a Clinical Pharmacy Service Expansion for Sexual Assault Patients in the Emergency Department. *Deborah Larison, Pharm.D., BCPS*; Sarasota Memorial Hospital, Sarasota, FL

PURPOSE: Implement an emergency department (ED) clinical pharmacist–driven program to educate ED nurses, physicians, technicians, and pharmacists about Centers for Disease Control and Prevention (CDC) recommendations regarding treatment of sexual assault victims; facilitate consistently and accurately meet these recommendations; and measure and report our results. Our overall purpose was to improve the accuracy, timeliness, and ease of treating sexual assault victims.

METHODS: This 2-year quality improvement program began with an evaluation of our current state of practice through retrospective chart review and presentation of this evaluation to the ED Performance Improvement Committee (PIC), where it was determined that this committee would oversee the development and evaluation of the program. Six target areas were identified:

1. Baseline laboratory tests
2. Risk stratification
3. First-dose HIV postexposure prophylaxis (PEP)
4. Hepatitis vaccinations
5. Emergency contraception (EC)
6. Antibiotic PEP

Continuing education was provided to our emergency department staff of more than 300 nurses, technicians, pharmacists, physicians, and registration and security personnel. An HIV PEP "First Dose Kit" was developed and implemented. A "red packet" (consent forms, order forms, prefilled laboratory requisitions, etc.) was implemented. Currently under development is an 8-minute video to educate patients on arrival to help them understand the care to be provided and the options regarding PEP.

RESULTS: Improved baseline laboratory test values, 100% compliance with risk stratification, more patients receiving PEP within the 2-hour CDC goal, a 5-fold increase in meeting hepatitis treatment guidelines, almost 100% compliance with EC, and a 50% increase in compliance with antibiotic guidelines.

CONCLUSIONS: This easily implementable program for treating sexual assault has dramatically improved patient care by ensuring receipt of treatment according to appropriate guidelines. Goals that are not at 100% compliance have readily identifiable causes, and the process continues to improve.

251. Pharmacy Resident and Student Activities in an Emergency Eepartment. *Michael J. Peeters, Pharm.D., BCPS*; University of Toledo Medical Center, Toledo, OH

PURPOSE: Clinical pharmacy in the emergency department (ED) was recently added as a resident and student rotation site at the University of Toledo Medical Center (UTMC). The rotation focus has been to investigate and gather complete medication histories for patients likely to be admitted to UTMC. Using better information to build medication histories and potentially identifying drug-related illnesses (DRIs) were two key advantages for including pharmacy students and residents. The objective of this pilot analysis was to quantify resident and fourth-year Pharm.D. student activities within this new rotation site.

METHODS: Students and a postgraduate year 1 (PGY1) resident documented their medication-related activities during shifts in the ED. This documentation was collated in an Excel database. As well, it served to record for later entry of prominent student activities in the institutional clinical pharmacy activities database.

RESULTS: Five Pharm.D. students and one PGY1 resident (without students) completed this rotation in the academic year 2007–2008. Students collected between 102 and 150 medication histories, whereas only 54 histories were collected by the resident. The patient was the significant source of information in 80% of cases (range 72–87%). Family members, patients' medication lists, other facility medication lists (i.e., hospital records and Medication Administration Records), patients' medication containers, and physicians' office records were additional information sources for medication histories. Students identified between zero and seven DRIs (median 3), whereas the resident found nine ($p=0.0037$). After the histories, the resident more often gave physicians verbal feedback based on the medication history findings (37% vs. 13%, $p<0.0001$).

CONCLUSIONS: This activity fostered student involvement in drug information and patient care participation with the ED staff, effectively using pharmacy students' skills. ED involvement has noteworthy potential to improve patient care by identifying DRIs before an admission or further evaluations (i.e., diagnostics), therefore providing the best medication histories for continued care within the hospital.

252. Management of Warfarin in a University-Affiliated Emergency Department. *Elena Meeker, Pharm.D.*, Steven R. Kayser, Pharm.D., Ellen J. Weber, M.D., Cathi Dennehy, Pharm.D.; University of California, San Francisco, San Francisco, CA

PURPOSE: This study aimed to (1) characterize patients who present to the emergency department (ED) taking warfarin, (2) determine the frequency with which international normalized ratios (INRs) are obtained, (3) evaluate the ED management of these patients, and (4) evaluate discharge planning.

METHODS: Two hundred forty-one patients who had warfarin documented among their drugs presented to the ED between June and August 2007. Patients at high risk of hemorrhage or thrombosis were identified using established criteria. Patients who required

hospitalization were excluded. A retrospective chart review was performed to collect information including patient demographics, admission diagnosis, rationale for warfarin, medications, comorbidities, ED course, and discharge instructions.
RESULTS: One hundred eleven patients were included in the analysis. Fifty-four percent of patients were older than 65, 58% had hypertension, and 29% were taking antiplatelet agents in addition to warfarin. Although 71% of all patients had INRs obtained, values were therapeutic in less than half of these patients; INRs were obtained for more than 80% of patients in most high-risk subgroups, except for patients admitted for a suspected fall or fracture (57%) and patients with cardiac valve replacements (50%). Warfarin dose adjustment, bridging, or anticoagulation reversal was performed for 33% of patients with nontherapeutic INRs. Administration of medications with the potential to interact with warfarin occurred during the ED visit in 17% of patients. On discharge, only 17% of patients had arrangements made for anticoagulation follow-up. For 15 patients discharged on a potentially interacting medication, only one-third were advised to follow up for anticoagulation management.
CONCLUSIONS: There are numerous areas in which warfarin management can be improved in the ED, including consistent identification of high-risk patients, evaluation of INRs for these patients, and more proactive warfarin management to address nontherapeutic INRs. Discharge planning was the weakest area of ED warfarin management.

Geriatrics

253. Prospective Review of All Emergency Department Admissions for Beer's Criteria Drugs. *Dan Moellentin, Pharm.D.*, Benjamin Miles, Pharm.D.; Eastern Maine Medical Center, Bangor, ME
PURPOSE: Prospective review of all patients 65 years or older admitted through the emergency department (ED) for the presence of Beer's criteria medications as part of pharmacist medication reconciliation.
METHODS: All patients admitted through the ED during December 2007 who were 65 years or older had a medication review of drugs that was taken within 30 days of admission. Reason for admission or admitting diagnosis was included in the review. Causes for admission diagnosis were determined to be possibly correlated, or not likely correlated, to medications. Potential drug-drug interactions (DDIs) seen on admission were noted whether on Beer's list or not.
RESULTS: One hundred ninety-seven patients 65 years or older were admitted during the review period. Average age was 78.5 years. Thirty-six patients were admitted (18%) who were on Beer's medications. Twenty-three were women. DDIs likely involved in admission were fentanyl-clarithromycin (acute narcosis), fluoxetine-carvedilol (symptomatic bradycardia), and sildenafil-doxazosin (MI). Non-DDIs included amiodarone—pulmonary toxicity (two cases); propoxyphene—hip fracture (two cases in which creatinine clearance was less than 20 mL/minute; routine dosing of propoxyphene ileus; hydrochlorothiazide 50 mg without potassium supplement – cardiac arrest (K = 2.3); NDAIDs – gastritis (1); central nervous system changes (1); unopposed estrogens – pulmonary embolism (1) and arm numbness or edema (1); scopalamine patch – profound hallucinosis (1); donepezil-worsened respiratory function in asthma (1) – not Beers; nitrofurantoin – drug fever (1); and triazolam – hip fracture (1). Other Beer's drugs were involved. Prescribers were notified of the potential drug-related diagnosis and altered prescriptions in all but two cases (amiodarone and thyroid). A total of 32 of 36 patient admissions with a recent history of Beer's medications were likely related to an adverse drug event.
CONCLUSIONS: A prospective review of medications taken before admission in patients 65 years and older with the Beer's list as a guide provides the pharmacist performing medication reconciliation a valuable screening tool for evaluating drug-related causes of admission.

Health Services Research

254. Patient Comfort with Health Literacy Skills Assessment. *Jill S. Wallace, Medical Student,*[1] Darcie L. Keller, Pharm.D., BCPS,[2] Julie M. Wright, Pharm.D., FCCP[1]; (1) University of Missouri–Kansas City, School of Medicine, Kansas City, MO; (2) Kansas City Veterans Affairs Medical Center, Kansas City, MO
PURPOSE: Health literacy (HL) is a person's ability to read and understand information necessary to make decisions about his or her health. Patients with low HL are at risk of worse health outcomes and increased use of the health care system. Asking patients about their level of HL is a sensitive topic, and little is known about how patients feel about being asked such questions. The purpose of this study was to determine if patients are uncomfortable with having their HL skills assessed.
METHODS: A 6-item survey using a 5-point Likert scale was used to assess patients' comfort with being asked about their HL skills in an urban primary care clinic. Age, sex, race, education, insurance, and employment status were also collected. A standardized test was used to determine their level of HL. Demographic and HL data were summarized. Spearman's correlation was used to evaluate the relationship between these characteristics and survey scores.
RESULTS: Among 227 subjects, the mean age was 52, 69% were women, 73% were African American, 25% had completed less than the 12th grade, 93% had no or government insurance, and 67% were unemployed. Most (77%) had adequate HL. The mean comfort scale score was 11 (range 6–28); possible score range was 6–30; more than 18 indicated feeling not comfortable with at least one aspect of communicating about HL. The comfort scale score was not correlated with HL status or demographic factors ($\rho < 0.1$ for all). Only 10 subjects selected any response indicating discomfort; no demographic characteristics were associated with that group (Fisher's exact, $p>0.10$ for all).
CONCLUSIONS: This study showed that even in a diverse population, most patients (95.5%) are comfortable being asked about their HL skills. Primary care providers should be encouraged to inquire about this important topic to optimize patient care.

255. A Reliable Scale to Measure Patient Comfort with Communicating About Their Health Literacy Status. *Julie M. Wright, Pharm.D., FCCP, BCPS,*[1] Darcie L. Keller, Pharm.D., BCPS,[2] Mary M. Gerkovich, Ph.D.,[3] Radhika K. Ravindran, Medical Student,[1] Jill S. Wallace, Medical Student,[1] Beena Shekar, Medical Student,[1] Mimi Moon, Medical Student,[1] Maria Posada, Medical Student,[1] Joomee Shim, Medical Student,[1] Heather Cha, Medical Student[1]; (1) University of Missouri–Kansas City, School of Medicine, Kansas City, MO; (2) Kansas City Veterans Affairs Medical Center, Kansas City, MO; (3) University of Missouri–Kansas City, Kansas City, MO
PURPOSE: Low health literacy (HL) has been associated with shame and embarrassment. As a result, clinicians are reluctant to inquire about patients' level of HL. However, studies have shown that HL status may be associated with health outcomes. The objective of this study was to test the reliability of and validate a survey tool that was developed to measure patients' comfort with communicating with health care providers about their HL status.
METHODS: A 13-item survey with a 5-point Likert response scale was used to assess patient comfort with provider evaluation of their ability to read, understand health information, and assess their confidence in their own HL. The survey was completed by 227 subjects as part of an HL-related study in an urban internal medicine clinic. Factor analysis was used to extract the best combination of survey items to compose a reliable scale. Chronbach's a was computed to assess the consistency of the selected items. A score was created to represent patients' degree of comfort with assessment.
RESULTS: Six of the 13 items were found to make up a common factor reflecting patients' comfort with communicating about their level of HL. Cronbach's a for this 6-item scale was 0.78. The resulting scale score range was 6–30; higher scores indicated discomfort with communicating about HL. The comfort scale score did not correlate with demographic factors such as age, race,

educational level, sex, or insurance status (rho < 0.20 for all).
CONCLUSIONS: We were able to validate a reliable 6-item survey tool that can be used to evaluate patients' comfort with communication about their ability to read and understand health information and to assess patients' confidence in their own HL. The scale provides patient-related HL data that should be integrated into HL research.

Hematology/Anticoagulation

256. Prospective Study Comparing Prevalence of Low B_{12} Levels in African Americans With and Without Sickle Cell Disease. *Salome K. Bwayo, Pharm.D.,*[1] Hemamalini Karpurapu, M.D.,[2] Suguna Chirla, M.D.,[2] Fredric Lombardo, Pharm.D.,[1] Victor Gordeuk, M.D.[2]; (1) Howard University School of Pharmacy, Washington, DC; (2) Howard University College of Medicine, Washington, DC
PURPOSE: To determine if mean B_{12} levels are lower in African Americans with sickle cell disease (SCD) than their controls as well as determine if the proportion of cases with low B_{12} levels is higher in patients with SCD than their controls.
METHODS: This was a prospective case-control study that enrolled 40 patients aged 18 years or older in a local teaching hospital from July 2006 to December 2007. An institutional review board was obtained from 2006 to 2008. All patients and controls had their hemoglobin type determined by hemoglobin electrophoresis. The participants also underwent a comprehensive history and physical examination. The data collected were stratified for gender, age, and hemoglobin electrophoresis.
RESULTS: Forty patients were enrolled in the study. However, data for interim analysis were only available for 24 patients. Seventeen (71%) men and seven (29%) women participated in the interim analysis. Six (25%) participants were controls, and 18 (75%) participants had SCD. The ages of the participants with SCD ranged from 21 to 58 years (mean age 38 years). The ages of the controls ranged from 27 to 63 years (mean age 36 years). The mean cobalamin concentration for the participants with sickle cell was 460 ± 305 pg/mL, and that of the controls was 513 ± 292 pg/mL ($p<0.715$). The men in the study had a mean cobalamin concentration of 477 pg/mL; the women in the study had a mean cobalamin concentration of 465 pg/mL.
CONCLUSIONS: There was a difference in cobalamin levels between the men and the women as well as the between the SCD participants and the non-SCD controls. However, more participants are needed to detect a power of 80% and a two-sided significance level of 0.05.

HIV/AIDS

257. Prevalence of Genotypic Drug Mutations Among a Cohort of HIV-Infected Pregnant Women. *Joshua Sawyer, Pharm.D.,*[1] Yu-Ching Hsia, Pharm.D. Candidate,[1] Darowan Akajagbor, Pharm.D. Candidate,[1] Patty Fan-Havard, Pharm.D.[2]; (1) University at Buffalo, Amherst, NY; (2) Univeristy at Buffalo and Ohio State University, Amherst, NY
PURPOSE: Genotypic drug resistance testing is now recommended for all pregnant women infected with HIV-1. Data are lacking on the prevalence of drug mutations in pregnant women infected with HIV. The purpose of this study was to compare the prevalence of genotypic drug mutations among a cohort of pregnant women infected with HIV before the initiation of antepartum chemoprophylaxis before and after 2004.
METHODS: Pregnant women with HIV infection who had a genotypic assay performed before receiving antepartum ART chemoprophylaxis were evaluated at the HIV Pregnancy Programs, Erie County Medical Center (ECMC), Buffalo, New York, and Nationwide Children's Hospital, Columbus, OH. Patient demographics, ART regimens, and virologic, immunologic, and genotypic data were retrospectively collected. Mutations conferring resistance to nucleoside reverse transcriptase inhibitors (NRTIs), nonnucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) were compared before and after 2004.
RESULTS: A total of 31 of 89 pregnant women with HIV infection met the inclusion criteria at the ECMC HIV Pregnancy Clinic. Genotypic assays were performed in 37 pregnancy events, of which 14 and 23 assays were obtained before and after January 1, 2004, respectively. The prevalence rate of mutations conferring resistance to NRTIs and NNRTIs decreased from 71.4% to 21.7% and from 35.7% to 13.0% before and after 2004, respectively. A decrease in the prevalence of M41L and M184V variants was observed. Conversely, the prevalence of multi-PI mutations (more than four) increased from 28.6% to 43.5% after 2004. Data collection and analysis are under way at the Nationwide Children's Hospital.
CONCLUSIONS: The increase in genotypic resistance testing reflects the recent changes of the mother-to-child transmission guidelines. Further studies are needed to determine the contributing factors to the prevalence of drug mutation differences among pregnant women with HIV infection before and after 2004.

Humanism in Medicine

258. Send in the Clowns! *Carolyn C. Brackett, Pharm.D., BCPS*; The Ohio State University College of Pharmacy, Columbus, OH
PURPOSE: To explore an expanded, creative approach to patient care and teaching through the practice of clowning.
METHODS: In November 2007, 40 individuals from 11 countries accompanied Dr. Hunter "Patch" Adams on a clowning outreach trip to Russia. Clowns ranged in age from 9 to 74 years. About one-third of them were health care providers, and most had no prior clowning experience. For 14 days, participants clowned in hospitals and orphanages in Moscow and St. Petersburg. We worked with children and young adults, seeking to bring comfort and pleasure to a relatively companionless subset of Russian society. Clowns visited two institutions each day, working in groups or individually to make personal, loving contact with people who spend months or even an entire lifetime separated from friends, family, and opportunity.
RESULTS: During the trip, clowns interacted with more than 1000 individuals. Participants learned that laughter and care absolutely reduce pain and that the contact sometimes affords long-lasting changes in people who have been isolated. We learned to establish meaningful, caring contact with others even without makeup or magic. We learned strategies that allowed these meaningful connections to occur irrespective of language, age, and social divisions. Since returning from Russia, clowns have written papers, presented symposia, and developed service groups, extending human care and contact into their communities and workplaces. I have established a Therapeutic Clowning group of pharmacy and medical students at The Ohio State University. I use clowning techniques to establish a more immediate relationship with my patients and a more trusting relationship with my students.
CONCLUSIONS: The clowning experience cultivates more direct, compassionate, discerning contact with students, patients, and colleagues. It offers a unique opportunity to allow care and concern to become the intention of our daily interactions.

Infectious Diseases

259. Implementation of an Extended Infusion Piperacillin/Tazobactam Policy at a Tertiary Academic Medical Center. *Elizabeth Marino, Pharm.D.*, Jason C. Gallagher, Pharm.D., BCPS, Stephanie J. Costante, Pharm.D., BCPS, Kazumi Morita, Pharm.D., BCPS, Courtney Vincent, Pharm.D., BCPS, Christina M. Rose, Pharm.D., BCPS; Temple University Hospital, Philadelphia, PA

PURPOSE: Piperacillin/tazobactam is a commonly used β-lactam antibiotic to treat pseudomonal infections. It is a time-dependent antibiotic, and a previous study evaluating the use of a pharmodynamically optimized extended infusion (EI) demonstrated a decrease in mortality in critically ill patients. The objective of this study was to implement an EI dosing policy for piperacillin/tazobactam in the intensive care units (ICUs) of our institution and assess its feasibility.

METHODS: All patients who received EI piperacillin/tazobactam during the study were monitored to evaluate whether the EI was being used correctly. Orders for piperacillin/tazobactam in the ICUs were reviewed daily for appropriateness in the ordering process. Patient charts and nursing records were evaluated prospectively to determine if infusions were being administered correctly. An appropriately administered infusion was defined as: drug infused without any incompatible drugs, drug administered as an EI over 4 hours every 8 hours, and infusion not interrupted for more than 30 minutes at any given time.

RESULTS: Forty-six patients received EI piperacillin/tazobactam between January and April 2008. Ninety-four percent (43 of 46) of patients received the EI correctly. All three cases of incorrect administration were caused by the infusion being given for less than 4 hours. Fifty-two percent (24 of 46) of orders were ordered incorrectly and required intervention by pharmacists to correct.

CONCLUSIONS: An EI piperacillin/tazobactam protocol was found to be feasible in our institution. Although incorrect ordering by physicians was common, it would likely have been avoided with an updated piperacillin/tazobactam order screen in the computer system that is pending. Nursing errors were infrequent and were likely because of unfamiliarity with EI dosing.

Managed Care

260. Benchmarking: Leveraging Best-Practice Strategies to Implement Anticoagulant and Antibiotic Management Tools. *Karen Miller, Pharm.D.*,[1] Bea Dys, Pharm.D.,[2] Charlene A. Hope, Pharm.D., BCPS[1]; (1) Comprehensive Pharmacy Services, Memphis, TN; (2) Medication Management/Comprehensive Pharmacy Services, Dracut, MA

PURPOSE: This study examined benchmarking methodologies of previously implemented initiatives, as the process of learning lessons about achieving the intended goal improving performance but not ensuring best practice. The second objective involved applying these lessons to the anticoagulant and antibiotic management tools.

METHODS: We evaluated retrospectively the benchmarking measurement methodologies and their respective outcomes used in implementing three previous clinical initiatives (antibiogram development, intravenous to oral conversion, and renal dosing) for 2 years. The second evaluation was a retrospective survey of a group of hospitals and their metrics data including their anticoagulation and select antimicrobial drug spend data.

RESULTS: A review of the outcomes revealed that only 50% of the hospitals tasked with implementing the three clinical initiatives (antibiogram, intravenous to oral conversion, and renal dosing) were able to accomplish the basic goal during a 2-year period. The review identified less than 1% who were able to convert this basic initiative to best practice. Benchmarking of these hospitals based on bed size showed that sites with a larger bed size were more likely to accomplish best practice. Combining the drug spend data and survey showed that those sites with a program in place were more likely to have a more proficient drug spend of the anticoagulation or antimicrobial drug classes.

CONCLUSIONS: Benchmarking focuses on how to improve any given process by exploiting "best practices" versus measuring the best performance. We have been able to illustrate through our first analysis that best performance has not always implied best practice. However, in our second analysis, we have been able to show how best practices are the cause of best performance. Studying best practices provides the greatest opportunity for gaining a strategic, clinical, operational, and financial advantage.

Medication Safety

261. Benefit of Pharmacist-Obtained Medication Histories in the Intensive Care Unit. *Jacob B. Hatch, Pharm.D.*, Jeffrey T. Fish, Pharm.D.; University of Wisconsin Hospital and Clinics, Madison, WI

PURPOSE: This study aimed to quantify the differences between medication histories obtained by physicians and pharmacists from critically ill patients in the intensive care unit (ICU) and to identify patient types at greatest risk of medication errors.

METHODS: The medical records of 200 critically ill patients admitted to the medical and surgical ICU were retrospectively reviewed. The history and physical (H&P) home medication list was compared with the pharmacy home medication history. Variations in the H&P relative to the pharmacy history were recorded including the number of drugs identified, drug formulation, dose, and frequency of administration. Medication orders were reviewed to obtain the number and accuracy of home medications prescribed in the ICU. Patients were divided into predefined groups (i.e., trauma, medical, and nontrauma surgical) to assess the risk of medication error by patient type.

RESULTS: Pharmacists identified 981 home medications compared with 665 by physicians. Pharmacists identified 1.7, 1.4, and 1.6 times more home medications than physicians in trauma, nontrauma medical, and nontrauma surgical patients, respectively. Variances in the H&P relative to the pharmacy history totaled 1628. The number of variances per home medication identified was 2.4, 1.4, and 1.8 for trauma, nontrauma medical, and nontrauma surgical patients, respectively. The distribution of variances by type included the number of drugs identified 25.9%, drug formulation 2.5%, dose 34.6%, and frequency of administration 37.0%.

CONCLUSIONS: Pharmacists identified 47.5% more medications than physicians. The relative incidence of variances in the H&P for each home medication identified was higher in trauma patients; however, medical patients had more medications and therefore the greatest number of variances overall.

Nephrology

262. Concurrent Iron Supplementation with Epoetin Alfa Treatment. *Salome K. Bwayo, Pharm.D.*, Bisrat Hailemeskel, Pharm.D., Anthony K. Wutoh, Ph.D., Euni Lee, Ph.D., Pharm.D.; Howard University School of Pharmacy, Washington, DC

PURPOSE: The goal of this retrospective multicenter study was to evaluate the patterns of recombinant human erythropoietin (r-huEPO) use and the concurrent iron supplementation among inpatients in acute care settings.

METHODS: A retrospective chart review was conducted at seven hospitals and medical centers in a northeast metropolitan area of the United States. The study included all inpatients 18 years and older prescribed r-huEPO between August and December 2003. Collected data included patient-related information (demographics and insurance), laboratory values, (i.e., hemoglobin, hematocrit, iron indices, erythropoietin level, serum creatinine, and blood urea nitrogen), status of iron supplementation, blood transfusions, other applicable diagnoses, medications used, indications, and dose/frequency of r-huEPO treatment.

RESULTS: A total of 518 patients were evaluated, with almost an equal distribution of male and female patients (49 vs. 51%, respectively). About 56% of the patients in this study were elderly. Renal impairment was the most common indication (71.3%) for the use of r-huEPO. Despite current guidelines, more than 63% of the

patients received no iron supplementation despite the use of r-huEPO. For patients who did receive iron supplementation, most received oral iron preparation, with ferrous sulfate (41.2%) being the most common form. Only 36% of patients had serum iron analysis conducted before or during r-huEPO therapy. The average serum iron and serum ferritin levels were very low (38 + 27.2 ng/mL and 20 mg/mL, respectively) in this study.
CONCLUSIONS: There was a lack of consistency in iron supplementation and monitoring practices among the hospitals studied. Future efforts should be placed to create clinical guidelines and improve awareness of iron supplementation during r-huEPO therapy.

263. Implementation of a Template Ordering Process to Improve Medication Safety with Erythropoiesis Stimulating Agents (ESAs) in a Veteran Population. *Heather Ourth, Pharm.D., CGP,*[1] Matthew Cantrell, Pharm.D.[2]; (1) VA Central Iowa Healthcare, Des Moines; (2) VA Medical Center, Iowa City, IA
PURPOSE: Eryrthropoiesis-stimulating agents (ESAs) such as epoetin alfa and darbepoetin alfa are essential in the management of anemia. Despite reducing the need for red blood cell transfusions and improving quality of life, the CHOIR and CREATE trials demonstrated an increased cardiovascular risk in patients with chronic kidney disease when hemoglobin values were normalized. The ensuing U.S. Food and Drug Administration (FDA) warnings and further evidence of increased risk of tumor progression in oncology patients prompted the need to ensure that guideline adherence was occurring within the VA health care system.
METHODS: A template ordering process was designed and implemented in April 2008 within Veterans Integrated Service Network 23 (VISN 23). The template was specifically designed to improve medication safety, promote guideline adherence, and reduce costs associated with misuse of ESAs. The ESA template encourages appropriate laboratory assessment by requiring completion of monthly hemoglobin concentrations and iron studies when indicated. The most recent blood pressure measurements are incorporated because hypertension can be a serious side effect. Because a proportion of patients receive shared care by nephrology or oncology specialists outside the VA, the template allows free text fields to enter these laboratory values and promote continuity of care. The provider may access ordering menus for ESAs only on completion of the template, of which refills are limited. For provider convenience, quick orders for patient return laboratory values are incorporated to ensure that follow-up is completed.
RESULTS: The completed template generates a medical note incorporated in the computerized patient record system for convenience in reviewing patient data and ensuring safety before dispensing. Preceding implementation, pharmacists and providers were educated about the FDA warnings, current treatment guidelines, and instructions on accessing and completing the template.
CONCLUSIONS: A baseline medication use evaluation was conducted with plans for follow-up to document the effectiveness of the template.

Pediatrics

264. Evaluation of the Current Treatment of Neonatal Abstinence Syndrome (NAS) and Development of a Standard of Care for the Neonatal Intensive Care Unit (NICU). *Brian Curran, Pharm.D.,*[1] Paul Mangino, Pharm.D.,[2] Lori A. Devlin, D.O.[2]; (1) Mayo Clinic, Rochester, MN; (2) University of Louisville Healthcare, Louisville, KY
PURPOSE: Evaluate current practice at the University of Louisville Hospital for the treatment of neonatal abstinence syndrome (NAS) in the neonatal intensive care unit (NICU), develop a standard of care for the treatment of opiate withdrawal in these patients, and evaluate treatment of NICU patients after the implementation of the standard of care.
METHODS: This project was reviewed and approved by the institutional review board in September 2005. The project was performed in three phases. Phase I was a retrospective chart review of NICU patients who were treated for NAS in the past 3 years (July 2002–July 2005) to obtain information related to current practice and length of stay for the treatment of NAS. Phase II involved assisting in the development of multidisciplinary treatment guidelines and the education of NICU staff about these guidelines. The guideline included a protocol for dosing morphine based on the Finnegan neonatal abstinence score. Phase III consisted of a postimplementation retrospective chart review to evaluate patients who have received treatment in accordance with the newly developed guidelines compared with the patients identified in phase I. The primary end point was length of treatment.
RESULTS: Twenty-one infants were identified for the retrospective portion of this project. The average length of treatment for NAS was 43.7 days. A multidisciplinary standard of care was developed and implemented. Nineteen infants have been treated after implementation of the standard of care. The length of treatment decreased to 31 days. Mean abstinence scores per day also decreased, indicating that the infants encountered fewer withdrawal-type symptoms.
CONCLUSIONS: Implementation of a standard of care for the treatment of NAS has decreased infants' length of treatment for NAS, length of hospital stay, and cost of hospital stay.

265. A Clinical Pharmacist's Role in Screening for Metabolic Syndrome in a Pediatric Ambulatory Clinic. *Sandra Benavides, Pharm.D.,*[1] Garry Souffrant, M.D.[2]; (1) Nova Southeastern University, Ft. Lauderdale, FL; (2) Su Clinica Familiar, Harlingen, TX
PURPOSE: Identification of metabolic syndrome (MetS) in children is crucial given the substantial increase of obesity in children. Screening and early detection of MetS in children are critical to prevent future cardiovascular disease. In children, the process can be cumbersome because of the necessity of normalizing values for a child's specific age and sex and, as a result, may not be diagnosed. Therefore, the purpose of this pilot study was to evaluate the role of a clinical pharmacist (CP) in screening children for MetS in a pediatric ambulatory clinic in a rural community health center.
METHODS: A CP screened all pediatric patients, aged 10–18, with a risk factor for insulin resistance. On consent and assent, participants were asked to complete a medical history and a physical examination by the primary care provider and to return for fasting laboratory analysis. The definition of MetS used in this study included body mass index (BMI), triglycerides, high-density lipoprotein, blood pressure, and an oral glucose tolerance test. Patients were classified as having MetS if three of the parameters were abnormal. Treatment recommendations were made by the CP to the primary care provider. The study was approved by the clinic and the university institutional review board.
RESULTS: Twenty-five children (aged 13.7 ± 2.3 years) were enrolled during a 3-month period. Fifteen males and 10 females were included. Eight participants (32%) met none of the criteria for MetS, 10 (40%) met one, 6 (24%) met two, and only 1 (4%) met four. As a result, only one patient received a diagnosis of MetS. The criterion most commonly met was a BMI z-score greater than 2 (n=17). All 17 obese children were referred to a dietician.
CONCLUSIONS: CPs can have an active role in screening and identifying MetS in a pediatric ambulatory clinic.

Pharmacoeconomics/Outcomes

266. Medication Errors: A Cost Analysis Examining Malpractice Claims and Reduced Errors with Bar Code Medication Administration (BCMA) Technology. *Gerald J. Rebo, Pharm.D.*, Jeffery E. Carter, M.D., Kimberly A. Benson, MSN, Alexis D. Smith, M.D., James H. Holmes IV, M.D.; Wake Forest University Baptist Medical Center, Winston Salem, NC
PURPOSE: National patient safety goals include improving the safety of medication administration. According to recent reports from the National Practitioner Data Bank and Institute of Medicine, medication-related errors represent about 5% of malpractice claims and result in 7000 deaths/year. Bar code medication administration (BCMA) has reduced medication errors in previous studies. We sought to demonstrate the cost-effectiveness of BCMA by comparing its costs with projected savings through a reduction in medication errors and potential litigation.

METHODS: Inpatient medication errors in an academic medical center were examined pre- and postimplementation of BCMA. The study group consisted of nurses in four selected units during three 4-day blinded observational periods at 2 months preceding and 3 and 6 months after BCMA implementation. Direct observation of 1473 medication administrations were recorded and compared with electronic documentation. Medication errors were defined as any variance in the drug or dose. We reviewed national indemnity awards for medication errors published in *Medical Malpractice Monthly* from 1989 to 2006.
RESULTS: Twenty-two medication errors occurred before BCMA implementation, with reductions to 17 errors at 3 months and 5 errors at 6 months postimplementation (p=0.001). The total cost of BCMA implementation was $2.1 million. Median indemnity awards were $1 million (range $14,500–$52 million).
CONCLUSIONS: BCMA technology reduced medication errors by more than 400%, which represents a potential cost savings of $14.9 million in the first 6 months alone after BCMA implementation. Our study population represented less than 10% of all inpatient medications administered in our hospital during the analysis; thus, system-wide annual projected savings are even greater. By reducing the risk of medication errors to patients and potential subsequent litigation, BCMA technology more than offsets its costs and demonstrates a significant cost-prevention for health care systems. This technology should be embraced to improve the safety, quality, and cost of patient care.

267E. Cost-Effectiveness of Colesevelam HCl Plus Metformin Compared with Metformin Alone Using a Validated Model from a Third-Party Payer Perspective in the USA. *Michael E. Minshall, MPH,*[1] Michael Hagan, Ph.D.,[2] Kevin Mayo, Ph.D.,[2] Sam Misir, Pharm.D.,[2] Meaghan St. Charles, Ph.D.[1]; (1) IMS Health®, Noblesville, IN; (2) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: Type 2 diabetes mellitus (T2DM) is a chronic disease that often leads to long-term complications and premature death. Colesevelam HCl is indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-c) in patients with primary hyperlipidemia. Using colesevelam HCl as an add-on treatment for T2DM in four randomized controlled clinical trials also decreases glycosylated hemoglobin, potentially bringing more patients with T2DM into glycemic control.
METHODS: The present analysis was conducted to evaluate the long-term cost-effectiveness of colesevelam HCl in treating T2DM patients with inadequate glycemic control on metformin monotherapy or metformin combination therapy using a validated model. A 40-year time horizon was used with U.S. $2006 costs and clinical outcomes discounted at 3% *per annum*. Clinical efficacy and baseline data were taken from a phase 3 study of colesevelam HCl added to metformin in patients with T2DM. The primary input variables were glycosylated hemoglobin and lipid reductions. A series of Markov constructs simulated the progression of diabetes-related complications (cardiovascular, neuropathy, renal, and eye disease).
RESULTS: The analysis found that the incremental life-years (LY) gained for colesevelam HCl increased by 0.351 at an overall increased cost of $20,422 per patient during the simulation period. The incremental cost-effectiveness ratio was $58,103/LY gained for colesevelam HCl. The relative risks for a myocardial infarction (MI) event, peripheral vascular disease (PVD), and end-stage renal disease (ESRD) were 0.88, 0.87, and 0.85, respectively. Calculated numbers needed to treat to avoid one case of MI, PVD, and ESRD were 30, 34, and 55, respectively, for colesevelam HCl.
CONCLUSIONS: This analysis demonstrates the potential cost and clinical effectiveness of colesevelam HCl as an add-on therapy in patients with T2DM inadequately controlled on metformin-based therapy.
Presented at the American Diabetes Association 68th Scientific Sessions, San Francisco, CA, June 6–10, 2008.

268. Cost Savings Through the Implementation of Low-Flow Inhalation in General Anesthesia. *Stephanie N. Davis, Pharm.D.,*[1] Heidi Smith, Pharm.D.,[2] Lois Connolly, M.D.,[3] Harvey Woehlck, M.D.[3]; (1) Pharmacy Healthcare Solutions, Madison, WI; (2) Froedter Memorial Lutheran Hospital, Milwaukee, WI; (3) Medical College of Wisconsin, Milwaukee, WI
PURPOSE: This evaluation was to document cost savings achieved through use of low-flow anesthesia in procedures requiring general anesthesia with isoflurane, desflurane, and sevoflurane.
METHODS: Surgical records were retrospectively reviewed in July 2007 and March 2008 to evaluate the impact of measures taken to implement low-flow inhalational anesthesia with isoflurane, desflurane, or sevoflurane. A convenience sample of 10% of adult patients undergoing general anesthesia in each month was obtained, totaling 196 in July 2007 and 167 in March 2008, and carrier flow rates were obtained from the operative report. Purchase data, adjusted for total surgical cases and total surgical minutes, were compared for the quarters June through August 2007 and February through April 2008.
RESULTS: Data collected provided a representative sample of practicing anesthesiologists. Gas carrier flow rate goals for isoflurane and desflurane of less than 1.5 L/minute were achieved in 16 (30%) of 53 patients in July 2007 and 23 (59%) of 39 patients in March 2008 (p<0.005). The goal for sevoflurane, less than 2 L/minute, was achieved in 58 (40%) of 143 patients in July 2007 and in 84 (65.6%) of 128 patients in March 2008 (p<0.005). Anesthetic costs, adjusted to surgical cases performed and total surgical minutes, were reduced by 25%, and $140,000 in annual savings is projected.
CONCLUSIONS: Education and concurrent promotion of low-flow rates by anesthesiology staff were effective. Using low-flow anesthesia results in an overall cost reduction in anesthetic gases.

Regional Chapter Issues

269E. Expanding the Frontiers of ACCP Regional Chapter Membership: Northern California College of Clinical Pharmacy's Experience in 2007. *Tina Denetclaw, Pharm.D., BCPS,*[1] Katherine Yep, Pharm.D.,[2] Sharya Bourdet, Pharm.D., BCPS,[3] Jodi Bryner, Pharm.D.,[4] Scott Pollock, Pharm.D., B.S.,[5] Audrey Lee, Pharm.D., BCPS,[3] Cecily Allmon, Pharm.D.,[2] Wendy Sui, Pharm.D. Student,[6] Christine Bang, Pharm.D. Student,[6] Ellena Mar, Pharm.D. Student,[7] Helen Kim, Pharm.D. Student,[7] Stephanie Yoo, Pharm.D. Student,[7] Michelle Ho, Pharm.D. Student,[8] Allen Ho, Pharm.D. Student,[8] Joy Pimentel, Pharm.D. Student,[8] Yvonne Phan, Pharm.D. Student[8]; (1) Marin General Hospital, El Sobrante, CA; (2) California Pacific Medical Center, San Francisco, CA; (3) Veterans Medical Center, San Francisco, CA; (4) Kaiser Permanente, Walnut Creek, CA; (5) Johnson and Johnson, San Francisco, CA; (6) University of California, San Francisco, CA; (7) Touro University College of Pharmacy, Mare Island, CA; (8) University of the Pacific School of Pharmacy, Stockton, CA
PURPOSE: Increase hospital, ambulatory, community, and student pharmacist membership in the Northern California College of Clinical Pharmacy (NCCCP).
METHODS: In 2007, the NCCCP provided a 5-hour continuing education program on the care of heart attack and stroke patients for pharmacists across the spectrum of practice, including clinical pharmacists, hospital staff pharmacists, ambulatory pharmacists, and community pharmacists. Efforts to expand student membership activities are also described.
RESULTS: In progress.
CONCLUSIONS: In progress.
Presented at the ACCP 2008 Spring Forum.

Regional Chapter Report

270. Mid-South College of Clinical Pharmacy: Enhancing Clinical Pharmacy Practice for Our Members. *Joseph M. Swanson, Pharm.D., BCPS,*[1] Shannon W. Finks, Pharm.D., BCPS,[1] Amy H. Manguso, Pharm.D.,[2] Carrie S. Oliphant, Pharm.D., BCPS[3]; (1) University of Tennessee Health Science Center, Memphis, TN; (2) Baptist Memorial Healthcare – Memphis, Memphis, TN; (3) Methodist University Hospital, Memphis, TN

PURPOSE: The Mid-South College of Clinical Pharmacy (MSCCP) seeks to gather clinical pharmacists with common interests in practice, education, and research.
METHODS: The primary goals of MSCCP are to promote clinical pharmacy, provide a forum for opinions and perspectives of clinical pharmacists, and provide an advanced level of continuing education programs.
RESULTS: MSCCP is a regional chapter composed of 55 members whose practice encompasses the spectrum of clinical pharmacy. MSCCP offers multiple services designed to address the organization's primary goals. Continuing education remains the main component of activities. MSCCP encourages scholarly activity by offering a Travel Award that, each year, provides $500 to a member presenting original research at a national scientific or professional meeting. In 2007, funds were allocated to two student members for research presented at the American College of Clinical Pharmacy (ACCP) annual meeting. Members interested in board certification are supported through the Board of Pharmaceutical Specialties (BPS) Award. One $600 award is offered to any member who receives a passing score on a BPS examination in any of the recognized specialty practice areas. The MSCCP Excellence in Clinical Pharmacy Award is presented to a graduating pharmacy student who consistently demonstrates exemplary clinical skills during his or her fourth-year clerkships. The award is accompanied by a 1-year membership in ACCP and MSCCP. In 2008, MSCCP has focused on fundraising to support independent education events and to bring together members in a social setting. A wine-tasting fundraiser totaled $900 for future programs. Finally, the MSCCP Task Force on Anticoagulation was formed to bring together clinicians from Memphis area hospitals to share approaches to address the Joint Commission's National Patient Safety Goal on Anticoagulation. The task force has met numerous times and hosted nationally recognized experts in this area.
CONCLUSIONS: MSCCP offers regional services that enhance the overall ACCP experience.

RESIDENTS AND FELLOWS RESEARCH IN PROGRESS

Adult Medicine

271. Impact of a Pharmacist-Managed Renal Dosing Protocol in a 317-Bed Full-Service Tertiary and Acute Care Referral Center. *Kimball Owens, Pharm.D.*, C. Dustin Waters, Pharm.D., BCPS; Intermountain Healthcare, McKay-Dee Hospital Center, Ogden, UT
PURPOSE: To determine the impact of a pharmacist-managed renal dosing protocol on enoxaparin renal dosing guideline compliance rates at McKay-Dee Hospital Center. The impact of the protocol on financial savings for the hospital by the avoidance of excessive medication doses was also determined.
METHODS: The percentage of enoxaparin doses appropriately adjusted on the basis of renal function between October 1 and December 31, 2007 (preprotocol), and between February 1 and April 30, 2008 (postprotocol), was collected. Pre- and postprotocol compliance rates were compared. Cost avoidance was calculated by subtracting the drug acquisition cost of the adjusted regimen from that of the original regimen and multiplying by the number of days the adjusted regimen was received.
RESULTS: During the preprotocol period, enoxaparin therapy was prescribed for 155 patients (455 doses) with impaired renal function (creatinine clearance less than 30 mL/minute). A greater proportion of patients received enoxaparin for deep venous thrombosis (DVT) prophylaxis (83%). Preprotocol enoxaparin renal dosing compliance rates were 33% for all indications, 38% for DVT prophylaxis, and 10% when enoxaparin was used for treatment.
CONCLUSIONS: In the 3 months before implementation of a pharmacist-managed renal dosing protocol, 67% of all enoxaparin doses administered were not adjusted in patients with impaired renal function. Most enoxaparin prescribed was for DVT prophylaxis. Better compliance rates were observed when enoxaparin was given for this indication. Although a smaller percentage of doses were used for treatment, only 10% were adjusted in patients with renal impairment. Postprotocol compliance rates and cost-avoidance data will be presented.

Ambulatory Care

272. A1c Outcomes of Patients Switched from Rosiglitazone to Insulin. *Amol D. Joshi, Pharm.D.*, Thomas J. Worrall, Pharm.D., BCPS; Ralph H. Johnson VA Medical Center, Charleston, SC
PURPOSE: In fall 2006, this VA facility performed a medication use evaluation to determine if rosiglitazone was being appropriately prescribed. All patients receiving rosiglitazone with an A1c greater than 9% were switched to insulin because these patients were not likely to achieve an A1c less than 7% (American Diabetes Association [ADA] recommendation for A1c) on rosiglitazone therapy. This study assessed whether changing patients from rosiglitazone to insulin helped patients move toward and achieve their A1c goal.
METHODS: This was a retrospective evaluation of patients seen in primary care clinics between November 2005 and December 2007. To be included in the evaluation, patients needed to have an A1c measured at least 52 weeks before the conversion and 10–20 weeks after the conversion. Patients served as their own control group. Baseline A1c measurements before the switch were compared with those at the end of the study period to determine the mean change in A1c concentrations and the percentage of patients meeting the ADA A1C goal of less than 7%. A1c measurements were accepted for up to 1 year before the most recent A1c before the switch was used.
RESULTS: One hundred fifty-four patient charts were reviewed, and 16 patients met inclusion and exclusion criteria. The mean A1c dropped from an average of 11.3% before the switch to 9.3% after the switch (p=0.002, CI: 0.829–3.033). No patients were able to achieve the ADA A1c goal of less than 7% during the follow-up period.
CONCLUSIONS: This retrospective chart review demonstrates that 16 patients were able to achieve a lower mean A1c with insulin compared with rosiglitazone. Switching poorly controlled patients with A1c concentrations of more than 9% from rosiglitazone to insulin may be an effective method to reduce A1c concentrations and possibly the future incidence of microvascular complications.

Cardiovascular

273. Use of Heparin Levels Versus aPTT in Patients with Acute Coronary Syndrome. *Leslie A. Hamilton, Pharm.D.*, Julie B. Cooper, Pharm.D., BCPS; Moses H. Cone Health System, Greensboro, NC
PURPOSE: Anti-Xa heparin levels are the emerging standard for monitoring unfractionated heparin (UFH), historically monitored using activated partial thromboplastin time (aPTT). The purpose of this study was to evaluate outcomes associated with UFH therapy in high-risk patients with acute coronary syndrome (ACS), comparing therapy monitored with aPTT to therapy monitored with anti-Xa heparin levels.
METHODS: A retrospective chart review was conducted of all patients admitted to Moses Cone Memorial Hospital in Greensboro, NC, with high-risk ACS who received UFH between November 2006 and November 2007. The primary efficacy measure was the composite of all-cause mortality and nonfatal myocardial infarction (MI) at hospital discharge. The primary measures of safety included GUSTO severe bleeding and TIMI major and minor bleeding. Data were compared with reported 48-hour outcomes in the UFH arm of the Superior Yield of the New Strategy of Enoxaparin, Revascularization, and Glycoprotein IIb/IIIa Inhibitors (SYNERGY) trial. Noninferiority was defined using the primary efficacy measure, and the noninferiority margin was set at a risk difference of 4%.
RESULTS: UFH monitored by anti-Xa heparin levels was not inferior to heparin monitored by aPTT, with a nonsignificantly different event rate for the primary efficacy measure. UFH monitored by anti-Xa heparin levels was also associated with lower rates of bleeding.

	Moses Cone (n=185)	SYNERGY (n=4985)	Risk Difference (95% CI)	p for Noninferiority
	No. of patients (%)		Percent	
All-cause mortality or nonfatal MI	11 (5.9)	324 (6.5)	-0.6 (-4.0 to 2.9)	0.01
Bleeding:				
GUSTO severe	0 (0)	110 (2.2)	-2.2 (-2.6 to -1.8)	
TIMI major	0 (0)	379 (7.6)	-7.6 (-8.3 to -6.9)	
TIMI minor	19 (10.3)	613 (12.3)	-2.0 (-6.5 to 2.4)	

CONCLUSIONS: Outcomes for high-risk patients with ACS receiving heparin monitored by anti-Xa heparin levels are noninferior to heparin monitored by aPTT.

274. Effect of Hydrochlorothiazide on Endothelial Expression of Insulin Signaling Genes. *Julio D. Duarte, Pharm.D.,*[1] Issam Zineh, Pharm.D.[2]; (1) University of Florida College of Pharmacy, Gainesville, FL; (2) University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, FL

PURPOSE: Thiazide diuretics are one of the most commonly used classes of antihypertensive drugs in the United States. A growing body of evidence suggests that thiazide diuretics confer a risk of new-onset diabetes. Thiazide modulation of insulin signaling genes at the endothelial level may represent a mechanism of this untoward drug effect. We will test whether hydrochlorothiazide (HCTZ) alters the endothelial expression of insulin signaling pathway genes.

METHODS: Human umbilical vein endothelial cells (HUVECs) (Cambrex Corp., New York, NY) will be treated with HCTZ (50, 100, 200, 300, and 400 ng/mL) or control. Cytotoxicity studies will be performed, followed by 24-hour dose-ranging cell culture. Gene expression analysis will be performed using an RT-PCR (reverse transcriptase-polymerase chain reaction) array for genes involved in insulin signaling (SuperArray Bioscience Corp., Frederick, MD). Fold changes in expression in response to HCTZ will be calculated by the $2^{-\Delta\Delta Ct}$ method.

RESULTS: Data will be reported on gene expression changes for 84 genes functionally grouped as follows: insulin receptor-associated proteins; PI3 kinase pathway; MAPK pathway; target genes for PPAR-gamma and SREBP1; carbohydrate, lipid, and protein metabolism; cell growth and differentiation; and others. Because all funding and most supplies necessary to complete this experiment are already secured and investigators have experience with all methods mentioned above, it is extremely likely this study will be complete in time to present at the ACCP annual meeting.

CONCLUSIONS: If gene expression changes occur in response to HCTZ versus control, this study provides new insight into the mechanism of thiazide-induced diabetes.

Critical Care

275. An Evaluation of Time-to-Initation of Medication Admit Orders in Adverse Outcomes of Critically Ill Patients Boarded in the Emergency Eepartment. *Valerie A. San Luis, Pharm.D., BCPS*, Jill M. Hara, Pharm.D., BCPS; Huntington Memorial Hospital, Pasadena, CA

PURPOSE: Delayed transfer of an admitted patient because of hospital overcrowding, known as boarding, is an increasingly common practice in emergency departments (EDs). Boarding of critically ill patients has been associated with adverse outcomes. The purpose of this study was to determine if time to initation of medication admit orders is a significant determinant of adverse outcomes in this population.

METHODS: This is a retrospective, case-control study. Patients admitted to the intensive care unit (ICU) between August 2003 and July 2005 were identified through electronic databases and categorized as follows: delayed (ED boarding 2 hours or more) versus nondelayed (transferred to the ICU in less than 2 hours). The primary outcome is ICU length of stay (LOS). Secondary outcomes include ICU mortality and hospital LOS.

RESULTS: Data collection is ongoing. Eighty-four patients were identified on the basis of inclusion and exclusion criteria (delayed, n= 20; nondelayed, n=64). Demographics and acuity, assessed by Sequential Organ Failure Assessment, were not different. Among hospital survivors, ICU LOS was significantly higher in the nondelayed group (4.2 ± 6.1 vs. 2.3 ± 1.3 days; $p<0.05$). ICU mortality (delayed 15% [n=3] vs. nondelayed 4.7% [n=3], p=0.74) and hospital LOS (delayed 9.9 ± 16.6 vs. nondelayed 11.4 ± 11.5 days; p=0.74) were similar between groups. Differences in time to initiation (delayed 11.4.4 ± 122.8 vs. nondelayed 161.1 ± 212.3 minutes; p=0.27) and completion of medication admission orders (delayed 413.5 ± 366.5 vs. nondelayed 399.0 ± 323.2 minutes; p=0.89) were also similar.

CONCLUSIONS: Preliminary results suggest that time to the initiation of medication admit orders is not a significant determinant of adverse outcomes in boarded patients. However, the small sample size and low incidence of boarding at our institution must be considered. The identification of specific factors of adverse outcomes of boarded patients is difficult, and further investigation is needed.

276. Mortality and Management of Non-ICU Patients with Severe Sepsis. *Chris Tawwater, Pharm.D.*, Krystal K. Haase, Pharm.D.; Texas Tech University Health Science Center School of Pharmacy, Amarillo, TX

PURPOSE: In 2004, the Surviving Sepsis Campaign published evidence-based treatment bundles for acute resuscitation and management of patients with severe sepsis. To date, these interventions have focused solely on patients in the intensive care unit (ICU) and emergency department (ED) settings. Little is known about the treatment and outcomes for patients with severe sepsis who are initially admitted to the general ward setting. This study compared treatment outcomes and practice patterns in patients with severe sepsis initially admitted to a general ward (ward) versus ICU setting.

METHODS: This was a retrospective cohort analysis of 209 patients admitted to a tertiary medical center who developed severe sepsis. Subjects were identified using a validated ICD-9 search strategy for severe sepsis, and medical records were used to confirm the diagnosis of severe sepsis and evaluate treatment patterns and outcomes. The primary outcome, in-hospital mortality, was compared for ward versus ICU patients. Secondary outcomes included compliance with select components of 6-hour and 24-hour sepsis bundles and length of hospital and ICU stay.

RESULTS: At interim analysis, 122 subjects were screened, and 43 (33 ICU, 10 ward) met inclusion criteria. ICU subjects had more dysfunctional organ systems (1.8 vs. 1.1, p=0.028) and fewer DNR/DNI orders (3% vs. 30%, p=0.034). Mortality was lower than expected in ICU and ward patients (12.1% vs. 10%, p=NS). Overall bundle compliance was 4% for the 6-hour bundle and 68% for the 24-hour bundle. Component compliance was 62.7% for antibiotics within 1 hour, 28.6% for insulin therapy, 50% for steroid administration, and 33% for drotrecogin alfa administration. Complete results will be presented at the meeting.

CONCLUSIONS: Severe sepsis was not uncommon on the ward. Bundle compliance was suboptimal in both groups, including antibiotic selection and completion of the 6-hour bundle. Both ward and ICU patients may benefit from implementation of comprehensive sepsis protocols.

HIV/AIDS

277. AREMIND: A Personalized Cell Phone System to Remind for Adherence. *Elke S. Backman, Pharm.D.,*[1] Mari-Lynn Drainoni, Ph.D.,[2] Anela Stanic, Pharm.D.,[3] Vikram S. Kumar, M.D.,[4] Daniel Myung, AB,[4] Helene Hardy, Pharm.D., M.Sc.,[3] Paul R. Skolnik, M.D.,[3] Betsy L. Adams, R.N.[3]; (1) Boston Medical Center, 771 Albany Street, Boston, MA; (2) Boston University School of Public Health, Boston, MA; (3) Boston Medical Center, Boston, MA; (4) Dimagi Inc., Cambridge, MA

PURPOSE: The aim of this pilot study was to evaluate usability and message content for the ARemind prototype. ARemind is a personalized cell phone–based reminder system developed to motivate and track adherence to antiretroviral drug therapies in patients with HIV/AIDS.

METHODS: Eight subjects were recruited for key informant interviews. During the interviews, subjects were asked to discuss their interests in cell phone text message content and its utility as an adherence reminder. Key informant interview data were analyzed using standard qualitative analytic techniques.
RESULTS: Six men and two women participated in the study. The median age was 49. The participants were well educated (having some college education), except for one. All subjects reported that they rarely, if ever, missed doses of their HIV drugs. Reasons for missing doses included sleeping late, thinking they already took their dose, and being busy. Four of the participants reported regular use of pillboxes, and all felt confident they could continue to take their HIV drugs every day. Four subjects had their own cell phone, and three others had experience using a cell phone. Only two of the participants currently used cell phones for text messaging, and two indicated no interest in text messaging. Some subjects stated they would prefer a specific ring tone as a reminder rather than a content-based text message. A wide array of answers relating to the types of reminder messages they would like to receive was obtained.
CONCLUSIONS: Although some subjects did not appear to completely understand the utility of coded adherence reminder messages, most did after it was explained to them. Most subjects considered the cell phone a useful and confidential adherence reminder and favored a personalized text message.

Infectious Diseases

278. Susceptibility Profile of Vaginal Isolates of *Candida albicans* Before and Following Fluconazole Introduction—Impact of Two Decades. *Catharine C. Bulik, Pharm.D.,*[1] Jack D. Sobel, M.D.,[2] Michael D. Nailor, Pharm.D.[1]; (1) Detroit Receiving Hospital, Detroit, MI; (2) Division of Infectious Diseases, Wayne State University School of Medicine, Detroit, MI
PURPOSE: Current treatment options for uncomplicated vulvovaginal candidiasis caused by *Candida albicans* include over-the-counter antifungal agents and prescription fluconazole. Fluconazole has been used extensively for uncomplicated disease with an unknown impact on susceptibility. The purpose of this study was to investigate the susceptibility trends in clinical isolates of *C. albicans* from women presenting with vulvovaginitis. A secondary objective was to assess susceptibility trends in other antifungal agents.
METHODS: Unique single isolates from 1986 to 2008 were randomly selected from a clinical culture bank. Microdilution susceptibility was performed according to Clinical and Laboratory Standards Institute guidelines. Minimum inhibitory concentrations (MICs) of the isolates were determined for fluconazole, flucytosine, clotrimazole, miconazole, ketoconazole, itraconazole, amphotericin B, and voriconazole. The MIC_{90} (the MIC required to inhibit the growth of 90% of organisms) for each drug was then calculated for the periods (per) 1986–1989 (per1), 1992–1996 (per2), and 2005–2007 (per3).
RESULTS: A total of 250 isolates were included in the study: n=100 for per1, n=50 for per2, and n=100 for per3. The MIC_{90} (µg/mL) for fluconazole was 0.25, 0.5, and 0.5 for per1, per2, and per3, respectively. The corresponding MIC_{90} for flucytosine was 1, 2, and 8; for miconazole, 0.03, 0.03, and 0.03; for itraconazole, 0.03, 0.03, and 0.06; and for amphotericin B, 0.25, 0.125, and 0.5. The MIC_{90} for clotrimazole, voriconazole, and ketoconazole remained 0.03 across all periods. Of note, the percentage of isolates with MIC of 1 or more and 2 or more for fluconazole increased from 3% to 9% during the study period.
CONCLUSIONS: Although the *C. albicans* MIC_{90} to fluconazole in vaginal isolates has not increased significantly since 1986, there is an increasing number of isolates with elevated MICs. The implications of this increase are unknown, but given the breakpoint of fluconazole, reduced susceptibility may have clinical relevance.

279. Clinician Response to Positive Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surveillance Cultures in the Intensive Care Unit (ICU). Eyerusalem Yemane, Pharm.D.,[1] *Kristi Kuper, Pharm.D., BCPS*[2]; (1) Suburban Hospital, Bethesda, MD; (2) Cardinal Health CT&S, Houston, TX
PURPOSE: The objectives of this study were to determine the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization after admission to a community hospital intensive care unit (ICU), assess practitioner response to screening results, and quantify the frequency of systemic antibiotic use for the treatment of colonization.
METHODS: This was a retrospective study of patients admitted to a 24-bed ICU between August and October 2007. Electronic medical records of all patients with a positive MRSA nasal swab obtained within 48 hours of ICU admission were analyzed. Medical history, patient demographics, clinical indicators of infection, previous history of MRSA, and active antibiotic therapy were also documented.
RESULTS: MRSA nasal surveillance cultures were obtained in 462 patients. Rate of positivity was 13% (n=50). Of these patients, 48% (n=24) received intravenous vancomycin. Thirty-eight percent (n=9) of these patients had a documented MRSA infection and were excluded from the study. The remaining 62% (n=15) were classified as colonized yet received vancomycin. Thirteen of these patients had one or more clinical infection indicators but no documentation of active MRSA infection. Average vancomycin dose for this group was 1 g/day, and average duration of therapy was 6 days. There were two patients with no clinical infection indicators or documentation of infection; they were treated with vancomycin for a total of 13 days (combined).
CONCLUSIONS: Empiric vancomycin therapy may be appropriate for patients who are identified as MRSA colonized on admission to ICU and are at high risk of infection. However, opportunities exist to streamline vancomycin therapy once active infection has been ruled out in patients who are colonized with MRSA.

280. Use of Cytomegalovirus Intravenous Immune Globulin (CMV-IVIG) for the Treatment of Cytomegalovirus (CMV) in Hematopoietic Stem Cell Transplant (HSCT) Patients. *Bryan T. Alexander, Pharm.D.,*[1] Kristan M. Augustin, Pharm.D., BCOP,[1] Ed Casabar, Pharm.D., BCPS,[1] Lindsay M. Hladnik, Pharm.D., BCOP,[1] Peggy S. McKinnon, Pharm.D., BCPS,[1] Richard M. Reichley, R.Ph.,[1] David J. Ritchie, Pharm.D., FCCP, BCPS,[2] Peter Westervelt, M.D., Ph.D.,[3] Erik R. Dubberke, M.D.[3]; (1) Barnes-Jewish Hospital, St. Louis, MO; (2) Barnes-Jewish Hospital and St. Louis College of Pharmacy, St. Louis, MO; (3) Washington University School of Medicine, St. Louis, MO
PURPOSE: Studies supporting the use of adjunctive cytomegalovirus intravenous immune globulin (CMV-IVIG) in the treatment of CMV disease in hematopoietic stem cell transplant (HSCT) patients are needed. This study describes the characteristics and clinical outcomes of HSCT patients who received adjunctive CMV-IVIG for probable or proven CMV disease.
METHODS: A retrospective chart review of all adult HSCT patients receiving at least one dose of CMV-IVIG for the adjunctive treatment of clinically suspected or histologically proven CMV disease between January 1, 1999, and December 31, 2007, was conducted. All-cause mortality at hospital discharge was the primary outcome evaluated. Univariate analyses were conducted to determine patient characteristics associated with all-cause mortality.
RESULTS: Thirty-five patients met study criteria. All patients received an allogeneic HSCT. Twenty-six patients had pneumonitis (74%), 9 had enteritis (26%), and 29 had CMV viremia (83%). All patients received concomitant antiviral therapy; 31 (89%) received ganciclovir, and 14 (40%) received foscarnet (some received both). All-cause mortality at hospital discharge was 49%. Patient characteristics associated with mortality included requiring intubation for CMV pneumonia (79% of nonsurvivors vs. 29% of survivors; p=0.016) and earlier disease onset after HSCT (48 days for nonsurvivors vs. 108 days for survivors; p<0.001). CMV-IVIG was attributed with a low rate of adverse events, specifically mild hypertension (2.9%) and erythema/chills (2.9%).
CONCLUSIONS: The mortality rate in our population is similar to previous reports in the literature and is lower than rates reported with antiviral monotherapy. Preliminary analysis suggests that factors associated with mortality include the need for intubation

and earlier onset of CMV disease after HSCT. CMV-IVIG appears to be well tolerated in HSCT patients. These findings support further trials of CMV-IVIG efficacy in this setting.

281. Antibiotic Use in Critically Ill Patients Colonized with Multidrug Resistant Organisms. *William R. Vincent III, Pharm.D.,*[1] Craig A. Martin, Pharm.D.,[1] Aaron M. Cook, Pharm.D.,[1] Jeremy D. Flynn, Pharm.D.,[1] R. Scott Morehead, M.D.,[2] P. Shane Winstead, Pharm.D.[1]; (1) UK HealthCare, Pharmacy Services, University of Kentucky, Lexington, KY; (2) University of Kentucky College of Medicine, Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine, Lexington, KY

PURPOSE: The collection and analysis of antimicrobial consumption data are an important component of efforts to limit antimicrobial resistance. We measured antimicrobial use in critically ill patients to test the hypothesis that intensive care unit (ICU) patients colonized with multidrug-resistant organisms (MDROs) are exposed to more antibiotics than noncolonized critically ill patients.

METHODS: Retrospective review of antimicrobial computerized prescribing for ICU patients at a tertiary, 473-bed, academic medical center. MDRO colonization was identified using active surveillance cultures (ASCs), and a comparison was conducted of antimicrobial exposure expressed in days of therapy/1000 patient-days (DOT/1000 PD) between colonized patients and noncolonized patients. Correlation analysis examined the relationship between APACHE III score and antibiotic exposure.

RESULTS: During the study period, 134 critically ill patients had positive ASCs for MDROs. Of those, 109 MDRO(+) patients met inclusion criteria and were matched by APACHE III score quartiles to 109 MDRO(–) patients who were not infected or colonized with MDROs. Overall, measured antibiotic use in all patients (n=218) was 1420 DOT/1000 PD. Antibiotic use in MDRO(+) patients was 1538 DOT/1000 PD compared with 1135 DOT/1000 PD in MDRO(–) patients, p=0.009. Use of amikacin, colistimethate, daptomycin, meropenem, and tigecycline were all greater in MDRO(+) patients. MDRO(+) patients had longer median ICU (14 vs. 4 days, p<0.0001) and median hospital (27 vs. 10 days, p<0.0001) lengths of stay.

CONCLUSIONS: Antibiotic use was greater in ICU patients colonized with MDROs than in noncolonized critically ill patients matched for APACHE III. Patients colonized with MDROs should be further studied to better understand the causes of increased antibiotic exposure.

282. Assessment of Empiric and Directed Fluconazole and Caspofungin Usage Patterns in Patients with Candidemia. *Lisa A. Keller, Pharm.D.,*[1] Douglas Slain, Pharm.D., BCPS,[2] Maurice L. Moffett, Ph.D.,[2] Kimberly B. Blake, Pharm.D., M.B.A.[2]; (1) West Virginia University Hospitals/West Virginia University School of Pharmacy, Morgantown, WV; (2) West Virginia University School of Pharmacy, Morgantown, WV

PURPOSE: Fluconazole and caspofungin are antifungals recommended for the treatment of candidemia. Most cases of candidemia are caused by fluconazole-susceptible strains (minimum inhibitory concentration [MIC] less than16 µg/mL). *Candida* species with fluconazole MICs in the range of 16–32 µg/mL (susceptible-dose dependent [S-DD]) can complicate dosing and drug selection but may be successfully treated with higher doses of fluconazole. Caspofungin has a broader spectrum of activity against *Candida* species; however, it is considerably more expensive, and its use in the empiric window has not correlated with a survival benefit over fluconazole. The objectives of this study were to assess antifungal prescribing trends and evaluate antifungal treatment costs based on empiric and directed therapy.

METHODS: A retrospective study was performed of adult patients with candidemia from 2002 to 2008. Only patients treated with fluconazole and/or caspofungin were included in this study. Patients receiving antifungal prophylaxis were excluded. Key parameters assessed included choice and dose of antifungal, therapy changes, length of therapy, *Candida* species, susceptibility data, and cost of therapy. A cost-minimization analysis was performed to assess potential antifungal cost savings for alternative prescribing patterns.

RESULTS: Seventy-three cases of candidemia were evaluated; 50% of evaluated patients had *C. albicans* (fluconazole MIC 0.125–8 µg/mL), and 36% had *Candida glabrata* (fluconazole MIC 16–128 µg/mL or higher). Sixty percent of isolates were fluconazole sensitive, 30% were S-DD, and 10% were resistant. Twenty-two percent of patients had antifungal therapy changed based on susceptibility report. If patients had been treated in the empiric window with fluconazole rather than caspofungin, the average potential antifungal cost savings would have been $845.20–$1126.17 per patient. Pharmacoeconomic sensitivity analysis based on fluconazole susceptibility breakpoints will be presented at the meeting.

CONCLUSIONS: Empirically treating candidemic patients with fluconazole instead of caspofungin may result in a substantial drug cost savings.

283. Assessment of Imipenem-Cilastatin 500 mg q6h, Meropenem 500 mg q6h, and Meropenem 1000 mg q8 Hours in Adult Patients with Neutropenic Fever. *Heather M. Arnold, Pharm.D.,*[1] Peggy S. McKinnon, Pharm.D., BCPS,[1] Kristan M. Augustin, Pharm.D., BCOP,[1] Lindsay M. Hladnik, Pharm.D., BCOP,[1] Ed Casabar, Pharm.D., BCPS,[1] Richard M. Reichley, R.Ph.,[1] Erik R. Dubberke, M.D.,[2] Peter Westervelt, M.D., Ph.D.,[2] David J. Ritchie, Pharm.D., BCPS[3]; (1) Barnes-Jewish Hospital, St. Louis, MO; (2) Washington University School of Medicine, St. Louis, MO; (3) Barnes-Jewish Hospital and St. Louis College of Pharmacy, St. Louis, MO

PURPOSE: Meropenem exhibits time-dependent killing, supporting lower, more frequent dosing to obtain pharmacodynamic exposure similar to traditional regimens while decreasing drug dose and medication costs. Limited studies support alternatively dosed meropenem, even fewer of which address the oncology population. Therefore, the study goal was to compare clinical outcomes between adult neutropenic fever patients treated second line with imipenem-cilastatin (I/C), alternatively dosed meropenem (M500), and traditionally dosed meropenem (M1000) after failure or intolerance of cefepime.

METHODS: This retrospective, single-center, observational cohort study evaluated 128 patients: 40 patients treated with I/C from September 1, 2005, to August 31, 2006, and 88 patients treated with meropenem (M500 = 58, M1000 = 30) from September 1, 2006, to August 31, 2007.

RESULTS: Current analysis includes the I/C and M500 arms; evaluation of the M1000 arm is scheduled to be complete August 1, 2008. Primary outcomes including time to defervescence (median 3 vs. 3 days), need for additional antibiotics (20% vs. 12%), and time to addition of antibiotics (median 5 vs. 2 days) were not statistically different between the I/C and M500 groups, respectively. Differences in secondary outcomes including treatment duration (median 10 vs. 8 days), seizure incidence (0% vs. 0%), in-hospital mortality (3% vs. 7%), and 30-day mortality (8% vs. 7%) were not identified.

CONCLUSIONS: Alternatively dosed M500 is as safe and efficacious as I/C for the treatment of adult patients with neutropenic fever. Comparisons of M500 with M1000 are forthcoming.

Nephrology

284. Urinary Markers for Renal Damage in Patients Undergoing Cardiac Catheterization Receiving Contrast Dye. Paula Simoni, Pharm.D.,[1] Allen Cunningham, Pharm.D.,[2] Jan Simoni, D.V.M., Ph.D.,[3] Audie Kilpatrick, Pharm.D.,[2] Shalyn Cox, Pharm.D.,[2] *Charles F. Seifert, Pharm.D.*[1]; (1) TTUHSC School of Pharmacy, Lubbock, TX; (2) Covenant Health System, Lubbock, TX; (3) TTUHSC School of Medicine, Lubbock, TX

BACKGROUND: Although percutaneous coronary intervention (PCI) has improved clinical outcomes, the development of contrast induced nephropathy (CIN) is associated with increased morbidity and mortality in these patients. However, to date, no specific criteria exist to help determine the extent of CIN or possible preventive strategies.

PURPOSE: To determine which urinary marker can be the best predictor of CIN in PCI patients.
METHODS: Spot urine was collected in patients undergoing PCI at baseline, immediately post-PCI procedure, and every 6 hours until hospital discharge. Glomerular function was determined by measuring urinary protein. Tubular function was estimated by urine *N*-acetyl-β-D-glycosaminidase (NAG). Oxidative stress was measured by 8-iso $PGF_{2\alpha}$ urinary excretion. Vascular tone parameters were established by urine nitric oxide (NO) and endothelin-1 (ET-1). All tested parameters were corrected for urine creatinine.
RESULTS: To date, data have been collected on 25 patients (median age = 65, median integer score = 8.0). Median estimated glomerular filtration rate (GFR) was 72 mL/minute, ranging from 10 to 90. Baseline urinary protein correlated with estimated GFR (r = -0.47, p=0.0215), and baseline urinary protein correlated with baseline urinary NAG (r=0.63, p=0.0010). In this patient population, urinary protein measurement diagnosed glomerular dysfunction within 6 hours postcardiac catheterization, and NAG determined tubular damage after 30 hours. Whereas the level of 8-iso PGF2a increased significantly immediately postcardiac catheterization, the NO level remained low throughout the study. There were no marked changes in ET-1.
CONCLUSIONS: The results indicate that glomerular damage occurs in most patients receiving intravenous contrast, especially in those who had normal kidney function before the PCI procedure. Tubular damage occurred within 30 hours. A larger study population monitored for longer periods is necessary to determine if these urinary markers can predict CIN.

Oncology

285. Evaluation of Safety and Efficacy of Active Hexose Correlated Compound (AHCC) in Combination with Liposomal Doxorubicin. *Rodney J. Hunter, Pharm.D.,*[1] Jing Hong Chen, Ph.D.,[1] Hajime Fugii, Ph.D.,[2] Koji Wakame, Ph.D.,[2] Judith A. Smith, Pharm.D., FCCP, BCOP[1]; (1) The University of Texas, M.D. Anderson Cancer Center, Houston, TX; (2) Amino Up Chemical Company, Ltd., Sapporo, Japan
PURPOSE: This preclinical study was designed to evaluate the in vivo growth inhibition of active hexose correlated compound (AHCC) as a single agent and in combination with liposomal doxorubicin (Doxil) in a human ovarian cancer xenograft mouse model. In addition, the safety and tolerability of AHCC in combination with liposomal doxorubicin was evaluated.
METHODS: Six groups of 10 athymic nude mice were injected with 9×10^6 $SKOV_3IP1$ cells, and the treatment was initiated 10 days posttumor injection. The six groups included untreated control, intravenous vehicle–only control, oral lavage vehicle control, AHCC treatment, liposomal doxorubicin treatment, and AHCC plus liposomal doxorubicin treatment groups. The total weight (mg) and waist circumference (cm) were evaluated 3 times/week for 28 days posttreatment initiation. After the 28-day treatment period, the tumors were collected, weighed (mg), and frozen.
RESULTS: The combination of AHCC with liposomal doxorubicin showed a 64.1% reduction in tumor growth compared with the untreated animal subjects (p=0.03). The liposomal doxorubicin single-agent treatment group showed a 48.9% tumor reduction compared with the untreated group (p<0.05). The tumor reduction translates to a 31.2% improvement in liposomal doxorubicin activity when used in combination with AHCC. No toxicity or safety concerns were observed in the control or treatment groups during the study.
CONCLUSIONS: The combination of AHCC and liposomal doxorubicin improved the growth inhibitory activity compared with liposomal doxorubicin single agent. All treatment arms and control arms tolerated treatment, and no major adverse drug effects were observed. Exploratory studies to confirm the mechanism of additive tumor reduction with AHCC are ongoing.

286. Evaluating Patient Characteristics Associated with Sunitinib Adverse Events Requiring Dosing Modification. *James Hart, Pharm.D.*, Brad J. Atkinson, Pharm.D., Tam Bui, Pharm.D., Lianchun Xiao, M.S., Eric Jonasch, M.D.; The University of Texas M. D. Anderson Cancer Center, Houston, TX
PURPOSE: A first-line option for the treatment of advanced renal cell carcinoma (mRCC), sunitinib demonstrated improved progression-free survival and response rates compared with interferon-α in its phase III registration trial. Although better tolerated overall, patients receiving sunitinib experienced more adverse effects (AEs) of all grades with the U.S. Food and Drug Administration–approved fixed oral dose of 50 mg daily for 4 weeks of a 6-week cycle. These common AEs often lead to dose interruptions and/or dose reductions. There are no formal recommendations for the management of sunitinib-related AEs, including dose adjustments. Potential patient characteristics that may predispose to these AEs have also not yet been reported in the literature.
Objectives: The objectives of this study were to (1) identify specifically those sunitinib-related AEs that require dose modification and (2) identify patient characteristics that may predispose to sunitinib-related AEs.
METHODS: A total of 220 clear cell mRCC patients evaluated at our institution from January 2006 to February 2007 have been queried from pharmacy records for retrospective review. Patient characteristics including demographics, medical history, tumor specifics, laboratory data, and treatment history are all being assessed as potential predisposing factors. Univariate and multivariate logistic regression are being used for the primary analysis.
RESULTS: More than half (56%) of the initial 100 patients reviewed experienced a sunitinib-related AE requiring a dose modification. Of note, 86% of these AEs occurred within the first three treatment cycles. Fatigue, mucositis, hand-foot syndrome, and nausea/ vomiting were the most common AEs experienced. Initial statistical analysis has failed to detect any significant differences in patient characteristics between those who experienced an AE and those who did not.
CONCLUSIONS: Initial results reveal a considerable number of patients started on the standard 50-mg dosing regimen require dose modification early within their treatment course. Final data collection and statistical analysis are ongoing.

Pharmacogenomics/Pharmacogenetics

287. Utilization of UGT1A1 Testing Before Irinotecan Dosing and Administration. *Ebtesam Ahmed, Pharm.D.*; UCSF Medical Center, San Francisco, CA
PURPOSE: The primary end point was to determine the current state of UGT1A1 testing before irinotecan administration among National Cancer Institute (NCI)-designated cancer centers. In addition, this study determined the current barriers and current strategies to implementing such testing.
METHODS: Using the NCI's comprehensive list of nationwide oncology centers, colorectal oncologists were identified. A questionnaire was developed and distributed using online electronic survey software through e-mails. The e-mail contained a brief introduction that defined the purpose of the questionnaire, and the questions focused on the familiarity and use of UGT1A1 testing in each colorectal oncology practice. Surveys were sent to 63 cancer centers in the United States between February 25, 2008, and April 7, 2008. All data were collected and analyzed anonymously; SAS v. 9.1 software (SAS Institute, Cary, NC) was used to analyze the results. Descriptive summary statistics and Fisher's exact tests were performed.
RESULTS: A total of 100 surveys were sent to 63 cancer centers, and 29% (18 of 63) of the centers responded. Only two (11%) respondents reported testing for UGT1A1, and neither required informed consent. In addition, physicians from private institutions were mostly familiar with UGT1A1 testing (3 [50.0%]); however, one respondent (5.5%) reported that he/she was unfamiliar with the testing. Our study revealed that the main barriers for not using UGT1A1 testing in clinical practice appeared to be availability (11 [68.75%]), unclear utility (13 [81.25%]), and impracticality (10 [62.5%]), respectively.

CONCLUSIONS: Despite the U.S. Food and Drug Administration modification of the manufacturer's prescribing information for irinotecan to include testing for UGT1A1, our study showed that UGT1A1 testing is not currently being used in clinical practice. This highlights the need for research studies to elucidate some of the barriers shown in our study. Pharmacogenetic testing for UGT1A1 would potentially predict the risk of adverse effects from irinotecan therapy and would help improve patient outcomes and reduce health care costs.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

288. Determination of Minimum Effective Dose and Optimal Dosing Schedule for Liposomal Curcumin in a Mouse Model of Pancreatic Cancer. *Claire M. Mach, Pharm.D.,*[1] Lata Mathew, M.S.,[1] Scott A. Mosley, B.S.,[1] Lawrence Helson, M.D.,[2] Razelle Kurzrock, M.D.,[1] Judith A. Smith, Pharm.D., BCOP, FCCP, FISOPP[1]; (1) University of Texas M.D. Anderson Cancer Center, Houston, TX; (2) SignPath, New York, NY

PURPOSE: Curcumin is a food chemical present in turmeric (*Curcuma longa*) that has pharmacological activity to suppress carcinogenesis and inhibits multiple signaling pathways such as NF-κB, COX-2, and interleukin 8 (IL-8). Oral curcumin has poor oral bioavailability, limiting its clinical activity; however, a patented liposomal formulation of curcumin was developed to improve drug delivery and has demonstrated activity in multiple cancers. This study was designed to determine the minimum effective dose (MED) as well as the optimal dosing schedule of liposomal curumin in a mouse xenograft model of human pancreatic cancer.

METHODS: The MED determination and optimal schedule were evaluated in female athymic nude mice injected with MIA PaCa-2 cells. Dosing was initiated at an average tumor size of 5 mm. For the MED, mice were treated with the following doses of liposomal curcumin: no treatment, liposome only, and 1, 2, 5, 10, 20, and 40 mg/kg given by tail vein injection 3 times/week. For the optimum dosing schedule, three additional schedules were evaluated and compared with the control of 3 times/week: once daily, every 4 days, and once weekly. All mice were weighed, and tumor measurements were taken 3 times/week to evaluate toxicity and efficacy.

RESULTS: The 20-mg/kg dose had the greatest decrease in tumor growth at a 52% decrease in tumor growth compared with no treatment control mice. MED was determined to be 20 mg/kg and was used for the optimal dosing schedule determination, for which results are pending. This dose was well tolerated.

CONCLUSIONS: The MED for liposomal curcumin is 20 mg/kg. Optimal dosing schedule results are pending.

Public Health

289. National Survey of Pharmacy Services in Free Medical Clinics. *Ann M. Wiesner, Pharm.D.,*[1] Douglas T. Steinke, Ph.D.,[2] William R. Vincent III, Pharm.D.,[1] Kenneth E. Record, Pharm.D.,[2] Kelly M. Smith, Pharm.D.[2]; (1) University of Kentucky HealthCare, Lexington, KY; (2) University of Kentucky College of Pharmacy, Lexington, KY

PURPOSE: Free medical clinics provide local health services to the poor and uninsured. Pharmacy services are a major component of health care, yet the role of pharmacists and medication provision in the free clinic setting is unclear. Research objectives were to characterize the contemporary model of pharmacy services in free medical clinics; identify the extent to which free clinics serve as training sites for pharmacy students and residents; elucidate specific pharmacy service gaps in free clinics; and compare results with previous surveys.

METHODS: Clinics registered in the Free Clinic Foundation Directory (www.freeclinicfoundation.org) were included in this voluntary, pilot-tested, institutional review board–approved survey. The 26-point questionnaire addressed clinic and pharmacy demographics; pharmacy services; medication storage and distribution process; and systems management. Survey invitations were extended by means of postal mail, with responses submitted either by hard copy (self-addressed, stamped envelope) or the Internet (Survey Monkey). Nonresponders were sent a second mailing 4 weeks later. Survey results were analyzed using descriptive statistics and bivariate analysis.

RESULTS: Forty-one percent (214 of 519) of clinics responded. The median annual clinic budget was $145,000, with 1–20% spent on medications. Thirty percent of clinics had a licensed pharmacy, staffed on average by 3.4 pharmacist volunteers and 0.1 pharmacist employees. Of the 83% (174 of 212) that dispensed drugs, 53 prescriptions per day were filled, with cardiovascular, gastrointestinal, and anti-infective agents as top classes. Pharmacy personnel provided mainly traditional services (62.1%), and 20% of clinics reported training pharmacy students. Compared with previous data, the number of free clinics (355 vs. 519) and prescriptions dispensed (29 vs. 53/day) has increased, but the percentage of clinics with a licensed pharmacy (33% vs. 30%) and average number of pharmacist volunteers/employees (3.8/0.1 vs. 3.4/0.1) have remained relatively constant.

CONCLUSIONS: Preliminary data reveal that the current model of free clinic pharmacy services is a modified community practice.

Transplant/Immunology

290. Early Detection of Persistent Post Kidney Transplant Anemia. *Whitney Y. Hung, Pharm.D.,*[1] Shelby L. Corman, Pharm.D., BCPS,[1] Kristine Schonder, Pharm.D.[2]; (1) University of Pittsburgh Medical Center, Pittsburgh, PA; (2) University of Pittsburgh, Pittsburgh, PA

PURPOSE: Anemia after kidney transplantation is expected to resolve within 2–6 months; however, 30–40% of patients will have persistent anemia. Posttransplantation anemia (PTA) may increase the risk of cardiovascular events and is associated with worsening graft function. The use of erythropoiesis-stimulating agents (ESAs) immediately after transplant is controversial because of the lack of clinical evidence, safety concerns, and high cost of these agents. The early identification of patients at risk of persistent PTA could aid in the selection of patients most appropriate for ESA therapy.

METHODS: This retrospective, case-cohort study included patients who received kidney transplants at the University of Pittsburgh Medical Center between January 1, 2002, and June 30, 2007, who did not receive ESAs within 2 months posttransplant. Deidentified data were collected from inpatient and outpatient electronic medical records. Patients with persistent PTA, defined as hemoglobin less than 11 g/dL 2 months posttransplant, were identified. The characteristics of these patients will be compared with those without persistent PTA using univariate and multivariate analysis to determine which demographic and clinical characteristics, if present in the first week posttransplant, are predictors of persistent PTA.

RESULTS: A total of 417 kidney transplant patients were identified for inclusion. Of these patients, 208 (50.1%) had PTA at posttransplant day 7, and 51 (12.2%) remained anemic at 2 months posttransplant. Significant predictors of persistent PTA will be reported.

CONCLUSIONS: Only 12% of patients have persistent PTA at 2 months posttransplant. It is expected that this project will identify predictors of persistent PTA that can be identified within 1 week after kidney transplant. Identifying these factors will help clinicians determine the patients most likely to benefit from ESA therapy.

STUDENT SUBMISSIONS

ADR/Drug Interactions

291. Irreversible Atorvastatin-Induced Hearing Loss: A Case Report. *Cheuk H. Liu, Pharm.D. Candidate,*[1] Antonia Alafris, B.S., Pharm.D., CGP,[2] Anthony J. Longo, B.S., Pharm.D.,[3] Henry Cohen, M.S., Pharm.D., FCCM, BCPP, CGP[4]; (1) Arnold & Marie Schwartz College of Pharmacy and Health Sciences of Long Island University, Brooklyn, NY; (2) Kingsbrook Jewish Medical Center, Arnold & Marie Schwartz College of Pharmacy and Health Sciences of Long

Island University, Brooklyn, NY; (3) Astellas Pharma US, Lynbrook, NY; (4) Arnold & Marie Schwartz College of Pharmacy and Health Sciences of Long Island University and Kingsbrook Jewish Medical Center, Brooklyn, NY

PURPOSE: Drug-induced auditory ototoxicity is a potentially irreversible adverse event associated with loop diuretics, aminoglycosides, macrolide antibiotics, and platinum-based chemotherapies. A MEDLINE search from 1950 to present revealed no case reports of statin-induced ototoxicity. The manufacturer of atorvastatin has reported three cases of deafness (0.1%) in unpublished clinical trials. However, none were thought to be associated with atorvastatin. We report a case of a patient developing hearing loss after initiating atorvastatin.

METHODS: A 32-year-old man was started on atorvastatin 20 mg every night. Six months later, he complained of occasional transient tinnitus lasting 5–10 minutes, which resolved spontaneously. An audiogram was performed, and it was normal. Fourteen months later, the tinnitus became continuous, and the following month, an audiogram revealed "cookie-bite" bilateral hearing loss. The patient could hear low- and high- but not mid-frequency sounds. Liver function was normal. Atorvastatin was discontinued, and the patient was fitted with hearing aids. Presently, the hearing loss has not progressed. Application of the Naranjo's nomogram yields a score of 6/10, indicating *probable* atorvastatin-induced ototoxicity.

RESULTS: Drug-induced auditory ototoxicity manifests as tinnitus, or hearing loss. Cookie-bite hearing loss is sensorineural, characterized by a downward slope in an audiogram affecting mid-, but not low- and high-frequency, sounds. Most common causes of sensorineural hearing loss include presbycusis and medications. Currently, there are no published case reports of statin-associated ototoxicity. The manufacturer has received spontaneous reports of deafness, but a causal relationship could not be established. Our patient experienced hearing loss that progressed for 13 months, however, which did not worsen on discontinuation of atorvastatin.

CONCLUSIONS: For patients taking atorvastatin, it is prudent to monitor for tinnitus as a sign of ototoxicity. An annual hearing test with a physical examination should be performed. Further research is needed to elucidate possible atorvastatin-induced ototoxicity.

Cardiovascular

292. Deferasirox Attenuates Iron-Induced Oxidative Stress and Prevents Cardiotoxicity in the Iron-Overloaded Gerbil. *Rabaa M. Al-Rousan, B.S.Pharm., M.S.*,[1] Satyanarayana Paturi, BVSC,[2] Joseph P. Laurino, Ph.D.,[3] Anil K. Gutta, BVSC,[2] Ravi Kumar Arvapalli, BVSC,[2] Sunil K. Kakarla, M.S.,[1] Devashish H. Desai, M.S.,[1] Ernest M. Walker, Ph.D.,[4] Eric R. Blough, Ph.D.[5]; (1) Department of Pharmacology, Physiology and Toxicology, School of Medicine, Marshall University, Huntington, WV; (2) Department of Biological Sciences, School of Medicine, Marshall University, Huntington, WV; (3) Department of Chemistry, University of Tampa, Tampa, FL; (4) Department of Pathology, School of Medicine, Marshall University, Huntington, WV; (5) Department of Biological Sciences, School of Medicine & Cell Differentiation and Development Center, Marshall University, Huntington, WV

PURPOSE: Iron overload arises from a sustained excess of iron supply over iron requirement and causes serious cellular and tissue damage through its ability to promote oxidative stress. Cardiac failure is a major, life-threatening complication of iron overload and is the leading cause of death in patients with thalassemia major. We investigated whether deferasirox was capable of effectively removing excess iron from heart and other tissues while reversing or reducing the severity of iron-induced cardiovascular alterations.

METHODS: Gerbils were divided into control, iron-overloaded, and deferasirox-treated groups. Iron dextran was injected at 100 mg/kg intraperitoneally/5 days for 10 weeks. Treatment groups received deferasirox 100 mg/kg/day orally. Cardiac and hepatic iron contents were determined by inductively coupled plasma atomic emission spectrometry. Pearls iron staining was performed to examine iron deposition in the corresponding tissues. Immunoblotting analysis was used to examine intracellular protein oxidation and the expression and activation of signaling molecules, which were previously shown to be affected by oxidative stress in response to iron overload.

RESULTS: Deferasirox treatment for 3 months resulted in a 23.5 and 43.5% decrease in cardiac and hepatic iron levels, respectively ($p<0.05$). These results were consistent with the decrease in cellular iron deposition observed after histologic iron staining. Deferasirox significantly decreased protein oxidation in cardiac tissue. Similarly, deferasirox tends to decrease expression and phosphorylation levels of multiple indices of oxidative stress in cardiac myocytes including p38-, JNK-, and ERK1/2-MAPK.

CONCLUSIONS: Taken together, these results suggest that deferasirox is useful for protecting the heart against iron-induced pathogenesis.

293. Assessment of Amiodarone Monitoring in Accordance with North American Society of Pacing and Electrophysiology (NASPE) Guidelines at the Veterans Affairs Medical Center, Memphis. *Sarah E. Mizne, B.A.*, Shannon W. Finks, Pharm.D., Kelly C. Rogers, Pharm.D.; University of Tennessee College of Pharmacy, Memphis, TN

PURPOSE: Amiodarone is commonly used for atrial and ventricular arrhythmias. Adverse effects occur in up to 50% of patients on long-term therapy. Pulmonary toxicity occurs in 1–17% of patients and requires immediate discontinuation of the drug. Monitoring criteria based on North American Society of Pacing and Electrophysiology (NASPE) guidelines should be followed in patients initiated on amiodarone. At the VA Medical Center, computerized clinical reminders to monitor baseline and follow-up parameters are in place. Whether these recommendations are being followed is worthy of study with regard to quality patient care.

METHODS: Patients prescribed oral amiodarone from January 1, 2006, to December 31, 2006, were identified. Demographic data, baseline and follow-up laboratory data, indication, comorbid conditions, concomitant medications, adverse events, and hospitalizations were recorded.

RESULTS: Fifty-seven patients were identified. Thirty-nine (68.4%) had atrial arrhythmias, 15 (26.3%) had ventricular, and 3 (5.3%) had both. Appropriate baseline laboratory test values were completed as follows:

Baseline (n=57) Test	Adherence (%)
Liver function tests (LFTs)	5 (9)
Thyroid	41 (72)
Ophthalmologic	14 (25)
Chest x-ray (CXR)	40 (70)
PFTs with DLCO	7 (12)

DLCO = diffusion capacity of carbon monoxide; PFTs = pulmonary function tests.

Follow-up LFT and thyroid assessment included only patients (n=36) receiving amiodarone for more than 6 months and were appropriate in 21 (58%) and 10 (28%), respectively. Follow-up eye examinations and CXR included patients (n=29) on amiodarone more than 12 months and were appropriate in 12 (41%) and 14 (48%), respectively. Before initiation, 32 (56%) patients had heart failure, 41 (72%) had coronary artery disease, 49 (86%) had hypertension, 5 (88%) had thyroid dysfunction, and 14 (25%) had chronic obstructive pulmonary disease. Thirty-eight (67%) were concomitantly receiving simvastatin, of which 14 (25%) were taking greater than the recommended maximum dose of 20 mg/day. Additional analyses will include adverse events and all-cause hospitalizations.

CONCLUSIONS: Baseline and follow-up monitoring are not consistently being performed for patients initiated on oral amiodarone despite computerized clinical reminders. Current procedures for starting amiodarone should be evaluated, and new strategies should be implemented to increase monitoring in accordance with NASPE guidelines.

294. Deferasirox Attenuates Age-Associated Increases in Cardiac and Hepatic Iron Accumulation and Improves Blood Glucose Regulation. *Ravi kumar Arvapalli, B.V.Sc.*,[1] Rabaa M. Al-Rousan,

B.S.Pharm., M.S.,[2] Joseph P. Laurino, Ph.D.,[2] Sunil K. Kakarla, M.S.,[2] Anjaiah Katta, M.S.,[2] Satyanarayana Paturi, M.S.,[1] Anil K. Gutta, M.S.,[1] Lucy Dornon, B.S.,[3] Kevin M. Rice, M.S.,[2] Ernest M. Walker, Ph.D.,[4] Eric R. Blough, Ph.D.[2]; (1) Department of Biological Sciences, Marshall University, Huntington, WV; (2) Department of Pharmacology, Physiology and Toxicology, School of Medicine, Marshall University, Huntington, WV; (3) Department of Cardiology, School of Medicine, Huntington, WV; (4) Department of Pathology, School of Medicine, Marshall University, Huntington, WV

PURPOSE: Cardiovascular disease is the leading cause of death in people older than 65, and the identification of an agent(s) able to diminish the incidence would be extremely valuable. Recent studies have demonstrated that aging in humans and rats is associated with marked iron accumulation. We hypothesized that chronic deferasirox administration would be associated with decreases in age-associated iron accumulation and indices of tissue reactive oxygen species and that these changes would, in turn, be associated with the attenuation of age-associated cardiovascular dysfunction.
METHODS: Twenty-seven-month-old male F344xBN rats were divided into two groups (control and deferasirox treated [100 mg/kg/day, oral]) and followed for 6 months. Cardiac and hepatic iron contents were determined by inductively coupled plasma atomic emission spectrometry. Using Western blot analysis, changes were followed in activity of anti- and pro-apoptotic proteins including Bcl-2, Bad, and Caspase-12.
RESULTS: Deferasirox treatment for 6 months resulted in a 37 and 56% decrease in cardiac and hepatic iron levels, respectively ($p<0.05$). These results were consistent with the decrease in cellular iron deposition observed after histologic iron staining. In addition, TUNEL staining of heart sections detected a profound decrease in TUNEL-positive nuclei in 33-month–treated rats compared with age-matched controls. All these alterations are in correlation with regulation of Bcl-2, Bad, and Caspase-12 with treatment. Defersirox-treated rats showed an 11.3% increase in expression of Bcl-2 and a 45.0 and 49.0% decrease in expression of Bad and Caspase-12, respectively, compared with control rats.
CONCLUSIONS: These data suggest that chronic deferasirox treatment is useful for cardioprotection against iron overload. The protective role may be through counteracting against apoptotic mechanisms associated with iron overload.

295. Statins and Diuretic Response in Heart Failure Patients. *Apra Jain, Student*, Sheryl L. Chow, Pharm.D., BCPS; Western University of Health Sciences, Pomona, CA

PURPOSE: Several studies have examined the use of statins and their effect on the progression of renal disease independent of their lipid-lowering effect. Pleiotropic effects on vasodilatory prostaglandins may provide additional beneficial effects in the kidney as a mechanism to improve diuretic resistance.
METHODS: Medical records were obtained and reviewed for 3500 patients admitted in Centinela hospital between January 1, 2006, and July 19, 2007, and 1500 patients receiving a loop diuretic, statin, and aspirin were identified. Patients with heart failure were included for analysis if they were at least 18 years old at the time of admission, had serum creatinine of less than 2.0 mg/dL, daily urine output, actual body weight, statin initiated during hospitalization, and availability of daily serum creatinine. The baseline mean fluid balance and mean diuretic doses were compared with values after statin therapy.
RESULTS: Nine patients (mean age 59 years; 56% women, 44% men; mean EF 24%) were evaluated on the basis of current inclusion criteria and time course of statin use. Atorvastatin (67%) or simvastatin (33%) was initiated during hospitalization in addition to furosemide therapy (100%). Average baseline serum creatinine was 1.2 mg/dL. Pairwise comparisons showed no significant difference in urine output between the prestatin versus poststatin groups (-761.5 vs. -802.7 mL/day, p=0.914); however, the average doses of intravenous furosemide demonstrated a nonsignificant trend toward dose reduction during statin therapy (95.6 vs. 55.6 mg/day, p=0.067), respectively.
CONCLUSIONS: Statins do not appear to improve short-term diuresis in patients with heart failure receiving loop diuretics; however, further studies with larger sample sizes are warranted.

Critical Care

296. Evaluation of Bleeding Events in Surgical Patients Receiving Recombinant Human Activated Protein C. *Brittany L. Warrick, Pharm.D. Candidate,*[1] Rachel C. Stratman, Pharm.D.,[2] Aaron M. Cook, Pharm.D.,[3] P. Shane Winstead, Pharm.D.[4]; (1) University of Kentucky College of Pharmacy, Lexington, KY; (2) UK HealthCare, Lexington, KY; (3) University of Kentucky HealthCare, Lexington, KY; (4) UK HealthCare, Pharmacy Services, University of Kentucky, Lexington, KY

PURPOSE: Recombinant human activated protein C (rhAPC) has been associated with bleeding complications because of its antithrombotic and profibrinolytic effects, particularly in high-risk patients. The purpose of this project was to define the rate of bleeding complications with rhAPC therapy at our institution.
METHODS: We conducted a retrospective analysis of surgical patients receiving rhAPC from January 2003 to October 2007.We defined surgical patients as those who had undergone a surgical procedure during the same hospital admission as the infusion of rhAPC. Bleeding complications were assessed by evidence of serious bleeding events including receipt of 3 or more units of packed red blood cells on 2 or more consecutive days, early discontinuation of rhAPC, and the documented presence of excessive blood loss. Bleeding events were assessed during the infusion and the postinfusion period of rhAPC. Statistical analysis was performed by a χ^2.
RESULTS: On interim analysis, 23 charts have been completed of the 69 charts that were identified. Bleeding events during the infusion were encountered by 34.8% (8 of 23) of the patients, with 30.4% (7 of 23) encountering a bleeding event that led to early discontinuation of the infusion. Bleeding events during the postinfusion period were encountered by 8 (34.8%) of 23 patients. Of these patients, 73.9% (17 of 23) underwent an emergency surgical procedure.
CONCLUSIONS: The final results of this trial will report bleeding complications in surgical patients and identify characteristics of patients who experience bleeding events.

297. Venous Thromboembolism Risk Assessment and Prophylaxis in the Surgical Intensive Care Unit. *Ann Marie B. Prazak, M.S.*, Steven E. Pass, Pharm.D., FCCM, BCPS; University of Houston College of Pharmacy, Houston, TX

PURPOSE: This study documented the use of a venous thromboembolism (VTE) risk assessment and anticoagulation dosing protocol based on American College of Chest Physicians (ACCP) consensus guidelines. The objective was to assess the proportion of patients who received proper VTE prophylaxis based on their risk assessment in the surgical intensive care unit of a private teaching hospital participating in the Surgical Care Improvement Project.
METHODS: We performed an initial assessment of the use of VTE prophylaxis during a 4-week period in August 2007 in our unit based on a draft of a new DVT prophylaxis order set. The order set was approved and implemented together with a concentrated staff educational initiative in September 2007. A second assessment was performed during a 4-week period in January–February 2008 to assess the compliance with the new order set.
RESULTS: A preliminary evaluation of the VTE order set indicated that about 39% of patients (10 of 26) received the appropriate prophylactic therapy based on our institution's protocol. Four months postimplementation, almost 77% of patients (49 of 64) were receiving the appropriate prophylactic therapy for their risk level. In addition, 48 of the 64 patients were assigned to the highest risk category, of which 79% were ordered the proper prophylactic regimen.
CONCLUSIONS: Implementation and use of a deep venous thrombosis prophylaxis protocol significantly improved the number of patients who received proper therapy based on their risk assessment. The order set will be updated to reflect the 2008 ACCP

evidence-based consensus guidelines, additional staff education will be provided, and a 1-year assessment will be performed in September 2008. Finally, the updated protocol will satisfy the Joint Commission's National Patient Safety Goal 3E for reducing patient harm from anticoagulation therapy.

Drug Information

298. Adapting the Formulary Decision-making Process to Evaluate an Evidence-Based Medicine Database for Use in a College of Pharmacy. *Kathryn M. Ruf, Pharm.D. Candidate*, Kelly M. Smith, Pharm.D., BCPS, FASHP; University of Kentucky College of Pharmacy, Lexington, KY

PURPOSE: Institutions today often are faced with a plethora of competing drug information resources coupled with limited funds for subscriptions; thus, a process is needed to evaluate drug databases for potential subscription. The structured approach to evaluating drug products for use in a clinical setting commonly used by Pharmacy and Therapeutics (P&T) Committees was adapted to evaluate an evidence-based medicine database (EBMD) for use at a college of pharmacy.

METHODS: *Natural Standard* was considered for adoption and use throughout the curriculum in a college of pharmacy. A monograph was developed to describe the key features of the database as well as its comparisons with other available references. Indications for drug use were noted as potential uses of the resource. Efficacy for each indication was examined using position statements from key organizations (e.g., Medical Library Association) as a foundation. Safety was evaluated by examining the quality of cited references and frequency of updates. Cost was then compared with other databases currently available throughout the institution and with other, similar resources.

RESULTS: The monograph was presented to the Curriculum Committee, akin to the P&T Committee, to make a "formulary" decision, together with creating a strategy to evaluate the new database's use. A pharmacy student led this initiative, and in the process, she expanded both her drug information and formulary evaluation process experience.

CONCLUSIONS: By implementing a structured evaluation modeled on the formulary evaluation process, an EBMD can be effectively considered for subscription and integration into a college of pharmacy's curriculum.

Education/Training

299. Clinical and Translational Pharmacogenomics: Integrating a Seminar Program with Undergraduate Pharmacogenomics Research. *Elizabeth L. Sanders, Pharm.D. (2011),*[1] Qing Ma, Ph.D.,[1] Daniel A. Brazeau, Ph.D.,[1] Gene D. Morse, Pharm.D., FCCP, BCPS[2]; (1) University at Buffalo, Buffalo, NY; (2) University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY

PURPOSE: Clinical and translational pharmacogenomics is a rapidly expanding field that is at the interface of genomics, proteomics, and biomedical research. To facilitate access to faculty conducting research in this field, a seminar series was developed to introduce undergraduates to clinical and translational pharmacogenomics, encourage participation in pharmacogenomics research, and assess the acceptance of the novel course format and material.

METHODS: The seminar series was composed of presentations by faculty in their specialty fields summarizing the current status and promoting discussion about pharmacogenomic research. A weekly evaluation survey was obtained for feedback and attendance. The participants were also encouraged to work with faculty members to design and implement pharmacogenomic research projects.

RESULTS: Twenty-one students from different departments (n=7) including pharmacy, pharmaceutical sciences, pharmacology and toxicology, chemistry, medicinal chemistry, biomedical sciences, and psychology enrolled. The faculty members (n=10) involved in the seminar program represented seven departments: Pharmacy, Pharmaceutical Sciences, Medicine, Pediatrics, Cell and Molecular Biology, Psychiatry, and Neurology. Five students (24%) are currently conducting pharmacogenomics research. A student survey indicated that, on average, 92% of participants felt the seminars provided new knowledge, 90% felt the lectures made them want to learn more, 91% found the lectures interesting and informational, and 83% reported that the lectures inspired them to explore further research opportunities. Ten of the 14 seminars had 86% or greater attendance through the course. One of the research projects conducted by a student received an award for excellence in undergraduate research.

CONCLUSIONS: The integration of a seminar program and translational pharmacogenomics research has proved to be a valuable mechanism for exposing undergraduates to this field and has promoted interest in seeking out projects as well as faculty members who can serve as potential mentors.

Endocrinology

300. Safety of Zoledronic Acid in the Management of Osteoporosis. *Meaghan L. Fox, Pre-Med,*[1] Michael P. Kane, Pharm.D.,[2] Robert S. Busch, M.D.,[3] Gary Bakst, M.D.,[3] Jill M. Abelseth, M.D.[3]; (1) Northeastern University, Boston, MA; (2) Albany College of Pharmacy, Albany, NY; (3) The Endocrine Group, LLP, Albany, NY

PURPOSE: Zoledronic acid (ZA) was approved for the once-yearly treatment of postmenopausal osteoporosis in August 2007. The purpose of this report was to evaluate the safety of ZA in osteoporosis patients of an ambulatory care practice. Drug efficacy will be assessed later.

METHODS: This retrospective review was approved by the Albany College of Pharmacy Investigational Review Board. Review of the electronic medical records of three private-practice endocrinologists was conducted to identify osteoporosis patients treated with ZA. All patients received therapy at the infusion center of a local hospital per hospital protocol. The protocol calls for pretreatment with 650 mg of acetaminophen and 5 mg of ZA to be diluted into 100 cc of normal saline and infused over 30 minutes. Drug safety was evaluated by review of documented reports of side effects and by patient telephone interview.

RESULTS: Review of electronic medical records identified 176 patients who discussed once-yearly ZA therapy with their physicians. As of June 12, 2008, 59 patients had received therapy. Patient demographics included the following: average age 69 ± 13 (range 46–92) years, 86.4% women, and 93.2% white. Eleven (18.6%) of 59 patients reported postinfusion adverse events, including flu-like symptoms (11.9%, n=7), bone and muscle pain (5.1%, n=3), and headache (1.7%, n=1). New-onset atrial fibrillation and osteonecrosis of the jaw were not reported after a mean 154 ± 71 (range 13–283) days of follow-up. Flu-like and musculoskeletal symptoms occurred in 25% (5 of 20) of patients who were bisphosphonate naïve, 15.4% (6 of 39) of patients with previous oral bisphosphonate exposure, and 0% of patients (n=6) who received previous intravenous bisphosphonate therapy (p=0.33).

CONCLUSIONS: Overall, the use of ZA was well tolerated in this osteoporotic ambulatory care practice. Postinfusion flu-like and musculoskeletal adverse effects occurred with similar frequencies in patients with or without previous bisphosphonate exposure.

301. Evaluation of Glycemic Control in Cardiac Patients with Admission Hyperglycemia. *Catherine A. Goulding, H.B.Sc., B.Sc.Phm., ACPR*, Jenny Chiu, B.Sc.Phm., ACPR, Dave Hallett, M.Sc., Lisa Burry, Pharm.D., Holly Leung, B.Sc.Phm., Doret Cheng, Pharm.D.; Mount Sinai Hospital, Toronto, ON, Canada

PURPOSE: About 40% of patients with diabetes mellitus will develop an acute coronary syndrome (ACS) and/or heart failure (HF). Evidence demonstrates that blood glucose of 11.1 mmol/L or more during an acute illness is a marker for poor clinical outcome. On admission to hospital, 50% of those with diabetes and 30% with no history of diabetes present with hyperglycemia, which can lead to a cycle of poor control and worsening of the acute illness, contributing to increased health care costs. The objective of this study was to determine if glycemic control was achieved in cardiology patients with admission hyperglycemia.

METHODS: This retrospective study included all patients admitted in the cardiology ward at Mount Sinai Hospital during a 9-month period, with an admission random blood glucose of 10.0 mmol/L or greater, fasting blood glucose of 8.0 mmol/L or greater, and/or hemoglobin A1c more than 7% and glucometer readings ordered at least twice daily.
RESULTS: Seventy-eight patients met inclusion criteria (mean age 71 years; 67% men), all with a previous diagnosis of diabetes. Target glycemic control (daily weighted mean glucometer readings between 4 and 7 mmol/L) was achieved in 45% of patients. An average of 2.4 days was required to achieve any blood glucose reading between 4 and 7 mmol/L. Patients had a hyperglycemic episode (fasting blood glucose more than 11.1 mmol/L) for a greater percentage of time (48%) during their hospital stay. Most patients did not have orders for hemoglobin A1c (97.4%). Despite patients presenting with hyperglycemia on admission, blood glucose control was not assessed in patients without a previous diagnosis of diabetes because glucometer readings were not ordered.
CONCLUSIONS: Glycemic control was achieved in less than one-half of cardiology patients presenting with hyperglycemia on admission. Efforts should be made to identify patients with hyperglycemia and improve glycemic control in all hyperglycemic patients admitted with ACS and/or HF, regardless of previous diagnosis of diabetes.

Infectious Diseases

302. Risk Factors and Clinical Features of Urinary Tract Infections in Solid Organ Transplant Recipients: A Retrospective Cohort Study. *Elyn Choa Tan, Pharm.D. Candidate,*[1] Rosemary Cross, Pharm.D., BCPS,[2] Vanthida Huang, Pharm.D., BSPHM[1]; (1) Department of Pharmacy Practice, Mercer University College of Pharmacy and Health Sciences, Atlanta, GA; (2) Piedmont Hospital, Atlanta, GA
PURPOSE: Although urinary tract infections (UTIs) are among the most common infectious complication in solid organ transplant recipients, few studies have formally evaluated the clinical characteristics and outcomes of UTIs in this population. This study aimed to assess the epidemiology and outcomes of UTIs in a large cohort of solid organ transplant recipients.
METHODS: We conducted a retrospective cohort study of 500 consecutive patients who underwent kidney, liver, pancreas, kidney-liver, or kidney-pancreas transplantation from 2005 to 2007 to assess posttransplant UTIs occurring within 1 year after transplant. Univariate odds ratios were determined, and multivariate logistic regression was performed to identify independent risk factors. Clinical and microbiologic characteristics of all patients treated for UTI were reviewed.
Preliminary RESULTS: A total of 50 patients of 180 patients studied to date developed one or more UTIs up to 1 year posttransplantation. This represented 27.8% of all transplant recipients and included 31 (27.4%) of 113 kidney recipients, 13 (27.7%) of 47 liver recipients, 1 (50.0%) of 2 pancreas recipients, 3 (30.0%) of 10 kidney-liver recipients, and 2 (25.0%) of 8 kidney-pancreas recipients. Twenty-two patients had recurrent posttransplant UTIs. A total of 86 UTIs were diagnosed, of which 57 (66.3%) were diagnosed within 6 months after transplantation. Twenty-three (26.7%) were fungal infections, 30 (34.9%) were gram-positive infections, and 33 (38.4%) were gram-negative infections. Resistance rates to trimethoprim-sulfamethoxazole were 43.3 and 51.5% for gram-positive and gram-negative infections, respectively. Four (13.3%) of 30 gram-positive infections were resistant to vancomycin, whereas 8 (24.2%) of 33 gram-negative infections were resistant to levofloxacin.
CONCLUSIONS: Thus far, we found that 28% of transplant recipients developed UTIs posttransplantation, most of which were from kidney recipients within 6 months of transplantation. A large percentage of the gram-positive and gram-negative infections were resistant to trimethoprim-sulfamethoxazole. This study will provide a basis for the development of optimal strategies for preventing and managing UTIs in solid organ transplant recipients.

303. Impact of the Ica Operon on Biofilm Formation and Antibiotic Susceptibility in *Staphylococcus aureus* (SA) and *epidermidis* (SE). *Peter Poppens, Pharm.D. Candidate,*[1] Ryan M. Knier, B.S.,[1] Steven C. Ebert, Pharm.D.,[1] Richard A. Proctor, M.D.,[2] Warren E. Rose, Pharm.D.[1]; (1) University of Wisconsin School of Pharmacy, Madison, WI; (2) Univerisity of Wisconsin Department of Medicine, Department of Microbiology and Immunology, Madison, WI
PURPOSE: The high prevalence of staphylococcal biofilm colonization and infection on indwelling medical devices is a significant health care burden. The intracellular adhesion locus (ica) is a known gene regulator involved in staphylococcal biofilm formation; however, its relationship to antibiotic susceptibility and treatment outcome is unknown. This study investigated the impact of a positive ica gene locus on biofilm formation and antibiotic susceptibility of *Staphylococcus aureus* (SA) and *S. epidermidis* (SE) isolates from catheter-related bloodstream infections.
METHODS: Twenty-five staphylococci from infected catheters were analyzed. Minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) were determined for vancomycin, rifampin, and daptomycin by microbroth dilution. The presence of the *icaA* and *icaD* genes was determined by polymerase chain reaction and gel electrophoresis. Biofilm formation was evaluated by an adherent plate assay with crystal violet staining and Congo red agar detection.
RESULTS: Of the 25 isolates 16 were SE,and 9 were SA. The susceptibility of planktonic bacteria is shown in the Table.[a]

	Vancomcyin	Rifampin	Daptomycin
S. epidermidis			
MIC50	2	< 0.03	0.125
MIC90	2	< 0.03	0.125
MBC range	0.5–16	< 0.03–2	0.063–1
S. aureus			
MIC50	1	< 0.03	0.25
MIC90	1	< 0.03	0.25
MBC range	1–8	< 0.03–0.25	0.125–0.5

[a]Data are expressed in milligrams per liter.

No resistance to any agent was found. Molecular analysis showed that 87.5% of SE contained icaA, 75% icaD, and 75% icaA/D. One-half of these strains were high biofilm producers. All SA isolates produced high levels of biofilm. Slime production with the Congo red assay correlated to biofilm quantification in the adherent plate assay in 92% of strains tested.
CONCLUSIONS: Overall, SE exhibited greater tolerance than vancomycin, whereas rifampin and daptomycin susceptibility was comparable in SA and SE. In SE, icaA/D was present in a large number of strains but did not always correlate with biofilm production. Further research will be conducted with ica in SA biofilm production and susceptibility.

304. MRSA Colonization and Infection: A Molecular and Susceptibility Analysis. *Suhani K. Patel, Pharm.D. Candidate,*[1] Warren E. Rose, Pharm.D.,[1] Ryan M. Knier, B.S.,[1] Cybele Abad, M.D.,[2] Linda McKinley, R.N.,[2] Nasia Safdar, M.D.[3]; (1) University of Wisconsin School of Pharmacy, Madison, WI; (2) University of Wisconsin Hospital and Clinics, Madison, WI; (3) University of WIsconsin School of Medicine, Madison, WI
PURPOSE: Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization of the nares is a reservoir for initial and relapsing infections. The purpose of this study was to evaluate the molecular epidemiology and antibiotic susceptibility of the colonizing and corresponding infecting strains from the VA Medical Center in Madison, WI (UW VA).
METHODS: Twenty MRSA strains from the UW VA were evaluated. MRSA minimum inhibitory concentrations (MICs) were determined

by broth microdilution. Inducible resistance to clindamycin was determined by a D-test diffusion assay. Isolate molecular identification of SCCmec type was determined by polymerase chain reaction with gel electrophoresis. The agr function was evaluated by a qualitative delta hemolysin assay.
RESULTS: The susceptibility results are listed in the Table.[a]

	Mupirocin	Vancomycin	Daptomycin
% susceptible	85	100	100
MIC50	0.5	1	0.125
MIC90	32	1	0.5
MIC range	0.5–256	0.5–2	0.125–0.5

[a]Results are given in milligrams per liter.

The mupirocin minimum bacterial concentration (MBC) was 16 or greater in 70% of isolates, including those with an MIC less than 0.5. Isolates with vancomycin MBCs of 32 or more most often had a corresponding MIC greater than 1. Inducible clindamycin resistance was positive in 40% of the isolates. SCCmec II was detected in 90% of the study isolates, whereas the remaining isolates were mec IV. The agr function was negative in 20% of the isolates, which is consistent with our epidemiologic data.
CONCLUSIONS: At concentrations used for topical application, mupirocin will likely maintain bactericidal activity, even in the select isolates with low- to high-level resistance (15% MIC of 8 or more) in our study. Although no resistance to vancomycin was shown, the high MBCs in some strains warrant further evaluation of its impact on treatment. Hospital-associated MRSAs corresponding to SCCmec II are the most prevalent in colonized and infected VA patients; however, SCCmec IV (community-associated MRSA [CA-MRSA]) should also be considered. As CA-MRSA increases in most health care institutions, this pathogen will be more and more of concern.

305. Guideline Adherence of Antimicrobial Prescribing Patterns for Lower Respiratory Tract Infections and Local Resistance Pattern Correlation. *Heather Barnes, Pharm.D. Candidate*, Lauren Stansky, Pharm.D. Candidate, Scott E. Kincaid, Pharm.D.; South University School of Pharmacy, Savannah, GA
PURPOSE: The purpose of this research was to analyze the antimicrobial prescribing patterns for lower respiratory infections among physicians in the Savannah, GA, area. These patterns will be used to determine the adherence to community-acquired pneumonia (CAP) guidelines and the hospital acquired/ventilator-associated and health care–associated pneumonia (HAP/VAP and HCAP) guidelines published in 2007 and 2005, respectively, by the American Thoracic Society and the Infectious Diseases Society of America. In addition, these patterns will be analyzed to check for correlation with local levels of resistance seen on antibiograms from local health systems.
METHODS: A 10-question survey was distributed to all physicians in the Savannah-Chatham County area. The survey included seven questions regarding HAP, VAP, and HCAP and three questions regarding CAP. Question topics included perceived risk factors, common pathogens, and empiric therapy options for each type of pneumonia. On return of the survey, results will be compared with national guidelines to determine adherence and analyzed in comparison with local antibiograms to correlate resistance.
RESULTS: The results of this research will be presented at the ACCP annual meeting.
CONCLUSIONS: The discussion of this research will be presented at the ACCP annual meeting.

306. Staphylococcal spp. Biofilm Formation in the Presence of Heparin or Tissue Plasminogen Activator (tPA). *Kevin W. McConeghy, Student,*[1] Carol Moore, Pharm.D.,[2] Kerry L. Laplante, Pharm.D.[1]; (1) University of Rhode Island and Veterans Affairs Medical Center, Providence, RI; (2) Henry Ford Hospital, Detroit, MI
PURPOSE: Heparin or tissue plasminogen activator (tPA) is often added to catheters to prevent clotting. Heparin enhances *Staphylococcus aureus* biofilm mass at concentrations of 1000 U/mL or less. It is unknown if increased concentrations of heparin, tPA, or diluents such as bacteriostatic water (0.9% benzyl alcohol) affect biofilm mass. We investigated heparin across a range of concentrations, tPA, and bacteriostatic water in the formation of biofilm.
METHODS: Biofilm-producing strains of *S. aureus* (ATCC 35556) and *S. epidermidis* (ATCC 35984), and a biofilm-nonforming *S. epidermidis* control (ATCC 12228) were evaluated against heparin (10,000–100 units/mL) and tPA (alteplase 1 mg/mL) alone and in combination with bacteriostatic water (benzyl alcohol 0.9%) Quantification of biofilm mass was conducted using the Christensen colorimetric microtiter plate assay (optical density 570). Minimum inhibitory and bactericidal concentrations (MICs, MBCs) were determined using the broth microdilution assay. The assays were run in quadruplicate, results were averaged, and SDs were calculated.
RESULTS: MICs and MBCs for benzyl alcohol were 0.45% for all isolates except *S. epidermidis* ATCC 35984, which had an MBC of 1.8%. Heparin concentrations of 5–10,000 units/mL inhibited biofilm mass, *S. epidermidis* (38% reduction). Alteplase inhibited biofilm mass (average 92% ± 10% reduction from growth control) for all isolates.
CONCLUSIONS: Heparin (5–10,000 units/mL) with 0.9% benzyl alcohol was inhibitory to tested isolates of *S. aureus*. However, *S. epidermidis* strains may not be inhibited by benzyl alcohol at these concentrations. Of interest, alteplase has merit to be evaluated as an alternative in preventing staphylococcus biofilm mass in catheter locks.

308. Levofloxacin: A Retrospective Evaluation of Indication and Dosage in Urinary Tract Infections. *Kevin W. McConeghy, Pharm.D. Candidate*, Mark A. Curtis, R.Ph., Jim J. Melfi, R.Ph., Pharm.D., Ph.D.; Roger Williams Medical Center, Providence, RI
PURPOSE: Levofloxacin is a common medication used in the inpatient setting to treat urinary tract infections (UTIs). National guidelines exist for levofloxacin treatment in UTIs. We performed a retrospective evaluation of levofloxacin therapy to determine opportunities for quality improvement.
METHODS: A retrospective chart review was performed by conducting a hospital-wide search of our 220-bed tertiary care center's electronic medical records (Meditech, Cambridge, MA, v. 5.5) for any adult patients who received a dose of levofloxacin from October 2007 to May 2008. Patients were screened for UTI using the International Classification of Diseases coding system (ICD) and medical chart review. Patients were classified as complicated with any of the following: indwelling urinary catheter, male, pregnant, renal failure, prostate hyperplasia, or any urinary obstruction by ICD code. Evaluation of dose adjustment was based on the package insert.
RESULTS: The search yielded 21 patients with an uncomplicated UTI and 9 patients (43%) who received a dose of levofloxacin 250 mg once daily for 3 days. The remaining patients received extended therapy (average 5 ± 1 day) and/or were administered 500 mg. Thirty-eight patients were identified with a complicated UTI, and 11 received a dose of 500 mg for 10–14 days. Twenty-six patients received 250 mg, were dosed for less than 10 days of therapy, or were inappropriately renally adjusted.
CONCLUSIONS: Some patients with an uncomplicated UTI received doses for more than 3 days or more than 250 mg. Prescribers may benefit from education on the recommendations for treating an uncomplicated versus complicated UTI. Patients with a reduced creatinine clearance and complicated UTI could benefit from renal adjustment, and education could focus on appropriate dosing in this population and maintaining 10–14 days of therapy. Otherwise, inappropriate use of these antimicrobials could lead to increased resistance and more serious infections, making these antimicrobials ineffective for future use.

Intravenous Compatibility and Particulate Matter

309. Intravenous Infusion Combinations and Particulate Matter. *Kate Conway, Pharm.D. Candidate*, Jimmi Hatton, Pharm.D., FCCP, FCCM, Aaron M. Cook, Pharm.D., BCPS; University of Kentucky, Lexington, KY

PURPOSE: USP 788 specifies that all parenteral preparations must be free of visible particles (more than 50 µm) and have limited numbers of subvisible particles to avoid clinical complications from intravenous particulate matter. These guidelines are applicable to singular intravenous preparations. However, many patients, particularly those who are critically ill, require combinations of drugs that often are coinfused through the same intravenous catheter. The precise interaction of coinfused medications and the occurrence of particulate matter under these conditions are unknown. The purpose of this study was to identify the most common drugs that occur in combination in the intensive care units (ICUs) of our academic medical center.
METHODS: Medical records of adult ICU patients admitted to an academic medical center were reviewed to identify the most common combinations of medications. This was done retrospectively by identifying the medications given to the patient and determining which ones were being administered in the same line.
RESULTS: All of the patients studied (n=50) were in an ICU at an academic medical center. Numerous combinations of medications were infused through the same intravenous catheter. The most common medications coinfused were midazolam, morphine, norepinephrine, phenylephrine, insulin, and vasopressin. Full data analysis is ongoing and will be presented.
CONCLUSIONS: This study describes combinations of intravenous medications often coinfused in ICU patients. It is the first step in investigating the combination of intravenous medications in critically ill individuals and the effect on intravenous particulate matter when these commonly used medications are coinfused.

Medication Safety

310. Predictors of Vancomycin Dosage Adjustment in Hospitalized Type-II Diabetic Patients. Cyrus Yazdani, M.S.,[1] *Arthur T. Shelton, Pharm.D. Candidate,*[2] Nancy Hanna, Pharm.D.,[1] Roger Bentler, B.S.[1]; (1) John C. Lincoln North Mountain Hospital, Phoenix, AZ; (2) Midwestern University College of Pharmacy – Glendale, Phoenix, AZ
PURPOSE: This retrospective study was designed to determine whether patient demographics, laboratory data, or oral antidiabetic therapy was associated with vancomycin dosage adjustments after the initiation of therapy in hospitalized patients with type 2 diabetes.
METHODS: Existing medical records from two acute care facilities were used for the analysis. Patients admitted between March 1, 2007, and February 1, 2008, who received vancomycin for a duration exceeding 24 hours and underwent pharmacokinetic monitoring while receiving oral antidiabetic agents during the same admission were eligible for inclusion. Information on the number of doses and duration of vancomycin treatment was collected as well as demographic information and medication and laboratory data. Dosage change was defined as an alteration to the total daily dose of vancomycin after the measurement of vancomycin serum trough concentration. Stepwise ordered logistic regression was used to determine variables for multivariate analysis, and multinomial logit model was used to examine the association between independent variables and probability of vancomycin dosage increase or decrease.
RESULTS: From 152 patients who met the inclusion criteria, 46 (30.26%) had their dose increased, and 21 (13.82%) had their dose reduced. Dosage adjustment was performed on an average of 4.72 (±2.74) doses after the initiation of therapy. Age was associated with dosage reduction after adjusting for other variables (relative risk ratio = 1.92, p=0.050). Patients in one institution were more likely to have their dose increased (relative risk ratio = 2.70, p=0.019), indicating a more conservative approach to dosing. No statistically significant association between oral antidiabetic agents and probability of dosage adjustment was observed.
CONCLUSIONS: The results suggest that elderly patients with type 2 diabetes should be treated more cautiously when receiving vancomycin because they are at higher risk of experiencing elevated serum trough concentrations, even after adjusting for renal function.

Oncology

311. Preliminary Evaluation of Patient-Reported Outcomes Among Patients Treated for Cancer-Related Pain at a Multidisciplinary Symptom Management Clinic. *Jennifer L. Hendricks, Pharm.D. Candidate,*[1] Jane Pruemer, Pharm.D., BCOP, FASHP,[1] Kyra Whitmer, R.N., Ph.D.,[2] Linda McCaig, R.N., CNP,[2] Cheryl Wilhelm, R.N., CNP,[2] Jennifer Hester, R.N., DPN[2]; (1) University of Cincinnati, James L. Winkle College of Pharmacy, Cincinnati, OH; (2) The University Hospital-Health Alliance of Greater Cincinnati, Cincinnati, OH
PURPOSE: This study examined quality-of-life (QOL) and subjective pain scores in patients treated for cancer-related pain in a multidisciplinary symptom management clinic (SMC).
METHODS: Medical records of all patients treated at the SMC between February 2005 and March 2008 were reviewed. Thirty-four patients who had completed at least three QOL questionnaires were included in the study. Patients completed the Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire and rated their current pain, best pain in 24 hours, and worst pain in 24 hours on an 11-point Likert scale during their admission visit and again at 6 months or on discharge from the clinic.
RESULTS: There was a statistically significant difference between the baseline and final FACT-G scores in all domains except for social/family well-being. The mean change in the FACT-G composite score from baseline to final visit was 10.6 (95% CI: 4.9–16.3, p=0.001). The mean changes in FACT-G Physical, Emotional, and Functional Domain Scores were 3.0, 2.6, and 4.5, respectively, and all of these changes were statistically significant (p<0.01). There was no statistically significant difference in current or "best in 24 hours" pain scores between baseline and final assessments, but there was a statistically significant decrease in "worst in 24 hours" pain scores of 1.1 points (p=0.009) on the 11-point scale. There was no statistically significant difference in the number of patients who had a positive QOL response in any of the studied demographic categories (sex, cancer diagnosis, or race).
CONCLUSIONS: Based on this preliminary study, QOL is a more sensitive outcome measure than pain scores in this population. Routine measurement of QOL has the potential to improve care and should be incorporated into clinical oncology practice. The relationship of QOL measures with subjective pain scores and the utility of QOL measurement in clinical practice need to be further evaluated in future trials.

312. Psychological Distress as a Negative Factor for the Survival of Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. (Encore, presented at the International Congress of The Pharmaceutical Society of Korea, Jeju, Korea, May 1–3, 2008.) Ji Eun Park, M.S.,[1] *Tae Kyung Kim, B.S.,*[1] In Ja Son, Ph.D.,[2] JungMi Oh, Pharm.D.[1]; (1) College of Pharmacy, Seoul National University, Seoul, South Korea; (2) Department of Pharmacy, Seoul National University Hospital, Seoul, South Korea
PURPOSE: The objective of this study was to evaluate the influence of distress history before stem cell transplant (SCT) on mortality and morbidity and to predict the possible risk factors on the survival of patients undergoing allogeneic SCT for hematologic malignancies.
METHODS: We performed a retrospective case-control study of patients who underwent the allogeneic SCT in the Seoul National University Hospital in Korea from January 2000 to August 2007. Primary outcome was the overall survival, and secondary outcomes were the days to recover (defined as absolute neutrophil count more than 500/mL), hospital length of stay, and rate and total daily dosage of opioids until the hematologic recovery after allogeneic SCT.
RESULTS: A total of 20 patients and 57 control subjects were evaluated. Low-risk disease included acute leukemia in first complete remission, early myelodysplastic syndrome (refractory anemia or refractory anemia with ringed sideroblast), and chronic myeloid leukemia in first chronic phase. High-risk disease included all other malignancies. The high-risk group was defined as the patients with high-risk disease. The factors associated with survival in univariate analysis were high-risk group (hazard ratio [HR] 3.19;

95% CI: 1.63–6.25), umbilical cord blood stem cells (HR 18.64; 95% CI: 2.04–170.56), total body irradiation (TBI)-containing conditioning regimen (HR 0.14; 95% CI: 0.06–0.39), and higher educational background (HR 0.40; 95% CI: 0.17–0.92). Risk factors for survival in multivariate analysis were high-risk group (HR 3.92; 95% CI: 1.84–8.36) and TBI-containing conditioning regimen (HR 3.50; 95% CI: 0.17–0.92). History of psychological distress significantly hastened death in first year of transplantation (HR 3.05; 95% CI: 1.45–6.23).
CONCLUSIONS: The present study has demonstrated that the history of distress before allogeneic SCT is an important risk factor on the survival of patients undergoing SCT for hematologic malignancies.

313. Evaluation of the Educational Interventions on Medical Team Compliance with NCCN Myeloid Growth Factor Guidelines. *Aimee Hammerstrom, B.S.,*[1] Jaffar Syed, B.S.,[1] Rodney Hunter, Pharm.D.,[2] Diane C. Bodurka, M.D.,[2] Shiney Kurian, APN,[2] Charlotte Sun, Dr.PH.,[2] Mark Munsell, M.S.,[2] Charles Levenback, M.D.,[2] Judith A. Smith, Pharm.D., BCOP, FCCP, FISOPP[2]; (1) University of Houston College of Pharmacy, Houston, TX; (2) University of Texas M.D. Anderson Cancer Center, Houston, TX
PURPOSE: Chemotherapy-induced neutropenia (CIN) is often responsible for treatment delays and dose reductions in cancer patients receiving chemotherapy, potentially compromising treatment outcomes. The primary objective was to determine the current practice pattern use of granulocyte colony stimulating factors (GCSF) and establish if evidence-based educational interventions supported by practice of the National Comprehensive Cancer Network (NCCN) guidelines influenced change in practice in the Gynecology Oncology Center at M.D. Anderson Cancer Center (UTMDACC).
METHODS: The study included all patients receiving chemotherapy for the treatment of a gynecologic malignancy at UTMDACC. There were four phases to this study. First, the observation phase evaluated the current use of GCSF and the incidence of events including CIN and febrile neutropenia (FN). The educational phase provided a series of written, live, and online educational tools based on the updated NCCN guidelines, followed by two assessment phases, an initial and 6-month assessment, to determine the immediate impact and durability of educational interventions.
RESULTS: A total of 217 patient visits were included in the observational phase (OP) and 225 in the initial assessment phase (first AP). The overall incidence of neutropenia, anemia, and thrombocytopenia in patients receiving chemotherapy in the gynecologic setting during the OP were 13.1, 9.2, and 0.4%, respectively. During the first AP, the incidence of neutropenia and anemia decreased to 11.1 and 5.2%, respectively. However, no significant difference (21.6% vs. 20%) in the use of GCSF was observed. Evaluation of GCSF use based on guidelines after the educational intervention phase is still being evaluated. The incidence of FN and treatment delays decreased from 2.8 and 5% in the OP to 0.8 and 4% in first AP, respectively. No change in dose reductions was observed.
CONCLUSIONS: Preliminary results suggest intensive educational interventions benefited, decreasing the incidence of CIN and FN. A 6-month assessment and statistical analysis are ongoing.

Pain Management/Analgesia

314. Evaluation of Pain Medication Prescribing Practices in an Outpatient Clinic. *Laura A. Prather, Pharm.D.,*[1] Patricia Wigle, Pharm.D.,[2] Jeff J. Guo, Ph.D.[2]; (1) University of Cincinnati, Cincinnati, OH; (2) University of Cincinnati, 304 Wherry Hall, Cincinnati, OH
PURPOSE: The long-term use of opioids in the treatment of chronic nonmalignant pain is not well defined. The goal of this evaluation was to assess the policies and prescribing practices related to opioids in a primary care clinic to assist in the development of policies and procedures that would lead to more standardized prescribing and handling of these medications in the clinic to optimize patient outcomes.
METHODS: Retrospective chart review was performed on adult patients (n=47) being treated with opioids for chronic pain of a nonmalignant origin at University Family Physicians at Forest Park clinic. Patients were included if they were older than 18 years and had been treated in the past year with at least one opioid; patients were excluded if their pain diagnosis was related to a malignant disease. Study outcomes included organ function monitoring, use of urine drug screens and pain contracts, assessment of pain severity and efficacy of treatment interventions, early refill requests, and subsequent denial or approval of early requests for controlled substances.
RESULTS: Large variations in the policies and prescribing practices of opioids were found at the clinic. There was infrequent monitoring of organ systems important to the safety and efficacy of drug therapy. Likert scales were not used in 89% of cases, and only 38% of cases had any assessment of pain severity. Urine drug screens had not been monitored in the past year in 77% of patients, and only 28% of patients had a pain contract in their chart.
CONCLUSIONS: Ample opportunity exists to improve the handling of opioids at the clinic to optimize patient outcomes. Collaborative brainstorming with the residents and physicians in the clinic generated ideas to change clinic policies and procedures to improve handling of these medications.

Pharmacoeconomics/Outcomes

315. Inpatient Resource Utilization Associated with Bipolar Disorder in Children and Adolescents. *Edmund Berry, M.S., Finance, M.S., Quantitative, A*, Pamela C. Heaton, Ph.D.; University of Cincinnati, Cincinnati, OH
PURPOSE: Currently, there is a tremendous dearth of information differentiating the burden of bipolar disorder in children and adolescents versus adults with regard to key economic dimensions of length of stay, total costs, and total charges. Therefore, the objective of this study was to calculate total charges, total costs, and length of stay of inpatient hospitalizations for children and adolescents with a principal diagnosis of bipolar disorder, quantify these metrics by demographic characteristics, identify the most common comorbidities associated with bipolar disorder, and identify the variables that predict increased costs for inpatient hospitalizations among pediatrics.
METHODS: Using the 2003 Kids' Inpatient Database, 36,806 pediatric discharges from community nonrehabilitation hospitals with a principal diagnosis of bipolar disorder (ICD 9 296.0, 296.1, 296.4–296.8) were identified to determine national estimates of inpatient total costs, total charges, and length of stay (LOS). Further descriptive analysis for LOS, charges, and cost was performed on variables relating to age, gender, income, number of diagnosis, payer, race, hospital type, hospital region, hospital bed size, hospital location, hospital control, and key comorbidities. Poisson regression was used to determine rate ratios to identify key predictors of increased total costs along key patient demographic characteristics, specific hospital characteristics, and comorbidities.
RESULTS: Total inpatient LOS, charges, and cost were estimated at 299,432 days (mean 8.14), $415,164,517 (mean $11,280), and $165,081,787 (mean $44,850). Higher treatment costs were associated with the 0–5 age group compared with the 13–20 age group (RR = 1.277, 1.133–1.439), Medicaid compared with private insurance (RR = 1.182, 1.150–1.216), blacks compared with whites (RR = 1.099, 1.05–1.150), northeast versus south (RR = 2.045, 1.954–2.140), urban versus rural hospitals (RR = 1.115, 1.046–1.190), and patients with posttraumatic stress disorder (RR = 1.222, 1.175–1.271).
CONCLUSIONS: Costs associated with bipolar disorder in children and adolescents can be decreased by greater use of medication in an outpatient setting, potentially decreasing the overall burden to society.

Pharmacogenomics/Pharmacogenetics

316. Clinical and Genetic Risk Factors of New Onset Post Transplant Diabetes Mellitus in Adult Hispanic Renal Transplant

Recipients. *Mai T. Vuong, Pharm.D.,*[1] Jae-Wook Yang, Ph.D., Pharm.D.,[2] Vera Pravica, M.D., Ph.D.,[3] Ian V. Hutchinson, Ph.D., D.Sc.,[4] Tariq Shah, M.D.,[5] David Min, Pharm.D.[1]; (1) Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Los Angeles, CA; (3) USC/National Institute of Transplantation, Los Angeles, CA; (4) USC School of Pharmacy, Los Angeles, CA; (5) St. Vincent Medical Center and National Institute of Transplantation, Los Angeles, CA

BACKGROUND: New-onset posttransplant diabetes mellitus (NOPTDM) is a major complication in kidney allograft recipients, and ethnicity is one of the known risk factors.
PURPOSE: To determine clinical and genetic risk factors of NOPTDM in Hispanic renal transplant patients.
METHODS: We conducted a retrospective analysis of adult nondiabetic Hispanic kidney transplant patients who received their transplants between January 2000 and December 2006 at St. Vincent Medical Center, Los Angeles, California. Seven hundred sixty-nine (50.8%) of 1513 patients wereidentified as Hispanic kidney recipients, of which 449 met our inclusion and exclusion criteria. Together with a total of 15 clinical factors, recipients' DNAs were genotyped for a total of nine diabetes-associated genes related to insulin gene expression, insulin secretion, or insulin signaling. The multivariate Cox regression analysis was used to determine the relative risk (RR) for NOPTDM.
RESULTS: The mean follow-up of this study was 1392 days after transplant (range 46–2943). The mean onset time of PTDM was 314 days after transplant (range 31–2568). In our study, 239 patients (53%) developed NOPTDM during our follow-up period. Using multivariate Cox regression analysis, among 15 clinical risk factors, the following were significantly high: RR: patient age at transplant (50 years and older: RR = 1.44, p=0.029, 60 years and older, RR = 1.85, p<0.001); deceased donor organ (RR = 1.34, range 1.22–2.07; p=0.042); tacrolimus use (RR =1.31, p=0.044); and sirolimus use (RR = 1.8, p<0.001). The following genetic risk factors were also significant: IRS1 (rs1801278) (RR = 0.45, p=0.022) and KCNJ11 (rs5219) (RR = 0.49, p=0.001).
CONCLUSIONS: This study indicated that age, deceased donor source, and tacrolimus or sirolimus use were associated with a higher risk and that IRS1 and KCNJ11 genetic mutations were associated with a reduced risk for developing NOPTDM in Hispanic kidney transplant recipients.

317. Effect of Genetic Polymorphisms of MDR-1 and CYP3A5 on Tacrolimus Pharmacokinetics After Renal Transplantation. (Encore will be presented at XXII International Congress of the Transplantation Society, Sidney, Australia, August 10–14, 2008.)

Yoo Jin Moon, B.S.,[1] Yang Jin Park, M.D.,[2] Shi-hwa Kim, B.S.,[2] Hye-Jin Hong, B.S.,[2] Yu Jin Joeng, B.S.,[2] Eun Hee Ji, M.S.,[1] In Ja Son, Ph.D.,[3] Seung-Kee Min, M.D.,[2] Jongwon Ha, M.D.,[2] Sang Joon Kim, M.D.,[2] JungMi Oh, Pharm.D.[1]; (1) College of Pharmacy, Seoul National University, Seoul, South Korea; (2) Department of Surgery, Seoul National University College of Medicine, Seoul, South Korea; (3) Department of Pharmacy, Seoul National University Hospital, Seoul, South Korea

PURPOSE: The pharmacokinetics of the immunosuppressive drug tacrolimus vary greatly among individuals. Because of its narrow therapeutic index and large interindividual variability, patients receiving tacrolimus require strict therapeutic monitoring of its blood levels. As a substrate of cytochrome P450 3A5 (CYP3A5) and P-glycoprotein, it is suggested that tacrolimus pharmacokinetics are affected by the genetic polymorphism of *MDR1* and CYP3A5. Therefore, the objective of this study was to identify the impact of genetic variations of *MDR1* and CYP3A5 on the tacrolimus pharmacokinetics in Korean renal transplant recipients.
METHODS: Renal transplant recipients receiving tacrolimus-based immunosuppressants were genotyped for *MDR1* C1236T, G2677T/A, and C3435T and CYP3A5. Clinical data were collected retrospectively for 1 year after transplantation. Dose-adjusted trough concentrations (ng/mL per mg/kg) as well as doses (mg/kg) required to achieve target blood concentrations were correlated with each genotype.
RESULTS: A total of 104 kidney recipients were evaluated to characterize the genetic variation of *MDR1* and CYP3A5 on tacrolimus pharmacokinetics. The mean trough levels were higher in the TT than in the CC/CT genotype of *MDR1* C3435T (p=0.031) only at week 2, and the *3/*3 genotype of CYP3A5 had significantly higher trough levels at week 2 and month 1. The dose-adjusted trough levels at week 2 were significantly higher in the TT variant of *MDR1* C3435T (p=0.01), but there was no significant difference in the other single nucleotide polymorphisms of *MDR1*. Dose-adjusted trough levels were significantly higher in expressers (CYP3A5 *3/*3) than in nonexpressers (CYP3A5 *1/*1 and *1/*3) during the follow-up period.
CONCLUSIONS: We demonstrated that the polymorphism of CYP3A5 is significantly associated with the pharmacokinetic characteristics of tacrolimus. In addition, the early level of tacrolimus is affected by the genetic variation of *MDR1* C3435T. Genotyping for CYP3A5 to identify CYP3A5 expressers or nonexpressers has the potential to identify individuals with a high-dose requirement for tacrolimus and may be a useful tool for individualizing immunosuppressive drug treatment in Korean renal transplant recipients.

318. TPMT Pharmacogenetics and the Risk for Secondary Brain Tumors After Antileukemic Therapy.

Jonathan Lee, Ph.D., Allen Sills, M.D., Anand Kulkarni, M.D., Cameila Johns, M.D., Terreia Jones, Pharm.D.; University of Tennessee Health Science Center, Memphis, TN

PURPOSE: Cancer is dependent on a series of genetic alterations to develop, but it is also dependent on individual genetic predisposition. Thiopurine methyltransferase (TMPT) is important to the deactivation of thiopurine drugs commonly used in the treatment of leukemia. Patients having a dysfunctional TPMT phenotype can have an exceptionally high risk of secondary brain tumors when concurrent thiopurines and cranial irradiation are given (Relling et al.; Lancet 1999). We used TPMT knockout mice to study whether TPMT was an important risk factor for normal brain tissue toxicity after thiopurine drugs and cranial irradiation.
METHODS: We treated TPMT +/+ and TPMT –/– mice with thioguanine (TG), cranial irradiation (IR), or concurrent TG and IR for 6 weeks and followed the mice for the remainder of their life span. To assess the degree of treatment-induced tissue damage, we analyzed brain tissue for histopathology. In addition, DNA damage will be measured using the COMET assay to assess the extent of genotoxicity.
RESULTS: We found that TG-treated TPMT –/– mice had brain tissue pathology remarkable for hemorrhage, ischemic neurons, and increased microvasculature compared with TPMT +/+ mice. The extent of hemorrhage was directly correlated with cumulative TG dose (r^2= 84.5, p=0.0034). IR-treated mice showed minimal pathologic evidence of tissue toxicity. To further validate our findings, we will analyze previously collected mouse brains treated with concurrent TG and IR. The extent of genotoxicity will be assessed for all tissues and correlated with our initial findings during the next month.
CONCLUSIONS: Cancer therapy is cytotoxic by design and, hence, can induce unwanted genomic alterations in normal cells. One consequence of anticancer therapy is the risk of treatment-induced secondary neoplasms. These preliminary data suggest that TPMT is an important risk factor for toxicity of normal brain tissue after thiopurine drugs and irradiation.

319. High-Dose Atorvastatin Lowers Blood Pressure in a CXCL5 Genotype-Dependent Manner.

Gregory J. Welder, A.A.,[1] Richard S. Schofield, M.D.,[2] Issam Zineh, Pharm.D.[1]; (1) University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, FL; (2) Division of Cardiovascular Medicine, University of Florida College of Medicine, & Department of Veterans Affairs Medical Center, Gainesville, FL

PURPOSE: White blood cell (counts) (WBC) can be elevated with increasing blood pressure (BP), suggesting the role of inflammation in hypertension. It has been suggested that statins lower BP through anti-inflammatory mechanisms. We recently showed that

atorvastatin lowers endothelial *CXCL5* production. *CXCL5* is a potent chemokine that attracts and activates WBC, making this gene a candidate for the antihypertensive effects of statins. We tested whether the variability in the BP-lowering effects of atorvastatin results from polymorphisms in the *CXCL5* gene.
METHODS: Participants were eligible if they had no cardiovascular disease or contraindications to statins. Systolic BP (SBP) and diastolic BP (DBP) were assessed in 83 individuals at baseline and after 8 weeks of atorvastatin 80 mg/day. BP measurements were taken after at least 5 minutes of rest in duplicate separated by at least 5 minutes. The *CXCL5* genotype for the -156G>C [rs352046] functional polymorphism was determined by pyrosequencing. Statistical significance was set at $p<0.05$ in assessing overall BP response to atorvastatin and differences in response by genotype.
RESULTS: Subjects were 31 ± 13 years old, 63% women, and 73% white, with a baseline BP of 119/73 ± 11/8 mm Hg. The -156C allele frequency was 17%, and the genotypes were in Hardy-Weinberg equilibrium. There were no baseline BP differences by genotype. Overall, atorvastatin reduced SBP by 3 mm Hg ($p<0.001$) and DBP by 2 mm Hg ($p=0.018$). At 8 weeks, -156C carriers experienced a 5.7- and 3.7-mm Hg reduction in SBP and DBP, respectively, and nonvariant carriers experienced a 1.7- and 0.5-mm Hg reduction in SBP and DBP, respectively ($p<0.05$ for genotype differences).
CONCLUSIONS: High-dose atorvastatin significantly reduced BP after 8 weeks of treatment. The antihypertensive effect differed by a polymorphism in the inflammatory chemokine gene *CXCL5*. This pharmacogenetic association provides insight into the statin antihypertensive effect and the role of inflammation in drug response.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

320. Alterations in the Expression of Intestinal Transporters and Metabolic Enzymes in Cultured Intestinal Cells Treated with Green Tea Extract. *Shu Zhang, B.S.*,[1] Xiaomei Zheng, M.S.,[1] Lingling An, M.S.,[2] Andrea Rau, M.S.,[2] Paul Livermore Auer, M.S.,[2] R.W. Doerge, Ph.D.,[2] David R. Foster, Pharm.D.[1]; (1) Purdue University, Department of Pharmacy Practice, Indianapolis, IN; (2) Purdue University, Department of Statistics, West Lafayette, IN
PURPOSE: Green tea extract (GTE) and its major component, EGCG, are under evaluation as potential anti-inflammatory/antioxidants. The effects of GTE and EGCG on xenobiotic transporter and metabolizing enzyme expression are largely unknown. This study was conducted to study global gene expression profiles including transporter and metabolizing enzyme expression elicited by GTE and EGCG in cultured human intestinal cells (Caco-2 cells).
METHODS: Caco-2 cells were treated with GTE (Polyphenon E, 100 µM of EGCG component), EGCG (100 µM), or control media for 72 hours (n=4/group). RNA was extracted from samples, and the expression of more than 50,000 genes was assessed using the Affymetrix HG-U133 Plus 2.0 array. An analysis of variance model was used to identify statistically significantly differentially expressed genes. The type I error was controlled at 5% using both Holm's sequential Bonferroni procedure and false discovery rate (FDR). Alterations in expression of cytochrome P450 enzymes (CYPs) and solute carrier transporters were evaluated.
RESULTS: More than 30,000 genes were expressed in Caco-2 cells, including more than 45 transporters/CYPs. Treatment with GTE and EGCG resulted in a 2- to 5-fold induction/inhibition in the expression of at least 326 and 618 genes, respectively. Statistically significant changes in transporter/enzyme expression by the FDR approach and Holm's sequential Bonferroni procedure are shown below.

Category	Gene	Fold Change GTE	EGCG	
CYP isoenzymes	CYP1A1	Aryl hydrocarbon hydroxylase	(+)2.74	(+)4.48
	CYP1B1		(+)3.02	(+)2.63
	CYP19A1	Aromatase	(–)2.2	(–)3.29
Membrane transporters	SLCO2A1	Organic anion transporter	(+)3.47	(+)4.37
	SLC8A1	Sodium/calcium exchanger	NA	(_)2.21
	SLC22A15	Organic cation/carnitine transporter	(+)2.32	NA
	SLC28A3	Sodium-coupled nucleoside transporter	(+)2.49	(+)2.05
	SLC39A8	Zinc transporter	(+)2.09	(+)2.45
	SLC39A10		(+)3.14	NA

(+) = induction; (–) = suppression.

CONCLUSIONS: GTE and EGCG broadly alter gene expression in Caco-2 cells, including several CYPs and membrane transporters. This may result in alterations in xenobiotic transport and metabolism, and the clinical implications of these observations warrant further evaluation.

321. Mycophenolic Acid Pharmacodynamics in Nonmyeloablative Unrelated Donor Hematopoietic Cell Transplant Patients. *Jennifer A. Knutson, Pharm.D. Candidate*,[1] Brenda M. Sandmaier, M.D.,[2] Barry E. Storer, Ph.D.,[2] David G. Maloney, M.D.,[2] Rainer F. Storb, M.D.,[2] Meagan J. Bemer, M.S.,[2] Jeannine S. McCune, Pharm.D.[1]; (1) University of Washington, Seattle, WA; (2) Fred Hutchinson Cancer Research Center, Seattle, WA
PURPOSE: Mycophenolate mofetil (MMF) is a component of postgrafting immunosuppression in nonmyeloablative hematopoietic cell transplantation (HCT) patients. MMF is rapidly hydrolyzed to its active metabolite, mycophenolic acid (MPA), by plasma esterases. Previously, we reported a relationship between low total MPA concentration at steady state (Css) and low donor T-cell chimerism and graft rejection, whereas high unbound MPA Css correlated with cytomegalovirus (CMV) reactivation. We sought to confirm these findings in a larger patient population.
METHODS: We are conducting a retrospective evaluation of total and unbound MPA pharmacodynamics in recipients of unrelated donor peripheral blood stem cell grafts after nonmyeloablative conditioning from January 2000 to July 2006. MPA pharmacokinetic samples were obtained on days 7 and 21 and quantitated using high-performance liquid chromatography–ultraviolet detection; the total and unbound MPA Css was calculated using noncompartmental analysis. Clinical end points to be evaluated are T-cell chimerism, CMV reactivation, graft rejection, acute and chronic graft versus host disease (GVHD), disease progression/relapse, and survival. Statistical analysis is planned for August 2008.
RESULTS: One hundred eighty-three patients received FLU/TBI conditioning, either oral or intravenous MMF (dosed every 8 or 12 hours), and cyclosporine (n=151) or tacrolimus (n=32). Total and unbound MPA Css (average ± SD) were 3.2 ± 1.4 µg/mL and 35.4 ± 22.1 ng/mL on day 7 (n=79) and 3.0 ± 1.6 µg/mL and 30.3 ± 19.5 ng/mL on day 21 (n=90). Median time of follow-up was 733 days (range 19–2908). The occurrences of clinical end points (percentage of patients) were as follows: 4% graft rejection; 15% grade III or IV acute GVHD; and 66% chronic GVHD.
CONCLUSIONS: We hypothesize that increased total MPA Css predicts higher degrees of donor T-cell chimerism in this population. If our hypothesis is confirmed, this study will provide evidence that personalizing MMF based on pharmacokinetics may improve patient outcomes.

322. Ethinylestradiol-Mediated Regulation of Hepatic Cytochrome P450 Enzymes in Rats. *Su-Young Choi, B.S.*, Hyunyoung Jeong, Pharm.D., Ph.D.; University of Illinois at Chicago, Chicago, IL
PURPOSE: Ethinylestradiol (EE2), a major component in oral contraceptives, is known to alter the pharmacokinetics of coadministered drugs in humans. Current evidence suggests that these clinical findings are attributed to altered hepatic metabolism by EE2. In this study, to examine the effects of EE2 on hepatic drug metabolism, we investigated the effects of EE2 on the regulation of cytochrome P450 (CYP) expression in female rats.
METHODS: Female Sprague-Dawley rats were treated with EE2 (40

µg/kg/day intraperitoneally) or corn oil (control) for 4 days, and hepatic microsomes were prepared by differential centrifugation. Hepatic CYP activities were determined by conducting microsomal drug assays using isoform-specific probe drugs: ethoxyresorufin for cyp1a, benzoxyresorufin for cyp2b, diclofenac for cyp2c, midazolam for cyp3a, dextromethorphan for cyp2d, and *p*-nitrophenol for cyp2e. The metabolite concentrations were determined by liquid chromatography–mass spectrometry (diclofenac, midazolam, and dextromethorphan), fluorometer (ethoxyresorufin and benzoxyresorufin), or spectrophotometer (*p*-nitrophenol). Michaelis-Menten parameters were estimated on the basis of metabolite formation rates.

RESULTS: We found that apparent V_{max} values of cyp1a and cyp3a were increased by EE2 treatment (2.1-fold for cyp1a, 1.4-fold for cyp3a), but those of cyp2d and cyp2e did not change. For all cyp pathways, the Km values were not altered by EE2. These results indicate that EE2 regulated the expression level rather than the functions of these enzymes.

CONCLUSIONS: Taken together, our study shows that CYP enzymes are differentially regulated by EE2 in female rats. Of interest, these results obtained in rats do not correspond to the pharmacokinetic changes in oral contraceptive users, suggesting interspecies difference in hormonal regulation of drug metabolizing enzyme expression between rats and humans.

323. Mycophenolic Acid Pharmacodynamics in Nonmyeloablative, HLA-Matched Related Hematopoietic Cell Transplant (HCT) Recipients. *Cara L. McDermott, B.A.*,[1] Brenda M. Sandmaier, M.D.,[2] Barry E. Storer, Ph.D.,[2] David G. Maloney, M.D.,[2] Rainer F. Storb, M.D.,[2] Meagan J. Bemer, M.S.,[2] Jeannine S. McCune, Pharm.D.[1]; (1) University of Washington School of Pharmacy, Seattle, WA; (2) Fred Hutchinson Cancer Research Center, Seattle, WA

PURPOSE: Nonmyeloablative hematopoietic cell transplant (HCT) recipients receive postgrafting immunosuppression with a calcineurin inhibitor and mycophenolate mofetil (MMF) to prevent donor graft rejection and graft-versus-host disease (GVHD). The active metabolite of MMF is mycophenolic acid (MPA). Pharmacodynamic associations between total and free MPA concentration at steady state (Css) have been reported in HCT recipients. We seek to be the first to characterize MPA pharmacokinetics/dynamics in patients who receive nonmyeloablative HCT with HLA-matched related grafts.

METHODS: Patients received total body irradiation (TBI) with or without fludarabine monophosphate (FLU) preceding a related-donor hematopoietic graft infusion, plus a calcineurin inhibitor and MMF. Patients with MPA pharmacokinetic data available between January 1998 and December 2006 were included. Total and unbound MPA concentrations were quantitated using high-performance liquid chromatography–ultraviolet detection and were fit with a noncompartment model. Clinical end points including T-cell chimerism, graft rejection, acute and chronic GVHD, relapse/disease progression, and overall survival will be analyzed. Statistical analysis is planned for July 2008.

RESULTS: One hundred forty-nine patients, 86 male and 63 female, received TBI alone (n=52, 34.9%) or FLU/TBI conditioning (n=97, 65.1%) and MMF with cyclosporine (n=121, 81.2%) or tacrolimus (n=28, 18.8%). Oral or intravenous MMF was dosed every 8 hours (n=10, 6.7%) or 12 hours (n=139, 93.3%).Total and unbound MPA Css (average ± SD) were 2.46 ± 1.06 µg/mL on day 7 (n=115, 77.2%) and 2.42 ± 0.90 µg/mL on day 21 (n=90, 60.4%). Median time of follow-up was 820 days (range 18–3571). Five (3.4%) patients had graft rejection, 89 (59.7%) patients developed acute GVHD, and 96 (64.5%) patients developed chronic GVHD.

CONCLUSIONS: Considerable variability in MPA pharmacokinetics was observed, as expected. The rates of our clinical end points agree with previously reported data in unrelated HCT recipients. We will evaluate total and free MPA pharmacodynamics in the future, with the goal of determining whether personalized MMF dosing can improve clinical outcomes in nonmyeloablative HCT recipients.

324. Atorvastatin Regulates Global Inflammatory and Anti-inflammatory Gene Expression in Human Endothelial Cells. *Gregory J. Welder, AA*, Issam Zineh, Pharm.D.; University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, FL

PURPOSE: Endothelial inflammation that contributes to cardiovascular disease is a complex process involving genes that encode cytokines, chemokines, and their respective receptors. HMG CoA (3-hydroxy-3-methylglutaryl coenzyme A) reductase inhibitors (statins) exhibit anti-inflammatory properties; however, their simultaneous impact on the aforementioned mediators of inflammation is unknown. We investigated the effect of atorvastatin on the expression of 84 inflammatory and anti-inflammatory genes in human endothelial cells (HUVECs).

METHODS: HUVECs were treated with atorvastatin calcium 10 µM or control (dimethyl sulfoxide) for 24 hours (n=2 or 3 experiments). RNA was isolated, and 500 ng was reverse transcribed. Pathway-based gene expression profiling was performed by RT-PCR (reverse transcriptase-polymerase chain reaction). Changes in gene expression were determined by the $2^{-\Delta\Delta Ct}$ method, with $p \leq 0.05$ considered significant.

RESULTS: Atorvastatin significantly down-regulated the gene expression of five CXC chemokines (CXCL6, CXCL5, CXCL10, CXCL1, and IL8) by 4- to 47-fold ($p \leq 0.05$) and two CC chemokines (CCL7 and CCL2) by 5- to 18-fold ($p \leq 0.01$). The expression of two cytokine genes (SCYE1 and IL1B) and a member of the tumor necrosis superfamily (LTB), whose receptor has been recently implicated in regulating cholesterol homeostasis, were also down-regulated by 2- to 16-fold ($p \leq 0.05$). Atorvastatin up-regulated the gene expression of a CC chemokine, CCL23, by 2-fold and the anti-inflammatory IL10RA by 7-fold ($p \leq 0.01$).

CONCLUSIONS: Atorvastatin's ability to simultaneously regulate endothelial gene expression of multiple chemokines, cytokines, and their receptors could contribute to its pleiotropic effects and should be further explored.

Pulmonary

325. Evaluating the Risk of Right-sided Heart Failure or Edema with Ambrisentan Compared with Bosentan. *David M. Crowther, B.S., Physiology,*[1] Krystal L. Moorman, Pharm.D.[2]; (1) University of Southern Nevada, Midvale, UT; (2) Intermountain Medical Center, Murray, UT

PURPOSE: Endothelin receptor antagonists (ERAs) have been shown to cause edema. Our experience suggests that this adverse effect is caused more often with ambrisentan than bosentan. This study is designed to determine whether a greater proportion of patients require diuretic dose escalation after initiation of ambrisentan compared with bosentan, whether additional diuretic therapy (e.g., metolazone) is required more often with ambrisentan compared with bosentan, and whether treatment with bosentan or ambrisentan has a greater incidence of worsening edema or new or worsened right heart failure.

METHODS: Medical charts of 64 patients who have been prescribed either ambrisentan or bosentan by physicians at the Pulmonary Hypertension Center will be included in this study. The medical records will be analyzed for dose escalations in diuretics after initiation or dose increase of the ERA; addition of new diuretics after initiation or dose escalation of ERAs; indication in clinical notes that the patient has complained of worsening edema or noting increased edema or right heart failure on physical examination after ERA therapy initiation or dose escalation; and hospitalization for worsening edema or right heart failure (as indicated in clinic note or hospital discharge summary). These adverse effects will be evaluated using the Naranjo algorithm to determine the likelihood of causality. Results will be compared between groups as well as with national trends, obtained from MedWatch.

The likelihood of patients requiring diuretic dose escalation or additional diuretic therapy with worsening edema or right heart failure will be compared between groups using a multivariate analysis.

RESULTS: In progress.

CONCLUSIONS: To be presented.
This project will be completed by the date of presentation without difficulty.

326. Tissue Plasminogen Activator: Anti-inflammatory Agent via Modulation of Rac2. *Christine Kim, Pharm.D., 2010*, Joshua E. Pitzer, M.S., Regine L. Caruthers, Pharm.D., Kathleen A. Stringer, Pharm.D.; University of Michigan College of Pharmacy, Ann Arbor, MI
PURPOSE: Plastic bronchitis (PB) is a rare pediatric pulmonary disorder that can occur in children with single ventricular physiology who have received the Fontan procedure. PB is characterized by the presence of fibrin or mucin bronchial casts and pulmonary inflammation that can lead to obstruction and death. Inhaled tissue plasminogen activator (tPA) is an indiscriminate pharmacotherapy used to treat PB. Although the potential efficacy of tPA has been attributed to its fibrinolytic activity, tPA has also been shown to dampen the neutrophil-mediated inflammatory response by inhibiting NADPH oxidase superoxide anion (O2•-) production. The small G-protein, Rac2, which is required for robust O2•- production, has been implicated as the potential target of the observed anti-inflammatory activity of tPA. The purpose of this study was to test the hypothesis that the anti-inflammatory activity of tPA was due to its ability to suppress Rac2-GTP.
METHODS: Genetically engineered cells that contain the human components of the NADPH oxidase (COSphox) have been transiently transfected with constitutively active Rac2 (G12V). Experiments are currently being conducted to determine whether Rac2 G12V has the ability to rescue the NADPH oxidase from tPA-induced suppression. The production of O2•- will be measured by cytochrome C reduction.
RESULTS: Treatment of human neutrophils with tPA (100 µg/mL) decreased levels of active Rac2-GTP in the presence and absence of the O2•- stimulant phorbol myristate acetate (PMA): mean + SE of untreated cells: 57% + 11%; tPA: 47% + 3%; PMA: 98% + 10%; tPA+PMA: 71 + 4 compared with GTP controls (100%). Additional research is ongoing and is likely to be completed by the date of presentation.
CONCLUSIONS: Suppression of Rac2-GTP is a unique anti-inflammatory mechanism that could serve as a novel therapy for neutrophil-mediated inflammation. The dual anti-inflammatory and fibrinolytic activities of tPA could be particularly useful for the treatment of PB for which there is presently no proven pharmacotherapy.

Substance Abuse/Toxicology

327. Interaction of Ibogaine Analogs with the Nicotinic Acetylcholine Receptor. *Mary E. Ghafoori, Pharm.D. Candidate,*[1] Krzysztof Jozwiak, Ph.D.,[2] Irving W. Wainer, Ph.D.,[2] Hugo R. Arias, Ph.D.[1]; (1) Department of Pharmaceutical Sciences, Midwestern University College of Pharmacy-Glendale, Glendale, AZ; (2) Gerontology Research Center, NIA-NIH, Baltimore, MD
PURPOSE: Characterization of the binding sites for ibogaine analogs on the *Torpedo* nicotinic acetylcholine receptor (nAChR) in the resting and desensitized states.
METHODS: [^{3}H]18-methoxycoronaridine ([^{3}H]18-MC) Scatchard-plots using *Torpedo* nAChR membranes, [^{3}H]TCP (a well-characterized noncompetitive antagonist) competition binding experiments and Schild-type analysis, analog-induced binding modulation of the agonist [^{3}H]cytisine, and molecular modeling of the *Torpedo* nAChR ion channel and molecular docking of 18-MC.
RESULTS: (1) There is one (0.86 ± 0.13) high-affinity (K_d = 0.23 ± 0.04 µM) binding site for [^{3}H]18-MC in the desensitized nAChR. (2) The affinity (in µM) of each 18-MC congener for the [^{3}H]TCP locus in the desensitized state follows the sequence 18-MC (0.17 ± 0.01) > 2-methoxyethyl-18-MC (1.3 ± 0.1) ~ 18-methylaminocoronaridine (1.3 ± 0.2) > catharanthine (3.2 ± 0.4) ~ albifloranine (3.2 ± 0.3) > ibogaine (5.4 ± 0.3) > 19-OH-ibogamine (40 ± 2), whereas the affinity sequence in the resting state is 18-MC (12 ± 1) > 18-methylaminocoronaridine (19 ± 2) > albifloranine (31 ± 4) > catharanthine (48 ± 5) > 2-methoxyethyl-18-MC (82 ± 8) > ibogaine (182 ± 17) >> 19-OH-ibogamine (1300 ± 500). (3) Schild-type analysis suggests 18-MC interacts with the TCP site in a steric manner. (4) [^{3}H]Cytisine binding is enhanced by the 18-MC congeners when the nAChR is in the resting but capable of being activated state, but not in the desensitized state. (5) 18-MC interacts with a domain located between the valine (position 13') and leucine (position 9') rings.
CONCLUSIONS: Binding and modeling results indicate the 18-MC binding site overlaps the TCP locus located in the middle of the desensitized ion channel, and ibogaine congeners may inhibit the nAChR by inducing desensitization.

328. Interaction of Novel Ibogaine Analogs with the Human α3β4 Nicotinic Receptor. *Mary E. Ghafoori, Pharm.D. Candidate,*[1] Dominik Feuerbach, Ph.D.,[2] Hugo R. Arias, Ph.D.[1]; (1) Department of Pharmaceutical Sciences, Midwestern University College of Pharmacy-Glendale, Glendale, AZ; (2) Novartis Institutes for BioMedical Research, Switzerland
PURPOSE: This research is an attempt to characterize the binding site and inhibitory activity of ibogaine analogs on the human α3β4 nicotinic acetylcholine receptor (hα3β4 nAChR).
METHODS: [^{3}H]Ibogaine equilibrium binding and Scatchard plots, [^{3}H]ibogaine and [^{3}H]epibatidine competition binding, and ibogaine-induced inhibition of Ca^{2+} influx approaches were used.
RESULTS: (1) There is one high-affinity binding site for [^{3}H]ibogaine. (2) Ibogaine inhibits the hα3β4 with higher potency than the hα1β2γδ nAChR. (3) Ibogaine analogs inhibit the hα3β4 ion channel with high potency (EC_{50} = 0.6–2.6 µM). (4) [^{3}H]Ibogaine competition experiments indicate ibogaine and 18-methylaminocoronaridine (18-MAC), among ibogaine analogs, have the highest affinities for the hα3β4 in the resting state. (5) Imipramine and dextromethorphan, among other known noncompetitive antagonists, have the highest affinities for the ha3b4 in the resting state. (6) [^{3}H]Epibatidine competition experiments indicate ibogaine analogs interact with the agonist sites with very low affinities.
CONCLUSIONS: The results suggest ibogaine analogs mainly inhibit the open hα3β4 ion channel. In addition, 18-MAC and ibogaine could inhibit the hα3β4, inactivating the resting ion channel. These inhibitory mechanisms might be important for their anti-addictive properties.

329. Unknown Medication Ingestions in Children Less Than 6 Years: An 8-Year Retrospective Database Analysis. *Kristen E. Hillebrand, Pharm.D., B.A.,*[1] Jan Scaglione, Pharm.D., DABAT,[2] Alysha Behrman, BSN, RNII, CSPI, OCPS II, CARN,[2] Sheila Goertemoeller, R.Ph., CSPI, OCPS II[2]; (1) Cincinnati Children's Hospital Drug and Poison Information Center and University of Cincinnati College of Pharmacy, Cincinnati, OH; (2) Cincinnati Children's Hospital Drug and Poison Information Center, Cincinnati, OH
PURPOSE: Of the 13,381 exposures to unknown drugs logged by poison control centers in 2006, 4006 cases involved children younger than 6 years.[1] Defined protocols for observation and treatment of unknown pediatric medication ingestions do not exist. A retrospective analysis was performed to determine if children ingesting unknown medication can be discharged after 6–8 hours of hospital observation.
METHODS: This retrospective database analysis used Toxicall, an electronic access database, and evaluated exposures to unknown medications in children younger than 6 years at DPIC, a regional poison control center. Data collection included age, length of observation, decontamination, admission location, time to onset of symptoms, and symptom severity.
RESULTS: One hundred fifty-two cases were identified, with an age range of 4 months to 5 years and an average age of 25.2 months. Thirty-six of the included patients developed symptoms related to the unknown medication exposure; 80.6% of these were minor effects. Thirty patients underwent admission for observation; the severity of symptoms in these patients was more profound than those not admitted. Decontamination measures did not appear to affect symptom severity.
CONCLUSIONS: Most ingestion occurred in children aged 12–24 months, consistent with prior research.[2] Sixty-seven percent of

cases were observed for less than 8 hours and resulted in either minor or no effects. Although the study was limited by sample size and inconsistent documentation, it appears that children younger than 6 years who ingest unknown medication may safely be discharged if symptoms do not occur within the first 8 hours after ingestion.

References
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330. Implementation of a Student Pharmacist Tobacco Cessation Program. *Anthony M. Tardi, Pharm.D. Candidate*, Roy A. LaBarge, Pharm.D. Candidate, Ashley M. Fulton, Pharm.D. Candidate, Nancy S. Maylath, HSD, Alan P. Farkas, M.S., R.Ph., Karen S. Hudmon, Dr.PH., Alan J. Zillich, Pharm.D.; Purdue University, West Lafayette, IN

PURPOSE: To establish and evaluate a tobacco cessation program targeted to college students. The program is offered through a collaboration of the Purdue University Pharmacy, the Student Wellness Office, and the Purdue University Student Health Center.

METHODS: The program used age-appropriate advertising, X-Packs (smoking cessation kits), trained pharmacists and pharmacy students, and, if appropriate, pharmacological intervention to guide smokers through a series of four face-to-face counseling sessions to aid cessation. After implementation in fall 2007, the first 6 weeks of the program were evaluated through extracting self-reported data to assess age, gender, tobacco use history (concerning type, amount, length, and rationale), and cessation status.

RESULTS: Data from 46 college students were used in the initial assessment. The male-to-female-ratio was 3:1, with 72% men and 28% women. Most participants were younger than 20 years (average 19.9 years) and used cigarettes more than any other type of tobacco (91%). Stress was the most commonly reported reason to start and continue the use of tobacco. Fifty percent indicated health concerns as reasons to quit. All 46 students received the X-Pack, and 35 (76%) set a quit date; 99 counseling sessions (average two of four sessions) were provided by either the pharmacist or student pharmacist. Three participants received four sessions, and one participant completed five sessions. Through December 31, 2007, the self-reported quit rate was 22% (n=10) for 1 or more days (mean = 27 days, range 5–55 days).

CONCLUSIONS: A tobacco cessation program was successfully established for college students on a university campus. The program is ongoing; future research will further evaluate the effectiveness of the program.

Transplant/Immunology

331. 3-Year Outcomes of Basiliximab Induction in African American Kidney Transplant Recipients of Deceased Donor Transplants. *Kimberly A. DuBrueler, Pharm.D. Candidate*, Nicole Sifontis, Pharm.D., BCPS; Temple University School of Pharmacy, Philadelphia, PA

PURPOSE: To analyze long-term outcomes of basiliximab (BASI) induction in high-risk African American (AA) kidney transplant recipients of deceased donor transplants.

METHODS: A review of 57 consecutive deceased donor kidney transplants performed between November 2001 and November 2004 was conducted. All patients received BASI 20 mg intravenously on induction and a second dose on postoperative day 4. Maintenance immunosuppression consisted of oral tacrolimus adjusted on the basis of trough concentrations (8–12 ng/mL for 6 months and then 5–10 ng/mL); mycophenolate mofetil 1000 mg orally 2 times/day; and corticosteroids tapered to a minimum of 2.5 mg/day by 1 year. AA kidney transplant recipients were compared with non-AA kidney transplant recipients receiving BASI induction. Medication teaching was provided to each patient beginning after transplant. All patients were supplied with medication boxes that were carefully monitored/filled at each clinic visit to improve compliance.

RESULTS: Both groups were compared as depicted in the Table. With the exception of peak reactive antibody (PRA%), there was no difference between the two groups. The incidence of infections was also similar between the groups.

Comparison of 3-Year Outcomes in AA vs. non-AA Recipients of Deceased Donor Kidney Transplants

	AA (n=42)	Non-AA (n=15)
Age	57 ± 11 years	54 ± 17 years
Gender	27 M/15 F	10 M/5 F
DGF	21%	7%
DCD or ECD donors	36%	40%
Peak PRA (%)*	10 ± 14.5	3.8 ± 5.9
AR at 1 year	7%	13%
Mean time to AR (months)	6.1 ± 7.1	19.5 ± 11.0
SCr @ 6 months	1.6 ± 0.5	1.8 ± 0.7
SCr @ 1 year	1.8 ± 0.9	1.7 ± 1.2
SCr @ 3 years	2.4 ± 3.1	1.6 ± 0.5
GS @ 3 years	83%	80%
PS @ 3 years	88%[a]	87%

[a]All were deaths with functioning grafts.
*$p<0.05$.
AR = acute rejection; DCD = donation after cardiac death; DGF = duct growth factor; ECD = expanded criteria donor; GS = graft survival; PS = patient survival; SCr = serum creatinine.

CONCLUSIONS: This study suggests that BASI induction with low-dose maintenance prednisone provides equivalent 3-year graft and patient survival rates in AA kidney transplant recipients of deceased donor transplants compared with non-AA recipients. Similar acute rejection rates were noted. Basiliximab induction is effective in a carefully managed high-risk AA population.

332. Efficacy and Safety of Low-Dose Valganciclovir in Cytomegalovirus Prophylaxis in Kidney Transplantation Following Alemtuzumab Induction. *Shannon M. McLaughlin, Pharm.D. Candidate,*[1] Kristine S. Schonder, Pharm.D.[2]; (1) University of Pittsburgh School of Pharmacy, Canonsburg, PA; (2) University of Pittsburgh School of Pharmacy, Pittsburgh, PA

PURPOSE: To evaluate the efficacy and safety of low-dose valganciclovir for use of cytomegalovirus (CMV) prophylaxis in kidney transplant patients who received antibody induction with alemtuzumab.

METHODS: This retrospective study evaluated patients who received a kidney or kidney-pancreas transplant at the University of Pittsburg Medical Center between January 1, 2002, and January 1, 2007. Patients were included if they were 18 years or older at time of transplantation and received alemtuzumab induction before the transplant. Patients were excluded if follow-up laboratory values were not available. Patients received valganciclovir 450 mg/day, adjusted for renal dysfunction. Outcomes measured included incidence of CMV infection and the incidence of neutropenia, defined as a white blood cell count of less than 1.5 x 103/mm^3, to determine the safety of valganciclovir therapy.

RESULTS: The study population consisted of 863 patients. A total of 184 (21.3%) patients developed positive CMV results (CMV antigenemia or CMV polymerase chain reaction) posttransplantation. Of those patients, 72 were receiving an appropriate dose of valganciclovir based on renal function, indicating failure of the prophylactic regimen. Patients with neutropenia totaled 265 (30.7%), with 248 of them receiving growth colony stimulating factors to treat the adverse event.

CONCLUSIONS: Low-dose valganciclovir is an appropriate choice for CMV prophylaxis in patients receiving kidney transplantation when dosed according to changing renal function. This study is still in progress, and the collected data are currently being reviewed on a patient-specific basis to evaluate the significance of the incidence of infection and neutropenia.

333. Thymoglobulin® Induced Antibody Mediated Rejection in a Living Related Kidney Transplant Patient. *Anna Kipervasser, Pharm.D. Candidate*, Bethann Feist, Pharm.D. Candidate, Patrick J. McDonnell Jr., Pharm.D., Nicole M. Sifontis, Pharm.D., BCPS; Temple University School of Pharmacy, Philadelphia, PA

PURPOSE: Our report describes a rare case of antibody-mediated rejection (AMR) involving the use of Thymoglobulin in a kidney transplant recipient.

METHODS: A 26-year-old, 65-kg, black female, with a history of end-stage renal disease secondary to lupus nephritis received a 3 antigen-match kidney transplant from her brother. Patient had a history of blood transfusions, with no pregnancies or previous transplants. Pretransplant assessments of donor-reactive antibodies using complement-dependent cytotoxicity and flow cytometry were negative. Thymoglobulin was administered intraoperatively at 125 mg intravenously and then at 100 mg/day for two doses. Maintenance immunosuppression = mycophenolate sodium, tacrolimus (trough 5–10 ng/mL), and corticosteroid taper per protocol. Her postoperative course was uneventful, with serum creatinine (SCr) of 1.5 mg/dL by posttransplant day 5 (day of discharge).

RESULTS: Three days postdischarge, the patient presented with fevers and flu-like symptoms, SCr 2 mg/dL, and tacrolimus concentration 5 ng/mL. A biopsy showed acute cellular rejection (ACR) with intimal arteritis, Banff IIA, and negative CD4 staining. Patient was initiated on plasmapheresis, intravenous immunoglobulin (total 60 g), and 100 mg of Thymoglobulin for four doses; she subsequently became anuric. Hemodialysis (HD) was initiated; a second biopsy showed ACR type III with necrotizing vasculitis and extensive cortical infarction suggestive of combined ACR and AMR. Absence of CD4 staining argued against a conventional form of AMR, but because the intensity of the interstitial inflammatory process was not reduced with Thymoglobulin, the possibility was raised that the patient had developed anti-rabbit antibodies that reduced the efficacy of that agent. Patient subsequently reported exposure to a pet rabbit as a child. Anti-rabbit antibodies test was positive. Thymoglobulin was discontinued, HD was continued, and alemtuzumab 30 mg intravenously was given. On the day of discharge, patient was making urine with SCr 4.5 mg/dL off HD. Current baseline SCr 1.5 mg/dL (6 months posttransplant).

CONCLUSIONS: Clinicians should be made aware of the probability of antibody-mediated rejection after Thymoglobulin therapy and the importance of obtaining a thorough pet exposure history before transplantation.

RESEARCH INSTITUTE

ACCP Member Survey

334. Research Institute: ACCP Member and Frontiers Fund Donor Survey. *Jacqueline S. Marinac, Pharm.D.*; ACCP Research Institute, Lenexa, KS

BACKGROUND: In 2007, the Board of Trustees (BOT) of the Research Institute (RI) created a new strategic plan for the RI. This included the Focused Investigator Training (FIT) Program, Researcher and Scholarship Academy Programs (RSAP) & a nationwide practice-based research network (PBRN). Following BOT approval, a survey tool was created to get member feedback regarding Frontiers Fund (FF) development campaign and RI direction.

METHODS: Member respondents were stratified into 3 categories: Top-Tier (> $100) 2007 FF donors (n=186); Lower-Tier (< $100) 2007 FF Donors (n=343) & randomly selected 2005-2007 Non-donors (n=1250) were solicited via E-mail to complete the SurveyMonkey survey.

RESULTS: 227 members completed the survey. Response rates were 35%, 18% and 8% respectively. The duration of membership in ACCP was 13, (0-2 years) 38 (3-5 years) 42 (6-10 years) and 88 (10+ years). 77.5% have not received a grant or award from the RI. Overall the membership is satisfied to very satisfied with the Frontiers Fund and the RI. Over half have donated more than once, ¼ have not donated Most respondents are highly supportive of contributing to the RI. Many state competing donor priorities as reason why most members do not contribute. Majority prefer to be acknowledged for their donation via E-mail/letter and/or ACCP Report The #1 priority for both the individual and the organization was identified as Research demonstrating the value of clinical pharmacy services. The next highest priorities were the Academy Program, FIT & Investigator Development Grants and the PBRN. PRN mini-sabbaticals, traineeships and traditional fellowships received the lowest priority scores.

CONCLUSIONS: 2/3 of members surveyed are in support of the new direction of the RI, 1/3 being neutral at this time, the BOT has voted to move toward implementation of the new programs and services for 2008 and beyond.

Cardiovascular

335. Impact of Nesiritide Compared to Nitroglycerin on Renal Function in Patients with Acute Decompensated Heart Failure.

Text not available.

336. Renal Function and Neurohormonal Biomarkers Following Nesiritide vs. Nitroglycerin in Acute Decompensated Heart Failure: A Prospective Randomized Study. *Sheryl L. Chow, Pharm.D.,*[1] Stephen A. O'Barr, Ph.D.,[1] Jessica T. Peng, Pharm.D.,[2] Eric E. Chew, PA-C,[3] Firooz Pak, M.D.,[3] Paryus Patel, M.D.,[3] Mark Okamoto, Pharm.D.,[4] J. Thomas Heywood, M.D.[5]; (1) Western University of Health Sciences, Pomona, CA; (2) Western University of Health Sciences, College of Pharmacy and Centinela Freeman Regional Medical Center, Pomona, CA, Inglewood, CA; (3) Centinela Hospital, Inglewood, CA; (4) University of Hawaii at Hilo, Hilo, HI; (5) Scripps Clinic, La Jolla, CA

PURPOSE: A decline in renal function after nesiritide (NES) has been reported, but not with nitroglycerin (NTG). The current study compares the effect of NES versus NTG on renal function markers and their relationship to N-terminal pro-brain natriuretic peptide (NT-proBNP) in acute decompensated heart failure (ADHF).

METHODS: Eligible patients were randomized within 24 hours of hospital admission to either NES (0.01 µg/kg/minute with or without a 2-µg/kg bolus) or NTG (mean maximal dose 132 µg/minute) using a standard dosing protocol based on blood pressure monitoring. Standard renal function markers, Cystatin C (CystC), and NT-proBNP, were determined at baseline and at 24 and 48 hours of infusion.

RESULTS: Eighty-nine patients with ADHF (54% male, mean age 68 years, mean left ventricular ejection fraction 32%, 10% New York Heart Association II, 28% III, 58% IV, mean systolic blood pressure 133/75 mm Hg, and mean baseline brain natriuretic peptide 1695) were enrolled (45 NES, 44 NTG). Baseline values for serum creatinine, blood urea nitrogen, creatinine clearance, and intravenous furosemide doses were similar, although CystC levels were significantly different at baseline between the groups (1300 ± 1281 ng/mL for NES vs. 2081 ± 1922 for NTG group; p=0.045). There were no statistically significant changes from baseline in any of the renal function markers or between the NTG and NES groups at 24 and 48 hours of infusion. The mean baseline NT-proBNP levels were similar between the two groups; however, there was a greater reduction in NT-proBNP levels after NES versus NTG infusion (-22 ± 23*† vs. 8 ± 85% at 24 hours and -35 ± 29* vs. 10 ± 79%* at 48 hours, respectively [*p<0.05 compared with baseline, †compared with NTG]). No relationships between the percent change in NT-proBNP and renal function markers were observed.

CONCLUSIONS: NES or NTG treatment did not alter renal function in patients with ADHF; however, NT-proBNP was significantly reduced after NES infusion.

Infectious Diseases

337. Fluoroquinolone-Resistance (FQ-R) Is Linked to Increased Cytotoxicity of *Pseudomonas aeruginosa* (PA) Respiratory Isolates.

Annie Wong-Beringer, Pharm.D., Heather M. Owens, Pharm.D., M.S., Sam Lee, B.S.; University of Southern California, Los Angeles, CA

PURPOSE: *Pseudomonas aeruginosa* (PA) is a leading cause of ventilator-associated pneumonia. Patients infected with fluoroquinolone resistance (FQ-R) strains have poor outcomes, possibly related to the increased virulence of these strains. We investigated the relationship between FQ-R and cytotoxicity of respiratory isolates.

METHODS: Mechanisms of FQ-R were determined for 40 isolates by polymerase chain reaction analyses for mutations in *gyrA, gyrB, parC*, and *parE* genes and by testing with an efflux pump inhibitor (EPI; MC-04,128) for efflux pump overexpressed (EPO) phenotype. FQ-R was defined as levofloxacin minimum inhibitory concentration (MIC) of 8 µg/mL or more by broth microdilution. EPO was defined as 8-fold lower MIC in the presence of an EPI. Human lung epithelial cell line A549 was infected with PA, and cytotoxicity was measured using the Cytotox96 assay kit at 5, 1, 1.5, 2, 2.5, and 3 hours. PAO1 and PA103 were control strains. Isolates were grouped by the rate (fast vs. slow) at 1 hour and extent (weak vs. strong) at 3 hours of cytotoxicity.

RESULTS: Almost all (98%) isolates had EPO phenotype. Only 10% had no target site mutation (MIC 16–32 µg/mL); all showed slow-weak cytotoxicity. Isolates with a single mutation (11 [28%] of 40) were 73% *gyrA* (MIC 4–64 µg/mL) and 27% *parC* mutants (MIC 64–128 µg/mL). Half (52%) had two mutations (mostly *gyrA+parC*) with MIC 8–64 µg/mL. All four isolates with three target site mutations (*gyrA+parC+parE*) had MIC 64–128 µg/mL. As the number of mutations increases, the rate and extent of cytotoxicity increases, as indicated by the proportion with a fast rate (0, 18, 40, and 75%) and strong extent of killing (0, 36, 50, and 75%) for strains with zero, one, two, and three target site mutations, respectively.

CONCLUSIONS: Target site mutations, as they accumulate, appear to confer an additive cytotoxic potential to respiratory isolates of PA that are FQ resistant. Our data suggest that the expression of virulence and resistance genes is coregulated.