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ORIGINAL RESEARCH

ADR/Drug Interactions

1. Evaluation of the linezolid-serotonergic drug interaction in hospital inpatients. Amy C. Go, Pharm.D.,[1] *Larry K. Golightly, Pharm.D., BCPS*[2]; (1) University of Colorado Hospital, Anschutz Inpatient Pavilion, Aurora, CO; (2) University of Colorado Hospital, Center for Drug Information, Education, and Evaluation, Aurora, CO

PURPOSE: The oxazolidinone antibiotic linezolid is a nonselective reversible monoamine oxidase inhibitor. Prompted by the advent of life-threatening neuromuscular symptoms after the initiation of linezolid therapy in a patient receiving treatment with a selective serotonin reuptake inhibitor (SSRI) antidepressant, this evaluation was conducted to determine the incidence and characteristics of symptomatic serotonin toxicity among hospitalized patients receiving combined treatment with these medications.

METHODS: Patients admitted between January 1, 2006, and August 30, 2008, who received linezolid concurrently with citalopram or escitalopram were identified, and their medical records were examined. Patients were believed to have serotonin toxicity if their records contained documentation of clinical evidence adequate to fulfill the requisites of the Hunter Serotonin Toxicity Criteria (myoclonus, agitation, diaphoresis, tremor, and/or hyperreflexia [Dunkley et al. Q J Med 2003;96:635–42]). Severity of serotonin-related symptoms was graded according to standard criteria (Boyer et al., N Engl J Med 2005;232:1112–20).

RESULTS: During the period of observation, 24 patients received concurrent treatment with linezolid and citalopram or escitalopram. Of these patients, one (4%) treated with linezolid and citalopram met evidentiary requirements for diagnosis of serotonin toxicity. The severity of symptoms in this patient was graded as mild. No evidence of serious harm related to a possible drug interaction was identified.

CONCLUSIONS: As suggested by other surveillance reports, severe symptoms associated with serotonin toxicity were shown to be uncommon in patients receiving linezolid and selected SSRIs. Nonetheless, serious interaction-related toxicity has been reported in detail; accordingly, these medications in combination are categorized as contraindicated. When ordered, individual prescribers should be fully informed, and alternative antimicrobial therapy should be considered. If no suitable alternative is available, recipient patients should be carefully monitored.

2. Relationship between daily dosing frequency, compliance, and healthcare resource utilization: evidence from the treatment of chronic obstructive pulmonary disease (COPD). *Craig A. Plauschinat, M.S.*; Novartis, East Hanover, NJ

PURPOSE: To assess the relationship between daily dosing frequency (DDF) of chronic obstructive pulmonary disease (COPD) pharmacotherapies and treatment adherence and to estimate the effect of adherence on health care resource use.

METHODS: Patients with COPD were identified (ICD-9 491.XX, 492.XX, 493.2X, and 496.XX) using an administrative claims database covering 8 million privately insured lives (1999–2006). Patients were stratified on the basis of the recommended DDF (once daily, twice daily, 3 times/day, or 4 times/day) of their first COPD drug claim (index) post-COPD diagnosis. Continuous enrollment was required for 6 months before and 12 months after the index date. Comparisons of baseline demographics between groups were conducted using the Wilcoxon test for continuous outcomes and the χ^2 test for categoric outcomes. Adherence was measured using proportion of days covered (PDC). Health care resource use outcomes included inpatient days and medical visits. A multivariate negative binomial regression model assessed the relationship between adherence and 1-year health care resource use, controlling for demographics, comorbidities, and baseline health care resource use.

RESULTS: Sample sizes ranged from 3678 (once daily) to 21,843 (4 times/day). Adherence was strongly correlated with dosing frequency: PDCs for once-daily, twice-daily, 3 times/day, and 4 times/day patients were 43.3%, 37.0%, 30.2%, and 23.0%, respectively ($p<0.001$ for comparisons between once-daily and other dosing categories). Multivariate analysis showed that 1-year adherence was strongly correlated with health care resource use. For 1000 patients with COPD, a 5-percentage point increase in PDC reduced the number of inpatient visits by 30, hospital inpatient days by 190 days, and emergency department visits by 10; the estimated number of outpatient visits increased by 10 ($p<0.001$ for all comparisons).

CONCLUSIONS: Patients with COPD who initiated treatment with once-daily dosing had significantly higher adherence than those with more frequent dosing. Patients with higher adherence incurred less hospital- and emergency department–related health care resource use.

Adult Medicine

3. Evaluation of treatment practices for hyperkalemia in an acute care setting. Ted Walton, Pharm.D.,[1] *Kristy N. Fordjour, Pharm.D.,*[1] John Doran, M.D.[2]; (1) Grady Health System, Atlanta, GA; (2) Emory University School of Medicine–Nephrology Division, Atlanta, GA

PURPOSE: There are no uniform data regarding potassium (K^+) levels at which treatment of hyperkalemia is necessary. In addition, dosing for sodium polystyrene sulfonate (SPS) based on K^+ concentrations is lacking. There is also controversy surrounding the usefulness of electrocardiograms (ECGs) for detecting changes associated with hyperkalemia. This study sought to identify patients not treated with K^+ of 6.5 mEq/L or more, concentrations at which treatment is initiated, concentrations associated with ECG changes, and treatment practices for hyperkalemia.

METHODS: This was a retrospective, observational study of patients who developed hyperkalemia during July and October 2008. Patients who received treatment for hyperkalemia (defined as K^+ of 5.1 mEq/L or greater) were identified by medication use reports. A critical laboratory report was generated to capture patients not receiving treatment in the presence of a K^+ concentration of 6.5 mEq/L or greater. Medical records were assessed for ECG findings, causes of hyperkalemia, medications used in treatment, and concentrations pre- and posttreatment with SPS.

RESULTS: One hundred forty-eight episodes were evaluated. Two patients did not receive treatment for K^+ of 6.5 mEq/L or more. The mean K^+ prompting treatment was 6 mEq/L. Administration of 15-, 30-, and 60-g doses of SPS yielded reductions of 0.81 ± 0.58, 0.89 ± 0.64, and 1.04 ± 0.62, respectively. The ECG changes associated with hyperkalemia were six occurrences of peaked T waves, five prolonged PR intervals, and three widened QRS intervals when confounding variables were removed. Of 70 ECGs collected, 50% were normal when K^+ concentrations were greater or less than 6.5 mEq/L.

CONCLUSIONS: The most used treatment for hyperkalemia was SPS, and greater reductions in K^+ were achieved with increased doses. Treatment practices were targeted at reducing K^+ concentrations rather than using an ECG to determine when treatment was necessary. The ECG did not appear to be a sensitive indicator of elevated K^+ concentrations because half of the ECGs were normal regardless of the concentration.

4. Proton pump inhibitor use to reduce the gastrointestinal risks associated with dual antiplatelet therapy of clopidogrel and aspirin. *Kevin L. Forrester, Pharm.D.*, Jiwon W. Kim, Pharm.D., Emily Han, Pharm.D., Paula V. Phongsamran, Pharm.D., Marc Cosep, Pharm.D., Jennifer H. CupoAbbott, Pharm.D.; University of

Southern California School of Pharmacy and USC University Hospital, Los Angeles, CA

PURPOSE: Proton pump inhibitors are routinely prescribed to minimize gastrointestinal risks in patients receiving dual antiplatelet therapy with clopidogrel and aspirin. Recent studies suggest that proton pump inhibitors may interfere with the therapeutic activity of clopidogrel. Reevaluation of patients receiving dual antiplatelet therapy together with a proton pump inhibitor is, therefore, pertinent. The purpose of this retrospective study was to examine the appropriateness of proton pump inhibitor use to reduce the associated gastrointestinal complications in patients on dual antiplatelet therapy admitted to a tertiary care academic surgical hospital.

METHODS: A retrospective chart review was conducted of patients who received clopidogrel, aspirin, and proton pump inhibitors from February 2008 to April 2009. Baseline demographics, clinical history, and medication history were collected, and appropriateness of proton pump inhibitor indication was assessed. Appropriateness was based on criteria derived from published clinical practice guidelines.

RESULTS: A total of 128 patients (88 male; mean age, 68.3 ± 12.5 years) who received clopidogrel, aspirin, and a proton pump inhibitor were assessed. Fifty-five (43%) patients took a proton pump inhibitor before hospital admission. Of the 128 patients evaluated, 32 (25%) were taking a proton pump inhibitor with dual antiplatelet therapy before their hospital visit. The other 96 (75%) patients received therapy with clopidogrel, aspirin, and a proton pump inhibitor during hospital admission. Based on the developed criteria, an indication for proton pump inhibitor therapy was considered appropriate in 45 (35%) patients.

CONCLUSION: Among patients receiving dual antiplatelet therapy, a significant portion received a proton pump inhibitor, even though they did not meet criteria to be considered at-risk patients for gastroprotective therapy. With recent data suggesting reduced efficacy of clopidogrel with concomitant proton pump inhibitor use, it may be crucial to avoid unwarranted use of proton pump inhibitors in obtaining positive therapeutic outcomes with dual antiplatelet therapy, which includes clopidogrel.

Ambulatory Care

5. Evaluation of a pain management prescription service at a primary care clinic. *Zachary A. Weber, Pharm.D.,*[1] Philip T. Rodgers, Pharm.D., BCPS, CDE, CPP[2]; (1) Purdue University, Indianapolis, IN; (2) Duke University Medical Center, Durham, NC

PURPOSE: Determine the benefit of a clinical pharmacist for the management of pain within the C-II opiate contract-based prescription service (CBPS) in a primary care clinic.

METHODS: Eligible patients were all actively enrolled in the C-II opiate CBPS for treatment of nonmalignant pain from September 15, 2007, to September 15, 2008. Information collected included demographics, pharmacist and physician recommendations, drug-related problems (DRPs), patient-reported pain score, adverse drug reaction (ADR) frequency, and number of urine drug screens and physician visits. A physician survey was also completed. The primary end point was to compare patient-reported pain scores before and after pharmacist involvement in their pain management.

RESULTS: Fifty patients were included in this study. There was a significant reduction in patient-reported pain score after pharmacist involvement (7.6 vs. 6.0, p=0.0041). Pharmacists also improved adherence to CBPS standards by significantly increasing the number of urine drug screens (0.8 vs. 1.6, p<0.0001). The probability of patient-reported ADRs also significantly improved (27% vs. 33%, p=0.008). The most common opioid combination was methadone (34%) and oxycodone immediate release (44%). About 20% of patients were receiving monotherapy with either a short- or long-acting opiate for management of their chronic pain. Overall, pharmacists provided recommendations 44% of the time and identified DRPs 52% of the time. According to survey results, physicians like the current CBPS, with 97.3% stating that the CBPS is acceptable or that they would not change anything, and 88.9% like pharmacists' current role within this service. Physicians also report oxycodone as their short-acting opiate of choice and either MS Contin or OxyContin as their long-acting opiate of choice (56.8%, 37.8%, and 37.8%).

CONCLUSIONS: This study demonstrated an association between pharmacist involvement in the CBPS and decreases in patient-reported pain scores.

6. Medication management programs at a VA medical facility: effects on blood pressure, a retrospective analysis. *Jennifer H. Lai, Pharm.D.*, Timothy C. Chen, Pharm.D., Mark Bounthavong, Pharm.D.; Veterans Affairs San Diego Healthcare System, San Diego, CA

PURPOSE: To evaluate the impact of pharmacist-run medication management (PMM) versus standard care on hypertension in two scenarios: 1) medication management clinic (MMC) where pharmacists review all medications and 2) pharmacist-management clinic (PMC) where pharmacists have prescribing privileges.

METHODS: A retrospective analysis of patients evaluated by PMM in two separate clinics, MMC and PMC, from January 2004 to December 2007 compared with standard care (control group). Primary outcome was median time to blood pressure (BP) goal (tBPG). Secondary outcomes were change in BP and number of patients who reached BP goals. Univariate analyses were performed to identify covariates (p<0.10) for input into a logistic regression model.

RESULTS: In the MMC, tBPGs for PMM and control group were 72 and 188.5 days, respectively (p=0.319). In the PMC, the tBPGs for the pharmacist care group and control group were 110 and 182 days, respectively (p=0.011). The BP reduction in the MMC was seen in patients in the PMM (mean difference: systolic, –29.32, p<0.0005; diastolic, –13.74, p=0.09) and control group (mean difference: systolic, –27.68, p<0.0005; diastolic, –13.59, p=0.04). The BP reduction in the PMC was seen in patients in the PMM (mean difference: systolic, –26.51, p<0.0005; diastolic, –10.71, p<0.0005) and control group (mean difference: systolic, –27.06, p<0.0005; diastolic, –12.42, p<0.0005). In the MMC, a total of 27 of 34 patients reached BP goal in the PMM and 14 of 27 in the control group (p=1.000). In the PMC, a total of 122 of 128 patients reached BP goal in the PMM (60 of 122) and control group (62 of 122) (p=0.68). Low baseline diastolic BP (OR = 0.927; 95% CI: 0.844–0.996) and congestive heart failure (OR = 1.014; 95% CI: 3.438–183.301) were predictors of BP goal in the logistic regression model for the PMC.

CONCLUSIONS: PMC and MMC were able to reduce the time to BP goal compared with standard care.

7. Glycemic control in pharmacist-managed insulin titration versus standard care in an indigent population.

Jamie M. Pitlick, Pharm.D., Amie D. Brooks, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis, MO

PURPOSE: Assess the impact of a pharmacist-managed insulin titration program on achieving clinical goals in an indigent population with diabetes. The primary outcome is change in A1c over time. Secondary outcomes include clinical goal attainment and change in parameters over time.

METHODS: Medical records for subjects in the pharmacist-managed insulin titration program between August 2007 and August 2008 (n=48) were retrospectively reviewed. An equal number of control subjects were matched for age, titration time frame, and insulin regimen. A Student t-test was used to analyze the primary outcome. Descriptive statistics and χ^2 analyses were used to evaluate secondary outcomes.

RESULTS: Thirty-six pharmacist-managed subjects were included with 35 matched controls. Average subject at baseline was 51.7 years old (±10.3 years) and 223.7 lb (±56.1 lb), with body mass index 36.1 kg/m^2 (±8.7 kg/m^2). A1c was the only characteristic that differed significantly at baseline (intervention group, 10.1% [±2.1%]; control group, 9.0% [±2.1%]; p=0.04). Between-group comparison demonstrated a significant difference in mean change in A1c favoring pharmacist management at 3 months (–0.6%, 95% confidence interval [CI]: –1.1 to –0.05; p=0.03), 6 (–1.1%, 95% CI: –1.8 to –0.5; p=0.003) and 9 months (–0.9%, 95% CI: –2.1 to –0.8; p=0.046) but not 12 months (–0.7%, –2.1 to 0.6; p=0.20). Within-

group comparisons demonstrated a significant A1c reduction from baseline to each time point (3, 6, 9, and 12 months) in the pharmacist-managed group, with no significant changes observed in the control group.
CONCLUSIONS: Pharmacist-managed insulin titration demonstrated significant improvement in glycemic control compared with standard care in an indigent population.

8. Using a clinical reminder to increase statin use in diabetics. *Elizabeth J. Peterson, Pharm.D.,*[1] Thomas J. Worrall, Pharm.D., BCPS, FAPhA,[2] Dorothy E. Jenrette, Pharm.D., BCPS[2]; (1) Ralph H. Johnson VA Medical Center, Charleston, SC; (2) Ralph H. Johnson VA Medical Center, Charleston, SC
PURPOSE: This study determined whether a computerized medical record clinical reminder and a formal pharmacist-provider educational session influence statin prescribing in individuals with diabetes.
METHODS: Patients with diabetes were eligible for the study if they were seen by their primary care provider but were not prescribed a statin between November 1, 2007, and October 31, 2008, and had a follow-up visit between November 1, 2008, and January 31, 2009. A clinical reminder in the electronic medical record was implemented on November 1, 2008, prompting providers to prescribe statin therapy in statin-naïve individuals with diabetes. Concurrently, a pharmacist provided an educational session to a subset of providers highlighting the benefits of statins in patients with diabetes. It was determined whether the clinical reminder alone, or the clinical reminder in combination with pharmacist-led education, influenced statin prescribing in the follow-up period. χ^2 analysis was used.
RESULTS: We identified 557 statin-naïve patients with diabetes during the baseline period. In the 407 patients cared for by providers who were exposed to the clinical reminder only, 64 (16%) were prescribed a statin in the follow-up period (p=0.01). In the 150 patients cared for by providers exposed to the clinical reminder in combination with pharmacist-led education, 32 (21%) were prescribed a statin in the follow-up period (p=0.04). The electronic clinical reminder combined with pharmacist-led education did not statistically influence statin prescribing compared with the electronic clinical reminder alone (p=0.15).
CONCLUSIONS: An electronic clinical reminder alone or in combination with pharmacist-led education increases statin prescribing in patients with diabetes. One method was not statistically superior to the other.

9. Prescribing patterns for the outpatient treatment of constipation in the United States. *Katy Trinkley, Pharm.D.,*[1] Kyle Porter, MAS,[2] Milap Nahata, Pharm.D., M.S.[1]; (1) Ohio State University College of Pharmacy, Columbus, OH; (2) Ohio State University Center for Biostatistics, Columbus, OH
PURPOSE: We designed this study to 1) identify patterns in the treatment of constipation and 2) determine associations between treatment and demographic variables among U.S. outpatients.
METHODS: This was a retrospective cross-sectional study using data from the NAMCS (National Ambulatory Medical Care Survey) from 1997 to 2006 on treatment trends for constipation in different age groups. Information collected from each visit included demographic data, medications, and nonpharmacologic therapies for constipation. Statistical sampling weights were used to obtain estimates representative of all U.S. outpatient visits.
RESULTS: There were 52.7 million office visits related to constipation: 65% were from females, 26% from pediatric patients, 19% from patients 18–44 years old, 20% from individuals 45–64 years old, and 35% from elderly patients. Choices of treatments were medications and nonpharmacologic therapies for 17% of visits, medications for 21%, nonpharmacologic therapies for 23%, and no therapy for 39%. Medications used were 19% hyperosmolars, 7% fiber, 5% stool softeners, 3% stimulant laxatives, 3% tegaserod, 3% saline, and 1% prokinetics. From 1997–2001 to 2002–2006, there were significant shifts in treatments. Across all patients, use of medications increased, and nonpharmacologic therapies decreased. In pediatric patients and patients aged 18–44, hyperosmolars increased and saline decreased. In pediatric patients, fiber decreased. In patients aged 18–44, there were increases in stimulant laxatives and medication in general, with African Americans more likely to receive medications than whites were. Stool softeners decreased in patients aged 45–64. In elderly patients, medications increased while combination therapies decreased, with whites receiving some therapies more often than African Americans and being more likely to receive nonpharmacologic therapy than other races.
CONCLUSIONS: Constipation was most frequent among the elderly, followed by children. Medications increasingly replaced nonpharmacologic therapy. Hyperosmolars were most often prescribed, and their use increased over time. Age and race influenced treatment of constipation.

10E. Predictors of medication adherence in an urban community with healthcare disparities. *Fei Wang, Pharm.D.,*[1] Jennifer Colby, Pharm.D.,[2] Rafael Perez-Escamilla, Ph.D.,[3] Jyoti Chhabra, Ph.D.[2]; (1) Hartford Hospital/ University of Connecticut, Hartford, CT; (2) Hartford Hospital, Hartford, CT; (3) University of Connecticut, Storrs, CT
PURPOSE: To identify independent predictors of medication adherence in an urban Latino community with diabetes and health care disparities.
METHODS: This was a nested, cross-sectional retrospective study of a subsample of baseline data; it was gathered for a larger parallel, randomized, longitudinal study titled "Diabetes Among Latinos Best Practices" (DIALBEST). This trial was conducted at an urban primary care practice affiliated with a teaching hospital. Patients included in the larger study had a diagnosis of type 2 diabetes with a hemoglobin A1c of 7.0 or more. Baseline patients included in the subsample for this presentation were those who responded to a medication adherence scale (Morisky scale). Baseline demographic and medication use covariates were evaluated for eligibility into the multivariable logistic regression to predict medication adherence. (Medication nonadherence is defined as a Morisky score of less than 4.) Independent predictors of medication adherence are reported as adjusted odds ratios with 95% confidence intervals. Statistical analysis was performed with SPSS version 14 (SPSS Inc., Chicago, IL).
RESULTS: Multivariate logistic regression results revealed that medication adherence was strongly associated with support extended by a physician or health care team (adjusted odds ratio [aOR] = 9.32 [95% confidence interval (CI): 1.00–87.17]). In contrast, patients of lower socioeconomic status (as reflected by their participation in federal/state assistance programs) were associated with an 85% reduced odds of being adherent to their medications (aOR = 0.15 [0.025–1.02]).
CONCLUSION: Medication adherence is positively influenced by increased support extended by a physician or health care team and negatively influenced by a low socioeconomic background.
Presented at ASHP 2009 Summer Meeting, Chicago, IL, June 14–17, 2009.

11. Stroke and hypertension awareness in a high-risk population: influence of a pharmacist-initiated intervention in an anticoagulation clinic. *Jennifer L. Clemente, Pharm.D.,*[1] Jesse Shuster, Pharm.D.,[1] Candice L. Garwood, Pharm.D.,[2] Peter Whittaker, Ph.D.[3]; (1) Detroit Medical Center, Detroit, MI; (2) Wayne State University, Detroit, MI; (3) Wayne State University School of Medicine, Cardiovascular Research Institute and Department of Emergency Medicine, Detroit, MI
PURPOSE: African Americans (AA) are at risk of stroke, and hypertension and warfarin therapy increase this risk; however, regular attendance at an anticoagulation clinic provides an opportunity to receive education. Therefore, we sought to determine whether pharmacist-initiated interventions could increase patients' knowledge.
METHODS: AA patients on antihypertension therapy were given an oral questionnaire (OQ), which covered knowledge of stroke and hypertension, at a routine anticoagulation visit. The OQ was then readministered at the next scheduled visit. We randomized patients (n=60) to three groups: 1) control group (C) – no intervention, 2)

group in which patients' blood pressure (BP) was measured after the OQ was given at the first visit, and 3) group in which an education (ED) brochure on hypertension, anticoagulation, and stroke risk was provided, with additional counseling given at the first visit after administration of the OQ. We calculated the change in score (ΔS) between visits and examined how this was influenced by the initial score and time between visits.
RESULTS: The ΔS increased in the BP and ED groups ($p<0.05$) but not in the controls. In addition, all groups possessed inverse correlations between ΔS and initial score; the lower the initial score, the higher the ΔS. The gradient of these regression lines was similar for all groups; however, the C group line was below that of the BP group, which was below that of the ED group – consistent with increased knowledge; ED>BP>C. For controls, time between visits did not affect the ΔS. Similarly, the ED group showed no temporal change; however, the regression line was above that for controls – consistent with knowledge retained after education. Conversely, for the BP group, the ΔS decreased as time between visits increased – consistent with the concept that the apparent knowledge gain associated with BP measurement was gradually lost.
CONCLUSION: Regular anticoagulation clinic attendance provides pharmacists an opportunity to increase awareness of stroke and hypertension in a vulnerable population.

12. Impact of clinical pharmacy services on hypertension at a Veterans Affairs community based outpatient clinic. *William Joshua Guffey, Pharm.D.*, Beth Bryles Phillips, Pharm.D.; University of Georgia College of Pharmacy, Athens, GA
PURPOSE: The benefit of pharmacist-managed ambulatory care clinics on patient outcomes in large Veterans Affairs (VA) medical centers has been established. It is not known if similar outcomes extend to the growing number of smaller standalone VA community-based outpatient clinics (CBOCs). The purpose of this study was to evaluate the impact of a pharmacist-managed pharmacotherapy clinic (PC) on hypertension (HTN) management at a CBOC compared with usual primary care (UC).
METHODS: Patient data were evaluated retrospectively in 50 CBOC patients (n=25 PC, n=25 UC) at baseline, 3 months, and 6 months. UC patients were randomly selected on the basis of the ICD-9 code.
RESULTS: Patients (mean age, 61 ± 10 years) were taking 2.1 ± 1 antihypertensives: 68% angiotensin-converting enzyme inhibitors, 14% angiotensin receptor blockers (ARBs), 45% b-blockers, 30% thiazide, and 22% calcium channel blockers. Fewer PC patients were taking ARBs (8%) compared with UC patients (20%) ($p=0.02$). Blood pressure (BP) and percent at goal BP were not different between PC and UC at baseline. In the PC group, baseline systolic BP decreased from 141 ± 14 mm Hg to 132 ± 13 mm Hg at 3 months ($p=0.02$) and to 129 ± 12 mm Hg at 6 months ($p<0.001$). The percentage of patients achieving goal BP (less than 130/80 mm Hg) increased from 24% at baseline to 48% at 3 months ($p<0.001$) and 41% at 6 months ($p=0.02$). In the UC group, the percentage of patients achieving goal BP decreased from 36% at baseline to 28% at 3 months ($p>0.05$) and 4% at 6 months ($p<0.0001$). Compared with UC, PC patients had larger reductions in systolic BP (10.8 ± 13 vs. −5.1 ± 17 mm Hg, $p=0.003$) and diastolic BP (3 ± 12 vs. −2.1±15 mm Hg, $p=0.03$) at 6 months.
CONCLUSIONS: Pharmacy-managed HTN care at a VA CBOC resulted in lower blood pressure levels and greater achievement of BP goal over 6 months. These findings suggest clinical pharmacy services can optimize BP management in this practice setting.

13. Impact of clinical pharmacy services on diabetes mellitus at a Veterans Affairs community based outpatient clinic. William Joshua Guffey, Pharm.D.,[1] *Beth Bryles Phillips, Pharm.D.*[2]; (1) University of Georgia College of Pharmacy, Athens, GA; (2) University of Georgia, Athens, GA
PURPOSE: The benefit of pharmacist-managed ambulatory care clinics on patient outcomes in large Veterans Affairs (VA) medical centers has been established. It is not known if similar outcomes extend to the growing number of smaller standalone VA community-based outpatient clinics (CBOCs). The purpose of this study was to evaluate the impact of a pharmacist-managed pharmacotherapy clinic (PC) on diabetes mellitus (DM) management at a CBOC compared with usual care (UC).
METHODS: Patient data were reviewed retrospectively in 39 CBOC patients (n=14 PC, n=25 UC) at baseline and 6 months to evaluate the impact of the PC on A1c and attainment of goal A1c. The UC patients were randomly selected on the basis of the ICD-9 code.
RESULTS: Patients were 62 ± 9 years old and had a baseline A1c of 8.6% ± 1.7%. Patients in the PC group were taking more DM medications (2.3 ± 0.7) compared with UC (1.3 ± 0.8, $p<0.001$). Compared with UC patients, a higher percentage of PC patients were receiving insulin (80% vs. 24%, $p<0.0001$) and metformin (84% vs. 48%, $p<0.0001$); a lower percentage of patients were receiving thiazolidinediones (5% vs. 20%, $p=0.002$). In the PC group, A1c decreased from 8.9 ± 1.4 at baseline to 7.9 ± 1.1 at 6 months ($p<0.001$). The percentage of PC patients achieving goal A1c (less than 7%) increased from 11% at baseline to 29% at 6 months ($p=0.002$). In the UC group, changes in A1c and percent at goal were not significant.
CONCLUSION: Pharmacy-managed DM care at a VA CBOC resulted in greater reductions in A1c and a greater percentage of patients achieving A1c goals over 6 months. These findings suggest that clinical pharmacy services can optimize DM management in this practice setting.

14. Hepatitis C virus (HCV): evaluation of laboratory assessments before treatment and the effectiveness of a pharmacist-managed treatment program. *Lori B. Hornsby, Pharm.D.*,[1] Ryan Crossman, Pharm.D.,[2] Hardik Patel, P4,[3] Alison O. Baker, P4[3]; (1) Auburn University Harrison School of Pharmacy, Phenix City, AL; (2) Columbus Regional Healthcare System, Columbus, GA; (3) Auburn University Harrison School of Pharmacy, Auburn, AL
PURPOSE: To evaluate the appropriateness of hepatitis C virus (HCV) laboratory assessments conducted by primary care providers before treatment and outcomes of a pharmacist-managed treatment program in an indigent population.
METHODS: A retrospective chart review of 94 patients with HCV was conducted. Hepatitis panels, serum HCV RNA levels, and genotypes were evaluated for appropriateness considering indication, prior evaluations, contraindications to treatment, and outcomes. Patients treated through the pharmacist-managed clinic with peginterferon alfa and ribavirin were assessed for response to treatment and adverse effects.
RESULTS: Thirty-one HCV RNA levels and 17 genotypes were obtained in 58 patients either ineligible because of alcohol use (n=33) or lost to follow-up (n=25) before treatment. The remaining patients were receiving treatment or being assessed for treatment, had completed treatment or had undetectable HCV RNA levels at baseline, or had other reasons for delaying treatment. Fourteen patients were referred for pharmacist treatment between January 2007 and May 2009. Six experienced end-of-treatment response, two with genotype 2 (24 weeks) and four with genotype 1 (48 weeks). Two with genotype 1 had a sustained virologic response, with the remaining awaiting follow-up. Another four achieved an early virologic response at 12 weeks. Of these, one maintained undetectable HCV RNA levels and one was unresponsive at 24 weeks. Three were recently initiated on therapy with follow-up unavailable. Therapy was discontinued in one patient because of nonadherence to follow-up. Dose reductions because of a decrease in hemoglobin were necessary in three patients. Adverse effects included flu-like symptoms, cutaneous reactions, and weight loss (range, 6–40 lb; mean, 20 lb).
CONCLUSIONS: Although most HCV evaluations were appropriate, suggestions to decrease future laboratory assessments include screening for alcohol use before evaluation postdiagnosis and obtaining genotypes immediately before initiating treatment. To date, 14 patients have been referred for pharmacist-managed HCV treatment with overall positive results.

15. Anticoagulation stability is determined by the consistency and quantity of vitamin K consumption. *Jennifer L. Clemente, Pharm.D.*,[1] Candice L. Garwood, Pharm.D.,[2] Jennifer L. Johnson, Pharm.D., Candidate,[3] Peter Whittaker, Ph.D.[4]; (1) Detroit Medical

Center, Detroit, MI; (2) Wayne State University, Detroit, MI; (3) Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, MI; (4) Wayne State University School of Medicine, Cardiovascular Research Institute and Department of Emergency Medicine, Detroit, MI

PURPOSE: Warfarin-treated patients are counseled to have consistent vitamin K consumption (VKC). The hypothesis is that VKC consistency results in anticoagulation (AC) stability. Nevertheless, there are no data to indicate if consistency alone or a combination of consistency and quantity is the key factor. Therefore, we sought to examine the role of quantity in VKC consistency.

METHODS: Our retrospective chart review identified patient cohorts who claimed VKC consistency during a 1- to 5-year follow-up. Precise microgram VKC measurement over protracted periods is impractical, so we divided patients into three VKC categories: 1) those with zero weekly (ZW); 2) those with some weekly (SW), one or two servings; and 3) those with lots weekly (LW), servings at least every other day. To minimize influences of parameters that can affect stability, we restricted enrollment to patients younger than 70 years, 2.0–3.0 target international normalized ratio (INR), and glomerular filtration ratio more than 60 mL/minute. We evaluated AC stability by calculating the percentage of clinic visits with INR of 4.0 or greater as well as the standard deviation (SD) of each patient's INR; the lower the SD, the greater the stability. Diet stability was assessed by calculating the number of days between VKC changes.

RESULTS: SW patients had 3-6-fold increases in INRs more than 4.0 versus the other groups (SW = 5.7 ± 1.6, ZW = 0.9 ± 0.6, LW = 1.8 ± 1.0; p<0.02). Furthermore, INR SD was higher in SW patients (SW = 0.68 ± 0.06, ZW = 0.48 ± 0.04, LW = 0.52 ± 0.06; p=0.03). The time between VKC diet changes was longer in the ZW group (ZW = 904 ± 147, SW = 195 ± 51, LW = 142 ± 23 days; p<0.0001).

CONCLUSION: Patients with zero VKC demonstrated greater INR stability. Conversely, patients who reported some weekly VKC were more likely to have elevated INRs and hence increased bleeding risk. Large weekly VKC achieved AC stability similar to zero VKC, even with diet fluctuations, indicating that VKC quantity plays a role in achieving stability. Therefore, stressing diet consistency may not be the correct approach for achieving AC stability.

Cardiovascular

16E. Beta-Blocker Evaluation of Survival Trial (BEST) findings show benefit of bucindolol in moderate to severe HF patients, according to pre-specified statistical analysis plan. *Bruce R. Koch II, Pharm.D.*,[1] Eric Eichhorn, M.D.,[2] Hector Ventura, M.D.,[3] Gordon Davis, MSPH,[1] Mona Fiuzat, Pharm.D.,[4] Alastair D. Robertson, Ph.D.,[5] Michael R. Bristow, M.D., Ph.D.[6]; (1) ARCA biopharma, Inc., Broomfield, CO; (2) Dallas Heart Group, Dallas, TX; (3) Oschner Medical Center, New Orleans, LA; (4) Duke University Medical Center, Division of Clinical Pharmacology, Durham, NC; (5) University of Colorado Health Sciences Center, Denver, CO; (6) ARCA biopharma, University of Colorado Health Sciences Center, Denver, CO

PURPOSE: Preliminary results from the Beta-Blocker Evaluation of Survival Trial (BEST) were reported in 2001, after an early termination of the study for loss of investigator equipoise; however, results analyzed according to the U.S. Food and Drug Administration–negotiated prespecified statistical analysis plan (SAP) have never been reported. This paper presents results from that analysis.

METHODS: A total of 2708 patients with heart failure (HF) designated New York Heart Association (NYHA) functional class III (92%) or IV (8%) and a left ventricular ejection fraction of T35% were randomly assigned to double-blind treatment with either bucindolol (1354 patients) or placebo (1354 patients) and were observed for the primary end point of death from any cause as well as the highest ranking secondary end point of HF progression.

RESULTS: Analysis of study results according to the prespecified SAP indicated a near-significant reduction in all-cause mortality with bucindolol compared with placebo (hazard ratio [HR], 0.87, p=0.053), despite the availability of only 92% of the projected number of primary end points based on the pretrial sample size calculations. Analysis of the composite end point of HF progression indicated that bucindolol was significantly superior to placebo for slowing progression of HF (HR, 0.80; p=0.00003) and its components of HF-related mortality (HR, 0.85; p=0.042), HF-related hospital admission (HR, 0.77; p=0.00002), and HF-related emergency department visit (HF, 0.74; p=0.024). Bucindolol also demonstrated significant superiority over placebo for eight secondary end points.

CONCLUSIONS: In a demographically diverse group of primarily U.S. patients with NYHA class III and IV heart failure, bucindolol resulted in near-significant overall survival benefit as well as significant benefit in slowing progression of HF, despite premature termination of the study. These findings are contrary to the common belief that BEST was terminated early because of futility.

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17. Comparison of a treatment strategy using amlodipine/valsartan fixed dose combination therapy (Exforge®) with conventional therapy. *Mark A. Malesker, Pharm.D., FCCP, BCPS*, Daniel E. Hilleman, Pharm.D., FCCP; Creighton University Medical Center, Omaha, NE

PURPOSE: Single-pill combination antihypertensive drug products have many potential advantages including improved adherence. The purpose of this study was to compare clinical and economic outcomes associated with the use of a single-pill combination of amlodipine-valsartan (A/V) against conventional therapy in patients whose initial monotherapy failed with either a dihydropyridine calcium channel blocker or an angiotensin receptor blocker.

METHODS: We conducted a retrospective cohort study of patients either switched to A/V (Exforge) or receiving individual antihypertensive agents (controls), none of which could be single-pill combination therapy. The groups were matched for age, gender, race, baseline blood pressure (BP), and comorbidities. The primary outcomes of the study included the proportion of patients achieving BP targets, the absolute change in BP from baseline compared with the final follow-up visit, the proportion of patients discontinuing drug therapy because of adverse effects, the proportion of patients nonadherent to drug therapy, and health care resource use and costs.

RESULTS: Each group included 100 patients, with 58 patients receiving the single-pill combination achieving BP goals compared with the 47 control patients (p=0.119). The absolute reduction in BP was significantly greater with A/V (–22.8‡6.9/–19.3‡5.2 mm Hg) compared with controls (–20.6‡6.4/–17.8‡5.6 mm Hg) (p<0.03). Significantly fewer patients discontinued antihypertensive therapy for adverse effects and nonadherence with A/V compared with the control group (both p=0.042). A/V patients accrued fewer clinic visits, laboratory tests, and electrocardiograms but had higher drug acquisition costs. Median medical therapy costs were not significantly different between the groups at the end of the 6-month follow-up.

CONCLUSIONS: A/V was associated with greater absolute BP reductions, improved adherence, and fewer drug discontinuations, clinic visits, laboratory tests, and electrocardiograms. In light of a higher acquisition cost, the total cost of A/V therapy was not significantly greater than the use of the individual agents.

18E. The AGELESS Study: the effect of aliskiren vs ramipril alone or in combination with hydrochlorothiazide and amlodipine in patients ≥ 65 years of age with systolic hypertension. *Mark A. Munger, Pharm.D.*,[1] Daniel A. Duprez, M.D.,[2] Jaco Botha, Ph.D.,[3] Alan N. Charney, M.D.[3]; (1) University of Utah, Salt Lake City, UT; (2) University of Minnesota Medical School, Minneapolis, MN; (3) Novartis Pharmaceutical Co., East Hanover, NJ

PURPOSE: To demonstrate noninferiority between monotherapy with the direct renin inhibitor aliskiren and the angiotensin-converting enzyme inhibitor ramipril on the change from baseline in mean sitting systolic blood pressure (msSBP) after 12 weeks of treatment in patients 65 years and older. If noninferiority was demonstrated, then superiority was tested. The proportion of patients achieving their BP goal (msSBP less than 140/90 mm Hg), the proportion of patients requiring add-on therapy, and safety/

tolerability were also assessed.
METHODS: In this 36-week, double-blind, multicenter study, patients 65 years and older with an msSBP of 140 mm Hg and more and less than 180 mm Hg were randomized to aliskiren 150 mg/day or ramipril 5 mg/day for 4 weeks. If SBP was not at goal at 4 weeks, doses were doubled, and SBP was evaluated at 12 weeks. If SBP was still not at goal, hydrochlorothiazide (HCTZ) (12.5–25 mg/day), followed by an amlodipine (5–10 mg/day) regimen (after week 22), was added, and SBP was evaluated at 36 weeks.
RESULTS: Nine hundred one patients were randomized (aliskiren n=457, ramipril n=444). Mean age was 72.1 years, 52% were female, 21% were diabetic, 40% were obese (body mass index more than 30 kg/m^2), and 85% were white. Patients older than 75 years made up 33% of the total population. Changes from baseline in msSBP (mm Hg) at the week 12 end point were –13.96 and –11.64 for aliskiren monotherapy and ramipril monotherapy, respectively (p=0.0241). Significantly more patients on aliskiren-based therapy achieved their BP goal at week 12, 22, and 36 end points (p<0.05 for each end point), and significantly fewer required add-on HCTZ by the week 22 end point (p=0.0048) or amlodipine by the week 36 end point (p=0.0481). Both treatments were well tolerated, but significantly more patients on ramipril had cough at week 12 and 36 end points (p<0.0001).
CONCLUSIONS: Direct renin inhibition with aliskiren provided greater reductions in SBP and diastolic BP, brought greater attainment of BP goal, and required fewer add-on therapies compared with ramipril in elderly patients with hypertension.
Published in Duprez DA, Davis P, Botha J. The AGELESS Study: the effect of aliskiren vs ramipril alone or in combination with hydrochlorothiazide and amlodipine in patients > 65 years of age with systolic hypertension. Circulation 2008;118(Suppl 18): S886.

19E. Efficacy of olmesartan medoxomil and hydrochlorothiazide in elderly (≥65 years) patients with hypertension: age and gender subgroups. *Dean J. Kereiakes, M.D.,*[1] Joel M. Neutel, M.D.,[2] Kathy A. Stoakes, RN, BSN, CCRA,[3] William F. Waverczak, M.S.,[3] Jianbo Xu, M.S.,[3] Ali Shojaee, Pharm.D.,[3] Robert Dubiel, Pharm.D.[3]; (1) The Christ Hospital Heart and Vascular Center and The Carl and Edyth Lindner Center for Research and Education at The Christ Hos, Cincinnati, OH; (2) Orange County Research Center, Tustin, CA; (3) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: Evaluate the antihypertensive efficacy of olmesartan medoxomil (OM) and hydrochlorothiazide in a prespecified subgroup analysis by age (75 years and younger and older than 75 years) and gender in an elderly patient population (65 years and older) with hypertension.
METHODS: Blood pressure (BP)-lowering efficacy was determined by mean 24-hour ambulatory BP monitoring (ABPM) and mean seated cuff BP (SeBP) in this open-label, dose-titration study of OM with or without hydrochlorothiazide. The primary end point was the mean change from baseline in systolic BP (SBP) assessed by ABPM after 12 weeks. Some secondary end points included mean change from baseline in diastolic BP (DBP) by ABPM, change in SeSBP/SeDBP, and proportion of patients achieving prespecified ambulatory BP targets (less than 140/90, less than 135/85, less than 130/80, less than 125/75, <120/80 mm Hg). After a 2- to 3-week placebo period, patients started OM 20 mg, uptitrated to OM 40 mg, and then added hydrochlorothiazide 12.5–25 mg in a stepwise manner at 3-week intervals. Patients with SeBP less than 120/70 mm Hg did not uptitrate.
RESULTS: Efficacy cohort: 176 patients (ABPM available for 150) with mean age (±SD) 71.9 ± 5.2 years and 65.9% stage 2 hypertension. At study end, the OM-based regimen significantly reduced mean 24-hour ambulatory SBP/DBP for those 75 years and younger by 26.0/12.5 mm Hg and older than 75 years by 24.9/12.0 mm Hg (p<0.0001). For ages 75 years and younger, 45.5%–86.4% of patients achieved mean 24-hour ambulatory BP targets ranging from less than 120/80 to less than 140/90 mm Hg, and 40.0%–95.0% of patients older than 75 years achieved the same targets. The OM-based regimen reduced mean 24-hour ambulatory SBP/DBP for men by 26.0/13.0 mm Hg, and for women, by 25.4/11.5 mm Hg. Furthermore, 47.6%–88.1% of men achieved mean 24-hour ambulatory BP targets ranging from less than 120/80 mm Hg to less than 140/90 mm Hg, and 39.4%–89.4% of females achieved the same targets. OM/hydrochlorothiazide therapy was well tolerated irrespective of age or gender.
CONCLUSIONS: OM/hydrochlorothiazide provided comparable significant reductions in ambulatory BP and achievement of ambulatory BP targets regardless of age or gender.
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20E. Differential effects of nesiritide versus nitroglycerin on inflammatory biomarkers in patients with acute decompensated heart failure. *Sheryl L. Chow, Pharm.D., BCPS,*[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 P. Okamoto, Pharm.D.,[1] J. Herbert Patterson, 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) UNC-Chapel Hill, Chapel Hill, NC; (5) Scripps Clinic, La Jolla, CA
PURPOSE: The purpose of the present study was to evaluate the differential response of inflammatory markers to nitroglycerin (NTG) versus nesiritide (NES) treatment in acute decompensated heart failure (ADHF).
METHODS: Patients were prospectively 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. The inflammatory biomarkers, high-sensitivity C-reactive protein (hsCRP), tumor necrosis factor alpha (TNF-α), transforming growth factor beta-1 (TGF-β), and interleukin-6 (IL-6), were evaluated at baseline and during infusion at 24 and 48 hours.
RESULTS: Eighty-nine patients with ADHF (54% male; mean age, 68 years; mean left ventricular ejection fraction, 32%; 10% New York Heart Association [NYHA] II, 28% III, and 58% IV; mean systolic blood pressure, 133/75 mm Hg; and mean baseline brain natriuretic peptide, 1695) were enrolled (44 NTG, 45 NES). Mean baseline values were not significantly different between NTG and NES (1.3 vs. 1.3 mg/dL for SCr, 135 vs. 130 mm Hg for systolic blood pressure, and 51 mg vs. 51 mg/day of intravenous furosemide). All four inflammatory markers were elevated in these patients with ADHF, and their responses to NES or NTG infusion are shown in the table below. All patients survived the acute episode of ADHF and were discharged from the hospital with no significant changes in creatinine.
CONCLUSIONS: NES significant reduced IL-6 and hsCRP levels compared with NTG. Conversely, TNF-α and TGF-β did not change significantly with either therapy. The differential effects of NES versus NTG on these inflammatory markers during ADHF may have important implications and should be the basis for further research.
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21E. Aliskiren monotherapy lowers blood pressure independently of baseline plasma renin activity: subgroup analysis of a 6-month, double-blind trial. Karl Andersen, M.D., Ph.D.,[1] Myron H. Weinberger, M.D.,[2] Christian M. Constance, M.D.,[3] Melanie Wright, MSC,[4] Margaret F. Prescott, Ph.D.,[5] *Marc Israel, Pharm.D.*[5]; (1) Landspitali University Hospital, Reykjavik, Iceland; (2) Indiana University School of Medicine, Indianapolis, IN; (3) Maisonneuve-Rosemont Hospital, Montreal, Quebec, Canada; (4) Novartis Pharma AG, Basel, Switzerland; (5) Novartis Pharmaceuticals Corporation, East Hanover, NJ
PURPOSE: The direct renin inhibitor aliskiren (ALI) has demonstrated antihypertensive efficacy in a broad range of patients with hypertension, but its utility for patients with low baseline plasma renin activity (PRA) has not been reported.
METHODS: This was a post hoc analysis of a subset of patients (n=232) in a 6-month double-blind study in which 842 patients with a mean sitting diastolic BP (msDBP) of 95–109 mm Hg were randomized to ALI 150 mg or ramipril (RAM) 5 mg. Optional uptitration to ALI 300 mg or RAM 10 mg was permitted at week 6,

together with add-on hydrochlorothiazide from week 12 in patients with a BP of 140/90 mm Hg or more. Biomarkers, including PRA, were measured in a subset of patients, and least-squares mean changes from baseline in msS (systolic) BP/DBP were assessed by a subgroup of baseline PRA (0.65 or less or more than 0.65 ng/mL/hour).

RESULTS: At the week 12 end point, the BP-lowering effect of ALI monotherapy was independent of baseline PRA (interaction p=0.79 and p=0.49 for msSBP and msDBP, respectively). ALI provided significantly greater (p≤0.05) least-squares mean BP reductions than RAM in patients with either baseline PRA (Table).

CONCLUSIONS: In this post hoc analysis, aliskiren monotherapy (150–300 mg) provided effective BP lowering superior to RAM and independent of baseline PRA.

	n		LSM Change from Baseline		LSM difference	
Parameter	ALI	RAM	ALI	RAM	(95% CI)	p-value
msSBP (mm Hg)						
ITT	414	418	-14.0	-11.3	-2.7 (-4.4, -0.9)	< 0.01
PRA ≤ 0.65 ng/mL/hour	44	43	-13.0	-7.7	-5.3 (-10.7, 0.0)	0.05a
PRA > 0.65 ng/mL/hour	71	74	-13.7	-9.3	-4.4 (-8.5, -0.3)	0.04
msDBP (mm Hg)						
ITT	414	418	-11.3	-9.7	-1.6 (-2.7, -0.5)	0.01
PRA ≤ 0.65 ng/mL/hour	44	43	-12.5	-8.4	-4.2 (-7.5, -0.8)	0.02
PRA > 0.65 ng/mL/hour	71	74	-12.1	-9.5	-2.7 (-5.3, -0.1)	0.04

[a]p=0.0503.

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22. Do statins reduce the incidence of post-operative atrial fibrillation following cardiac valve surgery?

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PURPOSE: Statins reduce the incidence of postoperative atrial fibrillation (POAF) in patients undergoing cardiac surgery; however, data assessing patients undergoing isolated cardiac valve surgery are scarce.

METHODS: A retrospective, dual-center, case-control study of patients undergoing isolated cardiac valve surgery was performed. Excluded were patients receiving antiarrhythmic drug therapy or those with preoperative atrial fibrillation. Patients were included within the statin group if therapy was initiated by postoperative day 1 and continued throughout hospitalization and discharge. Patients in the control group received no statin therapy during the study period. The primary outcome was the incidence of POAF. Secondary outcomes included postoperative length of stay (LOS), myocardial infarction (MI), cerebrovascular events (CVAs), mortality, and the effect of statin dose on outcomes. Multivariate logistic regression was performed.

RESULTS: Of the 382 patients evaluated, 90 met exclusion criteria. The median age of the study population was 67.5 (56–75) years. Patients in the statin group were more likely to have a medical history of hypertension (74.8% vs. 58.2%, p=0.004) and diabetes (29.6% vs. 11.9%, p<0.001). There was no difference in the frequency of POAF between the statin and control group (46.1% vs. 42.4%, respectively, adjusted odds ratio [aOR] = 0.79; 95% confidence interval [CI]: 0.47–1.34). Higher doses of statin therapy (equivalents of atorvastatin 40 mg or greater) were associated with a lower incidence of POAF (aOR = 0.26; 95% CI: 0.07–0.96). There was no difference in median postoperative LOS (5 days vs. 5 days, p=0.637), MI (1.7% vs. 1.1%, p=0.648), CVA (1.7% vs. 0%, p=0.154), or mortality (0% vs. 2.8%, p=0.161) between groups. Results were comparable among both study centers.

CONCLUSIONS: Use of high-dose statins may be associated with a reduction in POAF after isolated cardiac valve surgery. Further investigation through multicenter, randomized, controlled trials is needed.

23. Heart failure associated hypervolemia does not cause increased INRs in patients taking warfarin.

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PURPOSE: Bleeding complications from anticoagulation (AC) with warfarin therapy can be catastrophic. Some studies suggest heart failure (HF) may be associated with excessive AC, even though causation has not been confirmed prospectively. This study further characterizes the association between HF-associated hypervolemia and international normalized ratio (INR) elevations in patients taking warfarin.

METHODS: We prospectively observed the effects of HF-associated hypervolemia on INR values in 40 patients taking warfarin enrolled in the HF Treatment Program at The University of Oklahoma Health Sciences Center for 14.5 ± 9 months. Visits were excluded if complete data regarding HF or AC could not be obtained; INR values were excluded if they were associated with a known cause for INR fluctuation. INR increases of 50% and more were considered clinically significant. Hypervolemia was classified as mild, moderate, or severe if diuretics were increased less than 50% or 50% or more or if the patient required intravenous diuretics, respectively.

RESULTS: Fifty-seven episodes of HF-associated hypervolemia with corresponding INR data were evaluable (71% of all hypervolemic episodes); most episodes were mild or moderate. INR elevations of 50% or more occurred 8 times during hypervolemia (Pearson χ^2 test, p=0.85; effect size = 0.021). There were no differences in average INR change among patients classified as mild, moderate, or severe or among patients classified as New York Heart Association (NYHA) II, III, or IV (p=NS for all). Patients classified as NYHA III had lower weekly warfarin doses than those classified as NYHA II (p<0.01).

CONCLUSIONS: Mild to moderate HF exacerbations do not appear to cause an exaggerated response to warfarin, yet those with advanced HF required lower weekly warfarin doses. These results challenge hypotheses from prior research suggesting HF exacerbations cause an exaggerated response to warfarin. To our knowledge, this is the first study since 1949 to prospectively characterize causation between HF and excessive AC. The effect of severe hypervolemia requires further study.

24E. Diuretic dose is not predictive of worsening renal function in patients with heart failure receiving nesiritide.

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PURPOSE: Concerns about worsening renal function have been raised in patients with heart failure (HF) who receive nesiritide (NES). Loop diuretics have also been shown to decrease creatinine clearance and increase adverse neurohormone production. The interaction between NES administration and loop diuretic dose has not been well studied. This study evaluates changes in serum creatinine (Crt) in patients with HF receiving either high-dose (HD) or low-dose (LD) loop diuretics while being treated with NES.

METHODS: We recorded the data of 71 consecutively hospitalized patients who received NES for HF. Patients were divided into LD (equivalent daily intravenous furosemide dose of 120 mg or less) or HD (daily furosemide of 160 mg or more). Baseline data, together with Crt at pre- and post-NES infusion and at discontinuance, were analyzed.

RESULTS: Thirty-nine patients received LD furosemide (mean, 66 ± 38 mg) daily, and 32 received HD (mean, 242 ± 82 mg) daily. There was no significant difference between the LD and HD groups with respect to age, sex, ejection fraction (0.32 vs. 0.30, p=0.59), baseline brain natriuretic peptide (pg/mL) (1672 vs. 2047, p=0.29), b-blocker use, baseline Crt (1.8 vs. 1.8 mg/dL, p=0.91), NES bolus administration, infusion dose, or duration of infusion. There was a trend toward more angiotensin-converting enzyme/angiotensin receptor blocker use in the HD group (56% vs. 73%, p=0.08). There was no significant difference in Crt between LD and HD groups post-NES infusion or at discharge. There was a nonsignificant trend

toward an increase in Crt from baseline to post-NES within the HD group.
CONCLUSIONS: There is no association between loop diuretic dose and significant changes in Crt in patients with heart failure receiving nesiritide. Hypotension is a common adverse effect regardless of diuretic dose.
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25E. Safety and tolerability of olmesartan medoxomil and hydrochlorothiazide in elderly (≥65 years) patients with stage 1 and stage 2 hypertension. *Joel M. Neutel, M.D.*,[1] Deanna Cheung, M.D.,[2] Kathy A. Stoakes, RN, BSN, CCRA,[3] William F. Waverczak, M.S.,[3] Jianbo Xu, M.S.,[3] Ali Shojaee, Pharm.D.,[3] Robert Dubiel, Pharm.D.[3]; (1) Orange County Research Center, Tustin, CA; (2) Long Beach Center for Clinical Research, Long Beach, CA; (3) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: In addition to investigating the efficacy of antihypertensive agents in the elderly (65 years and older), it is important to verify safety because of concerns about increased risk of adverse events (AEs). This was an open-label, dose-titration study investigating safety and efficacy of olmesartan medoxomil (OM) with or without hydrochlorothiazide (HCTZ) in patients 65 years and older with hypertension.
METHODS: The primary safety end point was incidence of treatment-emergent AEs (TEAEs) during the 12-week study. After a 2- to 3-week placebo run-in, patients started OM 20 mg, uptitrated to OM 40 mg, and then added HCTZ 12.5–25 mg in a stepwise manner at 3-week intervals. Asymptomatic patients with BP less than 120/70 mm Hg remained on the current dose.
RESULTS: Safety cohort included all patients who received one or more doses of drug (n=178). Mean age (±SD) was 72.0 ± 5.3 years; 65.2% of patients had stage 2 hypertension. Results are in Table. TEAEs occurring in 2% or more of patients overall included dizziness (n=8, 4.5%), diarrhea, upper respiratory tract infection, headache, and hypotension (n=4, 2.2% each). Among individual regimens, headache and dizziness (n=4, 2.4% each) were reported for OM 40 mg, and dizziness (n=6, 3.8%) was reported for OM/HCTZ 40/12.5 mg. Orthostatic hypotension occurred in only one patient (0.6%) with OM/HCTZ 40/12.5 mg.
CONCLUSIONS: In elderly patients for whom AEs are often a concern, OM was safe and well tolerated alone or with HCTZ.
Table: TEAEs

TEAEs, n (%)[a]	OM 20 mg (n=178)	OM 40 mg (n=169)	OM/HCTZ 40/12.5 mg (n=159)	OM/HCTZ 40/25 mg (n=125)	Overall[b] (n=178)
≥ 1 TEAE	25 (14.0)	27 (16.0)	36 (22.6)	25 (20.0)	58 (32.6)
≥ 1 drug-related TEAE)	6 (3.4)	5 (3.0)	12 (7.5)	8 (6.4)	21 (11.8
≥ 1 severe TEAE	0	2 (1.2)	1 (0.6)	0	3 (1.7)
Serious AEs	0	1 (0.6)	0	0	1 (0.6)
Discontinuations because of AEs	1 (0.6)	4 (2.4)	3 (1.9)	1 (0.8)	9 (5.1)

[a]Calculated using number of subjects in respective period as denominator.
[b]During entire active treatment period.

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26E. Efficacy of olmesartan medoxomil and hydrochlorothiazide in elderly (≥65 years) patients with hypertension as assessed by ambulatory blood pressure monitoring. *Dean J. Kereiakes, M.D.*,[1] Jaime Sandoval, M.D.,[2] Deanna Cheung, M.D.,[3] Kathy A. Stoakes, RN, BSN, CCRA,[4] William F. Waverczak, M.S.,[4] Jianbo Xu, M.S.,[4] Ali Shojaee, Pharm.D.,[4] Robert Dubiel, Pharm.D.[4]; (1) The Christ Hospital Heart and Vascular Center and The Carl and Edyth Lindner Center for Research and Education at The Christ Hos, Cincinnati, OH; (2) Padre Coast Clinical Research, Corpus Christi, TX; (3) Long Beach Center for Clinical Research, Long Beach, CA; (4) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: The effect of olmesartan medoxomil (OM) with or without hydrochlorothiazide on attaining prespecified blood pressure (BP) targets in patients 65 years and older with hypertension was evaluated by mean 24-hour ambulatory BP monitoring in an open-label, dose-titration study.
METHODS: Secondary end points included ambulatory BP change from baseline and proportion of patients achieving prespecified ambulatory BP targets (less than 140/90, less than 135/85, less than 130/80, 125/75, and less than 120/80 mm Hg) during the daytime (8:00 am–4:00 pm), nighttime (10:00 pm–6:00 am), and final 2, 4, and 6 hours of the dosing interval. After a 2- to 3-week placebo run-in, patients started OM 20 mg, uptitrated to OM 40 mg, and then added hydrochlorothiazide 12.5–25 mg in a stepwise manner at 3-week intervals. Patients with BP less than 120/70 mm Hg did not uptitrate.
RESULTS: Efficacy cohort included 176 patients (ambulatory BP available for 150) with mean age (±SD) 71.9 ± 5.2 years and 65.9% stage 2 hypertension. Mean baseline ambulatory BP for daytime and nighttime was 155.7/86.2 and 140.5/74.6 mm Hg, respectively, and during the last 2, 4, and 6 hours, it was 152.8/84.2, 147.4/80.3, and 143.9/77.7 mm Hg, respectively. Mean (±SEM) changes from baseline in ambulatory BP for daytime and nighttime were –26.5 (±1.1)/–13.0 (±0.7) and –24.4 (±1.0)/–11.5 (±0.6) mm Hg, respectively, and for last 2, 4, and 6 hours, values were –24.2 (±1.4)/–11.4 (±0.8), –24.4 (±1.2)/–11.8 (±0.7), and –24.1 (±1.1)/–11.6 (±0.6), respectively ($p<0.0001$ vs. baseline for all comparisons). Ambulatory BP targets of less than 120/80 mm Hg to less than 140/90 mm Hg were achieved by 22.7%–80.0% of patients during the daytime, 66.0%–95.3% during the nighttime, and 24.7%–78.7%, 42.7%–84.7%, and 54.0%–88.0% during the last 2, 4, and 6 hours, respectively, of the dosing interval.
CONCLUSIONS: In patients 65 years and older with hypertension, an OM-based treatment algorithm produced statistically and clinically significant reductions in BP during the daytime, nighttime, and last 2, 4, and 6 hours of the dosing interval that enabled patients to achieve ambulatory BP targets throughout this 24-hour dosing period.
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27E. Effect of age, gender, race and ethnicity on efficacy of amlodipine/valsartan/hydrochlorothiazide triple combination therapy in patients with moderate to severe hypertension. David Calhoun, M.D.,[1] *Robert Glazer, M.D.*,[2] Joseph Yen, Ph.D.,[2] Yves Lacourciere, M.D., FRCPC, FACP[3]; (1) University of Alabama at Birmingham, Birmingham, AL; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) Centre Hospitalier de l'Universite Laval, Ste. Foy, Quebec, Canada
PURPOSE: Around 30% of hypertensive patients require three or more drugs to achieve blood pressure (BP) control. Limited data are available on the efficacy of triple antihypertensive therapy in patient subgroups according to age, gender, race, and ethnicity.
METHODS: This was an 8-week, multinational, double-blind, parallel-group trial in patients with BP of 145/100 mm Hg or more and less than 200/120 mm Hg who were randomized to receive a once-daily dose of amlodipine-valsartan-hydrochlorothiazide (A/V/H) 10/320/25 mg, V/H 320/25 mg, A/V 10/320 mg, or A/H 10/25 mg. Post hoc subgroup analyses were performed between treatment for change in systolic BP (SBP) and diastolic BP (DBP) from baseline to week 8 end point and overall BP control rate (BP less than 140/90 mm Hg) at end point.
RESULTS: Of the 2271 randomized patients with mean baseline BPs of 170/107 mm Hg, 14% were 65 years and older, 55.3% were males, 71.6% were whites, and 17.1% were blacks. Disposition by ethnicity included 25.9% Hispanics and 72.9% patients classified as "Others." Regardless of age, gender, and race, reductions in both SBP and DBP were greater with triple therapy compared with each of the dual therapies, with statistical significance achieved for all comparisons except some in the 65 and older and black subgroups, possibly because of smaller patient numbers (Table).
CONCLUSIONS: The overall BP control rates were significantly greater with A/V/H (64%–76%) compared with V/H (38%–51%), A/V (41%–63%), and A/H (37%–55%) across all subgroups. Consistent findings were observed in Hispanic patients. In conclusion, A/V/H triple combination effectively reduces BP and improves BP control across diverse patient subgroups.

	A/V/H 10/320/25 mg	V/H 320/25 mg	A/V 10/320 mg	A/H 10/25 mg
Age < 65 years (n=1925)	38.9/24.4	31.7*/19.6*	32.4*/21.0*	30.5*/18.7*
Age ≥ 65 years (n=311)	43.9/26.3	33.9*/20.0*	40.5/24.0	37.3*/23.4*
Male (n=1234)	36.0/24.0	30.2*/18.9*	30.3*/20.5*	27.6*/17.9*
Female (n=1002)	44.1/25.4	34.2*/20.4*	37.5*/22.5*	36.4*/21.3*
Whites (n=1516)	40.0/25.1	32.3*/19.5*	34.0*/21.7*	30.6*/18.6*
Blacks (n=375)	35.4/21.8	29.3*/19.3	27.2*/18.5*	31.0*/20.2
Hispanics (n=580)	42.7/25.8	32.0*/19.9*	37.3*/22.5*	35.3*/21.5*

*p<0.05 vs. A/V/H.

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28E. Effect of prescription omega-3 fatty acids coadministered with escalating doses of atorvastatin on non–HDL-C in patients with hypertriglyceridemia. *Harold E. Bays, M.D., FACP, FACE,*[1] James J. McKenney, Pharm.D.,[2] Ralph Doyle, B.A.,[3] Roderick N. Carter, M.D.,[3] Evan A. Stein, M.D., Ph.D., FRCP(C), FCAP[4]; (1) Louisville Metabolic and Atherosclerosis Research Center, Louisville, KY; (2) School of Pharmacy, National Clinical Research, Inc., Richmond, VA; (3) Reliant Pharmaceuticals, Inc., Liberty Corner, NJ; (4) Metabolic and Atherosclerosis Research Center, Cincinnati, OH

PURPOSE: Non–high-density lipoprotein cholesterol (non–HDL-C) is a secondary treatment target for patients with mixed dyslipidemia and persistent hypertriglyceridemia. This study assessed the effects of prescription omega-3 fatty acids (P-OM3) when coadministered with escalating doses of atorvastatin (atorva) in n=243 subjects with baseline non–HDL-C more than 160 mg/dL and triglyceride (TG) concentrations 250–599 mg/dL.

METHODS: Multicenter, randomized, double-blind, placebo-controlled, parallel-group, 16-week study. After a 4-week diet lead-in, dyslipidemic subjects 18–79 years old received blinded P-OM3 (4 g/day; n=122) or placebo (PBO; n=121) plus open-label atorva (10, 20, and 40 mg/day at weeks 1–8, 9–12, and 13–16, respectively). The primary end point was the difference between groups in non–HDL-C based on median percent change from baseline (%CFB) at week 8. Secondary end points included safety assessments and differences between groups in other lipid/lipoprotein-related parameters at week 8.

RESULTS: P-OM3 plus atorva significantly reduced non–HDL-C in patients compared with those receiving PBO plus atorva (–40.2% vs. –33.7%, respectively, p=0.0002). P-OM3 produced similar trends for TG (–45.4% vs. –26.9%, p<0.0001), very low-density lipoprotein cholesterol (VLDL-C; –54.3% vs. –37.0%, p<0.0001), TC (–31.5% vs. –27.4%, p=0.0015), apolipoprotein (Apo) CIII (–29.4% vs. –16.0%, p<0.0001), and elevated inflammatory enzyme (Lp-PLA_2) (–20.7% vs. –9.7%, p<0.0001), but not for LDL-C (–29.3% vs. –31.5%, p=0.2416) or Apo B (–32.1% vs. –30.7%, p=0.1314). P-OM3 plus atorva also significantly increased HDL-C compared with PBO plus atorva (+12.4% vs. +10.0%, respectively, p=0.0066). P-OM3 also significantly improved non–HDL-C, VLDL-C, TC, Apo CIII, and Lp-PLA_2 when coadministered with atorva 20 and 40 mg/day. The coadministration of P-OM3 and atorva (all doses) was generally well tolerated.

CONCLUSIONS: P-OM3 significantly reduces non–HDL-C when coadministered with atorva 10, 20, and 40 mg/day.

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29. Comparison of the effects of energy drink and caffeine supplementation on indices of 24-hour ambulatory blood pressure. *Amy M. Franks, Pharm.D.,*[1] Julia M. Schmidt, Pharm.D.,[1] Keith R. McCain, Pharm.D.,[1] Mony Fraer, M.D.[2]; (1) University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR; (2) University of Arkansas for Medical Sciences College of Medicine, Little Rock, AR

PURPOSE: To compare the effects of energy drink versus caffeine supplementation on blood pressure (BP) as measured by 24-hour ambulatory BP monitoring (ABPM).

METHODS: Healthy, nonsmoking, normotensive volunteers taking no prescription or nonprescription medications were enrolled in an open-label crossover pilot study. During each 24-hour study period, subjects received four doses of energy drink (Red Bull Energy Drink, each dose containing 80 mg of caffeine and 1000 mg of taurine in an 8.3-oz serving) or control (compounded caffeine solution, each dose containing 80 mg of caffeine solution in 8 oz of bottled water) dosed at 0800, 1100, 1500, and 1900 hours. Subjects underwent 24-hour ABPM during each supplementation period, beginning 1 hour before supplementation and continuing until the next morning. The two ABPM study periods were separated by 4–30 days. Subjects refrained from caffeine and physical exertion during the two study supplementation periods. Descriptive statistics were used to describe the demographic data, and paired t-tests were used to analyze ABPM data.

RESULTS: Nine subjects (five females, 27.7 ± 5.0 years) completed the study. Mean 24-hour systolic (117.4 vs. 123.2 mm Hg, p=0.04), diastolic (68.2 vs. 73.6 mm Hg, p=0.02), and mean arterial (84.8 vs. 90.1 mm Hg, p=0.03) BP values were significantly higher during energy drink supplementation. Trends in higher daytime systolic (121.9 vs. 127.0 mm Hg, p=0.05) and mean arterial (88.6 vs. 93.6 mm Hg, p=0.05) BP were found with energy drink supplementation. Daytime diastolic BP (72.0 vs. 77.0 mm Hg, p=0.04) was significantly higher with energy drink supplementation. Nighttime BP, BP load, and nocturnal dipping status did not differ significantly between supplementation periods in these normotensive subjects.

CONCLUSIONS: Single-day energy drink supplementation increased mean 24-hour and daytime BP compared with supplementation with a control containing equivalent doses of caffeine. BP elevations were not sustained into the nighttime hours.

30E. Effect of baseline systolic blood pressure on response to triple combination amlodipine/valsartan/hydrochlorothiazide in patients with moderate-to-severe hypertension. Yves Lacourciere, M.D., FRCPC, FACP,[1] Robert Glazer, M.D.,[2] *Nora Crikelair, Ph.D.,*[2] Joseph Yen, Ph.D.,[2] David Calhoun, M.D.[3]; (1) Centre Hospitalier de l'Universite Laval, Ste. Foy, Quebec, Canada; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) University of Alabama at Birmingham, Birmingham, AL

PURPOSE: Several studies have demonstrated that the risk of cardiovascular events is more closely related to systolic blood pressure (SBP) than to diastolic BP (DBP). Despite the growing evidence regarding the importance of SBP, control rates remain low. The use of two or more antihypertensive drugs from different therapeutic classes may provide additive or synergistic BP-lowering effects.

METHODS: The present study was an 8-week, multinational, double-blind, parallel-group trial in patients with BP of 145/100 or more and less than 200/120 mm Hg who were randomized to receive once-daily doses of amlodipine-valsartan-hydrochlorothiazide (A/V/H) 10/320/25 mg, V/H 320/25 mg, A/V 10/320 mg, or A/H 10/25 mg. Post hoc subgroup analyses were performed to evaluate change from baseline in BP, SBP control rate (SBP less than 140 mm Hg), and overall BP control rate (BP less than 140/90 mm Hg) at end point according to baseline SBP categories.

RESULTS: Randomized patients (n=2271) had a mean age of 53.2 years; 55.3% were men, and 71.6% were white. Overall, baseline BP was 170/107 mm Hg. Greater reductions in SBP and greater rates of SBP control were observed with triple A/V/H therapy compared with each dual therapy across the entire SBP range analyzed. All treatment comparisons were statistically significant, with some exceptions in the less than 160 mm Hg subgroup (Table). Consistent results were observed for reductions in DBP and overall BP control rates.

CONCLUSIONS: In conclusion, triple antihypertensive therapy with A/V/H is more effective than dual therapy, particularly for patients with higher baseline SBP.

Reduction in Mean SBP (mm Hg)[§] and SBP Control Rates (%)[#] Across Different Baseline SBP (mm Hg) Subgroups

	< 160 (n=635)		160–169 (n=541)		170–179 (n=414)		≥ 180 (n=646)	
	mm Hg	%	mm Hg	%	mm Hg	%	mm Hg	%
A/V/H 10/320/25 mg	28.1	85	37.6	85	44.7	78	49.6	71
V/H 320/25 mg	25.5	81	29.8*	62*	32.3*	48*	39.9*	34*
A/V 10/320 mg	24.6*	80	29.3*	67*	36.4*	54*	43.6*	42*
A/H 10/25 mg	20.5*	71*	27.5*	60*	35.4*	54*	42.5*	44*

p<0.05 vs. A/V/H.
[§]Least-squares mean from analysis of covariance model.
[#]Logistic regression model.

Presented at American Society of Hypertension 24th Annual Scientific Meeting and Exposition, San Francisco, CA, May 6–9, 2009.

31E. Twenty-four hour ambulatory BP control of therapy with amlodipine/valsartan/Hctz triple combination compared to dual therapy in patients with moderate to severe hypertension. Yves Lacourciere, M.D., FRCPC, FACP,[1] *Robert Glazer, M.D.,*[2] Joseph Yen, Ph.D.,[2] David Calhoun, M.D.[3]; (1) Centre Hospitalier de l'Universite Laval, Ste. Foy, Quebec, Canada; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) University of Alabama at Birmingham, Birmingham, AL

PURPOSE: Ambulatory blood pressure monitoring (ABPM) is the most accurate measure for assessment of the effectiveness of an antihypertensive therapy and is a strong predictor of cardiovascular events and mortality. This substudy evaluated the efficacy of amlodipine-valsartan-HCTZ (A/V/H) triple combination as assessed by 24-hour ABPM compared with dual therapy (V/H, A/H, or A/V) in patients with moderate to severe hypertension.

METHODS: This was an 8-week, multinational, double-blind, parallel-group trial in patients with clinic diastolic BP of 100 or greater and less than 120 mm Hg and systolic BP of 145 or greater and less than 200 mm Hg. Eligible patients were randomized in equal ratios to receive once-daily doses of A/V/H 10/320/25 mg, V/H 320/25 mg, A/V 10/320 mg, or A/H 10/25 mg for 8 weeks. ABPM was performed in a subgroup of patients, and BP was measured every 20 minutes over 24 hours.

RESULTS: A total of 2271 patients were randomized (14% 65 years and older; 55% males; 72% whites; and 17% blacks, with mean baseline clinic BP of 170/107 mm Hg). ABPM was assessed in a subgroup of 283 patients at baseline and end point. All treatment groups produced statistically significant reductions from baseline (p<0.0001 for all) in 24-hour ABP at end point (Table). Triple therapy produced significantly greater reductions in both systolic and diastolic 24-hour mean ABP (p<0.0001 for all) as well as daytime and nighttime ABP (p<0.003 for all) compared with each dual therapy. Furthermore, greater reductions in ABP were observed with triple therapy compared with the dual therapies for every hourly mean over the 24-hour period.

CONCLUSIONS: A/V/H triple combination therapy provides effective 24-hour BP control that is superior to each respective dual therapy in moderate and severe hypertensives.

ABP	A/V/H (n=67)	V/H (n=69)	A/V (n=71)	A/H (n=76)
Baseline	149.6/94.4	146.4/92.8	149.7/93.1	147.3/93.4
End point	119.1/74.5	123.8/77.9	125.1/78.7	129.1/81.9
Difference	–30.3/–19.7	-23.9/-15.5	–24.1/-14.9	-18.8/-11.7
Comparison of Triple Combination vs. Dual Therapy (LSM ± SE [95% CI])				
SBP	-	–6.4 ± 1.01 (–8.40, –4.41)*	–6.2 ±1.00 (-8.13,-4.19)*	-11.5 ±0.99 (-13.45,-9.56)*
DBP	-	–4.2 ± 0.70 (-5.61, –2.87)*	–4.8 ±0.69 (-6.19,-3.47)*	-8.0 ±0.68 (-9.38,-6.71)*

*p<0.0001 vs. triple; A/V/H = 10/320/25 mg; V/H = 320/25 mg; A/V = 10/320 mg; A/H = 10/25 mg

Presented at ESH (European Society of Hypertension) Annual Scientific Meeting 2009, Milan, Italy, June 12–16, 2009.

32. Coronary artery bypass graft surgery and bleeding outcomes with recent clopidogrel exposure. *Charles H. Hayes III, Pharm.D.*, Danielle Blais, Pharm.D., Michael Firstenberg, M.D., Kerry K. Pickworth, Pharm.D.; The Ohio State University Medical Center, Columbus, OH

PURPOSE: Clopidogrel administration before coronary artery bypass grafting (CABG) may increase the risk of postoperative bleeding; guidelines recommend that patients receiving clopidogrel have surgery delayed for 5–7 days. Studies investigating clopidogrel administration and postoperative bleeding have had conflicting results. Patients undergoing isolated CABG with recent clopidogrel exposure were compared with those without recent exposure, with respect to the use of blood products and bleeding complications.

METHODS: A case-matched retrospective cohort study was conducted from January to December 2008 in patients undergoing isolated CABG. Patients were case matched on the basis of age (±5 years), gender, and Society of Thoracic Surgeons (STS) risk score (±5%). The primary end point included receiving 2 U or more of blood intraoperatively and up to 48 hours post-CABG. Any blood product use, bleeding complications, and outcomes were reviewed. Statistical analysis for categoric data was conducted using the McNemar test, whereas a paired *t*-test was used for continuous variables. Statistical significance was determined at p<0.05.

RESULTS:

Clopidogrel Within 5 days of CABG	Not Exposed (n=45)	Exposed (n=45)	p-value
Age (mean ± SD)	62 ± 11	61.8 ± 11.2	0.83
Male, n (%)	36 (80)	36 (80)	
STS score (mean ± SD)	14.7% ± 9.08	14.7% ± 9.2	0.96
Intraoperative and 48-Hour Post-CABG Blood Product Use			
Any blood product, n (%)	21 (46.6)	27 (60)	0.24
≥ 2 U PRBC, n (%)	17 (37.7)	23 (51)	0.21
Platelets, n (%)	5 (11)	12 (26.6)	0.14
FFP, n (%)	6 (13.3)	11 (24.4)	0.26
Cryoprecipitate, n (%)	1 (2.2)	3 (6.6)	0.61
Bleeding Complications			
≥ 3 g/dL drop in Hgb, n (%)	24 (63)	24 (63)	0.77
≥ 5-g/dL drop in Hgb, n (%)	6 (16)	7 (18)	1.0
Surgical reexploration, n (%)	2 (4.4)	0	0.48

*Seven patients/group excluded because of missing preoperative Hgb value. Compared with baseline preoperative hemoglobin up to 48 hours post-CABG.

CONCLUSION: Results suggest patients undergoing isolated CABG with recent clopidogrel exposure at our institution are not at increased risk of bleeding, nor do they require significantly greater amounts of blood products compared with patients without recent exposure.

33. Platelet response to aspirin in healthy volunteers. *Rebecca D. Moote, Pharm.D., BCPS*, Laurajo Ryan, Pharm.D., M.S., BCPS, CDE, Christopher R. Frei, Pharm.D., M.S., BCPS, Robert L. Talbert, Pharm.D., FCCP, BCPS, FAHA; University of Texas at Austin and University of Texas Health Science Center at San Antonio, San Antonio, TX

PURPOSE: Aspirin is effective therapy for preventing cardiovascular events; however, some patients still experience events on therapy. We investigated platelet response to aspirin 81 mg versus 325 mg for 7 days in healthy volunteers. We hypothesized platelet response would not differ between doses.

METHODS: A randomized, double-blind crossover study was conducted in healthy volunteers age 18–65. Subjects were given 7 days of 81 mg and 325 mg each and were randomly assigned to dose order. We collected baseline demographics, complete blood cell count, and medication use. Platelet function was evaluated with Accumetrics VerifyNow at baseline and on days 4 and 7. Platelet response was compared using the Wilcoxon signed-rank non-parametric test.

RESULTS: Nineteen volunteers completed the study. Response to aspirin therapy was defined as aspirin reaction units (ARUs) less than 550. A significantly greater median platelet response was seen with 325 mg on both day 4 (399 vs. 410 ARUs; p=0.03) and day 7 (395 vs. 419 ARUs; p=0.008). There was also a 3-fold greater intrasubject variability to 81 mg than to 325 mg (median difference of 24 vs. 9 ARUs; p=0.1), suggesting that 325 mg achieves more predictable platelet response than 81 mg. We evaluated the impact of body mass index (BMI), age, and gender on baseline platelet

function and response to aspirin. Baseline platelet function and response to aspirin 325 mg were similar regardless of BMI; however, subjects with a BMI greater than 25 kg/m^2 had a blunted response to aspirin 81 mg compared with BMI less than 25 kg/m^2. Subjects younger than 30 had less response to aspirin 81 mg compared with those older than 30. Men had less response to 81 mg than women had and showed more variable responses.
CONCLUSION: Healthy volunteers taking aspirin 325 mg daily experience more platelet inhibition and less variability than those taking 81 mg daily.

34. Evaluation of postoperative atrial fibrillation in patients undergoing cardiac surgery. *Wesley R. Zemrak, Pharm.D.*, Danielle M. Blais, Pharm.D., Kerry K. Pickworth, Pharm.D.; The Ohio State University Medical Center, Columbus, OH
PURPOSE: To assess the incidence, risk factors, current treatment strategies, and outcomes of cardiac surgery patients developing postoperative atrial fibrillation (POAF).
METHODS: Patients undergoing coronary artery bypass, valve surgery, or both from October 1, 2007, to September 30, 2008, were identified and screened for POAF. Data were collected through the Society of Thoracic Surgery database, electronic medical records, and patient charts. Data collected included demographics, comorbidities, procedure details, medication use, frequency of POAF, length of stay, morbidity, and mortality. Statistical analysis included descriptive statistics, Student t-test for continuous data, and χ^2 test for categoric data.
RESULTS: A total of 452 patients underwent bypass (n=254), valve surgery (n=120), or both (n=78). The incidence of POAF was 20% (91 patients) and was more common in patients with advanced age (p<0.001), prior myocardial infarction (p=0.03), and combined CABG/valve surgery (p<0.001). Median time to onset of POAF was 54.5 hours, and time to initial therapy was 30 minutes. Initial treatment strategies were intravenous amiodarone (73.6%), b-blocker (24.2%), and cardioversion (4.4%). Most patients (95.6%) received amiodarone at any time during their hospitalization, and 75.6% were discharged on oral amiodarone. Preoperative and postoperative b-blocker use was 89% and 96.7%, respectively. Median (range) length of stay was 11 (4–90) for patients with POAF versus 9 (1–6) for patients without POAF (p=0.03). There was no difference in mortality between patients with POAF and those without (3.3% vs. 1.7%, p=NS).
CONCLUSIONS: Overall, the incidence of atrial fibrillation after bypass, valve, or combined surgery was 20% at our institution, consistent with reported rates in the literature. There was a high variability in the treatment of POAF; therefore, a treatment algorithm has been designed and implemented. Targets for education and continuous quality improvement have been identified.

35E. Colesevelam's effect on lipid parameters in monotherapy or combination therapy: a meta-analysis. Julie M. Strickland, Pharm.D.,[1] *Daniel M. Riche, Pharm.D., BCPS, CDE,*[2] Krista D. Riche, Pharm.D., BCPS,[3] Honey E. East, M.D.[4]; (1) University of Mississippi School of Pharmacy, Jackson, MS; (2) University of Mississippi Schools of Pharmacy and Medicine, Jackson, MS; (3) Mississippi Baptist Medical Center, Jackson, MS; (4) University of Mississippi School of Medicine, Jackson, MS
PURPOSE: Colesevelam is indicated for use as monotherapy or in combination with statins; however, colesevelam is often prescribed in combination with other cholesterol-lowering agents, particularly when statin intolerance exists. To date, there are few randomized, controlled trials that evaluate the efficacy of colesevelam in combination with other agents. The purpose of this study was to assess the effect on lipid parameters and adverse drug reactions (ADRs) when colesevelam is used in monotherapy or combination.
METHODS: A systematic literature search of PubMed and MEDLINE was performed to identify trials evaluating colesevelam. Trials were included if they met the following criteria: 1) randomized, controlled trial, 2) well-described protocol, and 3) data reported on lipid parameters. A DerSimonian-Laird random-effects model effect size meta-analysis was used to analyze lipid parameters, and an odds ratio (OR) meta-analysis was used for ADRs. Lipid data are reported in milligrams per deciliter with 95% confidence intervals (CIs), whereas ADR data are reported as ORs with 95% CIs.
RESULTS: Three studies evaluated colesevelam monotherapy (n=229) and statin combination (n=283), whereas only two studies (n=102) reported data in combination with ezetimibe. Low-density lipoprotein (LDL) is significantly reduced when colesevelam is used in both statin combination (–20.96 mg/dL; 95% CI: –26.28, –15.64) and monotherapy (–17.8 mg/dL; 95% CI: –25.88, –9.75); however, colesevelam combined with ezetimibe (–14.33 mg/dL; 95% CI: –29.33, 0.67) demonstrated a nonsignificant reduction in LDL but was significant after sensitivity analysis. Colesevelam did not affect triglycerides in any group.
CONCLUSIONS: Colesevelam used as monotherapy or in combination with statins significantly decreases LDL without detriment to triglycerides or severe adverse effects. The lipoprotein effect of colesevelam in combination with ezetimibe is underpowered with differing results based on sensitivity analysis. The authors encourage more controlled studies evaluating colesevelam in combination with other cholesterol-lowering therapies.
Presented at the American Society of Health-Systems Pharmacists 43th Midyear, Orlando, FL, December 2008. Presentation #SP–270.

36E. Decreased hospital readmission with nitroprusside in acute decompensated heart failure. *Anne P. Spencer, Pharm.D., BCPS,*[1] Robert L. Page III, Pharm.D., MHA, BCPS,[2] Adrian Van Bakel, M.D., Ph.D.[3]; (1) Roper Saint Francis Healthcare, Charleston, SC; (2) University of Colorado School of Pharmacy, Denver, CO; (3) Medical University of South Carolina, Charleston, SC
PURPOSE: Despite its inclusion in the latest clinical guidelines for the management of acute decompensated heart failure (ADHF), nitroprusside is inconsistently used in the treatment of this patient population. The purpose of this investigation was to evaluate the outcomes associated with the use of nitroprusside in patients with ADHF.
METHODS: In this multicenter, case-control study, 48 patients with ADHF were included. Twenty-four patients who received nitroprusside were identified and matched to patients who did not receive nitroprusside in a 1:1 fashion by age, sex, race, ejection fraction (EF), serum creatinine (SCr), and heart failure (HF) etiology. Outcomes were compared by bivariate analysis, and secondary analyses stratified by race were performed.
RESULTS: Of the 48 patients included, 38% were African American, 38% had ischemic HF, and 67% were male with an average age of 48 years, EF of 23%, and SCr of 1.3. In the control group, ADHF therapies consisted of nitroglycerin, diuretics, nesiritide, and/or inotropic agents. Hospital readmission at 30 days was significantly lower in patients receiving nitroprusside (4.2% vs. 29.2%, OR = 0.11; 95% CI: 0.012–0.941). This difference is largely driven by an increase in hospitalizations in the African American patients who did not receive nitroprusside compared with whites (44% compared with 20%). No difference existed between nitroprusside and control groups regarding the number of days of intravenous vasodilator/diuretic therapy (2.8 ± 1.96 vs. 2.9 ± 1.85, respectively) and LOS (6.1 ± 2.83 days vs. 6.4 ± 2.92 days, respectively). When adjusting for race, both end points remained unchanged. No metabolic or organ toxicities were noted in the nitroprusside group.
CONCLUSION: Compared with standard management of ADHF, the use of nitroprusside was associated with a significantly lower probability of hospital readmission at 30 days. This phenomenon was most pronounced in African Americans. The use of nitroprusside had no impact on the length of intravenous therapies or hospital stay.
Presented at the Annual Scientific Meeting of the Heart Failure Society of America, Boston, MA, September 13–16, 2009.

37E. Modified clopidogrel desensitization following percutaneous coronary intervention (PCI): a novel approach to the management of clopidogrel allergy. *Denis Brouillette, BPharm, DPH*; Montreal Heart Institute, Montreal, Quebec, Canada
PURPOSE: Over the years, the combination of aspirin and

clopidogrel has become standard practice in the prevention of stent thrombosis and as treatment of secondary coronary artery disease prevention. Interruption of combination therapy, primarily in stent carriers, is associated with considerable morbidity, mainly sudden death and myocardial infarction. In the presence of a suspected hypersensitivity to clopidogrel, clinicians face the difficult decision of suspending clopidogrel and/or using a less optimal treatment.
METHODS: We evaluated a strategy in patients receiving clopidogrel and presenting with a hypersensitivity reaction. The approach consisted of maintaining clopidogrel treatment, accompanied by symptomatic treatment, and evaluating the need for reexposure (e.g., graded rechallenge, desensitization).
RESULTS: This approach was evaluated in 42 patients (29% STEMI, 33% unstable angina, and 38% angina) who underwent a PCI (37% DES, BMS 51%, and 7% both). The presentation was mainly rash (69%) or accompanied by pruritus (28.6%) with no cases of angioedema. The median time for the presentation of the hypersensitivity reaction was 6 days. Thirty-nine patients were maintained on clopidogrel without interruption. Substitution with an alternative was necessary for only one patient (2.4%). No patient required premature cessation of the treatment.
CONCLUSION: A treatment strategy based mainly on the symptomatic treatment and maintenance of clopidogrel during hypersensitivity reaction is safe and effective.
Presented at ACCP 2009, Orlando, FL, April 3–5, 2009.

Critical Care

38E. Nicardipine in the management of hypertension in critically ill patients. *Mark A. Malesker, Pharm.D., FCCP, BCPS*, Robyn R. Kondrack, Pharm.D., Daniel E. Hilleman, Pharm.D., FCCP; Creighton University Medical Center, Omaha, NE
PURPOSE: Critically ill patients with acute hypertension require rapid blood pressure reductions using parenteral medications. Nicardipine has been demonstrated to be safe and effective in such situations, but it is more expensive than most alternatives. The purpose of this study was to evaluate the short-term clinical outcomes of nicardipine compared with other acute hypertension drug therapies and to assess the relative cost in critically ill patients.
METHODS: Consecutive patients receiving nicardipine in the intensive care unit at two hospitals were identified, together with an equal number of consecutive patients receiving other antihypertensives. The non-nicardipine group (NNG) was selected based on age, gender, ethnicity, baseline blood pressure, and indication for antihypertensive therapy. Demographic and clinical characteristics were collected from the medical record together with hospital billing charges.
RESULTS: From January 2007 to December 2007, 159 patients received nicardipine, and 435 patients received another parenteral antihypertensive agent. Of the 435, 159 were matched to the patients receiving nicardipine. The number of patients requiring either a second antihypertensive or a substitution of agents was significantly higher in the NNG group (59%) compared with the nicardipine group (34%) (p=0.001). The time to initiation of oral antihypertensives was significantly shorter in the nicardipine group (p<0.001). The total length of hospital stay was significantly reduced by around 30 hours in the nicardipine group (p<0.001). Major complications were also more common in the NNG group, with cardiac arrhythmias being significantly more prevalent (18% vs. 8%, p=0.018). After sequential multiple regression, nicardipine use was found to significantly decrease inpatient hospital costs by 17% compared with other antihypertensive agents (F = 4.22, p<0.001).
CONCLUSIONS: The higher acquisition cost of nicardipine is offset by a greater monotherapy treatment success rate and a lower rate of complications. Nicardipine was associated with an overall lower cost of treatment in critically ill, hospitalized patients with acute hypertension.
Presented at the American College of Chest Physicians, San Diego, CA, October 31–November 5, 2009.

39E. Economic impact of dexmedetomidine vs. midazolam in adult ICU patients with prolonged mechanical ventilation: an economic model. *Joseph Dasta, M.S.,*[1] Paula Bokesch, M.D.,[2] Sandra L. Kane-Gill, Pharm.D., M.S.,[3] Michael Pencina, Ph.D.,[4] Richard Riker, M.D.[5]; (1) The University of Texas College of Pharmacy, Austin, TX; (2) Hospira, Inc., Lake Forest, IL; (3) University of Pittsburgh, Pittsburgh, PA; (4) Boston University, Boston, MA; (5) Maine Medical Center, Portland, ME
PURPOSE: The objective of this study was to determine the cost-effectiveness of intravenous dexmedetomidine (DEX) compared with intravenous midazolam (MID) in patients requiring greater than 24 hours of continuous sedation in the intensive care unit (ICU).
METHODS: Within the double-blind, multicenter SEDCOM study, 366 ventilated adult ICU patients were randomized to receive DEX or MID. This pharmacoeconomic analysis (blinded to treatment assignment) compared actual resource use by patients multiplied by U.S. representative costs using Medicare schedules, IMS drug prices, and peer-reviewed literature. Additional analyses characterized costs associated with ICU and mechanical ventilation duration and treatment of study-related adverse events. Censored lengths of ICU stay and mechanical ventilation were imputed using a nonparametric adjustment algorithm. Crude and multivariate median regressions were performed to relate total cost of treatment with adjustment for patient (age, gender, race, and APACHE II score) and hospital characteristics (location, affiliation, size, and type).
RESULTS: DEX was shown to be cost-effective compared with MID, with a median cost savings of $9679 (95% CI: $2314–$17,045). Unadjusted total costs from time of randomization to ICU discharge were reduced ($30,232 DEX vs. $37,931 MID, p=0.031). The primary drivers of cost savings included reduced ICU length of stay (median savings, $6584; 95% CI: $727–$12,440) and reduced length of mechanical ventilation (median savings, $2958; 95% CI: $698–$5219).
CONCLUSIONS: Despite a higher acquisition price, DEX is cost-effective compared with MID for ICU patients requiring more than 24 hours of ICU sedation, mainly because of decreased lengths of mechanical ventilation and ICU stay.
Published in Dasta J, Pencina M, Kane-Gill S, Bokesch P, Riker R. Economic impact of dexmedetomidine vs. midazolam in adult ICU patients with prolonged mechanical ventilation: an economic model. Anesth Analg 2009;108:S51.

40. Modification of diet in renal disease, modified Cockcroft-Gault and 24-urine formulas are poor predictors of aminoglycoside elimination in critically ill surgical patients. *Anthony Gerlach, Pharm.D., BCPS*, Claire V. Murphy, Pharm.D., Stanislaw Stawicki, M.D., Charles H. Cook, M.D.; The Ohio State University Medical Center, Columbus, OH
PURPOSE: Bookstaver and colleagues recently demonstrated that the six-variable Modification of Diet in Renal Disease (M6) formula was more accurate in predicting aminoglycoside clearance compared with the modified Cockcroft-Gault (CGm) formula in hospitalized patients. This retrospective study compared M6, CGm, and 24-hour urine creatinine collection estimations of creatinine clearance (CrCl) for predicting aminoglycoside elimination constant (ke) to actual ke from measured aminoglycoside concentrations in critically ill surgical patients.
METHODS: Patients admitted between July 2004 and June 2008 to the SICU with aminoglycoside concentrations were evaluated retrospectively for 24-hour urine collection, age, gender, race, serum creatinine (SCr), blood urea nitrogen, and albumin. Patients were excluded if they were pregnant, received concurrent dialysis, did not have an albumin within 7 days of aminoglycoside concentrations, or did not have a 24-hour urine collection within 48 hours of aminoglycoside concentrations. Statistical analyses were performed by the Student t-test, Spearman correlation, and logistic regression analysis.
RESULTS: Sixty-one patients (43 male) were included for analysis. The mean ± standard deviation age, weight, body surface area, SCr, and albumin were as follows: 58.7 (±15) years, 83.3 (±24.4) kg, 1.95 (±0.26) m^2, 0.9 (+0.5) mg/dL, and 1.7 (±0.4) g/dL. The estimated CrCl was 78.9 (±55.2) mL/minute/1.73 m^2 for M6, 102.5

(±59.2) mL/minute/1.73 m^2 for CGm, and 90.7 (±65.2) mL/minute/1.73 m^2 for 24-hour urine.

	Calculated	M6	CGm	24-Hour Urine
Ke	0.145 ± 0.077	0.205 ± 0.157	0.253 ± 0.146	0.228 ± 0.156
Spearman coefficient		0.41	0.53	0.85
p-value		< 0.01	< 0.01	< 0.01
R^2		0.166	0.214	0.56
p-value		< 0.01	< 0.01	< 0.01

CONCLUSIONS: In critically ill surgical patients, there is a wide variation in estimation of CrCl using M6, CGm, and 24-hour urine collection. These methods appear to poorly predict aminoglycoside ke. Further studies are needed.

41. Predictors of inappropriate initial antibiotic therapy in patients with gram-negative bacteremia complicated by severe sepsis or septic shock. *Scott T. Micek, Pharm.D.,*[1] Junaid Khan, M.D.,[2] Mubashir Pervez, M.D.,[1] Richard M. Reichley, RPh,[1] Joshua A. Doherty, B.A.,[1] Marin H. Kollef, M.D.[3]; (1) Barnes-Jewish Hospital, St. Louis, MO; (2) St. Luke's Hospital, Chesterfield, MO; (3) Washington University School of Medicine, St. Louis, MO

PURPOSE: Inappropriate initial antibiotic therapy (IIAT) is a significant variable linked to mortality in patients with severe sepsis (SS) and septic shock (SSh). The Surviving Sepsis Guidelines recommend empiric combination therapy as a means to decrease the likelihood of IIAT. The goal of the study was to identify predictors of IIAT in patients with gram-negative (GN) bacteremia complicated by SS or SSh.

METHODS: A retrospective analysis of 760 episodes of GN bloodstream infection in patients between 2002 and 2007. SS and SSh were defined by ICD-9 discharge codes indicating acute organ dysfunction, with the latter having the administration of vasopressors within 48 hours of blood culture collection.

RESULTS: Two hundred thirty-eight (31.3%) patients received IIAT. Variables significantly associated with IIAT included nosocomial acquisition, chronic hemodialysis, chronic liver disease, malignancy, diabetes, need for mechanical ventilation, and receipt of prior antibiotics (all comparisons p<0.05 vs. appropriate initial therapy [AIT]). Bacteria significantly linked to IIAT included extended-spectrum β-lactamase–producing *Klebsiella* sp., *Achromobacter* sp., *Acinetobacter* sp., and *S. maltophilia* (all p<0.05). Infections with bacteria harboring resistance to one or more antipseudomonal antibiotics were more likely to receive IIAT. Patients receiving monotherapy were more likely to receive IIAT versus combination therapy (CT) (32.3% vs. 23.2; p=0.009). Mean hospital LOS (33 days vs. 21; p<0.001), mean LOS from culture date to discharge (17 days vs. 13; p<0.001), and hospital mortality (51.7% vs. 36.4%; p<0.001) were greater in the IIAT group versus the AIT group. Variables independently associated with IIAT included (adjusted odds ratio [95% confidence interval]) cefepime resistance 5.15 (2.73–9.71), carbapenem resistance 2.32 (1.16–4.65), chronic hemodialysis 2.31 (1.25–4.27), chronic liver disease 1.71 (1.01–2.89), and prior antibiotics 1.60 (1.01–2.53). Initial CT reduced the odds of IIAT 0.41 (0.27–0.63).

CONCLUSION: IIAT in patients with GN bacteremia complicated by SS or SSh occurred in almost one-third of patients and was associated with increased hospital LOS and mortality. Infections caused by antibiotic-resistant bacteria, receipt of prior antibiotics, and underlying antibiotic resistance were linked to IIAT. CT reduced the odds of prescribing IIAT.

42. Pharmacokinetics of enoxaparin following subcutaneous and intravenous administration in critically ill trauma patients. *Curtis E. Haas, Pharm.D.,*[1] Krishnan Raghavendran, M.D.,[2] Alan Forrest, Pharm.D.,[3] Edward Timm, Pharm.D.,[4] Charles W. Francis, M.D.[5]; (1) University of Rochester Medical Center, Rochester, NY; (2) University of Michigan Health Systems, Ann Arbor, MI; (3) University at Buffalo, Buffalo, NY; (4) Albany Medical Center, Albany, NY; (5) University of Rochester, School of Medicine and Dentistry, Rochester, NY

PURPOSE: Trauma intensive care unit (TICU) patients are at risk of venous thromboembolism. Recommended low-molecular-weight heparin regimens provide low, unreliable heparin activity in ICU patients, likely because of decreased subcutaneous bioavailability (F). The purpose of this study was to compare the pharmacokinetics (PK) of enoxaparin after subcutaneous and intravenous administration in TICU patients.

METHODS: An open-label, randomized, crossover study enrolling severely injured TICU patients. Enoxaparin 30 mg subcutaneously every 12 hours was routine care. Patients received either their subcutaneous dose or 0.2 mg/kg intravenously in the morning at steady state. The following morning, they were crossed over. Blood samples were collected over 12 hours after each dose. Samples were analyzed for plasma anti-Xa and anti-IIa activities, heparin activity by HEPTEST, and tissue factor pathway inhibitor. Anti-Xa activity results are being reported at this time. Noncompartmental PK analysis was performed. $AUC_{0-\infty}$, slope of the terminal phase (λ_z), elimination half-life ($t^1/_{2\lambda z}$), absolute F, and A_{max} and T_{max} were estimated by usual methods. Wilcoxon signed-rank test was used to compare between study periods.

RESULTS: Of the 10 TICU patients enrolled in the study, all completed it. Demographic and clinical characteristics (median [range], age [37 years (23–67)]; body mass index [27.5 kg/m^2 (22.6–33.8)]; serum creatinine [0.8 mg/dL (0.5–1.0)]; and injury severity score [38 (17–50)]. The median F after subcutaneous administration was 66.2% (33.8–205.8). Two subjects had an F-value much greater than 100%, without apparent explanation. Median λ_z was 0.33 h^{-1} (0.11–0.41) and 0.62 h^{-1} (0.10–1.05) after subcutaneous and intravenous doses (p=0.05), with a $t^1/_{2\lambda z}$ of 2.1 hours (1.7–6.5) and 1.1 hours (0.66–6.7). Median A_{max} values were 0.16 IU/mL (0.06–0.44) and 0.30 IU/mL (0.17–0.68) after subcutaneous and intravenous doses (p=0.03), and median T_{max} values were 2.5 hours (0.5–4.3) and 0.18 hours (0.17–1.5) (p=0.004).

CONCLUSION: Consistent with previous reports, the PK of enoxaparin was highly variable after subcutaneous administration. Variability in F_{abs} is an important contributor to this observation.

43. Review of colloid utilization in cardiac surgery. *Denis Brouillette, BPharm, DPH*, Nicolas Noël, BPharm, M.S., Sylvain Belisle, M.D., Jean-Sebastien Lebon, M.D.; Montreal Heart Institute, Montreal, Quebec, Canada

PURPOSE: Colloids are an important part of the fluid repletion strategy in cardiac surgery; however, there are limited comparative safety and efficacy data for the different colloid solutions available in cardiac surgery.

METHODS: A prospective, unblinded, observational study comparing Pentaspanâ, a pentastarch, and Voluvenâ, a tetrastarch, was conducted. Each colloid was used for 1 month alternately in adult patients scheduled for cardiac surgery for a 6-month period. Data were collected for colloid exposition (volume), renal safety (acute kidney injury and renal replacement therapy), and bleeding (blood loss and transfusion exposure).

RESULTS: Six hundred twenty-six patient files were reviewed. There was no statistical difference in patient demographics and surgery characteristics. Preoperative bleeding and renal risk assessment revealed no difference. Volume used to maintain hemodynamic stability was higher for Voluvenâ (3583 vs. 3357 cc, p=0.0065). No difference in acute kidney injury or need for postoperative renal replacement therapy was observed between the two groups. Postoperative blood loss was statistically lower for Voluvenâ (757 vs. 900 cc, p=0.0275). Differences in bleeding were more important in patients younger than 60 years (663 vs. 1000 cc, p=0.0137) and patients scheduled for elective surgery with a cardiopulmonary bypass (CPB) shorter than 60 minutes (720 vs. 910 cc, p=0.0064). Although patients in the Pentaspanâ group bled significantly more in the postoperative period, there were no differences in transfusion exposure.

CONCLUSION: Colloid choice can influence postoperative bleeding in cardiac surgery. Voluvenâ is associated with less postoperative blood loss without differences in transfusion exposure, particularly in younger patients with a shorter CPB. A larger study will be required to assess whether this product can promote blood conservation in this specific population where we actively want to restrict blood product use.

Education/Training

44. Assessment of pharmacy student's ability to critique drug advertisements. *Terri M. Wensel, Pharm.D.*, Maisha K. Freeman, Pharm.D., BCPS, Mary R. Monk-Tutor, Ph.D., RPh, FASHP; Samford University McWhorter School of Pharmacy, Birmingham, AL

PURPOSE: The purpose of this study was to determine the effectiveness of a didactic lecture in improving pharmacy students' ability to appropriately critique a direct-to-consumer (DTC) prescription drug advertisement.

METHODS: Third-year pharmacy students at Samford University were assessed on their ability to critique a DTC advertisement before and after a lecture on DTC. A 3-minute simulated pharmaceutical company sales representative "call" was used to introduce students to the topic; only claims published in a current published advertisement were mentioned. Students reviewed the advertisement and completed the presurvey. After an almost 40-minute lecture, students completed a postsurvey in which they reanalyzed the same advertisement. Paired survey data for each student were entered into SPSS (version 16.0) and were analyzed using descriptive statistics and a Wilcoxon signed-rank test for a comparison of pre- and postscores. All tests were two-sided with $\alpha < 0.05$ considered significant.

RESULTS: Both the pre- and postsurveys were completed by 80% (99 of 123) of the class with a usable response rate of 79% (78 of 99). Most respondents were female, aged 19–29 years, with previous pharmacy-related work experience. Changes in pre- and postsurvey scores were statistically significant on seven items, with student agreement increasing on six of the seven items. Although the mean of six items did not change significantly between pre- and post-scores, an increase in agreement was seen for two items, an increase in disagreement was seen for three items, and one item remained unchanged.

CONCLUSIONS: The use of didactic lectures significantly affected students' ability to critique DTC advertisements, particularly components related to regulatory requirements and presentation of safety information. For items not significantly changed from pre- to postsurvey, it is possible students will require additional lectures or practical applications to appropriately critique those specific components of DTC advertisements.

45. Reliability of a seminar grading rubric in a grand rounds course. *Eric J. MacLaughlin, Pharm.D.*,[1] David S. Fike, Ph.D.,[1] Carlos A. Alvarez, Pharm.D.,[2] Charles F. Seifert, Pharm.D.,[3] Amie T. Blaszczyk, Pharm.D.[2]; (1) Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX; (2) Texas Tech University Health Sciences Center School of Pharmacy, Dallas, TX; (3) Texas Tech University Health Sciences Center School of Pharmacy, Lubbock, TX

PURPOSE: Evaluations of student presentations are often viewed as subjective. In the past, this was a common complaint of students and faculty in the grand rounds course at Texas Tech University Health Sciences Center School of Pharmacy. In 2006, a new rubric was designed to objectively assess content and communication skills of students presenting a formal seminar. The objective of this study was to determine the reliability of the new rubric.

METHODS: Retrospective study of 252 student presentations given from fall 2007 to fall 2008. Data including student and faculty demographics, overall content score, overall communication scores, subcomponents of content and communication, and total presentation scores were collected. Internal consistency of the rubric was assessed using Cronbach α. The Pearson correlation coefficient was used to determine the correlation between the mean faculty presentation grade (average of two faculty graders) and students' self-evaluations. Statistical analyses were performed using SPSS, 16.0.

RESULTS: The rubric demonstrated a high degree of internal consistency (Cronbach $\alpha = 0.826$). The mean grade difference between faculty graders was 4.54 percentage points (SD = 3.614), with a 10-point or less difference for 92.5% of the evaluations. Student self-evaluations correlated with faculty scores for content, communication, and overall presentation ($r=0.513$, $r=0.455$, and $r=0.539$; $p<0.001$ for all). When comparing mean faculty scores with students' self-evaluations between quintiles (i.e., 19% or less, 20%–39%, 40%–59%, 60%–79%, and 80% or more), students with lower faculty evaluations overestimated their performance, and those with high faculty evaluations underestimated their performance ($p<0.001$).

CONCLUSIONS: The seminar rubric demonstrated a high degree of inter-rater reliability and internal consistency.

46. Assessing pharmacy students' beliefs and confidence levels before and after an elective course in infectious diseases. *Elias B. Chahine, Pharm.D., BCPS*, Allana J. Sucher, Pharm.D., BCPS, Adwoa O. Nornoo, Ph.D.; Palm Beach Atlantic University, West Palm Beach, FL

PURPOSE: Educating and training future pharmacists in the treatment of infectious diseases is essential in pharmacy education. An elective course was developed to enhance students' knowledge, skills, and attitudes in infectious diseases. This study was designed to assess students' beliefs and confidence levels before and on completion of this elective course.

METHODS: A 2-credit-hour elective course was offered to third-year pharmacy students who successfully completed microbiology and infectious diseases pharmacotherapy prerequisite courses. Course topics were discussed in a case-based fashion throughout the course, and students were required to deliver formal presentations in which they recommended an antimicrobial agent for a specific patient and for inclusion on an institution's formulary. At the end of the semester, two surveys were distributed to students to assess their beliefs and confidence levels regarding antimicrobial pharmacotherapy before and on completion of the course. In addition, pharmacists who precepted these students were asked to complete a survey to evaluate the students' knowledge and skills in infectious diseases. Statistical analysis of the surveys was performed with the Wilcoxon signed-rank test using the Origin Pro SR4 program (version 8.0951).

RESULTS: There were statistically significant improvements in the median preassessment and postassessment values of both students' beliefs and students' confidence levels regarding antimicrobial pharmacotherapy after taking the elective course ($p<0.05$). Eighty-eight percent of surveyed preceptors agreed that students who took this elective course were more knowledgeable in infectious diseases compared with other students they had precepted. Eighty-two percent of the preceptors agreed that these students were also better prepared to apply their knowledge in a pharmacy practice setting.

CONCLUSIONS: Incorporating an elective course in infectious diseases into the pharmacy curriculum enhances students' beliefs and confidence levels in this therapeutic area, improves their performances during clerkship rotations, and may better prepare them for future clinical practice.

47. Curriculum in pharmacogenetics and pharmacogenomics in colleges and schools of pharmacy in the United States. *Laura Adams, Pharm.D.*,[1] Robert Squire, Pharm.D.,[1] John E. Murphy, Pharm.D.,[1] James Green, Pharm.D.[2]; (1) The University of Arizona College of Pharmacy, Tucson, AZ; (2) Shenandoah University Bernard J. Dunn School of Pharmacy, Ashburn, VA

PURPOSE: The purpose of this study was to assess the breadth and depth of pharmacogenetics and pharmacogenomics (hereafter pharmacogenomics) curricular content as well as the level of faculty development relative to these areas in U.S. colleges of pharmacy and to compare pertinent results with those determined in a previous study.

METHODS: A questionnaire was developed based on one used in a 2004 study by Latif and McKay. The questionnaire was sent by e-mail to 90 contacts identified by their respective deans at U.S. colleges of pharmacy. Multiple follow-up approaches were used to enhance response.

RESULTS: Of the 90 questionnaires sent, 75 (83.3%) usable questionnaires were returned. There were significantly more of the responding colleges (69 [92.0%]) that included pharmacogenomic coursework in their Pharm.D. curriculum compared with the study by Latif and McKay (16 [39.0%]). The genetic basis of disease core competencies was being covered and considered important for the

curriculum by responding faculty. Ethical, social, and economic implications were also considered important, though this content was not covered as thoroughly. Depth of content coverage was less than 10 didactic hours for 28 (40.6%) colleges, whereas 29 (42.0%) provided 10–30 hours, and another 10 (14.5%) committed 31–60 hours. Respondents believed the state of pharmacogenomic instruction at other colleges was poor or not at all adequate (46 [61.3%]), whereas only 22 (29.3%) believed their own school was in a similar situation. Less than half (46.7%) of the colleges were planning to increase their pharmacogenomic coursework during the next 3 years, and 54.7% had no plans for faculty development in the area.

CONCLUSIONS: Although pharmacogenomic content is included in the curricula of most colleges of pharmacy today, the depth may be somewhat limited. Most colleges are not providing specific faculty development in the area.

48. Constructing a tool to assess deep student learning within advanced pharmacy practice experiences. *Danny McNatty, Pharm.D., BCPS,*[1] Michael J. Peeters, Pharm.D., MEd, BCPS[2]; (1) Midwestern University College of Pharmacy – Glendale, Glendale, AZ; (2) University of Toledo College of Pharmacy, Toledo, OH

PURPOSE: Measuring the quality of student learning in advanced pharmacy practice experiences (APPEs) is problematic – with no available quantitative instruments for assessment. The purpose of this investigation was to construct an evaluation tool to measure "depth of learning" among pharmacy students within their APPEs.

METHODS: By modifying a prior depth of learning instrument that had already been validated for didactic classroom instruction, an initial draft of the "Pharmacy Education Student Tool for Learning Experiences" (PESTLE) was created with the intent to evaluate the depth of student learning during APPEs. The PESTLE is a 20-item self-report survey instrument for students to complete in conjunction with APPEs. First, the tool was piloted with seven students from two colleges of pharmacy. Thereafter, in 2008–2009, each MWU-CPG APPE student completed the PESTLE at the conclusion of his/her Acute Care APPE rotation with the primary investigator and after his/her final evaluation. Responses were analyzed using the Winsteps software program (Chicago, IL) within the Rasch Measurement Model. The intent was to characterize the PESTLE's measurement properties in this small cohort. IRB approval was granted, and student responses remained confidential and anonymous.

RESULTS: Fourteen APPE students completed the PESTLE. In this small cohort, the tool separation was 2.02 with a reliability of 0.80; at least two categories of learning depth were measured with strong reliability. The probabilities for each category of the rating scales were stepwise and sufficiently distinct from one another. People and items fit the Rasch Measurement Model adequately within this linear, unidimensional construct (62% by Principal Contrast Analysis).

CONCLUSIONS: Within this small cohort of APPE students, the PESTLE provided ample measurement properties to adequately assess at least two levels (shallow vs. deep) of self-reported learning depth during APPEs. A future study will be conducted to test the PESTLE in a larger cohort of pharmacy students.

49. Development and implementation of an internal educational needs assessment for hospital pharmacists in an academic medical center. *Rebecca A. Taylor, Pharm.D., MBA, BCPS*, Jun-Yen Yeh, Ph.D., Morton P. Goldman, Pharm.D., FCCP, BCPS; Cleveland Clinic, Cleveland, OH

PURPOSE: To develop and implement an educational needs assessment tool for hospital pharmacists focusing on perceived importance and underlying knowledge base in the area of cardiovascular therapeutics.

METHODS: A registry-like survey was developed using an online commercial source and sent out by e-mail to all registered inpatient pharmacists. The 37-item questionnaire was adapted from published literature and covered nine therapeutic topics in cardiology chosen from the ACCP White Paper on Clinical Pharmacist Competencies. Each cardiology topic was rated for importance and knowledge on a 5-point Likert scale. Other questions related to delivery methods, satisfaction with present educational programs, and operational education needs were rated on a 3- or 4-point Likert scale. Internal reliability of the instrument was assessed.

RESULTS: The overall response rate was 56%. Mean importance ratings on nine topics ranged from 3.54 to 4.23, and mean knowledge ratings ranged from 3.38 to 4.27 on the 5-point scale. The coefficient α was 0.88. Of 69 pharmacists, 80%, 75%, 74%, and 70% rated stroke, atrial fibrillation, heart failure, and acute coronary syndromes very important or essential topics, and 20%, 29%, 26%, and 44% indicated poor or less knowledge to these topics, respectively. Thirty-six percent of pharmacists preferred Web-based courses, with 32% favoring full-day sessions. Only 56% of pharmacists indicated they were very satisfied or somewhat satisfied with ongoing educational programming.

CONCLUSIONS: The survey suggests therapeutic areas that pharmacists deem of highest importance and lowest knowledge level in cardiology. These data will help in the planning of future educational programs for the pharmacist staff. Additional plans include expanding the survey to cover other disease states, ensuring appropriate access to educational programs, and considering a full day of education or competency training for pharmacist education.

50. Experience-based pharmacist education needs assessment in an academic medical center. *Jun-Yen Yeh, Ph.D.*, Rebecca A. Taylor, Pharm.D., MBA, BCPS, Morton P. Goldman, Pharm.D., FCCP, BCPS; Cleveland Clinic, Cleveland, OH

PURPOSE: An education needs assessment survey was designed to assist in developing continuing cardiology educational programming for the hospital pharmacist staff. Future programming will be based on the results of the survey and may be able to target pharmacists with the most need and interest. To explore pharmacists' education needs in cardiology by years of experience as pharmacists and by practice sites.

METHODS: Hospital pharmacists at Cleveland Clinic main campus were asked to voluntarily, anonymously respond to a Likert-type Web-based survey that included questions about interest and knowledge level of various operational and cardiology topics. Data were analyzed by χ^2 tests and nonparametric Kruskal-Wallis rank tests. When responses were treated as continuous variables, analysis of covariance (ANCOVA) was performed to adjust responses for responsiveness (proxy: overall mean scores).

RESULTS: Significant differences in percentages of poor or less knowledge to *thromboembolic disorders* (p=0.015), *stroke* (p=0.005), *heart failure* (p=0.045), and *cardiopulmonary resuscitation* (p=0.018) were found among five groups based on years of experience. Pharmacists with less than 2 years' experience showed more interest in learning more about *nursing policies/procedures* (p=0.003) and *precepting/teaching students* (p=0.001), compared with pharmacists with more than 15 years' experience. Among pharmacists who rated a topic very important or essential, relatively higher percentages of pharmacists with experience between 10 and 15 years expressed poor or less knowledge to *thromboembolic disorders* (p=0.033), *stroke* (p=0.020), and *heart failure* (p=0.015) than the other groups. Pharmacists working at satellite pharmacies indicated less interest in *atrial fibrillation* (p=0.041), and they reported relatively lower knowledge levels of *hypertension* (p=0.021).

CONCLUSIONS: Pharmacists' knowledge and interest vary by years of experience as pharmacists and practice site for some topics. Pharmacist educational programs could be designed and prioritized based on these two factors.

51. Comparing colleges' of pharmacy didactic migraine education to the U.S. Headache Consortium's evidence-based migraine treatment guidelines. Richard G. Wenzel, Pharm.D.,[1] *Rosalyn S. Padiyara, Pharm.D., CDE,*[2] Jon C. Schommer, Ph.D.[3]; (1) Diamond Headache Clinic Inpatient Unit, Chicago, IL; (2) Midwestern University–Chicago College of Pharmacy, Downers Grove, IL; (3) Department of Pharmaceutical Care and Health Systems, Minneapolis, MN

PURPOSE: Evaluate doctor of pharmacy (Pharm.D.) candidates' didactic migraine training.

METHODS: Self-administered survey sent to all 90 ACPE-approved Pharm.D. programs in July 2008.
RESULTS: Seventy-seven programs responded (86%), and 69 usable surveys were identified (Table I). Exclusions were that this study's lead author provided two programs' migraine lecture, four programs did not provide migraine lectures, and two programs were "student self-directed learning," thus lacking a formal migraine lecture.
Table I (n=69)

Question	Written handout*	Verbally conveyed*
Are the U.S. Headache Consortium's evidence-based migraine treatment guidelines discussed?	55%	77%
Is the concept of stratified care explained?	77%	81%
Is the concept of step care explained?	65%	74%
Is information regarding the reason(s) for the selection of over-the-counter agents (OTC) vs. prescription agents explained?	49%	70%
Is the patient counseling point of limiting acute therapy use to 2 days or less per week explained?	74%	78%
Are the goals of acute migraine therapy explained?	88%	97%
Are the goals of preventive migraine therapy explained?	75%	81%
Are the indications of preventive migraine therapy explained?	87%	90%
Are patient counseling points for preventive therapy explained?	65%	75%
Is the need for patients to maintain a headache diary discussed?	70%	87%
Are nondrug treatments discussed (e.g., biofeedback)?	73%	81%
Are butalbital-containing products recommended for acute migraine attacks?	45%	48%
Are any tools that assess migraine-related debilitation discussed?	20%	32%

*Percentages indicate percentage of programs responding "yes" to the question.
CONCLUSIONS: Opportunities exist to improve Pharm.D. candidates' didactic migraine education. Particular attention is needed regarding 1) expanded dissemination of evidence-based care, 2) the rationale to select OTC versus prescription products, 3) the avoidance of butalbital-containing products, and 4) tools to assess migraine-related debilitation.

52. Use of wikis for advanced pharmacy practice experiences. *April D. Miller, Pharm.D.*, P. Brandon Bookstaver, Pharm.D., BCPS, AAHIVE, LeAnn B. Norris, Pharm.D.; South Carolina College of Pharmacy-USC Campus, Columbia, SC
PURPOSE: Wikis are an online tool used in various areas of health education and research communities. Their uses in pharmacy education are not well described. This study surveyed fourth-year pharmacy students on their experiences and overall satisfaction in using wikis on advanced pharmacy practice experiences (APPEs).
METHODS: Wikis were used during acute care rotations with three faculty preceptors in internal medicine/infectious diseases, critical care, and hematology/oncology. Students were asked to create and edit wiki pages based on daily questions that arose during patient care rounds or patient-specific evidence-based medicine care decisions. An anonymous survey was administered to students after clerkship completion using SurveyMonkey. Questions assessed student opinions on their effectiveness in reinforcing clerkship concepts, building collegiality, perception of wiki tasks, and interest in using wikis in other areas of pharmacy education.
RESULTS: Responses from the survey indicate that more than 90% of students (12 of 13) either agreed or strongly agreed that using wikis helped them review, understand, and reflect on clerkship concepts. Around 70% of students (9 of 13) agreed or strongly agreed that wikis helped create a sense of collegiality among their peers. In addition, more than 90% of respondents (12 of 13) reported agreement or strong agreement that they enjoyed using the wiki and that they would like to see them used in other areas of pharmacy education.
CONCLUSIONS: Students enjoyed using wikis during APPEs and felt that they helped reinforce clerkship concepts. Their interest in using them in other areas of pharmacy education indicates that wikis may be an effective tool in a variety of educational settings. Involved faculty share a common sentiment with the students, feeling the use of wikis enhances the overall clerkship experience.

53. Pharmacy students' work experience. *Michael Steinberg, Pharm.D.*, Anna K. Morin, Pharm.D.; Massachusetts College of Pharmacy and Health Sciences, Worcester, MA
PURPOSE: The purpose of this study was to assess the extent, type, and opinions of pharmacy students' extracurricular work experiences, both before and during their enrollment in an accelerated Pharm.D. program.
METHODS: A survey of 18 questions was prepared and made available through an online service. About 587 students attending a 3-year accelerated doctor of pharmacy program were solicited by the school's e-mail to access the survey by an Internet link during a 3-week period.
RESULTS: One hundred sixty-one students (first-year students, n=65 [40%]; second-year students, n=51 [32%]; third-year students, n=45 [28%]) participated in the survey. Before matriculation, 69% of students had worked in a pharmacy; of these, 78% had worked solely in the retail setting, 6% had worked in a hospital, 11% had worked in both, and 5% had worked in another type of pharmacy. Most of the students (55%) had worked in a pharmacy for more than 2 years before starting pharmacy school, but only 42% achieved Certified Pharmacy Technician status. While enrolled in classes, 62% of students found employment, 42% continued in a previous position, 34% began work during their first year of school, 18% began work during their second year, and only 3% began work in their third year. Sixty-eight percent of students worked less than 6 days/month, accounting for less than 8 hours/week working. Reasons provided by students for working included gaining experience (46%), earning money (40%), and hoping for future employment (13%). A majority of students (55%) felt working helped them better understand what they were learning in classes, whereas 5% felt working did not help them. Only 11% of students felt having a job prevented them from completing their studies.
CONCLUSIONS: Pharmacy students feel that having a job in a pharmacy before or during enrollment in an accelerated Pharm.D. program is an important contributor to their success.

54. Impact of an online self-paced lecture to deliver drug information. *Suzanne G. Bollmeier, Pharm.D., BCPS, AE-C*, Alicia B. Forinash, Pharm.D., BCPS, Philip J. Wenger, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis, MO
PURPOSE: Advances in classroom technology enable faculty to transition away from traditional lectures. A portion of the drug information (DI) sequence is covered in a 2-hour lecture in the Therapeutics II (T2) course. Traditionally, all topics are covered with an in-class lecture from the content expert. In the spring 2009 semester, the DI lecture (audio and slides) was only available online by the Camtasia program.
METHODS: Students were asked to view the Camtasia lecture online outside class and to individually complete four DI assignments. Each examination had questions covering DI. Students completed a survey regarding Camtasia at the end of the semester. Minutes of the Camtasia lecture viewed were analyzed in relation to DI portion of examination scores, DI homework scores, and final course grades. Multiple-choice DI question scores were compared with a historical control group.
RESULTS: Scatter plots and Pearson correlation coefficients revealed little correlation between minutes viewed and examination 1 (r=0.149), examination 2 (r=0.185), examination 3 (r=0.062), final examination (r = -0.05), course grade (r = -0.0148), and DI homework assignments (r=0.0114). Performance on DI multiple-choice questions was significantly higher in 2009 versus the historical control group in 2008 (p=0.04).
Of the 73 students completing the survey, 99% rated the Camtasia DI lecture as at least somewhat helpful in completing DI homework and 86% in studying for examinations. Eighty-one percent of students were willing to watch future lectures by Camtasia.
CONCLUSIONS: Having access to an online DI lecture throughout the semester did not correlate with student outcomes on homework assignments, DI portions of examinations, or course grade. Spring 2009 students did outperform the historical control group on DI-specific multiple-choice examination questions. Students subjectively saw benefit with the lectures and would welcome future lectures delivered in this manner.

55. Impact of online lecture viewing on student attendance in a therapeutics course. *Suzanne G. Bollmeier, Pharm.D., BCPS, AE-C*, Philip J. Wenger, Pharm.D., BCPS, Alicia B. Forinash, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis, MO

PURPOSE: Tegrity allows instructors to post lecture files (audio and video of PowerPoint slides) to course homepages; however, little is known about how posting lectures in a therapeutics course influences traditional class attendance.

METHODS: Second professional year students enrolled in the spring 2009 Therapeutics II (T2) course at St. Louis College of Pharmacy could view recorded files online up to 72 hours after the lecture. Attendance during traditional lectures was analyzed in relation to online lecture viewing minutes and total accessions. Students who opted to participate in the research study completed a brief survey.

RESULTS: Of the 112 participants (class size, 196), 68% commuted to campus from less than 10 miles, 19% commuted more than 10 miles, 14% lived on campus, and 45% lived with other students enrolled in T2. Self-reported number of lecture accessions was none (7%), once (15%), 2–5 (28%), 5–10 (27%), and more than 10 (23%). Of the 24 lectures (40 hours) during the semester, the average number of lecture accessions was 3.4 (range, 0–19) with an average viewing time of 2 hours 27 minutes (range, 0–13 hours 56 minutes). Twenty-eight percent of students self-reported that the availability of online lectures affected their lecture attendance. No correlation was found between class attendance and minutes of lecture viewed ($r = -0.2839$, $r^2=0.0806$) or between attendance and number of lecture accessions ($r = -0.2158$, $r^2=0.0465$)

CONCLUSIONS: Attendance at traditional T2 lectures did not correlate with either the number of lecture accessions or the minutes of online lectures viewed, and 72% of students reported that their attendance was not influenced by online lecture availability. Surprisingly, the use of this new online resource was low.

56. Implementation of "living with diabetes week" curriculum and its impact on student attitude related to diabetes. *Deirdre E. Delea, Pharm.D.*, Sarah Shrader, Pharm.D., BCPS, CDE; Medical University of South Carolina, Summerville, SC

PURPOSE: To assess student empathy toward those with diabetes and confidence in diabetic education before and after participation in "Living with Diabetes Week" curriculum.

METHODS: Third-year pharmacy students at the South Carolina College of Pharmacy took part in didactic diabetes lectures and interactive diabetes laboratory sessions. After the laboratory sessions, the students participated in a weeklong simulation of life as a patient with diabetes. The simulation included blood glucose monitoring, diabetic meal planning, and simulation of diabetic medication administration. Before the laboratory sessions and at the end of the weeklong simulation, students completed a survey assessing attitudes related to diabetes.

RESULTS: Overall, there was an increase in the belief that diabetes has a psychosocial impact, that patients with diabetes should have autonomy with respect to treatment of their disease state, and that type 2 diabetes is a serious disease state. Student confidence in diabetes education skills also increased on completion of the curriculum.

CONCLUSIONS: Implementation of a "Living with Diabetes Week" curriculum changed pharmacy students' attitudes toward patients with diabetes and increased confidence in diabetes education skills.

57. Pre-APPE assessment of students' clinical writing skills in a capstone course. *Jeannine M. Conway, Pharm.D.,*[1] Michael C. Brown, Pharm.D.[2]; (1) University of Minnesota, Minneapolis, MN; (2) Concordia University Wisconsin, Mequon, WI

PURPOSE: To assess students' clinical writing skills across a capstone pharmacotherapy course and determine their improvement through the course in preparation for APPEs.

METHODS: This semester-long course was offered immediately before APPEs. Every 2 weeks, students were presented with subjective and objective portions of a written case. Students were individually required to complete the assessment and plan. Residents used a rubric to assess the structure and clinical content of each student's submission, including rating each section's structure as satisfactory or not satisfactory. Assessment structure–required elements included status of condition, identification of problem(s), goals for condition, and rationale for therapeutic decision(s). The elements required by the plan structure included specific recommendation(s) and instructions for what/when to follow up. Although the type, number, and complexity of conditions changed throughout the semester, structure expectations remained constant, allowing comparative analysis. Ratings from the first and last cases were analyzed by the McNemar test for paired categoric data to determine whether documentation skills improved throughout the semester.

RESULTS: Data for two course offerings were available (n=316). One hundred eighty-five students (58.5%) received satisfactory ratings for both assessment and plan on case 1, and on case 6, 235 students received satisfactory ratings (74.4%) ($p<0.001$). Performance on assessment was satisfactory for 217 (68.7%) and 266 (84%) students, on case 1 versus case 6, respectively ($p<0.001$). Performance on plan was satisfactory for 259 (81.9%) and 268 (84.8%) students on case 1 versus case 6, respectively (NS). Improvement on assessment was driven predominantly by fewer students missing the provision of their therapeutic rationale (16 students case 1 vs. 1 student case 6 [$p<0.001$]).

CONCLUSIONS: Students' mastery of the structure of clinical writing is multifaceted. This capstone course helps students continue to build their documentation skills before their APPEs. Although student performance improved, continued writing practice on APPEs and residencies is essential for developing further expertise.

58. Impact of on-line lecture viewing on student outcomes. *Suzanne G. Bollmeier, Pharm.D., BCPS, AE-C*, Philip J Wenger, Pharm.D., BCPS, Alicia B. Forinash, Pharm.D., BCPS, CCD; St. Louis College of Pharmacy, St. Louis, MO

PURPOSE: Tegrity allows instructors to make lecture files (audio and video of PowerPoint slides) available through course Web pages; however, little is known about how posting lectures in a therapeutics course influences performance in that course.

METHODS: Second professional year students enrolled in the spring 2009 Therapeutics II (T2) course at St. Louis College of Pharmacy could view recorded files online up to 72 hours after the lecture. Students completed a brief survey about Tegrity at the end of the semester. Students' final examination and course grades were compared with a T2 historical control and their own performance in Therapeutics 1 (T1).

RESULTS: Of the 124 participating students (class size, 196), the average number of lecture accessions throughout the semester was 3.4 (range, 0–19; 24 lectures available), with an average viewing time of 2 hours 27 minutes (range, 0–13 hours 56 minutes; 40 available hours). No correlation was found between final course grade and number of accessions ($r=0.0014$) or minutes viewed ($r=0.033$). Students performed significantly better in T2 compared with T1 in final examinations (mean, 67% vs. 62%, respectively, $p<0.002$) but not in final course grades (79% vs. 78%, respectively, $p=0.07$). Compared with historical controls in T2, final course grades were similar. In student surveys, 67% felt the online lectures were at least somewhat helpful in preparing for examinations, 70% in completing homework, and 78% in completing lecture handouts. Eighty-eight percent stated they would enjoy access to Tegrity lectures in future courses.

CONCLUSION: Neither total number of accessions nor total minutes viewed correlated with final course grades. No difference was found in final course grades between years. Final examination grades in T2 were higher than in T1. Students subjectively found the online lectures helpful; although they would enjoy more lectures through Tegrity, the total accessions were surprisingly low.

59. Assessing the progression of pharmacy student achievement of the Center for the Advancement of Pharmaceutical Education (CAPE) outcomes in a senior capstone course. *Jennifer L. Donovan, Pharm.D.,*[1] Abir O. Kanaan, Pharm.D.,[1] Evan R. Horton, Pharm.D.,[1]

Cheryl Abel, Pharm.D.,[2] Paul Belliveau, Pharm.D., RPh,[1] Matthew A. Silva, Pharm.D., BCPS[1]; (1) Massachusetts College of Pharmacy and Health Sciences, Worcester, MA; (2) Massachusetts College of Pharmacy and Health Sciences, Worcester, MA

PURPOSE: Higher education is challenged with incorporating assessment at the institutional, programmatic, and course levels. The Accreditation Council for Pharmacy Education (ACPE) requires assessment as part of accreditation, and assessment must be consistent across all levels of a program. We evaluated the achievement of CAPE outcomes in a capstone course for third-year pharmacy students. We hypothesized that an improvement existed in student communication, knowledge, critical thinking skills, and professionalism between the beginning and completion of the course.

METHODS: A prospective, observational survey using a paired pretest, posttest evaluative model was constructed and administered to graduating third-year students during 2008–2009. Students identified clinical therapeutic topics of interest and conducted extensive research for a poster presentation. CAPE outcomes were used to construct course objectives, which were then mapped to evaluation rubrics used for poster assignments. The primary objective was to evaluate the proportion of students meeting CAPE objectives and then to evaluate student communication, knowledge, critical thinking, and professionalism based on assignment grades and survey responses. A minimum score of 70% was used to identify those meeting an objective, and we estimated that 70% of students would meet the set objectives in each evaluated category. The Pearson χ^2 test was used for proportional comparisons.

RESULTS: Complete information was collected from 117 students. Successful achievement of all CAPE objectives was observed by 85% of students (vs. 70% hypothesized, $p \leq 0.0001$). Communication and knowledge objectives were met by 87% (vs. 70% hypothesized, $p \leq 0.0001$). Critical thinking objectives were met by 77.4% (vs. 70% hypothesized, $p \leq 0.0001$), and professional objectives were met by 83% (vs. 70% hypothesized, $p \leq 0.0001$).

CONCLUSION: A senior capstone course centered on research and professional poster development is an effective teaching strategy that can be aligned with AACP's CAPE outcomes.

60. Relationship between faculty self assessments and students ratings of learner centered teaching during advanced pharmacy experiences. *Anna K. Morin, Pharm.D.*, Abir Kanaan, Pharm.D., Matt Silva, Pharm.D., Paul Belliveau, Pharm.D.; MCPHS, Worcester, MA

PURPOSE: Learner-centered teaching (LCT) requires active involvement of faculty and students. Tools assessing LCT allow faculty and students to reflect on teaching and learning practices. We hypothesized that a relationship existed between faculty self-assessments and student ratings of LCT during advanced pharmacy practice experiential education (APPE).

METHODS: A prospective observational survey was conducted from September 2008 to May 2009. Students and faculty, who were blinded, received a random number identifier. An administrative member remained unblinded and distributed the surveys. Student assessments of faculty LCT methods were performed at the end of each APPE. Faculty self-assessments were performed at the end of the first and last APPE. Ordinal data were evaluated with a Wilcoxon rank-sum test. Analysis of variance and repeated-measures regression were used for continuous data with confounding variables. Adjusted regression coefficients of at least 0.5 were considered indicative of a correlation between variables. Simple t-tests and Fisher exact analysis were used for proportional comparisons. A six-item survey using a five-point Likert scale defined the frequency of each LCT activity (1 = never, 5 = always). Proportions indicating "frequently" or "always" were combined and considered favorable.

RESULTS: Surveys were issued to 24 faculty and 135 students with participation rates of 83% and 42%, respectively. Nonparametric analysis revealed a difference in modes of student versus faculty LCT scoring (4.46 vs. 3.81, $p \leq 0.01$) and an overall increase in faculty awareness of learner needs when preparing materials (4.56 vs. 3.67, $p=0.009$). There were similar self-assessment scores among faculty ($p=0.24$) and similar scores according to practice site ($p=0.85$). Linear regression failed to demonstrate correlations between student and faculty scores ($r^2=0.04$).

CONCLUSION: Lack of correlation between student and faculty scores may be attributed to low rates of student participation. Faculty members consistently apply LCT methods, and this approach is recognized by learners.

61. Survey of the early entry program's influence on pharmacy student development. *Lauren S. Bloodworth, Pharm.D., BCPS*, T. Kristopher Harrell, Pharm.D., Alicia Bouldin, Ph.D.; University of Mississippi School of Pharmacy, Jackson, MS

Survey of the Early Entry Program's Influence on Pharmacy Student Development. Lauren S. Bloodworth, Alicia S. Bouldin, and T. Kristopher Harrell. The University of Mississippi.

PURPOSE: The University of Mississippi School of Pharmacy began an Early Entry Program for high school seniors in 1997. The purpose of this study was to evaluate how this program has influenced student development in current pharmacy students who participated in that program.

METHODS: Current PY3 and PY4 students who were a part of the early entry program were sent an e-mail requesting them to complete an anonymous online survey consisting of 20 questions. The survey questions examined student perception of the program's influence on academic performance, leadership, self-confidence, and career decisions.

RESULTS: Of the 40 students who were sent surveys, 39 responded (22 PY3 and 17 PY4). Most respondents perceived that they were better prepared in time management (62%), stress management (64%), leadership (67%), and self-confidence (72%) than had they chosen the regular entry pathway. Although perceptions were not negative regarding preparation for academic and rotation performance, they were more neutral (46% neutral for academics, 74% for rotations). Around 60% of the students reported they were somewhat interested in pursuing a residency after graduation.

CONCLUSIONS: These results suggest that the Early Entry Program may benefit student development in desired nonacademic skills, especially leadership, time management, stress management, and self-confidence.

Emergency Medicine

62. Drug information references used by emergency medicine clinicians to make prescribing decisions to pregnant patients. Lindsay Stansfield, Pharm.D., *Victor Cohen, Pharm.D.*, Samantha Jellinek, Pharm.D., Antonios Likourezos, M.A., MPH; Maimonides Medical Center, Brooklyn, NY

PURPOSE: Certain drug references may lead to inappropriate prescribing by emergency medicine clinicians because of exclusion of pregnancy registry data, limited clinical detail, and/or outdated information. The purpose of this study was to determine whether the drug information references used by clinicians in the emergency department (ED) provided the most up-to-date drug-related pregnancy information.

METHODS: A cross-sectional survey was completed by emergency medicine–attending physicians, physician assistants, and residents at Maimonides Medical Center. The three-part survey was approved by the institution's review board. In part I, clinicians listed the top three drug information references they routinely used in clinical practice. In part II, clinicians ranked their willingness to prescribe a category A, B, C, D, or X drug using a 5-point Likert scale. In part III, clinicians selected, from a list of electronic and print resources, the resources they considered available to them in the ED to find pregnancy-related drug prescribing information. Statistical analyses included frequency distribution and bivariate analysis by SPSS version 15.0.

RESULTS: Fifty-five clinicians with a median of 2.5 years (range, 1–38) in the profession filled out the survey. Forty-one (75%) respondents were men, and 26 (48%) were residents practicing in both the adult and pediatric EDs. Only 10 (19%) respondents stated that they would be willing to prescribe category C drugs, yet 40 (66%) of the most commonly used drugs in the ED are category C. The most commonly used references included Micromedex,

Tarascon Pocket Pharmacopoeia, and Epocrates (29%, 18%, and 14%, respectively). Among the five (63%) pregnancy-specific drug information references that were available in our EDs, only 20% of clinicians stated that these references were available to them.
CONCLUSIONS: Emergency medicine clinicians commonly use drug information references that may not incorporate pregnancy human data into their pharmacotherapy recommendations.

63. Effect of sedative and paralytic dosing on first attempt success rate during rapid sequence intubation in the emergency department. *Sara A. Stahle, Pharm.D.*,[1] Asad E. Patanwala, Pharm.D.,[1] Daniel P. Hays, Pharm.D.,[2] John C. Sakles, M.D.,[3] Brian L. Erstad, Pharm.D.[1]; (1) The University of Arizona College of Pharmacy, Tucson, AZ; (2) University Medical Center, Tucson, AZ; (3) The University of Arizona College of Medicine, Tucson, AZ
PURPOSE: This study evaluated the effect of sedative and paralytic dosing, as well as other intubation parameters, on first-attempt intubation success during rapid sequence intubation (RSI) in the emergency department (ED). The aims of this study were to determine dosing variability of etomidate, succinylcholine, and rocuronium for RSI; determine success rate of first intubation attempt; and identify factors predictive of successful first intubation attempt.
METHODS: Data were retrospectively obtained from medical records and a quality improvement database for all patients intubated in the ED between July 1, 2007, and October 31, 2008. Demographic data and information pertinent to each RSI were collected. The effects of independent variables on first-attempt intubation success were analyzed using univariate and multiple logistic regression analyses.
RESULTS: A total of 621 intubations were performed during the study period, and 327 patients met criteria for inclusion in the analysis. The mean dosages for RSI medications were etomidate, 0.27 ± 0.1034 mg/kg; succinylcholine, 1.68 ± 0.6047 mg/kg; and rocuronium, 1.24 ± 0.3900 mg/kg. Success rate of first intubation attempt was 72.8%. Independent variables predictive of first-attempt success were difficult airway parameters (odds ratio [OR] = 0.69, 95% confidence interval [CI]: 0.58–0.82, p<0.0001) and laryngeal view (OR = 0.16, 95% CI: 0.10–0.24, p<0.0001).
CONCLUSIONS: Factors found to be predictive of successful first intubation attempt were difficult airway parameters and laryngeal view. Choice of paralytic agent, as well as weight-based dose, was not found to be predictive of first-attempt success. Dosages for etomidate, succinylcholine, and rocuronium based on weight varied considerably.

Endocrinology

64E. Long-term use of colesevelam HCl in subjects with type 2 diabetes mellitus (T2DM) on metformin therapy. Harold E. Bays, M.D., FACP,[1] Allison B. Goldfine, M.D.,[2] Michael R. Jones, Ph.D.,[3] Stacey L. Abby, Pharm.D.,[3] *Soamnauth Misir, Pharm.D.*,[3] Sukumar Nagendran, M.D.[3]; (1) Louisville Metabolic and Atherosclerosis Research Center, Louisville, KY; (2) Joslin Diabetes Center, Boston, MA; (3) Daiichi Sankyo, Inc., Parsippany, NJ
PURPOSE: In three double-blind (DB), placebo-controlled T2DM studies, the addition of colesevelam HCl 3.75 g/day to existing metformin-, insulin-, or sulfonylurea-based therapy resulted in an additional hemoglobin A1c reduction of 0.5%. Subjects completing one of these studies could enroll in a long-term open-label extension (OLE) to evaluate the safety, tolerability, and efficacy of colesevelam.
METHODS: This post hoc analysis evaluated the long-term glycemic effects of colesevelam in the cohort completing the 26-week, metformin-based, DB study and subsequently entering the 52-week OLE. Efficacy evaluations included 1) change in hemoglobin A1c in the colesevelam and placebo groups during the 26-week DB study; 2) change in hemoglobin A1c for those who received colesevelam for 52 weeks (received placebo during DB study/open-label colesevelam during 52-week OLE); and 3) change in hemoglobin A1c for those who received colesevelam for 78 weeks (received colesevelam during DB study/open-label colesevelam during 52-week OLE).
RESULTS: A total of 316 subjects entered the 26-week, metformin-based, DB study; 222 subjects completed the study, and 146 (65.8%) entered the OLE. At baseline (before DB study), the colesevelam and placebo groups had hemoglobin A1c levels of 8.2% and 8.1%, respectively. At week 26 (end of DB study/beginning of OLE), colesevelam (n=81) or placebo (n=65) resulted in a hemoglobin A1c change from baseline of –0.6% or +0.1%, respectively. Subjects who received DB placebo and 52 weeks of open-label colesevelam achieved a hemoglobin A1c change from baseline of –0.6% (n=41). Subjects who received 26 weeks of DB colesevelam and an additional 52 weeks of open-label colesevelam (78 weeks total [n=56]) achieved a hemoglobin A1c change from baseline of –0.5%.
CONCLUSIONS: This post hoc analysis of data from a long-term OLE in subjects with T2DM supports that colesevelam, when added to a metformin-based regimen, is efficacious in glucose lowering, and suggests that this benefit may be durable for as long as 78 weeks.
Presented at the American Association of Clinical Endocrinologists' 18th Annual Meeting and Clinical Congress, Exploring New Frontiers in Endocrinology, Houston, TX, May 13–17, 2009.

65. Impact of pharmacist intervention on glycemic control and cardiovascular risks management in hypertensive type 2 diabetic patients in primary care settings. *Vivian W.Y. Lee, Pharm.D.*, Kitty K.Y. Chu, B.S., Sinki S.K. Lam, B.S., Wilson Y.S. Leung, Ph.D.; The Chinese University of Hong Kong, Shatin, Hong Kong
PURPOSE: To develop structured pharmaceutical care for patients with type 2 diabetes and hypertension in primary care settings in Hong Kong and to evaluate the effects of structured pharmaceutical care on glycemic control as well as cardiovascular risk.
METHODS: This was a prospective randomized, controlled trial conducted in hypertensive patients with type 2 diabetes in two general outpatient clinics. Patients randomized to the pharmacist group (PG) received structured pharmaceutical care including individualized patient education, review of drug regimen, and evaluation of drug adherence. Primary end point was the change in hemoglobin A1c. Secondary outcomes included the change in the 10-year cardiac risk scores, systolic and diastolic blood pressure (BP) measurements, random blood glucose, lipid panels, and the number of patients attaining the hemoglobin A1c and BP treatment goals.
RESULTS: After a follow-up of 34.1 ± 4.2 weeks, 109 patients completed the study. Patients in the PG (n=54) had a significantly greater absolute reduction in hemoglobin A1c compared with those in the control group (CG) (n=55) (PG, -1.0% ± 1.8% vs. CG, -0.2% ± 0.9%, p<0.05). Patients in PG showed a greater decrease in coronary heart disease (CHD) (PG, -4.16% ± 10.65% vs. CG, -1.18% ± 6.78%, p=0.13) and fatal CHD risk scores (PG, -3.46% ± 9.72% vs. CG, -0.94% ± 5.98%, p=0.14) than the control. No reductions were noted in cerebrovascular events (CVAs) (PG, 0.50 ± 1.82 vs. CG, 0.77 ± 2.41, p=0.33) and fatal CVA risk scores (PG, 0.16 ± 0.51 vs. CG, 0.07 ± 0.84, p=0.54) in either group. There was no statistically significant difference in BP, random blood glucose, or lipid panels between the two groups.
CONCLUSIONS: Structured pharmaceutical care in hypertensive patients with type 2 diabetes improved glycemic control in the primary care settings. The benefit in cardiac risks requires further investigation.

66. Vitamin D status and obesity. *Daniel M. Riche, Pharm.D., BCPS, CDE,*[1] Honey E. East, M.D.,[2] Krista D. Riche, Pharm.D., BCPS[3]; (1) University of Mississippi Schools of Pharmacy and Medicine, Jackson, MS; (2) University of Mississippi School of Medicine, Jackson, MS; (3) Mississippi Baptist Medical Center, Jackson, MS
PURPOSE: Inadequate vitamin D status is associated with a multitude of disease states, including cardiovascular disease. Obesity is one of the most common comorbidities in cardiovascular disease. It has been hypothesized that common obesity results from an atypical adaptive winter response because of a decrease in vitamin D. The connection between low vitamin D and obesity has not been formally assessed in adults; therefore, an investigation into an association is warranted.

METHODS: A retrospective chart review was conducted of 98 adults in a cardiometabolic clinic with a 25-(OH)D level drawn from December 2006 to April 2008. Patients were divided into two groups: 1) vitamin D insufficiency (30 ng/mL or less) and 2) vitamin D sufficiency (more than 30 ng/mL). A subgroup of vitamin D deficiency (20 ng/mL or less) was also evaluated. Descriptive statistics were used to quantify results. A t-test was used to compare average body mass index (BMI), and a Fisher exact test was used to compare dichotomous data.
RESULTS: Fifty-seven percent of patients with vitamin D insufficiency (n=56) had obesity (defined as a BMI greater than 30 kg/m^2), and the average BMI was 30.6 kg/m^2. Significantly fewer patients (29%) with sufficient vitamin D levels were classified as obese (p=0.046), and the average BMI of these patients (28.2 kg/m^2) was significantly lower than those with vitamin D insufficiency (p=0.0074). Although statistical significance was not achieved in the subgroup with vitamin D deficiency (n=29), this was likely owing to inadequate power because the percentage of obese patients (59%) and the average BMI (31 kg/m^2) remained consistent.
CONCLUSION: Vitamin D status is associated with BMI, particularly vitamin D insufficiency and obesity. Prospective research should clarify a causal or indirect effect of vitamin D on obesity.

67. Vitamin D status and statin-induced myopathy. *Daniel M. Riche, Pharm.D., BCPS, CDE,*[1] Honey E. East, M.D.,[2] Krista D. Riche, Pharm.D., BCPS[3]; (1) University of Mississippi Schools of Pharmacy and Medicine, Jackson, MS; (2) University of Mississippi School of Medicine, Jackson, MS; (3) Mississippi Baptist Medical Center, Jackson, MS
PURPOSE: Inadequate vitamin D status is associated with a multitude of disease states, including cardiovascular disease. Statin-induced myopathy is a major reason for drug discontinuation and nonadherence, and vitamin D deficiency has been associated with muscle weakness and severe myopathy. It has been reported that symptomatic myalgia in statin-treated patients with low vitamin D status (less than 32 ng/mL) reflects a reversible interaction between vitamin D and statins on skeletal muscle. Because there are few known risk factors for the development of statin-associated myopathy and no solidified treatment courses of action, investigation into potential confounders to elucidate the dynamics of statin-induced myopathy is warranted.
METHODS: A retrospective chart review was conducted of 84 patients in a cardiometabolic clinic with a 25-(OH)D level drawn from December 2006 to April 2008 and previous statin discontinuation because of myopathy. Patients were divided into two groups: 1) vitamin D insufficiency (less than 32 ng/mL; n=52) and 2) vitamin D sufficiency (32 ng/mL or more; n=32). A subgroup of vitamin D deficiency (less than 20 ng/mL) is also reported. A Fisher exact test was used to compare dichotomous data, and descriptive statistics were used to quantify results.
RESULTS: There were 43 statin-specific myopathies among 24 patients who could not tolerate statins. Vitamin D insufficiency (p=0.048) was significantly associated with statin-induced myopathy, documenting discontinuation in 37% of patients versus only 16% of patients with vitamin D sufficiency. After prescription vitamin D supplementation, statin tolerance rates were significantly higher (p=0.033) in patients with vitamin D deficiency (90%) than in those without deficiency (40%).
CONCLUSION: Vitamin D status plays an important role in muscle-related adverse effects of statins, and supplementation of vitamin D deficiency (20 ng/mL or less) can improve statin tolerance.

68E. Determining predictors of response to exenatide in type 2 diabetes. *Sarah L. Anderson, Pharm.D.,*[1] Jennifer Trujillo, Pharm.D.,[1] Joseph Saseen, Pharm.D.,[1] Michael T. McDermott, M.D.[2]; (1) University of Colorado Denver School of Pharmacy, Aurora, CO; (2) University of Colorado Denver, School of Medicine, Aurora, CO
PURPOSE: This retrospective observational cohort study was conducted to determine predictors of clinically meaningful glycemic response to exenatide. Secondary end points included change in A1c with exenatide use and whether weight loss with exenatide use correlated with glycemic response.
METHODS: Medical records were identified by the ICD-9 code for adult patients with type 2 diabetes prescribed exenatide between June 2005 and March 2008. Patients were grouped into the responder cohort or the nonresponder cohort based on change in A1c. Responders were defined as having an A1c reduction of 0.5% or more, and nonresponders, as having an A1c reduction of less than 0.5% from baseline to postinitiation (12–30 weeks) of exenatide. Gender, age, duration of diabetes, weight, serum creatinine, diabetes education, and concurrent diabetes medications were collected for each patient as potential predictors of response.
RESULTS: One hundred patients met inclusion criteria; 61 were responders, and 39 were nonresponders. Responders had a mean A1c decrease of 1.52%, and nonresponders had a mean A1c increase of 0.25% (p<0.001). Binary logistic regression analysis demonstrated that none of the a priori determined variables was a predictor of response to exenatide (all p-values > 0.05). Post hoc linear regression analysis revealed baseline A1c as a predictor of response to exenatide (p<0.001). Patients with a baseline A1c less than 7.4% ± 0.16% did not respond to exenatide. There was no correlation between weight loss with exenatide and glycemic response (p=0.63).
CONCLUSION: None of the a priori determined variables predicted glycemic response to exenatide; however, a post hoc analysis identified baseline A1c as a predictor of response to exenatide. This is consistent with what is seen with oral antihyperglycemic agents. Our data indicate that patients with a higher baseline A1c are more likely to have a glycemic response to exenatide compared with patients having a lower baseline A1c.
Presented at the Western States Conference for Pharmacy Residents, Fellows, and Preceptors, Pacific Grove, CA, May 21, 2009.

Gastroenterology

69. SSRI prophylaxis vs. rescue treatment of interferon-induced depression in hepatitis C patients. *Septima B. Hong, Pharm.D., BCPS,*[1] Michele M. Spence, Ph.D.,[1] Jim Chan, Pharm.D., Ph.D.[2]; (1) Kaiser Permanente Medical Care Program, Downey, CA; (2) Kaiser Permanente Medical Care Program, Oakland, CA
PURPOSE: To evaluate the frequency of SSRI prophylaxis versus rescue treatment in patients receiving peginterferon-2-a/b and ribavirin for hepatitis; to compare the likelihood of completing treatment and achieving treatment success; and to determine the most cost-effective strategy for managing interferon-induced depression.
METHODS: This was a retrospective electronic database study composed of about 4000 identified patients within an integrated health care organization from January 1, 2002, to June 1, 2008, who initiated peginterferon-ribavirin therapy. Patient demographics, prescription refill history, and hepatitis C laboratory values were analyzed. Hepatitis C therapy completion was based on genotype treatment duration and prescription refill history. Treatment success was defined as an undetectable hepatitis C viral load for 6 months (sustained viral response), after initial undetectable levels. Pharmacoeconomic analysis was performed using decision tree modeling.
RESULTS: The study cohort included 4055 patients; 4.96% received SSRI prophylaxis, 24.51% received SSRI rescue treatment, and 70.53% did not receive any SSRI during the study period. Between the SSRI prophylaxis versus rescue treatment groups, no significant difference was observed in a patient's ability to complete hepatitis C therapy (36.77% vs. 40.35%, p<0.4) or to achieve treatment success (54.29% vs. 70.76%, p=0.06). Cost per treatment success was about 3 times higher with prophylaxis.
CONCLUSION: SSRI prophylaxis is not as common as SSRI rescue therapy for the management of interferon-induced depression. There was no significant difference in completing hepatitis C therapy or successful treatment. SSRI rescue treatment was more cost-effective for managing interferon-induced depression.

Geriatrics

70. Use of Beers criteria to evaluate medical resident prescribing in elderly outpatients. Janice L. Hallenbeck, Pharm.D.,[1] *Alison M. Walton, Pharm.D., BCPS,*[2] Karie A. Morrical-Kline, Pharm.D.,[2] Toni K. Eash, Pharm.D.[2]; (1) St. Vincent Health, Indianapolis, IN; (2) St. Vincent Joshua Max Simon Primary Care Center, Indianapolis, IN

PURPOSE: Beers criteria has proved to be a useful tool in identifying potentially inappropriate medications (PIMs) and decreasing medication adverse events in older adults. This study examined the incidence of PIM prescribing, identified commonly prescribed PIMs, and identified patient factors that may influence prescribing of PIMs by medical residents in an ambulatory clinic.

METHODS: This observational, cross-sectional, retrospective study used the revised Beers criteria to evaluate PIM use in the elderly. St. Vincent Joshua Max Simon Primary Care Center internal medicine patients 65 years and older were assessed for inclusion. Two groups of patients were identified: patients taking one or more Beers criteria medications and patients not taking any Beers medications. One hundred patients from each group were randomly chosen for inclusion in the secondary outcomes. End points included the incidence of PIM prescribing, commonly prescribed PIMs and their indications, and patient risk factors for PIM prescribing.

RESULTS: Of the 390 patients in the study, 120 and 270 patients were in the Beers and non-Beers group, respectively, resulting in an incidence of PIM prescribing of around 31%. Antihypertensives (13.9%), NSAIDs (13.9%), and muscle relaxants (12.4%) were the most commonly prescribed PIMs. Pain (29%) was the most common indication, followed by hypertension (12.4%) and iron deficiency (7.3%). The total number of medications was identified as a significant patient risk factor for PIM use (p=0.001).

CONCLUSIONS: This study demonstrated that the incidence of PIMs prescribed to elderly outpatients by medical residents is similar to the prescribing rate of other practitioners and that PIM prescribing remains a common concern. In addition to polypharmacy, relatively younger elderly and individuals with more chronic diseases may have an increased risk of PIM use. The results of this study were used to develop educational initiatives to increase awareness of PIMs for elderly patients and improve prescribing practices of medical residents.

71E. Renal dysfunction in older patients is associated with reduced warfarin maintenance dose and decreased anticoagulation stability. *Peter Whittaker, Ph.D.,*[1] Candice L. Garwood, Pharm.D.,[2] Megan E. Kleinow, Pharm.D.,[3] Kristy Curtis, Pharm.D.,[4] Jennifer L. Clemente, Pharm.D.[3]; (1) Wayne State University School of Medicine, Cardiovascular Research Institute and Department of Emergency Medicine, Detroit, MI; (2) Wayne State University, Detroit, MI; (3) Detroit Medical Center, Detroit, MI; (4) Detroit Receiving Hospital, Detroit, MI

PURPOSE: Warfarin's considerable interpatient dosing variability contributes, in part, to its underuse in older patients. Although clinical and genetic factors have been identified as contributors to such variation, a large portion of the variability is not yet understood. Recent evidence suggests that renal dysfunction (RD) is an additional determinant of dose variability; specifically, warfarin doses were lower and anticoagulation (AC) instability was higher in middle-aged patients with RD versus matched controls. Therefore, because RD is relatively common in older patients, we aimed to determine whether these same effects occurred in this potentially vulnerable population.

METHODS: In a retrospective chart review, we examined 28 AC clinic patients. To minimize the influence of factors known to determine warfarin dose, we matched patients with RD (eGFR less than 60 mL/minute/1.73 m^2) with controls for the following dose determinants; age, body surface area (BSA), race, gender, and target international normalized ration (INR; 2–3). We then calculated, during the course of all recorded clinic visits, 1) the mean weekly dose used to maintain target INR and 2) the standard deviation (SD) of INR, a measure of AC stability.

RESULTS: Most patients (65%) had atrial fibrillation; 71% were female, 57% were African American, and 43% were white. The mean age was 80 ± 1 years, and BSA averaged 1.9 ± 0.1 m^2. The follow-up time was 660 ± 71 days, which covered 35 ± 4 clinic visits. Renal dysfunction was associated with an 18% reduction in weekly dose (†p=0.005) and an increase in INR SD (*p=0.045) versus controls.

CONCLUSIONS: RD not only contributes to warfarin dose variability, but also decreases AC stability in older patients. Appreciation of RD's impact on warfarin-treated patients may improve their AC management and hence encourage greater use of warfarin in this undertreated population.

	eGFR (mL/minute/1.73 m^2)	Weekly Dose (mg)	INR SD
Control	79 ± 7	37.3 ± 2.4	0.53 ± 0.04
RD	43 ± 2†	30.7 ± 3.6†	0.61 ± 0.06*

The abstract will be published in the *Journal of Thrombosis and Haemostasis* and presented at the XXII Congress of the International Society on Thrombosis and Haemostasis, Boston, MA, July 11–17, 2009.

72. Quality of medication use in older adults: findings from a longitudinal study. *Mary T. Roth, Pharm.D., MHS,*[1] Denise A. Esserman, Ph.D.,[1] Jena L. Ivey, Pharm.D.,[1] Morris Weinberger, Ph.D.[2]; (1) University of North Carolina, Chapel Hill, NC; (2) Durham VA Medical Center, Durham, NC, and University of North Carolina, Chapel Hill, NC

PURPOSE: Medication-related problems are prevalent in older adults, represent poor-quality medication use, and adversely affect patient outcomes. Most approaches to evaluating quality of medication use either 1) target specific drugs, medication problems, or disease states or 2) highlight predefined quality indicators; neither approach takes a patient-centered perspective. To assess the quality of medication use among community-residing older adults, both overall and by race.

METHODS: We conducted a prospective cohort study among 200 (100 white, 100 black) older adults residing independently in the community. We completed in-home interviews and medical record reviews at baseline, 6 months, and 12 months. Clinical pharmacists used implicit criteria to assess quality of medication use. We used mixed models with a log link (Poisson regression), adjusting for a fixed pharmacist effect, to model the longitudinal data.

RESULTS: Most respondents were female (77%) with mean age 76.9 years. Medication-related problems were prevalent at baseline (Table) and, despite not implementing interventions, increased over time (p=0.0053). Most of the increased prevalence, which was among whites, largely reflects the use of suboptimal drugs, the use of expensive drugs when less costly alternatives exist, and inadequate medication monitoring. Notably, although blacks took fewer prescribed medications at baseline than whites (9.7 vs. 11.6, p=0.0028), they had more medication-related problems (6.3 vs. 4.9; p=0.0027).

CONCLUSION: The prevalence of medication-related problems among older adults residing in the community suggests poor-quality medication use. The higher prevalence of medication problems among blacks, despite their taking fewer medications, is perplexing and warrants further study. Data from this study are being used to design and rigorously evaluate clinical pharmacy interventions to improve the overall quality of medication use and health outcomes in older adults.

Gout

73E. Documentation of fewer gout flares after long-term urate-lowering treatment. *Michael A. Becker, M.D.,*[1] H. Ralph Schumacher Jr., M.D.,[2] Saima Chohan, M.D.,[1] Patricia MacDonald, NP,[3] Barbara Hunt, M.S.,[3] Robert L. Jackson, M.D.[3]; (1) University of Chicago, Pritzker School of Medicine, Chicago, IL; (2) University of Pennsylvania School of Medicine, Veterans Affairs Medical Center, Philadelphia, PA; (3) Takeda Global Research & Development Center, Inc., Deerfield, IL

PURPOSE: Compare efficacy, gout flare rates, and safety of 6-month febuxostat or allopurinol treatment between subjects whose gout and hyperuricemia were successfully treated in prior trials with febuxostat or allopurinol for 3–5 years versus subjects not previously so treated.

METHODS: In the 6-month CONFIRMS trial, 2269 subjects with gout and hyperuricemia received daily febuxostat 40 or 80 mg or allopurinol (300 or 200 mg based on creatinine clearance). There were 276 subjects from the previous FOCUS (5 years) or EXCEL (3 years) trials maintaining serum urate levels (sUAs) less than 6 mg/dL for up to 5 years on febuxostat 40, 80, or 120 mg or allopurinol 300 mg. Randomization was stratified by renal function and prior long-term urate-lowering therapy (ULT) study participation. Subjects with previous ULT washed out for 30 days or more and had a baseline sUA of 8 mg/dL or more before entering CONFIRMS. Subjects received colchicine or naproxen for gout flare prophylaxis.
RESULTS: Demographics in this prior treatment subset were similar to those of the entire group. Proportions of subjects with prior participation who achieved sUA less than 6 mg/dL at final visit in the febuxostat 40 or 80 mg and allopurinol groups were 57%, 77%, and 52%, respectively, versus 43%, 66%, and 41%, respectively, among subjects without prior participation ($p \leq 0.05$). Overall, subjects with prior participation in each group had lower flare rates ($p \leq 0.001$) versus those without prior participation. The most frequent AEs were URIs, abnormal LFTs, musculoskeletal pain, and diarrhea, and rates of AEs were similar among subjects with and without prior participation.
CONCLUSIONS: The subset with 3–5 years of ULT achieved sUAs less than 6 mg/dL more often and had substantially fewer reported gout flares versus subjects without ULT. This demonstrates the clinical benefit of maintaining sUAs less than 6 mg/dL in reducing subsequent gout flare incidence and supports the likelihood of long-term urate pool depletion during successful ULT.
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Health Disparities

74. Warfarin outcomes in rural and urban Medicaid patients with new-onset atrial fibrillation. *Ann M. Wiesner, Pharm.D.,*[1] Tracy E. Macaulay, Pharm.D., BCPS,[1] Douglas T. Steinke, Ph.D.,[2] Daniel A. Lewis, Pharm.D., BCPS,[1] Aimee G. Adams, Pharm.D.[1]; (1) University of Kentucky HealthCare, Lexington, KY; (2) University of Kentucky College of Pharmacy, Lexington, KY

PURPOSE: Rural health disparities and intricacies of warfarin management may contribute to outcome differences in rural patients with atrial fibrillation (AF). The objective was to determine whether there was a difference in outcomes associated with warfarin use in rural and urban Medicaid patients with new-onset, nonvalvular AF.
METHODS: Retrospective cohort design used administrative claims of Kentucky Medicaid patients older than 18 years with AF (ICD-9 427.31) and warfarin prescriptions who were living in a county with a rural-urban continuum code of 1-3 (urban) or 7-9 (rural). Groups were frequency matched on age and $CHADS_2$ score. Primary outcome was incidence of thromboembolic events. Secondary end points were incidence of major and minor bleeds, mortality, time to death and stroke, hospitalizations and emergency department visits, and time to warfarin initiation. Subgroup analysis included age, gender, $CHADS_2$ score, and concomitant aspirin or amiodarone.
RESULTS: Subjects (n=1525) had a mean age of 69 years, a median $CHADS_2$ score of 2, and an average follow-up time of 2.8 years; they were primarily women. The rate of thromboembolic events was 9.1 per 100 person-years, double that of rates previously reported, with no difference between rural and urban groups (p=0.35). Mortality was higher in urban subjects (31.7 vs. 26.5%, p=0.029, RR = 0.84). Rural subjects were more likely to be hospitalized (3.2 vs. 2.96 per patient, p=0.037), but there was no difference in median emergency department visits (3.5 per subject). The annual risk of major bleed was 8.7%, 4 times higher than previously reported. There was no difference in incidence of bleeding events between the groups. Rural subjects had a shorter time to warfarin initiation (9 vs. 28 days, $p<0.001$).
CONCLUSION: There is no difference in rate of thromboembolic events between rural and urban populations. Significant disparities in health outcomes exist in the Medicaid population.

Health Services Research

75. Formation of a nationwide clinical pharmacist practice-based research network. *Grace M. Kuo, Pharm.D., MPH,*[1] Jacqueline S. Marinac, Pharm.D.[2]; (1) UCSD and ACCP, La Jolla, CA; (2) ACCP Research Institute, Lenexa, KS

PURPOSE: Practice-based research networks (PBRNs) are effective for investigating questions related to clinical practice and quality of patient care. Although there are more than 100 physician-based PBRNs in the United States, pharmacist PBRNs are in the emerging stage. The purpose of this study was to describe the formation and composition of the first nationwide clinical pharmacist PBRN and to characterize participating pharmacists, practices, and clinical services provided.
METHODS: An online network registry was implemented in February 2009. Through e-mail list messages, network investigators invited ACCP full and associate members to join the network by filling out the online registry questionnaire. The first 4 months of online registry data were input to Web-based programs and Excel files for descriptive analyses.
RESULTS: A total of 359 individual pharmacists from 43 states and 207 practice sites (61% inpatient and 36% outpatient) joined the network by the online registry in 4 months. Another 257 pharmacists joined in groups from 105 sites. Members represented 22 PRN specialty groups. About half (58%) indicated having PBRN research experience, and 84% were involved in clinical pharmacy services (average of 5.3 ± 3 half-days managing 45 patients/week), whereas 14% had no clinical responsibilities but had access to patients for research. Some practice sites (15%) accepted central IRB, and 66% used electronic billing and/or medical records. Few members (4%) billed for service, whereas 38% used practice agreements. Patients who were served by network pharmacists included whites (60%), African Americans (29%), and Asians (8%); Latino ethnicity was 20%. Most patients (78%) were adults. Pharmacist services included the management of pharmacotherapy/ polypharmacy (61%), anticoagulation (43%), diabetes (40%), hypertension (39%), hyperlipidemia (29%), and congestive heart failure (26%).
CONCLUSIONS: The newly formed nationwide clinical pharmacist PBRN included representations from different states in the United States and multiple clinical specialties. Most members had direct clinical care responsibilities managing patient care from multiethnic backgrounds with various medical conditions.

76. The impact of pharmacist-provided risk factor screening and education on health-promoting behaviors. *Leslie A. Mooney, Pharm.D.*, Amy M. Franks, Pharm.D.; University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR

PURPOSE: To investigate the impact of a community-based health screening and education program on participants' health-promoting behaviors.
METHODS: Participants of free health screenings were administered a prescreening survey to determine their baseline participation in health-promoting behaviors. All participants were screened for coronary heart disease (CHD) risk factors (lipid profile, blood glucose, body mass index, and blood pressure) by pharmacists and student pharmacists. Each participant was counseled on his/her screening results, encouraged to make heart-healthy changes when warranted, and educated on all CHD risk factors. Four to 8 weeks after the screening, a telephone survey was administered to determine changes in participants' health-promoting behaviors.
RESULTS: Of the 56 participants enrolled, 45 (80%) completed the postscreening telephone survey. Most participants were women (81%) and white (51%). Age ranged from 32 to 67 years (mean, 45.8). The participants were well educated, with 98% having completed high school and 67% having received a college degree. After the screening, 29 (64%) participants had either seen their primary care provider or scheduled an appointment. Although only five participants (11%) reported exercising more after the screening, half (51%) reported making change(s) in their eating habits. The most common changes included decreasing caloric intake (41%), decreasing fat intake (27%), and eating more fruits and vegetables (27%). Fourteen (31%) of the 45 participants made no healthy behavior changes.

CONCLUSION: Pharmacist-provided risk factor screening and education encouraged most participants to seek medical care and/or make behavioral changes, but a considerable proportion of participants made no change. These results demonstrate that education programs can have a positive impact on participants' behavior; however, more research is needed to design tailored programs that provide all participants with the information and tools necessary to make heart-healthy choices.

Hematology/Anticoagulation

77. Phytonadione for excessive anticoagulation: a community hospital's experience in improving utilization. *Luigi Brunetti, Pharm.D.,*[1] Fatema Dhanaliwala, RPh,[2] Nancy Doherty, RPh, M.S.,[2] Stuart Vigdor, RPh[2]; (1) Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ; (2) Somerset Medical Center, Somerville, NJ

PURPOSE: The purpose of this study was to evaluate the effectiveness of a multidisciplinary intervention on improving phytonadione administration route/dosage selection in a community-based hospital.

METHODS: A retrospective review of phytonadione patient orders at Somerset Medical Center was performed in an effort to identify prescribing patterns. Patients were excluded if their international normalized ratio (INR) was less than 5, if they received phytonadione in preparation for surgery, or if they had significant liver impairment. Data were obtained through electronic query of the pharmacy database (January 1, 2008, to December 31, 2008, excluding June 2008). During June 2008, a multidisciplinary intervention including physician, nursing, and pharmacy education; revision of computerized physician orders; presentation to various committees; and distribution of educational materials was implemented. Phytonadione orders were allocated to either the preintervention (PRE) (January 1, 2008, to May 31, 2008) or postintervention (POST) (July 1, 2008, to December 31, 2008) group as appropriate. PRE and POST groups were analyzed using descriptive statistics.

RESULTS: A total of 218 doses meeting inclusion criteria (PRE, 108; POST, 110) were included in data analysis. Baseline characteristics were similar between groups with the exception of age (PRE, 79.1 years ± 11.52; POST, 74.3 years ± 12.84; p=0.005). A statistically significant decrease in the percentage of orders for subcutaneous (PRE, 52.8%; POST, 5.5%; p<0.001) and intramuscular (PRE, 17.6%; POST, 1%; p<0.001) phytonadione was observed after the intervention period. The percentages of oral (PRE, 23.1%; POST, 57.2%; p<0.001) and intravenous phytonadione orders (PRE, 4.6%; POST, 36.4%; p<0.001) were significantly increased after the intervention period. Furthermore, a statistically significant decrease in mean phytonadione dosage was noted after the intervention (PRE, 6.67 ± 3.37 mg; POST, 5.24 ± 3.36 mg; p=0.002).

CONCLUSIONS: A multidisciplinary multimodal approach is effective in improving phytonadione use.

78. Thrombotic risk stratification in residents of long term care facilities. *Barbara Zarowitz, Pharm.D.*, Allen Lefkovitz, Pharm.D., Terrence O'Shea, Pharm.D., Eric Tangalos, M.D., Steven Deitelzweig, M.D., Henry Bussey, Pharm.D., Edith Nutescu, Pharm.D., Barbara Resnick, RNP, Arthur Wheeler, M.D.; Omnicare, Inc., Livonia, MI

PURPOSE: Hospitalized patients and residents of long-term care (LTC) facilities account for about 60% of all cases of venous thromboembolism (VTE). The primary aim of the study was to develop an evidence-based VTE risk stratification tool and definition of immobility for residents in LTC facilities.

METHODS: Using the Delphi process, a panel of vascular thrombotic and geriatric experts reviewed and ranked statements of VTE risk and immobility derived from the literature to arrive at a consensus for the importance of each statement. Rating was conducted before and during an on-site meeting. Statements that were rated high and very high were used to develop a VTE risk stratification and immobility tool.

RESULTS: A total of 1165 publications related to VTE risk were identified, from which 137 (12%) pertained to subjects with a median age of 60 years or older; 42 (31%) met study criteria. Eight (29.6%) of 79 publications pertaining to immobility met study criteria. VTE risk factors were age older than 60 years, active cancer, acute infectious disease, catheter in a central vein, chronic obstructive pulmonary disease, dehydration, history of VTE, having a first-degree relative with VTE, heart failure, hypercoagulable state, immobility, inflammatory bowel disease, obesity, rheumatoid arthritis and treatment with erythroid-stimulating agents to a hemoglobin value greater than 12 g/dL, aromatase inhibitor, hormone replacement therapy, megestrol acetate, or selective estrogen receptor modulators. Immobility was defined as the presence of at least one of the following: being bedridden or bedridden except for bathroom privileges, being unable to walk at least 10 feet, having a recent reduction in ability to walk at least 10 feet for at least 72 hours, and having a lower limb cast.

CONCLUSIONS: A risk stratification tool for VTE and immobility was developed to assist clinicians in caring for residents of LTC facilities. Validation in an LTC population is warranted.

79. Safety and efficacy of very low dose unfractionated heparin continuous infusion for the treatment of venous thromboembolism in hematologic malignancy patients with thrombocytopenia. *Jennifer Baldock, Pharm.D.*, Courtney Yuen, Pharm.D., BCOP, Helen Wu, Pharm.D., BCOP; University of California, San Francisco, San Francisco, CA

PURPOSE: Anticoagulants are normally contraindicated during severe thrombocytopenia. Patients with hematologic malignancies often become thrombocytopenic during treatment of malignancies. If these patients are concurrently being treated for venous thromboembolic (VTE) events, the common practice is to hold anticoagulants during thrombocytopenia. At the University of California, San Francisco (UCSF), however, we use a very low-dose unfractionated heparin continuous infusion (VLDHCI), dosed at 4 U/kg/hour, as continuation of VTE management during thrombocytopenia. The primary goal of this study was to assess the safety of the VLDHCI regimen in number of bleeding events, and a secondary goal was to assess the efficacy in the number of VTE events.

METHODS: This study was a retrospective chart review during a 1-year period of 13 patients with hematologic malignancies (leukemia, lymphoma, or multiple myeloma) undergoing chemotherapy or hematopoietic stem cell transplant who received VLDHCI for treatment of VTE during thrombocytopenia.

RESULTS: Within the 13 patients, a total of 18 therapy courses were analyzed. Patients had a mean duration of VLDHCI of 9.7 days. Platelet transfusion thresholds were set at clinician discretion, usually to maintain platelet counts above 50×10^9/L (mean platelet count during therapy was 61×10^9/L). Patients required a mean of 6 U of platelets transfused per course of VLDHCI. There were no major bleeding events and only three minor bleeding events during VLDHCI therapy: a single guaiac-positive stool, a small amount of blood in bronchoscopy, and a single event of epistaxis. All of these minor bleeding events resolved quickly and did not recur. During VLDHCI, there were no instances of VTE.

CONCLUSIONS: VLDHCI therapy may be safe and effective for the treatment of VTE during thrombocytopenia in patients being treated for hematologic malignancies.

80. Evaluation of a heparin dosing nomogram with emphasis on special patient populations. *Lynette R. Moser, Pharm.D.,*[1] Kathryn Weber, Pharm.D.,[2] Melissa Lipari, Pharm.D., Candidate, 2010,[3] Kathleen McGaffey, Pharm.D., Candidate,[3] Deborah Virant-Young, Pharm.D.[4]; (1) Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, MI; (2) St. John Hospital and Medical Center, Department of Pharmacy Services, Detroit, MI; (3) Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI; (4) St. John Hospital and Medical Center, Detroit, MI

PURPOSE: This project is designed to evaluate the heparin dosing nomogram used by the pharmacy anticoagulation service at a

community teaching hospital and to determine whether obesity, age, and decreased renal function alter heparin dosage requirements.
METHODS: A retrospective chart review was performed for patients who were dosed by the pharmacy anticoagulation service between October 2007 and June 2008. To be included, patients had to be dosed entirely by the dosing service, could not be pregnant or younger than 18 years, and had to have recorded PTT values while taking heparin. Patients were placed in categories according to their age, weight, and renal function. Therapeutic PTTs were defined by the institution's criteria. The therapeutic dose was determined as the time-averaged weight-based heparin dose associated with therapeutic PTT values. Bleeding episodes were also evaluated.
RESULTS: Eighty-two patients were assessed. In control patients (n=37), the average dose to achieve a therapeutic PTT was 7.8 ± 4.9 U/kg/hour. For patients with CrCl less than 30 mL/minute (n=19), weight more than 130 kg (n=6), or age older than 70 years (n=20), the average dose to achieve therapeutic PTT was 7.0 ± 5.9 U/kg/hour, 9.0 ± 7.1 U/kg/hour, and 6.6 ± 4.6 U/kg/hour, respectively. Initial PTTs were subtherapeutic for 35% of control patients, 47% of patients with CrCl less than 30 mL/minute, 67% of patients with weight more than 130 kg, and 35% of patients older than 70 years. Initial PTTs were supratherapeutic in 22% of control patients, 26% of patients with CrCl less than 30 mL/minute, 33% of patients with weight more than 130 kg, and 50% of patients older than 70 years. There were three bleeding events in the population studied.
CONCLUSIONS: Heparin dosage requirements vary depending on patient characteristics. Although initial PTT may be subtherapeutic using a protocol-defined dose, the average doses required to maintain a therapeutic PTT were lower than the protocol-defined initial doses.

81. Appropriateness of a weight-based heparin nomogram in obese patients. *Jennifer N. Riney, Pharm.D.*, James M. Hollands, Pharm.D., Jennifer R. Smith, Pharm.D., Eli N. Deal, Pharm.D.; Barnes-Jewish Hospital, St. Louis, MO
PURPOSE: The most appropriate dosing strategy for therapeutic heparin in the obese patient population is not clearly defined. At Barnes-Jewish Hospital, a large academic medical center, a heparin nomogram is currently in place, using actual body weight to determine infusion rates and adjustments. The objective of this study was to determine the safety and efficacy of this nomogram in obese patients.
METHODS: Patients with class III obesity receiving therapeutic doses of unfractionated heparin greater than 24 hours between September 1, 2008, and March 31, 2009, were evaluated. Two comparator groups were created by matching patients to the class III obesity group based on level of care (ICU vs. non-ICU) as well as whether a bolus dose had been administered. The first comparator group contained patients who were overweight or who had class I or II obesity, and the second contained normal or underweight patients. Doses and times to therapeutic aPTTs, bleeding rates, and mortality were assessed.
RESULTS: The mean infusion rate required to obtain a first therapeutic aPTT was 11.5 U/kg/hour in the class III obesity group (n=94) versus 12.5 U/kg/hour and 13.5 U/kg/hour for the overweight/class I/II obesity (n=92) and normal/underweight groups (n=87), respectively (p=0.001). The mean times to first therapeutic aPTT were 21.3, 22.1, and 29.9 hours, respectively (p=0.421). There was a statistically significant difference in the infusion rate required to obtain two consecutive therapeutic aPTTs between groups (p=0.016), with higher weight groups requiring smaller (per kilogram) infusion rates, but there was no difference in the time to reach two consecutive aPTTs (p=0.776). There was no difference in bleeding (p=0.517) or mortality (p=0.475) among groups.
CONCLUSIONS: Obese patients require smaller doses (per kilogram) of unfractionated heparin compared with patients with normal body weight. Our results indicate that heparin nomogram dosing recommendations should be modified to reflect body mass index classification.

82. Pre-test Probability Scoring System (4Ts) may assist in optimization of resource utilization in heparin-induced thrombocytopenia (HIT) in a community hospital. *Anna Dushenkov, Pharm.D.*, Agnes Koniecka, Pharm.D., Valeriy Kraydman, M.D., Nick Fitterman, M.D., Garry Stone, M.D., Jack Mateuynas, RPh; Hunthington Hospital NS LIJ Health System, Huntington, NY
PURPOSE: This study evaluated the clinical utility of 4Ts in the optimization of resource management in patients with heparin-induced thrombocytopenia (HIT).
METHODS: The 4Ts system (*Heparin-Induced Thrombocytopenia,* 4th edition, edited by Warkentin TE, Greinacher A, 2008) was used to retrospectively score the records of all admissions treated with fondaparinux or argatroban for presumptive HIT in 2008. Thirty-one complete records were evaluated. Scores were broken into three categories – high, intermediate, and low – and paired with the corresponding results of ELISA (PF4) immunoassays and treatment strategies. Scorers were blinded to treatments and immunoassay results. ELISA less than 0.4 OD was deemed negative.
RESULTS:

Scoring Categories	No. of Patients	No. of Positive ELISA (OD values)	Patients with Positive ELISA and Taking Argatroban	No. of Negative ELISA	Patients with Negative ELISA and on Argatroban
HIGH PRETEST PROBABILITY SCORE (6–8)	4	4 (1.347 to > 2.400)	3	0	0
INTERMEDIATE PRETEST PROBABILITY SCORE (4–5)	12	9 (7 cases – < 0.700; 1 case – 1.319; 1 case – > 2.400)	6	3	0
LOW PRETEST PROBABILITY SCORE (0–3)	15	5 (3 cases – < 0.451; 2 cases – 0.630 and 0.676 in patients with potentially contributing comorbidities)	3*	10	3*

*Argatroban use could have been avoided in a minimum of three patients and possibly up to six (20%–40% reduction).
CONCLUSIONS: Application of the Pre-test Probability Scoring System and guided laboratory testing can positively affect resource use in HIT management. The clinical scores correspond well with the immunoassay results. Raising the threshold of positive immunoassay may improve specificity without compromising sensitivity. Use of the 4Ts system can assist in appropriate identification of candidates for therapy with direct thrombin inhibitors and those who do not need therapy. The retrospective nature and low number of patients are potential limitations of this study. Additional studies are warranted.

83. Topical recombinant human thrombin at a concentration of 1000 IU/mL controls the negative effects of heparin and clopidogrel on hemostasis and clot durability. *Steven Hughes, Ph.D.*, Paul D. Bishop, Ph.D., Richard Garcia, B.S., Tracy Zhang, M.S., W. Allan Alexander, M.D.; ZymoGenetics, Inc., Seattle, WA
PURPOSE: This study evaluated the effect of recombinant human thrombin (rThrombin) concentration on time to hemostasis (TTH) and clot strength in settings that replicate heparinization and platelet inhibition often found in modern surgical populations.
METHODS: A modified, anticoagulated rabbit arteriovenous shunt preparation was selected to model vascular anastomotic bleeding. Animals (six per treatment group) were randomly assigned to treatment with heparin or heparin and clopidogrel. TTH was measured after topical application of a range of rThrombin concentrations (31.25, 62.5, 125, and 1000 IU/mL) or placebo in combination with absorbable gelatin sponge, USP. Clot burst assessment was conducted on hemostatic grafts in heparin plus

clopidogrel–treated animals. Clot viscoelastic strength and kinetics were measured in ex vivo samples using thromboelastographic (TEG) methods.
RESULTS: rThrombin decreased median TTH in a concentration-dependent manner. TTH decreased with increasing concentrations of rThrombin in both treatment groups (heparin, p<0.0001; heparin plus clopidogrel, p<0.0001; life test procedure). An rThrombin concentration of 1000 IU/mL significantly decreased TTH vs. 125 IU/mL in both experiments (heparin, p=0.0071; heparin plus clopidogrel, p<0.0001; log-rank test). In addition, significantly smaller variance in TTH was observed with 1000 IU/mL versus 125 IU/mL (heparin, p=0.0004; heparin plus clopidogrel, p<0.0001; folded F-test). In heparin plus clopidogrel–treated animals, clots that formed in the presence of 1000 IU/mL of rThrombin were significantly less likely to rupture during clot burst assessment than those formed in the presence of 125 IU/mL of rThrombin (0% vs. 79%, p<0.0001; Fisher exact test). TEG determinations of clot strength and kinetics were rThrombin concentration–dependent in the presence of either heparin or heparin plus clopidogrel.
CONCLUSION: Topical rThrombin resulted in a concentration-dependent reduction in TTH. rThrombin at 1000 IU/mL concentration reliably controlled the negative effects of heparin and heparin plus clopidogrel on TTH, clot durability, and clot strength compared with rThrombin at 125 IU/mL.

Herbal/Complementary Medicine

84. *Nigella sativa L* oil ameliorates methotrexate-induced intestinal toxicity in rats. *Rania M. Labib, M.S.*,[1] Hafez F. Hafez, Ph.D.,[1] Osama A. Badary, Ph.D.[2]; (1) National Cancer Institute, Cairo, Egypt; (2) Faculty of Pharmacy, Ain shams University, Cairo, Egypt
PURPOSE: The efficacy of methotrexate (MTX), a chemotherapeutic agent, is limited by adverse effects. In this study, *Nigella sativa* L. oil, a natural antioxidant, was studied as a protective agent against MTX-induced toxicity.
METHODS: Twenty-four male albino rats were divided into four groups: saline, *N. sativa* oil (10 mL/kg), saline plus MTX (20 mg/kg, intraperitoneal single dose), and *N. sativa* oil plus MTX. Blood samples were collected for hematologic assessment of hemoglobin (Hb%), RBCs, WBCs, and platelets as well as to determine serum MTX levels for the two groups injected with MTX. All rats were then sacrificed; sections from the intestine and liver were cut and homogenized for biochemical analysis of glutathione (GSH) content and superoxide dismutase (SOD) activity. In addition, sections from the intestine, liver, and kidney were removed for pathologic examination.
RESULTS: There was an increase in food consumption in the *N. sativa* group. Body weight loss in the *N. sativa* plus MTX–treated group compared with the MTX group was 12.7% versus 29.4% (p<0.05). Moreover, the severe degeneration of the intestinal mucosa, liver parenchyma, glomerular, and tubular epithelium observed in the MTX-treated group was improved by *N. sativa*. Parallel to these results, *N. sativa* showed a significant decrease in SOD content, which was elevated by MTX (p<0.05). At the same time, it increased in GSH content, which was decreased by 53% in MTX (p<0.05). Moreover, the addition of *N. sativa* did not significantly affect MTX level (p>0.05) excluding interaction. Furthermore, *N. sativa* increased total RBCs, WBCs, and Hb% (p<0.05) compared with MTX but did not cause a significant change in platelet count.
CONCLUSIONS: *N. sativa* oil before and after MTX injection ameliorated MTX-induced gastrointestinal toxicity through antioxidant activity. These results can lead to further clinical applications for the prevention of MTX-induced toxicities.

85. Characterizing adverse events associated with weight loss supplements reported to the Food and Drug Administration. *Cathi E. Dennehy, Pharm.D.*,[1] Candy Tsourounis, Pharm.D.,[2] Phebe Kwon, Pharm.D.[1]; (1) University of California, San Francisco, San Francisco, CA; (2) University of California, San Francisco, School of Pharmacy, San Francisco, CA
PURPOSE: To characterize all adverse event (AE) data associated with common dietary supplement weight-loss ingredients reported to the FDA after implementation of the 2007 Dietary Supplement and Nonprescription Drug Consumer Protection Act.
METHODS: The FDA Center for Food Safety and Applied Nutrition Adverse Events Reporting System (CAERS) was retrospectively reviewed for reports involving weight-loss supplements containing any of the following target ingredients: *Citrus aurantium*, *Citrus naringin*, caffeine, cola nut, guarana, Country mallow, Yerba mate, green tea, and Hoodia. Reports received from January 2008 to September 2008 were reviewed. Data were characterized for demographics, report source, product name/ingredients, regimen, AE type, level of care, outcome, and duration of use.
RESULTS: Seventy-seven of 507 reports met inclusion criteria. A total of 142 AEs were reported, with a target ingredient identified 188 times. All of the reports involved multi-ingredient weight-loss products, with 35% containing one target ingredient and 65% containing more than one target ingredient. Caffeine (36%), green tea (36%), and guarana (18%) were most commonly identified. Sixty-two percent of reports involved the use of a single weight-loss product, and 38% involved the use of multiple weight loss products. Cardiovascular AEs occurred in 21% of cases and typically involved elevated heart rate or blood pressure. Neurologic AEs occurred in 19% of cases and typically involved headache, anxiety, nervousness, panic attacks, or dizziness. Hospitalization was the most prevalent level of care (42%) among all reports, and outcomes were infrequently documented (44%).
CONCLUSIONS: Weight-loss products containing caffeine, guarana, and green tea most frequently resulted in cardiovascular and neurologic AEs. Products with one or more of these ingredients should include cautionary statements on package labeling so that consumers are aware of these potential adverse effects.

86. Arnica Montana not effective in leg pain. *Julie D. Adkison, Pharm.D.*, David W. Bauer, M.D., Ph.D.; Memorial Family Medicine Residency Program, Sugar Land, TX
PURPOSE: The herb arnica, in topical formulations, has been reputed to decrease bruising and muscle pain; however, this claim has been inadequately and incompletely addressed in the peer-reviewed medical literature.
METHODS: A randomized, controlled trial was performed. A total of 53 subjects participated in the study. Each participant received two tubes of cream, one with active arnica and one with placebo. The tubes were marked "LEFT" and "RIGHT" and were identical in appearance. Subjects were given an analog scale to rate their leg pain on the day of exercise (day 1). Active range of motion was measured in both ankles, and then a series of calf-raises were completed according to a protocol. The two creams were applied to the lower legs immediately after the exercise, according to the "RIGHT" or "LEFT" labels. The creams were reapplied 24 and 48 hours later (days 2 and 3), and subjects used the analog scale to rate their pain in each leg. At 48 hours postexercise, subjects returned to have their ankle range of motion remeasured. Muscle tenderness was also measured using a 5-lb weight. Subjects completed a final pain scale at 72 hours postexercise (day 4).
RESULTS: Pain scores on legs treated with arnica were higher than those receiving placebo 24 hours after exercise. No other significant differences were found.
CONCLUSION: The experimental hypothesis was not substantiated, and in fact, it appears that arnica may increase leg pain, at least in the first 24 hours after exercise. This effect did not extend to the 48-hour measurement.

HIV/AIDS

87E. Similar efficacy and tolerability of atazanavir (ATV) compared to ATV/ritonavir (RTV, r), each in combination with abacavir (ABC)/lamivudine (3TC), after initial suppression with ABC/3TC plus ATV/r in HIV-infected patients: 84 week results of the ARIES trial. *Mark S. Shaefer, Pharm.D.*,[1] Kathleen Squires, M.D.,[2] Benjamin Young, M.D., Ph.D.,[3] Edwin DeJesus, M.D.,[4] Nicholas C. Bellos, M.D.,[5] Daniel Murphy, M.D.,[6] Denise H.

Sutherland-Phillips, M.D.,[1] Henry Zhao, Ph.D.,[1] Lisa G. Patel, Pharm.D.,[1] Lisa L. Ross, Ph.D.,[1] Paul G. Wannamaker, B.S.[1]; (1) GlaxoSmithKline, Research Triangle Park, NC; (2) Thomas Jefferson University, Philadelphia, PA; (3) Division of General Internal Medicine, University of Colorado, Denver, CO; (4) Orlando Immunology Center, Orlando, FL; (5) Southwest Infectious Disease Associates, Dallas, TX; (6) Clinique Medicale L'Actuel, Montreal, Quebec, Canada

PURPOSE: Induction with a ritonavir (RTV)-boosted PI regimen, followed by simplification (without RTV), may offer sustained virologic suppression while minimizing potential long-term adverse effects associated with RTV.

METHODS: A large, open-label, multicenter, noninferiority study. ART-naïve subjects received ABC/3TC and ATV/r, followed by randomization (1:1) at week 36 to maintain or discontinue RTV for an additional 48 weeks. Eligibility for randomization required a confirmed vRNA less than 50 c/mL and no virologic failure. Protocol-defined VF after week 36 was a confirmed rebound of vRNA of 400 c/mL or more. Primary end point was the percentage of subjects with vRNA less than 50 c/mL at week 84 (TLOVR).

RESULTS: Baseline demographics of 419 subjects randomized at week 36 were mean age, 39 years; 84% male; 63% white; vRNA, 5.05 log c/mL; and median CD_4^+, 200 cells/mm^3, and they were similar between arms. Three hundred seventy-nine (90%) of 419 individuals completed 84 weeks.

Week 84 Results, ITT-E Population	ABC/3TC + ATV n=210	ABC/3TC + ATV/r N=209	p-value
	181 (86%)/	169 (81%)/	*p=0.140/
vRNA < 50/400, TLOVR, n (%)	194 (92%)	180 (86%)	p=0.036
BL vRNA < 100,000 c/mL	85%/88%	79%/84%	na
BL vRNA ≥ 100,000 c/mL	87%/96%	82%/88%	na
Protocol-defined VF, n (%)	1 (0.5%)	7 (3%)	na
Median CD_4^+ cell count (ΔBL), cells/mm^3	240	259	na
Any drug-related grade 2–4 AE from BL to week 84	63 (30%)	70 (33%)	na
Individual AEs in ≥ 10% Hyperbilirubinemia	34 (16%)	40 (19%)	na

*p-value from CMH test stratified by baseline viral load strata.

Median fasting lipid changes from weeks 36 to 84 were as follows for the simplification versus continuation arms, respectively: cholesterol –14 versus 6 mg/dL; HDL 1 versus 2 mg/dL; LDL –5 versus 4 mg/dL; and triglycerides –34 versus –4 mg/dL.

CONCLUSIONS: Similar and sustained efficacy was demonstrated regardless of BL vRNA in the simplification (ABC/3TC + ATV) and continuation (ABC/3TC + ATV/r) regimens at 84 weeks after achieving virologic suppression on the induction regimen; virologic failure was infrequent (2%).

Presented at the International AIDS Conference, Cape Town, South Africa, July 19–22, 2009.

88. Survey assessing HIV knowledge/skill and continuing education interest of pharmacists attending continuing education programs in Massachusetts. *Anela Stanic, Pharm.D.*,[1] Denis V. Rybin, M.S.,[2] Anita Young, MEd, RPh,[3] Caroline Zeind, Pharm.D.,[4] Helene Hardy, Pharm.D., M.S.[5]; (1) Boston Medical Center and Massachusetts College of Pharmacy, Boston, MA; (2) Boston University School of Public Health, Data Coordinating Center, Boston, MA; (3) Northeastern University School of Pharmacy, Boston, MA; (4) Massachusetts College of Pharmacy and Health Sciences, Boston, MA; (5) Boston Medical Center, Boston, MA

PURPOSE: To assess differences in knowledge/skill and continuing education (CE) interest in HIV of pharmacists attending Massachusetts CE programs in 2003 and 2008.

METHODS: Pharmacists completed an anonymous 19-item survey assessing perceived knowledge/skill and CE interest (low, medium, and high) in HIV and its management. Demographic data were collected for gender, time of pharmacy degree, preferred methods of learning, primary practice setting, and number of patients infected with HIV served monthly. Bivariate analyses with χ^2 tests were performed to compare 2003 and 2008 data.

RESULTS: The survey was completed by 170 pharmacists in 2003 and 92 pharmacists in 2008. Although a different audience was surveyed, gender and length of practice with most advanced pharmacy degree did not differ. Chain pharmacy was the practice setting for 62% of attendees in 2003 and 36% in 2008. Pharmacists surveyed in 2008 were seeing different numbers of patients with HIV/month compared with 2003 (10% vs. 4% were seeing more than 50 patients/month). Perceived knowledge was different in 2008 for metabolic complications (17% vs. 6% reported high knowledge, p=0.019), hepatitis coinfection (16% vs. 6%, p=0.045), and drug-drug interactions (18% vs. 5%, p=0.0019). More than 50% of surveyed pharmacists reported low knowledge about new therapies, virologic resistance, and HIV in special populations. In 2008, there was more interest in clinical case discussion (30% vs. 17%, p=0.009) and Web-based methods of learning (12% vs. 5%, p=0.003). CE topic interests did not differ; more than 50% of pharmacists were highly interested in treatment guidelines, adverse events (AEs), drug-drug interactions (DDIs), and new therapies.

CONCLUSIONS: Surveyed pharmacists appear to have an increased interest in learning about HIV by clinical case discussion and/or Web-based tools. HIV CE topics may be tailored toward DDIs, AEs, and new therapies, where most pharmacists had lower knowledge confidence, and high CE interest.

89. In vivo levels of ritonavir (RTV), lopinavir (LPV), efavirenz (EFV) over time after intraperitoneal (IP) injection of antiretroviral (AR) PLGA nanoparticle (NP). *Christopher J. Destache, Pharm.D., FCCP*, Todd Belgum, B.S., Annemarie Shibata, Ph.D., Alekha K. Dash, Ph.D.; Creighton University School of Pharmacy and Health Professions, Omaha, NE

PURPOSE: Our research was focused on combination antiretroviral drugs (RTV, LPV, and EFV) using a poly-DL-lactide/coglycolide (PLGA) NP method. A comparison of free (F) drugs (500 µg each) to antiretroviral (AR) NP time course in mice is presented.

METHODS: PLGA NPs containing RTV, LPV, and EFV were fabricated using an oil-in-water emulsion. Antiretroviral drug loading, particle size, and surface charge were determined using HPLC and light dynamic scattering. The particles (500 µg in PBS) were injected intraperitoneally (IP) into male BALB/c mice. At specific times (F 0.08, 0.167, 0.25, 0.33, 1, and 2 days; AR NP 0.167, 0.33, 1, 2, 4, 7, 14, 21, and 28 days), mice were euthanized, and organs/serum were harvested to determine AR drug levels. RTV, LPV, and EFV drug levels were compared. The results are presented as mean ± SEM.

RESULTS: ART NPs averaged 267 ± 14 nm in diameter and –9.4 ± 5.4 for surface charge. Drug loading averaged 63%, and loading efficiency averaged 65% for each of the three drugs. Free peak RTV, LPV, and EFV levels were at 2 hours after injection (7.9 ± 5; 6.3 ± 10; and 2.7 ± 5 mg/L). Serum (F) elimination half-lives were 1 hour for all ARTs. Free drugs were eliminated from tissues by day 3. Animals injected with PLGA NP had detectable RTV, LPV, and EFV levels in all tissues excised up to day 28 postinjection. Peak AR levels in serum were at day 1 postinjection (RTV, 50 ± 17 ng/mL; LPV, 432 ± 232 ng/mL; and EFV, 722 ± 290 ng/mL). The highest AR levels at day 28 were in the brain (RTV, 1.1 ± 0.4; LPV, 1.0 ± 0.2; and EFV, 1.2 ± 0.4 µg/mL).

CONCLUSIONS: These results demonstrate that PLGA NPs have sustained-release properties up to 28 days after injection in vivo.

90E. Similar reductions in markers of inflammation and endothelial activation after initiation of abacavir/lamivudine (ABC/3TC) or tenofovir/emtricitabine (TDF/FTC) in the HEAT study. *Parul Patel, Pharm.D.*,[1] Grace A. McComsey, M.D.,[2] Kimberly Y. Smith, M.D.,[3] Nicholaos C. Bellos, M.D.,[4] Louis Sloan, M.D.,[5] Phillip Lackey, M.D.,[6] Princy N. Kumar, M.D.,[7] Denise H. Sutherland-Phillips, M.D.,[1] Linda H. Yau, Ph.D.,[1] Mark S. Shaefer, Pharm.D.[1]; (1) GlaxoSmithKline, Research Triangle Park, NC; (2) Case School of Medicine, Cleveland, OH; (3) Rush University Medical Center, Chicago, IL; (4) Southwest Infectious Disease Associates, Dallas, TX; (5) North Texas IDC, Dallas, TX; (6) ID Consultants, Charlotte, NC; (7) Georgetown University, Washington, DC

PURPOSE: This analysis was conduced in a prospective, randomized study of ART-naïve subjects to compare the effects of ABC/3TC and TDF/FTC on biomarkers of inflammation and

endothelial dysfunction given recent data surrounding abacavir and cardiovascular risk.

METHODS: Available samples from subjects randomized to ABC/3TC or TDF/FTC each with lopinavir-ritonavir were analyzed at baseline (BL) and weeks 48 and 96 for sVCAM-1, IL-6, and hsCRP. Biomarker concentrations were measured by Quest Diagnostics using ELISA and fixed-rate nephelometry.

RESULTS: Four hundred seventy-six subjects were included; mean age was 39 years, 15% were women, and 45% were nonwhite, with BL median HIV-1 RNA and CD_4^+ of 4.88 log c/mL and 211 cells/mm^3, respectively. Mean percentage changes from baseline in sVCAM-1 and IL-6 were statistically significant at weeks 48 and 96 in both treatment arms. Reduction in hsCRP from baseline was statistically significant in the TDF/FTC arm only; however, these reductions were not significantly different between arms for any of the three biomarkers (p>0.05). The low number of CV-related events (none related to study drug), ABC/3TC:1; TDF/FTC: 2, prevented correlation with any biomarkers.

	ABC/3TC n=243			TDF/FTC N=233		
	Paired n (BL,48; BL, 96)	Mean % Change from Baseline Week 48	Week 96	Paired n (BL:48, BL:96)	Mean % Change from Baseline Week 48	Week 96
sVCAM-1 (ng/mL)	241, 211	-49	-51	228, 202	-48%	-50%
IL-6 (pg/mL)	220, 192	-26	-19	220, 197	-23%	-25%
hsCRP (mg/L)	235, 205	-12	-5	224, 199	-20%	-17%

CONCLUSIONS: Similar decreases in sVCAM-1, IL-6, and hsCRP were observed for 96 weeks of treatment with ABC/3TC or TDF/FTC. These data do not suggest that ABC/3TC or TDF/FTC contributes to an increase in cardiovascular risk mediated by inflammation or worsening endothelial activation. The findings from this randomized, prospective data set do not support the hypothesis of increased inflammation attributed to ABC from recent observational cohort studies.

Presented at The 16th Annual Conference of Retroviruses and Opportunistic Infections, Montreal, Quebec, Canada, February 8–11, 2009.

91E. Steady-state pharmacokinetics (PK) of maraviroc (MVC) and amprenavir (APV) alone and in combination after MVC is given twice daily with unboosted or ritonavir (r)-boosted fosamprenavir (FPV) once- or twice-daily in fasted healthy volunteers. Andrew D. Luber, Pharm.D.,[1] David V. Condoluci, D.O.,[2] P. Dawn Slowinski, MSN,[2] Stan G. Louie, Pharm.D.,[3] Nick Mordwinkin, Pharm.D.,[3] Keith A. Pappa, Pharm.D.,[4] *Gary E. Pakes, Pharm.D.*[4]; (1) Consultant, Division of Infectious Diseases, Voorhees, NJ; (2) Garden State Infectious Diseases Associates, P.A., Voorhees, NJ; (3) University of Southern California, School of Pharmacy, Los Angeles, CA; (4) GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: No study to date has evaluated whether there is an interaction between MVC and the protease inhibitor FPV, both of which are CYP3A4 and P-glycoprotein (P-gp) substrates.

METHODS: In a randomized, open-label, single-center, three-period, drug interaction study (COL112237), healthy, non-HIV infected subjects received MVC 300 mg twice daily for 7 days (period 1) and then were randomized to 14 days of either FPV 1400 mg twice daily, FPV/r 1400 mg/100 mg once daily, or FPV/r 700/100 mg twice daily with or without MVC (period 2). Subjects continued their randomized dose of FPV for 14 more days, adding or removing MVC based on whether or not it was received in period 2 (period 3). Twelve-hour PK sampling was done on day 7 of period 1 and on day 14 of periods 2 and 3 (24 hours for FPV/r once daily), with plasma MVC and APV PK determined by noncompartmental analysis. Geometric mean ratios (GMRs) (90% confidence intervals [CIs]) were calculated for each agent alone/in combination.

RESULTS: Thirty-five subjects completed all three treatment arms. After MVC coadministration, APV GMRs for unboosted FPV, FPV/r 1400 mg/100 mg once daily, and FPV/r 700 mg/100 mg twice daily were C_{min}, 1.00, 0.64, and 0.76; AUC, 0.56, 0.79, and 0.74; and C_{max}, 0.49, 0.68, and 0.69. APV C_{min} (GM 208, 591, and 1270 ng/mL, respectively) remained 1.4-, 4.1-, and 8.7-fold above the mean protein binding-corrected APV IC_{50} for wild-type virus. MVC GMRs after coadministering unboosted FPV, FPV/r 1400 mg/100 mg every day, and FPV/r 700 mg/100 mg twice daily were as follows: C_{min}, 0.72, 0.77, and 0.46; AUC, 0.87, 0.98, and 0.34; and C_{max}, 0.89, 0.93, and 0.30. MVC C_{min} values (GM 57, 54, and 62 ng/mL, respectively) were within the upper quartiles associated with virologic success in clinical trials of treatment-experienced CCR5-tropic patients. AEs were generally mild within all treatment groups and did not differ between treatment periods.

CONCLUSIONS: FPV and MVC coadministration led to decreases in plasma concentrations of both agents. The mechanism of this interaction is currently unknown, but it may be partly because of P-gp induction.

Presented at the 10th International Workshop on Clinical Pharmacology of HIV Therapy, Amsterdam, Netherlands, April 15–17, 2009.

92. Steady-state pharmacokinetics (PK) of fosamprenavir (FPV) and raltegravir (RAL) alone and combined with unboosted and ritonavir-boosted FPV in fasted healthy volunteers. Andrew D. Luber, Pharm.D.,[1] P. Dawn Slowinski, MSN,[2] Edward P. Acosta, Pharm.D.,[3] *Gary E. Pakes, Pharm.D.*,[4] Keith A. Pappa, Pharm.D.,[4] David V. Condoluci, D.O.[2]; (1) Consultant, Division of Infectious Diseases, Voorhees, NJ; (2) Garden State Infectious Diseases Associates, P.A., Voorhees, NJ; (3) University of Alabama at Birmingham, Birmingham, AL; (4) GlaxoSmithKline, Research Triangle Park, NC

PURPOSE: The integrase inhibitor RAL is eliminated by glucuronidation by *UGT1A1,* whereas FPV, a prodrug for the protease inhibitor amprenavir (APV), is metabolized by *CYP3A4.* This study is the first to investigate an FPV-RAL interaction.

METHODS: In an open-label, three-period drug interaction study, fasted, healthy, non-HIV–infected subjects received RAL 400 mg twice daily for 7 days (period 1) and then were randomized to 14 days of FPV 1400 mg twice daily, FPV/r 700 mg/100 mg twice daily, or FPV/r 1400 mg/100 mg once daily with or without RAL (period 2). Subjects continued their randomized dose of FPV for 14 more days, adding or removing RAL based on whether or not it had been received in period 2 (period 3). Twelve-hour PK was done on day 7 of period 1 and on day 14 of periods 2 and 3 (24-hour APV PK for FPV/r 1400/100 once daily), with RAL and APV PK determined by noncompartmental analysis. Geometric mean ratios (GMRs) (90% CI) were calculated from the PK of each agent alone/in combination.

RESULTS: Forty-one subjects completed all three treatment arms. After RAL coadministration, APV GMRs for unboosted FPV, FPV/r 1400 mg/100 mg once daily, and FPV/r 700 mg/100 mg twice daily were as follows: C_{min}, 0.57, 0.50, and 0.81; AUC, 0.64, 0.76, and 0.84; and C_{max}, 0.73, 0.82, and 0.86. Values of APV C_{min} (GM 111.2, 480.4, and 1436.3 ng/mL, respectively) were below and 2.1- and 6.3-fold above the APV EC_{90} for PI-naïve HIV-positive patients (228 ng/mL). RAL GMRs after the coadministration of unboosted FPV, FPV/r 1400 mg/100 mg once daily, and FPV/r 700 mg/100 mg twice daily were as follows: C_{min}, 0.62, 0.75, and 0.64; AUC, 0.63, 0.85, and 0.45; and C_{max}, 0.72, 1.06, and 0.49. RAL C_{min} (GM, 56.7, 49.6, and 44.4 ng/mL) were 3.9-, 3.4-, and 3-fold above the documented protein binding-corrected IC_{95} for RAL for wild-type HIV isolates (14.6 ng/mL [33 nM]).

CONCLUSION: FPV and RAL coadministration led to decreases in plasma APV and RAL concentrations. The clinical implications of these results have not been determined.

93. Immunologic response to hepatitis B (Hep B) vaccination in human immunodeficiency virus (HIV)-infected patients. *Bernadette Johnson, Pharm.D.*,[1] Renee Mercier, Pharm.D.,[1] Karla Thornton, M.D.,[1] Wenoah Veikley, BScN,[2] Trevor Hawkins, M.D.[2]; (1) University of New Mexico Health Sciences Center, Albuquerque, NM; (2) Southwest Care Clinic, Santa Fe, NM

PURPOSE: Current guidelines recommend hepatitis B (HepB) vaccination in all patients infected with HIV, regardless of CD_4 cell count. Investigated end points are as follows: 1) describe HepB vaccine response rates in patients infected with HIV; 2) determine

factors that affect response in this population; and 3) establish a potential cutoff for HepB vaccination deferment based on CD_4 cell count.
METHODS: This retrospective study included two clinics that serve most of the HIV population in New Mexico. Patients who received a complete vaccination series were included if they had documented prevaccination serologies and postvaccination antibody titers. Data collected included known risk factors for failed response (e.g., gender, smoking status, body mass index) as well as CD_4 cell count, nadir CD_4, viral load, and highly active antiretroviral therapy (HAART). The main outcome examined was response to vaccine, defined as HepB surface antibody (HBsAb) titer concentrations of 10 IU/L or more. Statistical analysis included logistic regression models and χ^2 test.
RESULTS: Sixty-nine patients were included for analysis (86% male; mean age, 43 [±8.3]; 96% on HAART; median CD_4 at vaccination, 319 [range, 53–1405]; median nadir CD_4, 174 [range, 2–671]). Overall response rate to the vaccine was 50.7%. Patients with CD_4 of 200 cells/mm^3 or less at time of vaccination had a diminished response rate of 29.4% compared with 57.7% in patients who had CD_4 greater than 200 cells/mm^3 (p=0.04). A 1-unit log change in CD_4 was associated with a 10-fold increase in chance of response, odds ratio (OR) of 10.31 (95% CI: 1.62–66.7). Nadir CD_4 of 100 cells/mm^3 or less had a negative effect on response rate (OR = 0.35; 95% CI: 0.13–0.95). HAART, age, and gender had no effect on response.
CONCLUSION: Patients with CD_4 more than 200 cells/mm^3 were significantly more likely to demonstrate an adequate response to the HepB vaccine. Vaccination deferment should be considered in patients with CD_4 cell counts of 200 cells/mm^3 or less.

94E. Therapeutic amprenavir (APV) and abacavir (ABC) concentrations in CSF of HIV-infected patients treated with fosamprenavir (FPV)-containing antiretroviral regimens. *Scott L. Letendre, M.D.,*[1] Edmund V. Capparelli, Pharm.D.,[2] Brookie M. Best, Pharm.D.,[2] Steven S. Rossi, Ph.D.,[2] Lauren F. Way, CMA,[3] Igor Grant, M.D.,[3] Ronald J. Ellis, M.D., Ph.D.[4]; (1) Department of Medicine, University of California, San Diego, San Diego, CA; (2) Department of Pediatrics, University of California, San Diego, San Diego, CA; (3) Department of Psychiatry, University of California, San Diego, San Diego, CA; (4) Department of Neurosciences, University of California, San Diego, San Diego, CA
PURPOSE: Demonstrating that CSF antiretroviral concentrations are in the therapeutic range strengthens the evidence that they are important components of neuroeffective anti-HIV treatment regimens.
METHODS: At the UCSD HIV Neurobehavioral Research Center, 71 frozen CSF and 75 blood plasma samples from 46 patients with HIV infection on FPV-containing regimens were evaluated by LC/MS and HPLC, respectively, for concentrations of APV (LLOQ 1 ng/mL). ABC concentrations were measured in 15 FPV-treated patients who had also received ABC. Concentrations were compared with the median IC_{50} for wild-type HIV (PhenoSense assay: APV 5.6 ng/mL; ABC 70 ng/mL). HIV-1 RNA levels were measured by RT-PCR (limit of quantitation, 50 copies/mL). Descriptive/bivariate statistics were calculated by standard methods.
RESULTS: Patients were mostly middle-aged (median, 47 years) white (59%) men (93%), with a median CD_4 count of 328/mm^3 and HIV-1 RNA detectable in 41% of blood and 16% of CSF specimens. Median FPV treatment duration was 11.3 months. APV was present in all CSF specimens, with median concentration 25 ng/mL (IQR 16,44). Median CSF-to-plasma ratio was 0.013 (IQR 0.009,0.019). CSF concentrations correlated with plasma concentrations (rho = 0.64, p<0.001). Patients taking ritonavir (n=70) had higher concentrations in plasma (median 2292 vs. 377, p<0.001) and CSF (median 27 vs. 7, p=0.004). ABC concentrations in CSF and plasma were similar (rho = 0.85, p<0.001) with a median CSF-to-plasma ratio of 1.03 (IQR 0.72,2.77). APV CSF concentrations were more than the IC_{50} of wild-type HIV in all but one CSF specimen by a median of 4.4-fold (IQR 2.9,7.8). ABC CSF concentrations were more than IC_{50} in 68% with a median CSF-to-IC_{50} ratio of 2.7 (IQR 0.33,7.4).
CONCLUSION: APV and ABC achieve therapeutic concentrations in CSF, with median CSF-to-IC_{50} ratios of 4.4 and 2.7, respectively.
Presented at the 10th International Workshop on Clinical Pharmacology of HIV Therapy, Amsterdam, Netherlands, April 15–17, 2009.

Infectious Diseases

95. Effect of renal function on the pharmacodynamics of piperacillin/tazobactam administered by intermittent and prolonged infusion. S. Christian Cheatham, Pharm.D.,[1] Katherine M. Shea, Pharm.D.,[2] Matthew F. Wack, M.D.,[3] David W. Smith, Pharm.D.,[4] Kevin M. Sowinski, Pharm.D.,[5] *Michael B. Kays, Pharm.D.*[5]; (1) St. Francis Hospitals and Health Centers, Beech Grove, IN; (2) University Medical Center at Brackenridge, Austin, TX; (3) Infectious Diseases of Indiana, Indianapolis, IN; (4) Clarian Health Partners, Inc., Methodist Hospital, Indianapolis, IN; (5) Purdue University School of Pharmacy, Indianapolis, IN
PURPOSE: Dosage adjustment for piperacillin-tazobactam is not recommended for creatinine clearance (CrCl) of 40 mL/minute or more. The purpose was to evaluate the effect of renal function on the pharmacodynamics of piperacillin-tazobactam, administered by intermittent (II) and prolonged (PI) infusion.
METHODS: Pharmacokinetic data were obtained from hospitalized patients with CrCl of 40 mL/minute or more. Patients were divided into two groups based on CrCl: group I, 70 mL/minute or more (n=7); group II, 40–69 mL/minute (n=6). Monte Carlo simulations (10,000 patients) were performed to calculate the probability of target attainment (PTA) at 50% *f*T greater than the minimum inhibitory concentration (MIC) for four II and four PI (4 hours) regimens at MICs ranging from 1 to 64 µg/mL.
RESULTS: Mean ± SD CrCl and piperacillin pharmacokinetic parameters for groups I and II were as follows: CrCl, 97 ± 18 vs. 54 ± 8 mL/minute (p<0.001); CL_s, 10.7 ± 2.1 vs. 6.2 ± 1.5 L/hour (p<0.01); t½, 1.3 ± 0.3 vs. 3.0 ± 1.2 hours (p<0.01); and V_β, 19.1 ± 3.8 vs. 24.8 ± 4.8 L (p=0.04). PTA for the regimens was as follows:

MIC (µg/mL)	8		16		32		64	
Group	I	II	I	II	I	II	I	II
4.5 g II every 8 hours	0.86	0.99	0.50	0.96	0.08	0.72	0.00	0.13
3.375 g II every 6 hours	0.97	0.99	0.72	0.98	0.14	0.73	0.00	0.06
4.5 g II every 6 hours	0.99	1.00	0.87	0.99	0.38	0.90	0.00	0.30
3.375 g II every 4 hours	1.00	1.00	0.98	0.99	0.65	0.94	0.03	0.21
2.25 g PI every 8 hours	1.00	1.00	0.58	1.00	0.00	0.36	0.00	0.00
3.375 g PI every 8 hours	1.00	1.00	0.99	1.00	0.11	0.90	0.00	0.06
4.5 g PI every 8 hours	1.00	1.00	1.00	1.00	0.58	1.00	0.00	0.35
6.75 g PI every 8 hours	1.00	1.00	1.00	1.00	0.99	1.00	0.11	0.91

CONCLUSIONS: Piperacillin-tazobactam pharmacodynamics of II and PI regimens are affected by renal function, but the magnitude is dependent on the dosing regimen and MIC.

96. Association of vancomycin trough concentrations and nephrotoxicity. Julia Munsch, Pharm.D.,[1] Jason Ellison, Pharm.D.,[1] Nam Nguyen, Pharm.D.,[1] Cinda Christensen, Pharm.D., BCPS-ID,[1] *Jenana Halilovic, Pharm.D., BCPS*[2]; (1) UC Davis Medical Center, Sacramento, CA; (2) University of the Pacific TJL School of Pharmacy and Health Sciences, Stockton, CA
PURPOSE: The purpose of this study was to determine whether vancomycin trough levels greater than 15 mg/L were associated with a higher incidence of nephrotoxicity compared with lower troughs (15 mg/L or less).
METHODS: One hundred five patients admitted to the UC Davis Medical Center between December 2005 and January 2006 were retrospectively studied. Patients were separated into two groups based on their vancomycin trough concentrations (group A, vancomycin troughs of 15 mg/L or less vs. group B, vancomycin troughs greater than 15 mg/L). Patients with renal insufficiency or those receiving nephrotoxic or myelosuppressive drugs were excluded. Demographic information, risk factors for nephrotoxicity, total vancomycin dose, duration of therapy, vancomycin trough, and serum creatinine levels were documented.
RESULTS: Mean vancomycin troughs were 8.9 mg/L ± 3.0 mg/L for group A and 20.9 mg/L ± 6.0 mg/L for group B. Nephrotoxicity was documented in 1 (2%) of 50 patients in group A and 12 (21.8%) of 55 patients in group B (p=0.0012). On average, patients in group B

received a higher cumulative dose of vancomycin (22.0 ± 21 vs. 17.7 ± 20.8 g), longer duration of treatment (22.1 ± 16 days vs. 18.3 ± 19.8 days), and longer hospitalization (13.2 ± 11.5 vs. 8.1 ± 8.4 days). Congestive heart failure, diabetes, or use of angiotensin-converting enzyme inhibitors was not associated with increased risk of nephrotoxicity in either group.
CONCLUSIONS: Vancomycin trough concentrations greater than 15 mg/L were associated with a higher risk of nephrotoxicity at our institution compared with trough concentrations of 15 mg/L or less. Practitioners should proceed cautiously to avoid nephrotoxicity when targeting higher vancomycin levels.

97E. Risk factors for extended spectrum β lactamase-producing *Klebsiella pneumoniae* (ESBL): a focus on previous antibiotic exposure (PAE). *Suprat Saely, Pharm.D.,*[1] Keith S. Kaye, M.D.,[2] Marilynn Fairfax, Ph.D.,[2] Teena Chopra, M.D.,[2] Jason M. Pogue, Pharm.D.[1]; (1) Sinai-Grace Hospital, Detroit Medical Center, Detroit, MI; (2) Detroit Medical Center/Wayne State University, Detroit, MI
PURPOSE: PAE has consistently been identified as a risk factor for ESBL isolation, but the exact definition of PAE remains unclear. The purpose of this study was to identify risk factors for ESBLs, with a focus on different definitions of PAE, based on varying periods of PAE before ESBL isolation.
METHODS: We conducted a retrospective case-control study at a 400-bed community hospital in Detroit, Michigan. Patients with cultures positive for *Klebsiella pneumoniae* from January 1 to December 31, 2007, were eligible for the study. ESBL cases were compared with patients with non–ESBL-producing *K. pneumoniae* (controls). Three PAE definitions were studied: PAEs occurring during 30, 60, and 90 days before organism isolation.
RESULTS: Eighty-eight cases and 88 controls were studied. The mean cohort age was 63.6 ± 16.9 years; 43% were male, and 86% were black. Bivariate analysis demonstrated that prior use of third- or fourth-generation cephalosporins was associated with ESBL isolation regardless of the PAE time frame analyzed; however, the odds ratio (OR) varied as a function of PAE definition for fluoroquinolones and ampicillin-sulbactam, with statistical significance found only at 90 days (OR = 2.16; p=0.042) for fluoroquinolones, whereas significance was seen at 30 days (OR = 0.185; p=0.001) and 60 days (OR = 0.34; p=0.018) for ampicillin-sulbactam. In multivariate analysis, regardless of the period analyzed, exposure to third-generation cephalosporins was an independent risk factor for ESBL isolation, whereas previous use of ampicillin-sulbactam was protective against ESBL isolation. Other independent risk factors were nursing home residence (OR = 9.30; p<0.001) and hemodialysis (OR = 13.60; p<0.001).
CONCLUSIONS: Third-generation cephalosporin use was an independent risk factor for ESBLs, and ampicillin-sulbactam was protective regardless of the time frame analyzed. In bivariate analysis, definition of time frame for PAE had a notable impact on associations between antibiotics and ESBL risk, but not in multivariate analysis.
To be presented at Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 12–15, 2009.

98E. Successful utilization of a prolonged course of nitazoxanide for the treatment of multi-recurrent Clostridium difficile infection. *Matthew Bardin, Pharm.D., BCPS,*[1] Bienvenido Yangco, M.D., MPH[2]; (1) Romark Institute for Medical Research, Tampa, FL; (2) Infectious Disease Research Institute, Inc., Tampa, FL
PURPOSE: *Clostridium difficile* infection (CDI) is a significant problem in hospitalized patients. Although reported *C. difficile* in vitro resistance to metronidazole and vancomycin is relatively nonexistent, currently observed outcomes with these drugs have been disappointing. Recent studies suggest at least 30% of patients treated with metronidazole will not respond to initial therapy. Furthermore, data indicate that patients with one treatment failure have a 33%–60% chance of multiple treatment failures. Although vancomycin is the drug of choice for severe CDI and taper dosing has been used for multirecurrent CDI, its frequent and prolonged use could potentially increase the incidence of vancomycin resistance among aerobic gram-positive organisms. Another antibiotic, rifaximin, has been used as chaser therapy after vancomycin; however, rifaximin resistance has been reported, and it has developed during therapy. Therefore, alternative antibiotics for CDI are needed. Nitazoxanide has proved to be an effective agent for the treatment of CDI as initial therapy and in patients whose metronidazole therapy has failed, but data are limited for prolonged dosing for multirecurrent CDI. This case series details the successful use of a prolonged course of nitazoxanide for the treatment of multirecurrent CDI.
METHODS: Five patients with multirecurrent CDI were treated with a prolonged course (mean treatment, 31 days) of nitazoxanide 500 mg twice daily. CDI was determined by positive stools for CD toxins A or B and clinical manifestations consistent with the disease. Previous CDI therapies consisted of two to four antibiotic regimens during the previous 1–4 months.
RESULTS: At the end of nitazoxanide therapy, all patients were considered clinical cures with no recurrence observed 60 days after therapy. No clinically significant adverse reactions attributable to nitazoxanide were identified.
CONCLUSIONS: A prolonged course of nitazoxanide appears to be a safe and effective therapy for the treatment of multirecurrent CDI. A larger prospective clinical trial may further validate this finding.
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99E. In vitro susceptibility of doripenem versus imipenem against *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in a 4-hospital system. *Hope T. Le, Pharm.D.*, Daniel Keays, M.S., CLS, Gonzalo Ballon-Landa, M.D., Harminder Sikand, Pharm.D.; Scripps Mercy Hospital, San Diego, CA
PURPOSE: The emergence of multidrug-resistant gram-negative bacilli such as *Acinetobacter baumannii* (ABAU) and *Pseudomonas aeruginosa* (PSA) continues to be problematic. In October 2007, the newest carbapenem, doripenem (DOR), received FDA approval for the treatment of complicated intra-abdominal and urinary tract infections. In vitro susceptibility data comparing DOR to imipenem (IMI) for these organisms are limited. The intent of this study was to assess susceptibility patterns of ABAU and PSA to two carbapenems, IMI and DOR, at a four-hospital system in San Diego, California.
METHODS: From August 2008 to April 2009, isolates of ABAU and PSA from blood, respiratory, urine, and wound/fluid cultures were collected. Isolates were tested for susceptibility by E-test using current FDA-approved susceptibility breakpoints. Isolates were sent to a reference laboratory to determine molecular characteristics of resistance mechanisms.
RESULTS: Of 49 PSA isolates, 81.6% were susceptible (MIC of 4 µg/mL or less) to IMI, and 83.7% were susceptible (MIC of 2 µg/mL or less) to DOR. Of 59 ABAU isolates, 47.5% were susceptible to IMI (MIC of 4 µg/mL or less), and 16.9% were susceptible (MIC of 1 µg/mL or less) to DOR. Three (33%) of nine PSA isolates were nonsusceptible to IMI but remained susceptible to DOR. Two (25%) of eight PSA isolates nonsusceptible to DOR remained susceptible to IMI. Of 31 nonsusceptible ABAU isolates to IMI, none was susceptible to DOR. Of the 49 isolates of ABAU nonsusceptible to DOR, 18 (36.7%) remained susceptible to IMI.
CONCLUSIONS: DOR and IMI demonstrated comparable in vitro activity against PSA. In ABAU, IMI showed greater activity in vitro than DOR. Resistance of ABAU to IMI may correlate with resistance to DOR.
Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, CA, September 12–15, 2009.

100E. Efficacy and safety of doripenem (DORI) versus comparators (COMP) in subjects with Acinetobacter baumannii: integrated analysis of six phase III clinical studies. Janet A. Peterson, Ph.D.,[1] Zhihai Qin, Ph.D.,[1] Alan C. Fisher, DrPH,[1] *Susan C. Nicholson, M.D.*,[1] Jörg Laeuffer, M.D.[2]; (1) Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ; (2) Janssen-Cilag, Baar, Switzerland

PURPOSE: Because some strains of *Acinetobacter baumannii* are resistant to almost all antibacterials, it is important to evaluate available agents for the treatment of infections caused by this pathogen. Doripenem (DORI) is a carbapenem with activity against gram-negative bacteria, including *A. baumannii*. The objective of this analysis was to report the clinical and microbiologic outcomes of DORI versus comparators (COMPs) in the treatment of infections caused by *A. baumannii*.
METHODS: An analysis was conducted of a subset of subjects with *A. baumannii* isolated at study entry and included in the microbiologic-modified intent-to-treat (mITT) population from six studies (complicated urinary tract infection [cUTI, two studies], complicated intra-abdominal infection [cIAI, two studies], nosocomial pneumonia [NP, one study], and ventilator-associated pneumonia [VAP, one study]). Clinical and microbiologic success at test-of-cure (TOC) was determined for subjects by disease, and the success rates for DORI versus COMP agents (imipenem [IMI], meropenem [MER], levofloxacin [LVX], and piperacillin-tazobactam [PIP/TAZO]) across the studies also were determined.
RESULTS: Forty-four (3.1%) of 1406 DORI-treated and 31 (3.0%) of 1043 COMP-treated mITT subjects had *A. baumannii*. At TOC for cUTI and cIAI, clinical and microbiologic success rates with DORI were high, although the number of pathogens was small. For NP/VAP in the CE population, clinical success rates were 82.4% and 61.5% for DORI versus COMPs (difference, 20.8; 95% confidence interval [CI]: –11.2, 52.9). Microbiologic eradication was 76.5% for DORI versus 61.5% for COMPs (difference, 14.9; 95% CIs: –18.3, 48.2). Adverse events were reported in 36 (78.3%) DORI and 29 (85.3%) COMP-treated subjects.
CONCLUSIONS: The current analysis suggests that DORI is a safe and effective antibacterial for the treatment of infections caused by susceptible strains of *A. baumannii*.
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101E. Clinical outcome of nosocomial pneumonia (NP)/ventilator-associated pneumonia (VAP) or health care–associated pneumonia (HAP) after treatment with doripenem (DORI) 1 g infused over 4 hours every 8 hours (Q8H) in a study that enriched for infection wit. Mary Ambruzs, RN, BSN, June Sambrowski, RN, Simrati Kaul, Ph.D., Mohammed Khashab, Ph.D., Jim Xiang, Ph.D., Janet A. Peterson, Ph.D., *Susan C. Nicholson, M.D.*; Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ
PURPOSE: Previous studies have shown the effectiveness of DORI 500 mg in NP/VAP treatment. Few pathogens with MICs of 4–8 µg/mL were evaluated in these studies. PK/PD modeling suggests 1 g of DORI may be effective for pathogens with MICs of up to 8 µg/mL.
METHODS: Adults with a diagnosis of NP, VAP, or HAP; a suitable respiratory specimen; and a risk of infection with a gram-negative pathogen (GNP) (hospitalization for 5 days or more, hospitalization in past 90 days, broad-spectrum antibacterial treatment within 30 days, immunosuppression, and COPD [VAP subjects]) were enrolled. Subjects were required to have a CPIS score of 6 or greater (VAP) and an APACHE II score of 8–35. DORI 1 g was given every 8 hours as a 4-hour infusion for 8–14 days. Optional de-escalation to 500 mg was based on the infecting pathogen MIC if Psa was not present. Concomitant therapy for Psa, *A. baumannii*, or MRSA was allowed. Primary outcome was clinical success at test of cure (TOC; 7–14 days after last dose).
RESULTS: One hundred eighty-five subjects (80 NP, 90 VAP, and 15 HAP) were enrolled in North America, Latin America, and Europe. Thirty-four subjects had Psa at study entry. Nine Psa had an imipenem MIC of 4 µg/mL or more. Mean age was 56.0 ± 20.2 years; mean CPIS was 7.8 ± 1.3 with a CPIS of 8, 9, or 10 in 56.1% of subjects; and mean APACHE II score was 18.3 ± 5.6. Clinical cure at TOC was 78 (63.9%) of 122 and 60 (67.4%) of 89 for clinically (CE) and microbiologically evaluable (ME) subjects. For CE subjects, 35 (66.0%) of 53 NP; 38 (64.4%) of 59 VAP; and 5 (50.0%) of 10 HAP were clinical cures. Cure rates for CE subjects with Psa were 14 (56.0%) of 25; 5 (71.4%) of 7 for NP; and 9 (50.0%) of 18 for VAP. Sixteen subjects (8.7%) discontinued therapy because of an adverse event.
CONCLUSIONS: DORI at an initial dose of 1 g infused over 4 hours was well tolerated and effective in treating NP, VAP, and HAP in a high-risk study population enriched for resistant GNPs including Psa.
Poster presented at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, CA, September 12–15, 2009.

102. Clinical experience with daptomycin for the treatment of methicillin-susceptible *Staphylococcus aureus* (MSSA). *Marianne Billeter, Pharm.D., BCPS,*[1] Joseph J. Kishel, Pharm.D.,[2] Ellie Hershberger, Pharm.D.,[2] Katie Holloway, Pharm.D.[2]; (1) Ochsner Clinic Foundation, New Orleans, LA; (2) Cubist, Lexington, MA
PURPOSE: β-Lactams are first-line therapy for methicillin-susceptible *Staphylococcus aureus* (MSSA). Vancomycin is used in patients intolerant of β-lactams; however, vancomycin has been associated with higher relapse rates and delayed responses compared with nafcillin. In controlled trials, daptomycin was noninferior to anti-staphylococcal β-lactams. This study evaluated outcomes with daptomycin in patients with MSSA infections.
METHODS: All patients with a confirmed MSSA infection in CORE 2005–2008, a retrospective, multicenter, observational registry, were studied. The primary outcome (cure, improved, failure, or non-evaluable) was the investigator's clinical assessment at the end of daptomycin therapy; a secondary outcome was the sponsor assessment, which additionally assessed daptomycin discontinuations because of an adverse event, death from any cause, and any indicator of lack of response as failures. Success was defined as cure or improved. The patient characteristics and efficacy analysis were based on the investigator-evaluable population; all patients were included in the safety analysis.
RESULTS: Four hundred seventeen patients with MSSA infection were identified, of whom 341 (82%) had an evaluable outcome. Twenty-six percent were older than 65 years; 11% had a creatinine clearance (CrCl) less than 30 mL/minute. Infection types were cSSSI 83 (24%) of 341, bacteremia 79 (23%) of 341, osteomyelitis 64 (19%) of 341 (19%), foreign body 40 (12%) of 341, and endocarditis 11 (3%) of 341. Twenty-one percent and 9% reported β-lactam and vancomycin allergies, respectively. Daptomycin median (min, max) initial dose was 6 mg/kg (3, 9), and length of therapy was 14 days (1, 166). Two hundred sixty-seven (78%) of 341 patients received prior antibiotics, and 26% experienced prior therapy failure. The primary outcome of success was reported in 91% (310 of 341), including 16 (84%) of 19 whose prior vancomycin therapy had failed. The secondary outcome of success was 84% (292 of 349). Twenty-nine patients (7%) experienced 29 adverse events possibly related to daptomycin; 7 were serious, and 16 (4%) of 417 discontinued therapy because of treatment-related adverse events.
CONCLUSIONS: Daptomycin is an effective treatment in patients with MSSA infections; therefore, it may be an appropriate empiric therapy for *S. aureus* infections.

103. Cardiac toxicity of echinocandin antifungals. *Kayla R. Stover, Pharm.D.,*[1] Huiling Liu, Ph.D.,[2] Jerry Farley, Ph.D.,[2] William Daley, M.D.,[2] John D. Cleary, Pharm.D.[3]; (1) University of Mississippi, Jackson, MS; (2) University of Mississippi Medical Center, Jackson, MS; (3) University of Mississippi Medical Center, Jackson, MS
PURPOSE: The echinocandins are a relatively new class of antifungal agents. Published literature does not identify cardiovascular toxicity at therapeutic echinocandin concentrations. Our purpose was to evaluate antifungal cardiac toxicity.
METHODS: Ex vivo live-heart studies were performed using Harlan Sprague-Dawley rats. Micafungin (MICA), anidulafungin (ANID), and caspofungin (CASP) were compared in multiple random crossover antifungal dose-ranging studies at 1, 4, and 10 times the therapeutic concentrations, with amphotericin B (AmB) as the positive control. Myocardial activity (contractility), ventricular filling pressure, heart rate, and arrhythmic activity were measured during medication infusion. All studies were performed in triplicate. Means for each agent were compared with the matched media control and assessed by Student t-test.
RESULTS: ANID, CASP, and AmB had a more than 50% reduction

in contractility at exposures equal to and greater than therapeutic concentrations. ANID and AmB often caused fatal events; CASP demonstrated a catastrophic event reversible with cessation of infusion. Contractility significantly decreased by 74.9% ± 10.8% and 57.2% ± 18.1%, and heart rate decreased by 40.3% ± 60.0% and increased by 120.6% ± 4.6%, for ANID and CASP, respectfully. During infusion of CASP, an increase in aortic perfusion pressure was seen. MICA did not have measurable toxicity.
CONCLUSIONS: ANID and CASP were associated with reductions in contractility, possibly associated with vascular histamine release. Clinically, patients receiving either agent by central venous catheter would be at higher risk of this complication. Further studies are necessary to elucidate this antifungal mechanism of toxicity.

104. Comparative sensitivity testing of *Escherichia coli* and *Pseudomonas aeruginosa* isolates from El Paso, Texas and Ciudad Juarez, Mexico. *José O. Rivera, Pharm.D.*,[1] Hoi Ho, M.D.,[2] Sureh Antony, M.D.,[2] Alan H. Tyroch, M.D.,[2] Melchor Ortiz, Ph.D.[2]; (1) University of Texas at El Paso and University of Texas at Austin, El Paso, TX; (2) Texas Tech University HSC, Paul L. Foster School of Medicine at El Paso, El Paso, TX
PURPOSE: Every month, more than 4 million Americans and Mexicans cross the border to work, shop, visit, and seek medical care. We hypothesized that factors stemming from uncontrolled and easy access to antibiotics in Ciudad Juarez, together with the enormous flow of traffic across the border, would make this a prime area for the development of bacterial resistance. We compared susceptibility patterns of two organisms from both sides of the border.
METHODS: Isolates were collected from patients seen and treated for community-acquired and hospital-acquired infections at two hospitals in El Paso and two in Ciudad Juarez. The samples were transported to a reference microbiology laboratory in El Paso, where samples underwent microbial identification and antimicrobial susceptibility testing according to NCCLS standards. Statistical analyses (Fisher exact tests) were performed using SAS to compare proportions of susceptible organisms between El Paso and Ciudad Juarez.
RESULTS: A total of 364 isolates of *Escherichia coli* and 285 isolates of *Pseudomonas aeruginosa* were identified and tested. *E. coli* isolates in Juarez were more frequently resistant to aztreonam, cefazolin, cefepime, cefotaxime, ceftriaxone, ciprofloxacin, and gentamicin ($p<0.05$) compared with those in El Paso. Extended-spectrum β-lactamase (ESBL)–producing *E. coli* were more prevalent in Ciudad Juarez compared with El Paso. *P. aeruginosa* isolates in Ciudad Juarez were more frequently resistant to amikacin, aztreonam, ceftazidime, ciprofloxacin, gentamicin, piperacillin-tazobactam, and tobramycin compared with those in El Paso ($p<0.05$).
CONCLUSIONS: We documented significant differences in the prevalence of bacterial resistance between the two cities for both *E. coli* and *P. aeruginosa* isolates. Although we encountered some variations, these differences supported our hypothesis that antimicrobial resistance is more prevalent in Ciudad Juarez, Mexico, than in El Paso, Texas, for these two gram-negative bacteria.

105. Do standard β-lactam dosing regimens achieve pharmacodynamic targets in hospitalized patients with faster creatinine clearances?
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PURPOSE: To evaluate pharmacodynamic exposures of standard intermittent (II) and prolonged (PI) infusion regimens of meropenem (MER), piperacillin-tazobactam (P/T), and cefepime (CEF) in hospitalized patients with good renal function.
METHODS: Monte Carlo simulations (10,000 patients) were performed using steady-state pharmacokinetic data from patients with mean creatinine clearances of 96, 97, and 98 mL/minute for MER, P/T, and CEF, respectively. Multiple II and PI regimens were evaluated, and PI regimens were infused over 3 hours for MER and 4 hours for P/T and CEF. Cumulative fraction of response (CFR) was calculated using MIC data for six gram-negative pathogens (MYSTIC 2005–2007, USA), and probability of target attainment (PTA) was calculated at MICs ranging from 0.5 to 64 µg/mL. Pharmacodynamic targets were 40%, 50%, and 60% *f*T more than MIC for MER, P/T, and CEF, respectively.
RESULTS: The lowest daily dosing regimens achieving 90% or more CFR for all *Enterobacteriaceae* evaluated were 0.5 g II and PI every 8 hours for MER and 1 g II every 6 hours and 2 g PI every 12 hours for CEF. The lowest daily dosing regimens achieving 90% or more CFR for *P. aeruginosa* were 1 g II and PI every 8 hours for MER and 2 g II every 8 hours and 2 g PI every 12 hours for CEF. None of the P/T regimens achieved 90% CFR or more for all *Enterobacteriaceae* or *P. aeruginosa*. The lowest daily dosing regimens achieving 90% or more PTA at the susceptibility breakpoint of each agent were 1 g II every 8 hours and 0.5 g PI every 8 hours for MER (4 µg/mL), 3.375 g II every 4 hours and 3.375 g PI every 8 hours for P/T (16 µg/mL), and 2 g II every 8 hours and 1 g PI every 8 hours for CEF (8 µg/mL).
CONCLUSIONS: In hospitalized patients with faster creatinine clearances, prolonging the infusion of MER, P/T, and CEF achieves desirable PTA at lower daily doses compared with standard intermittent infusion regimens.

106. An antimicrobial stewardship restriction protocol optimizes the use of daptomycin. *Elizabeth B. Hirsch, Pharm.D.*,[1] Jaye S. Weston, RPh,[1] Jessica M. Cottreau, Pharm.D.,[2] Kevin W. Garey, Pharm.D.,[2] Vincent H. Tam, Pharm.D.,[2] Hannah R. Palmer, Pharm.D.[1]; (1) St. Luke's Episcopal Hospital, Houston, TX; (2) University of Houston College of Pharmacy, Houston, TX
PURPOSE: In August 2008, a collaborative antimicrobial stewardship program was instituted within a large university-affiliated private hospital. Based on increased daptomycin use and rising minimum inhibitory concentrations (MICs) for vancomycin-resistant *Enterococcus* (VRE), a prospective medication use evaluation (MUE) was conducted during October 2008. In response to the MUE results, daptomycin was restricted to infectious disease (ID) physicians. The restriction was enacted February 24, 2009, together with an 8-mg/kg dosing regimen to optimize treatment of VRE.
METHODS: During October 2008 and April 2009, prospective chart reviews were conducted for all patients prescribed daptomycin. Data collected included indication, dose, frequency, microbiology, comorbidities, relevant laboratory values, and patient outcomes. Optimal dosing was defined according to indications in the package insert for the prerestriction data, with the addition of 8-mg/kg dosing for VRE in the postrestriction data. Before the restriction, pharmacists and ID physicians were educated on the rationale for the new dosing protocol. Data were compared to assess the effectiveness of the restriction protocol to optimize daptomycin use.
RESULTS: A total of 32 and 36 courses of daptomycin were prescribed in the pre- and postrestriction months. Percentage of empiric use decreased from 72% to 50% in the postrestriction period. Mean duration and empiric use duration decreased after the restriction protocol (8 ± 9.2 vs. 6.4 ± 4.5 and 6 ± 3.9 vs. 4.7 ± 2.9 days, respectively). Patients were more likely to have optimized dosing in the postrestriction period (OR = 2.175; 95% CI: 0.74–6.13; p=0.147).
CONCLUSIONS: Increased education and surveillance improved the use of daptomycin after a restriction protocol. An optimized dosing protocol using higher (8 mg/kg) doses may help decrease rising VRE MICs.

107E. Susceptibility of baseline *Pseudomonas aeruginosa* and *Acinetobacter baumannii* to doripenem and other antibiotics from six doripenem phase 3 clinical trials. *Koné Kaniga, M.D.*, Rebecca Redman, M.D., Ian Friedland, M.D., Alvaro Quintana, M.D.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ
PURPOSE: In six worldwide phase 3 clinical trials of doripenem

(DOR), the principal baseline nonfermenter isolates obtained were *P. aeruginosa* and *A. baumannii*. The distribution and susceptibilities of these pathogens to DOR and other antibiotics in regions where phase 3 DOR clinical trials occurred are reported.
METHODS: The distribution of nonfermenters in six multinational trials of complicated intra-abdominal infections, complicated urinary tract infections including pyelonephritis, and nosocomial pneumonia (including ventilator-associated pneumonia) in North America (NA), South America (SA), Europe (EU), and Australia and South Africa (AU/SA) was calculated. The minimum inhibitory concentrations (MICs) for *P. aeruginosa* and *A. baumannii* isolates were generated using Clinical and Laboratory Standards Institute broth microdilution methods.
RESULTS: The distributions of baseline nonfermenters were as follows: for *P. aeruginosa*, 27% (59 of 219) were from NA, 35% (77 of 219) were from SA, 35% (76 of 219) were from EU, and 3% (7 of 219) were from AU/SA. For *A. baumannii*, 29% (18 of 63) were from NA, 32% (20 of 63) were from SA, 29% (18 of 63) were from EU, and 11% (7 of 63) were from AU/SA. Overall, for all nonfermenters, DOR MIC50 and MIC90 were 0.5 and 16 mg/L, respectively, versus 1 and 32 mg/L for imipenem (IMI). For *P. aeruginosa*, DOR MIC50 and MIC90 were 0.5 and 4 mg/L, respectively, versus 1 and 16 mg/L for IMI. When DOR MIC was 4 mg/L (n=12), 25% of *P. aeruginosa* had IMI MIC of 4 mg/L or less. For *A. baumannii*, DOR MIC50 and MIC90 were 1 and 32 mg/L versus 0.5 and 32 mg/L for IMI, respectively.
CONCLUSIONS: In all regions, IMI MIC50 and MIC90 were generally double the DOR MIC50 and MIC90. Carbapenems had high MIC90 (32–64 mg/L) against *A. baumannii* across regions. Although IMI MIC90 varied from 4 to 16 mg/L across regions, DOR MIC90 for *P. aeruginosa* varied little (2–4 mg/L).
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108E. Doripenem clinical and microbiologic outcomes by baseline susceptibility for *Pseudomonas aeruginosa* and *Acinetobacter baumannii* from 5 phase 3 clinical trials. *Koné Kaniga, M.D.*, Rebecca Redman, M.D., Nzeera Ketter, M.D., Obiamiwe Umeh, M.D., Shin-Yir Tong, M.S., Michael Lee, Ph.D., Ian Friedland, M.D.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ
PURPOSE: Effective treatment options for infections caused by *P. aeruginosa* and *A. baumannii* are limited. A promising alternative to current agents could be doripenem (DOR), a new carbapenem approved for the treatment of adults with complicated intra-abdominal (cIAI) and urinary tract infections (cUTIs) in the United States, and cIAI, cUTI, and nosocomial pneumonia (NP) in Europe.
METHODS: Per-pathogen clinical cure (CC) and microbiologic cure (MC) rates for *P. aeruginosa* and *A. baumannii* from five phase 3 clinical trials were assessed. Rates for all isolates and for the subset susceptible to the study drug received were compared between DOR and pooled comparator agents in subjects who were microbiologically evaluable (ME) at the test-of-cure (TOC) visit as well as those in the microbiologic-modified intent-to-treat (mMITT) population.
RESULTS: CC rates for all *P. aeruginosa* and *A. baumannii* isolates combined in the ME at TOC were significantly higher for DOR versus pooled comparators (84.2% vs. 60.0%; 95% confidence interval [CI] 11.0–37.3) and for the subset of isolates with DOR minimum inhibitory concentrations (MICs) of 4 mg/L or less versus susceptible comparators (85.6% vs. 67.6%; 95% CI: 4.1–31.9). CC rates for all *P. aeruginosa* isolates were also significantly higher for DOR versus pooled comparators (83.8% vs. 60.3%; 95% CI: 8.7–38.3) and for isolates with a DOR MIC of 4 mg/L or less versus susceptible comparators (83.6% vs. 66.7%; 95% CI: 1.5–32.7). MICs for all *P. aeruginosa* and *A. baumannii* isolates combined were significantly higher for DOR versus comparators (81.2% vs. 66.3%; 95% CI: 1.7–28.1) and numerically higher for isolates with DOR MICs of 4 mg/L or less versus susceptible comparators (81.4% vs. 67.6%; 95% CI: –0.5 to 28.2)]. Parallel results occurred in the mMITT population.
CONCLUSIONS: DOR was clinically and microbiologically more effective than the pooled comparators in patients infected with *P. aeruginosa* and *A. baumannii* causing cIAI, cUTI, and NP, even when the pathogens were susceptible to the comparator drugs received.
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109E. Coordinate regulation of ERG11 and UPC2 in azole resistant isolates of *Candida albicans*.
Stephanie A. Flowers, Pharm.D., Katherine S. Barker, Ph.D., P. David Rogers, Pharm.D., Ph.D., FCCP; University of Tennessee, Memphis, TN
PURPOSE: Among the mechanisms of azole resistance in *Candida albicans* is the overexpression of *ERG11,* which encodes the azole target and key ergosterol biosynthesis enzyme lanosterol demethylase. One mechanism for overexpression of *ERG11* is extra copies of chromosome 5 on which *ERG11* resides. We recently showed that another mechanism by which *ERG11* is overexpressed in azole-resistant isolates is through mutations in the gene encoding the Upc2p transcription factor, resulting in its activation. The purpose of this study was to identify other clinical isolates that overexpress *ERG11* in association with azole resistance and determine whether these correspond with the activation of Upc2p.
METHODS: Fluconazole susceptibilities of clinical isolates were determined by the CLSI broth microdilution method. Expression of the efflux pump genes *CDR1*, *CDR2*, and *MDR1*, as well as *ERG11*, *UPC2*, and the putative Upc2p target genes *ERG24*, *DDR48*, and *CDR11* was measured by real-time RT-PCR.
RESULTS: Of 32 clinical isolates screened, 27 had a fluconazole MIC of 16 µg/mL or more. Of these, 5 had an average increase in *MDR1* expression, 22 had an average increase in *CDR1* and *CDR2* expression, and 16 had an average increase in *ERG11* expression by at least 2-fold compared with the average expression of the five fluconazole-susceptible isolates (MIC of 2 µg/mL or less). Of these, seven isolates also exhibited increased expression of *UPC2* and at least two of the putative Upc2p target genes *ERG24*, *DDR48*, or *CDR11*. Of interest, one azole-resistant isolate did not overexpress any of these genes.
CONCLUSIONS: Seven of 16 isolates identified in this study as overexpressing *ERG11* in association with fluconazole resistance also overexpress the *UPC2* gene itself and putative Upc2p target genes, suggesting constitutive activation of *UPC2* in these clinical isolates. Sequence analysis and further testing of putative gain-of-function *UPC2* alleles will identify novel mutations that arise clinically and contribute directly to fluconazole resistance.
Presented at Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 12–15, 2009.

110. Up-regulated genes of the ergosterol biosynthesis pathway associated with azole antifungal resistance in clinical isolates of *Candida albicans*. *Stephanie A. Flowers, Pharm.D.*, Katherine S. Barker, Ph.D., P. David Rogers, Pharm.D., Ph.D., FCCP; University of Tennessee, Memphis, TN
PURPOSE: Resistance to azole antifungals in the pathogenic fungus *Candida albicans* is often multifactorial and can include up-regulation of efflux pump genes *MDR1*, *CDR2*, and *CDR2* or the *ERG11* gene encoding the azole target enzyme lanosterol demethylase. We have previously shown that one way in which *ERG11* is up-regulated is by gain-of-function mutations in *UPC2* encoding the transcriptional regulator of sterol biosynthesis. Of interest, some isolates overexpressing both *UPC2* and *ERG11* do not contain mutations in *UPC2*, suggesting alternative mechanisms for constitutive up-regulation of these genes. In an effort to further delineate this process, we examined one such isolate pair using genome-wide gene expression profiling.
METHODS: Genetically matched isolate pairs used in this study were pretreatment isolate 945 (fluconazole MIC = 1 µg/mL) and posttreatment failure isolate 1619 (fluconazole MIC = 16 µg/mL). Isolates were grown to mid-log phase, and total RNA was extracted for microarray analysis. Differential gene expression was verified for selected genes by real-time (RT)-PCR.
RESULTS: Two hundred seventy genes were up-regulated and 227 genes were down-regulated reproducibly by at least 1.5-fold. Among the genes with increased expression were 12 putative transcription factors, which included *UPC2, HAP5, FCR1,* and *TAC1*. As expected, *ERG11* was up-regulated, as were other genes involved in sterol

biosynthesis (*ERG2*, *ERG5*, *ERG6*, *ERG24,* and *ERG25*). Of interest, representation of overexpressed genes that resided on chromosome 5 approached 44%, consistent with the presence of an isochromosome or trisomy.

CONCLUSIONS: In resistant isolate 1619, increased *ERG11* expression and azole resistance may be explained in part by the presence of a third copy of this gene through partial or complete trisomy for chromosome 5; however, this does not explain up-regulation of other genes in the ergosterol biosynthesis pathway or of *UPC2*. This study provides compelling evidence for an undescribed mechanism of azole resistance in this fungal pathogen.

111E. In vitro activity of colistin in combination with ceftazidime, ceftriaxone, clarithromycin, imipenem, linezolid and vancomycin against metallo-β-lactamase *Acinetobacter baumannii*. *David S. Burgess, Pharm.D., FCCP*, Warunee Srisupha-olarn, Pharm.D., Michael F. Carden, B.A.; University of Texas Health Science Center San Antonio, San Antonio, TX

PURPOSE: Carbapenem resistance mediated by production of metallo-β-lactamase is a worldwide problem that can make treating serious gram-negative infection caused by *Acinetobacter baumannii* extremely difficult. Although colistin (CST) is still very active microbiologically against MBL *A. baumannii*, resistance to CST can limit the utility of CST monotherapy to treat serious infections caused by MBL *A. baumannii*. Therefore, the objective of this study was to evaluate several antimicrobials in combination with CST against MBL *A. baumannii*.

METHODS: Clinical isolates of *A. baumannii* were collected from a tertiary care hospital in Bangkok, Thailand. MICs were determined against five MDR *A. baumannii* for CST, ceftazidime (CAZ), ceftriaxone (CRO), clarithromycin (CLR), imipenem (IPM), linezolid (LZD), and vancomycin (VAN) using broth microdilution. All five isolates were positive for MBL using the MBL E-strip. Time-kill curves were performed using a standard inoculum with the following antibiotic concentration (µg/mL) alone and in combination with CST (4): CAZ (16), CRO (1.5), CLR (1), IPM (4), LZD (7), and VAN (15). Bacterial densities were determined at 0, 4, 8, 12, and 24 hours.

RESULTS: CST MICs ranged from 0.5 to 2 µg/mL. The MICs for all other antimicrobials were more than 32 µg/mL. CST was rapidly bactericidal; however, there was regrowth for all isolates within 24 hours. All other monotherapy regimens resembled the growth control. Synergy occurred in all combinations with CST. Bactericidal activity at 24 hours was demonstrated for CSL in combination with CAZ, CLR, LZD, and VAN.

CONCLUSIONS: Colistin in combination with ceftazidime, clarithromycin, linezolid, and vancomycin was synergistic and bactericidal against MBL *A. baumannii*. These combinations warrant further investigation.

Presented at 49th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 12–15, 2009.

112E. Susceptibility profile of colistin-susceptible and colistin-resistant *A. baumannii* to several antibiotics. *David S. Burgess, Pharm.D., FCCP*, Warunee Srisupha-olarn, Pharm.D.; University of Texas Health Science Center San Antonio, San Antonio, TX

PURPOSE: Colistin (CST) resistance continues to increase worldwide for *A. baumannii*; however, as our group and others have observed, CST resistance can lead to a more susceptible profile for other antimicrobials. The objective of this study was to compare the susceptibility profile of several antimicrobials against CST^S and CST^R *A. baumannii*.

METHODS: *A. baumannii* ATCC 19606 and 27 CST^S *A. baumannii* clinical isolates from a tertiary care hospital in Bangkok, Thailand, were used. All isolates (n=28) were exposed to CST sulfate to create 28 CST^R strains. MICs were determined for CST, MEM, ASM, FEP, RIF, DOX, LVX, and AMK using broth microdilution according to CLSI guidelines (M7-A6) against all CST^S and CST^R *A. baumannii* (n=56).

RESULTS: MIC results for CST^S and CST^R isolates are displayed in the table.

Antibiotic	CST^S MIC_{50}/MIC_{90} (%S)	CST^R MIC_{50}/MIC_{90} (%S)	%S Incr.
CST	0.5/2.0 (100)	128/> 256 (0%)	
MEM	64/128 (4)	32/128 (43%)	39
SAM	64/256 (4)	16/128 (43%)	39
FEP	64/256 (0)	16/64 (43%)	43
RIF	32/128 (NA)	4/32 (NA)	NA
DOX	2/64 (57)	0.5/32 (79%)	22
LVX	8/64 (4)	8/32 (18%)	14
AMK	256/> 256 (4)	64/> 256 (21%)	17

About 50% of the CST^R strains demonstrated at least a two-dilution decrease in MICs compared with the CST^S isolates for MEM, ASM, FEP, RIF, and DOX. For AMK and LVX, 36% and 25%, respectively, demonstrated this decrease in MICs.

CONCLUSIONS: Because no new novel antibiotics are in the pipeline for CST^R *A. baumannii*, this study provides information about potential CST combinations that may be promising and warrant further investigation.

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113E. Impact of dosing strategies on the killing of multi-drug resistant *Acinetobacter baumannii* with colistin and amikacin in combination using a pharmacokinetic-pharmacodynamic model. *David S. Burgess, Pharm.D., FCCP*, Russell T. Attridge, Pharm.D., Warunee Srisupha-olarn, Pharm.D.; University of Texas Health Science Center San Antonio, San Antonio, TX

PURPOSE: Multidrug-resistant (MDR) *Acinetobacter baumannii* has been reported worldwide; the only rational approach to the treatment of MDR *A. baumannii* appears to be the use of combination therapy. We have previously demonstrated in time-kill studies that CST plus AMK demonstrates synergy against MDR *A. baumannii*; however, the combination was unable to maintain bactericidal activity over a 24-hour period. This investigation was to evaluate the impact of dosing strategies of CST and AMK in combination against MDR *A. baumannii* using a well-established PK-PD model.

METHODS: CLSI methodologies were used to determine MICs for 48 *A. baumannii* isolates against CST, AMK, cefepime (FEP), doxycycline (DOX), levofloxacin (LVX), meropenem (MEM), and piperacillin-tazobactam (TZP). Using a PK-PD model, CST (5 mg/kg every 12 hours) and AMK (15 mg/kg every 24 hours) were evaluated alone and in combination against an MDR *A. baumannii* clinical isolate. Three different strategies were evaluated for the combination of CST and AMK: 1) CST and AMK were given simultaneously, 2) AMK was administered 4 hours after CST, and 3) CST was administered 4 hours after AMK. Bacterial densities were determined at 0, 1, 2, 4, 8, 12, and 24 hours. Bactericidal killing was defined as a 3-log reduction in viable colony count.

RESULTS: MIC_{50}, MIC_{90}, and %S were as follows: CST (0.5, 1, 100%), AMK (128, more than 128, 4%), FEP (128, 128, 0%), DOX (8, 64, 50%), LVX (8, 32, 6%), MEM (64, 128, 6%), and TZP (1024, 2048, 0%). CST alone was bactericidal within 8 hours; however, regrowth occurred by 12–24 hours. AMK alone resembled the growth control. The addition of AMK to CST had no impact irrespective of the administration schedule.

CONCLUSIONS: The addition of AMK to CST provides no additional benefit compared with CST alone, irrespective of giving the combination simultaneously or staggered against this MDR *A. baumannii*.

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114E. Effects of gain-of-function mutations in PDR1 on fluconazole resistance and global gene expression in *Candida glabrata*. *Kelly E. Caudle, Pharm.D.,*[1] Nathan P. Wiederhold, Pharm.D.,[2] Kathy S. Barker, Ph.D.,[1] P. David Rogers, Pharm.D., Ph.D.[1]; (1) University of Tennessee Health Science Center, Memphis, TN; (2) The University of Texas Health Science Center at San Antonio, San Antonio, TX

PURPOSE: Azole antifungal resistance in *Candida glabrata* is primarily mediated by the fungal-specific zinc cluster transcription factor Pdr1p. Gain-of-function mutations in *PDR1* result in constitutive up-regulation of Pdr1p target genes. We used matched

azole-susceptible and -resistant isolates to delineate the Pdr1p regulon and to determine if different mutations in *PDR1* result in different levels of azole resistance and different target gene activation.
METHODS: Four azole-susceptible and -resistant matched isolate pairs were used in this study. *PDR1* alleles were sequenced to identify differences between matched susceptible and resistant isolates. *PDR1* alleles with putative gain-of-function mutations were expressed in a common background in which *PDR1* had been disrupted. Fluconazole susceptibilities were determined by the CLSI microdilution method. Expression of Pdr1p target genes was measured by real-time RT-PCR in these strains. Genome-wide gene expression profiles were determined by microarray analysis.
RESULTS: Two putative novel gain-of-function mutations were identified in two of the matched isolates. One resistant isolate had no *PDR1* mutation, and one susceptible isolate encoded a truncated Pdr1p. Introduction of the hyperactive alleles into a common strain disrupted for *PDR1* conferred different levels of resistance and resulted in increased expression of Pdr1p target genes, but to varying degrees. Microarray analysis comparing these re-engineered strains with their respective parent identified a core set of commonly differentially expressed genes as well as genes uniquely regulated by specific mutations.
CONCLUSIONS: These studies have defined a core set of genes regulated by Pdr1p and have demonstrated that different mutations in *PDR1* have different effects on both fluconazole susceptibility and target gene expression. Moreover, these results suggest the existence of a mechanism for constitutive activation of the Pdr1p regulon independent of mutations in *PDR1*.
Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 12–15, 2009.

115. Comparison of treatment efficacy with metronidazole monotherapy or metronidazole and oral vancomycin for *Clostridium difficile* associated diarrhea (CDAD). *Christopher J. Destache, Pharm.D., FCCP,*[1] Melissa Lapic, Pharm.D.,[1] Stephen Cavalieri, Ph.D.[2]; (1) Creighton University School of Pharmacy and Health Professions, Omaha, NE; (2) Creighton University Medical Center, Omaha, NE
PURPOSE: This retrospective study was performed to compare the efficacy of CDAD treatment success for patients receiving metronidazole monotherapy or a combination of metronidazole and oral vancomycin.
METHODS: Patients admitted to the hospital in 2007 with positive *C. difficile* EIA toxin A/B tests were identified from microbiology records. The patients' medical records were reviewed after IRB approval. Sixty-eight patients were identified and included in this study. Treatment success was defined as a minimum of 10 days of being symptom free after initiating treatment or well enough to be discharged from the hospital.
RESULTS: Of the 68 patients identified, 52 (76%) had treatment success (TS), and 16 (24%) had treatment failure (TF). A total of 38 (56%) patients were female. Baseline patient demographics showed that the TF group was significantly older than the TS group (68 ± 13 years vs. 55 ± 16 years, $p<0.01$). Fourteen (88%) of 16 patients in the TF group received combination therapy ($p<0.001$). Length of CDAD therapy for TF was 14.4 ± 7.5, and for TS, 8.9 ± 6.5 ($p<0.01$). Lengths of *C. difficile* treatment (-0.32), combination therapy (-0.63), and age (-0.38) were all significantly ($p<0.01$) correlated with treatment success. Thirteen patients (19%) died during their hospitalization, possibly because of CDAD.
CONCLUSIONS: Length of therapy, age, and combination therapy for CDAD are negatively correlated with treatment success. Elderly patients are at increased risk of mortality possibly because of CDAD.

116E. CANVAS-1: randomized, double-blinded, phase 3 study (p903-06) of the efficacy and safety of ceftaroline vs vancomycin plus aztreonam in complicated skin and skin structure infections. G. Ralph Corey, M.D.,[1] Mark Wilcox, BMedSci, BMBS, M.D.,[2] Tanya Baculik, M.D.,[3] Dirk Thye, M.D.,[3] *Joseph Laudano, Pharm.D.*[4]; (1) Duke Clinical Research Institute and Duke University Medical Center, Durham, NC; (2) Leeds Teaching Hospitals NHS Trust/University of Leeds, Leeds, United Kingdom; (3) Cerexa, Inc., Oakland, CA; (4) Forest Research Institute, Jersey City, NJ
PURPOSE: Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a common cause of complicated skin and skin structure infections (cSSSIs). Increasing antibiotic resistance and significant morbidity in cSSSIs have led to a need for new, effective, and safe therapies. Ceftaroline is a novel parenteral cephalosporin with excellent in vitro activity against MRSA, multidrug-resistant *Streptococcus pneumoniae*, and many gram-negative pathogens.
METHODS: Adult patients with cSSSI requiring intravenous therapy received ceftaroline (600 mg) or vancomycin (1 g) plus aztreonam (1 g) (V/A) every 12 hours for 5–14 days (randomized 1:1). Clinical and microbiologic response, adverse events (AEs), and laboratory tests were assessed. The primary objective was to determine noninferiority (lower limit of 95% CI: –10%) in clinical cure rate of ceftaroline to vancomycin-aztreonam at 8–15 days posttherapy in clinically evaluable (CE) and modified intent-to-treat (MITT) populations.
RESULTS: Of 702 enrolled patients, 353 received ceftaroline and 349 vancomycin-aztreonam. Baseline characteristics of treatment groups were comparable. Clinical cure rates were similar for ceftaroline and vancomycin-aztreonam in CE (91.1%, 288 of 316 vs. 93.3%, 280 of 300; 95% CI: –6.6 to 2.1) and MITT (86.6%, 304 of 351 vs. 85.6%, 297 of 347; 95% CI: –4.2 to 6.2) populations. Clinical cure rate for MRSA was 94.9% (75 of 79) for ceftaroline and 95.1% (58 of 61) for vancomycin-aztreonam. Microbiologic success was similar for ceftaroline and vancomycin-aztreonam overall (91.8%, 224 of 244, vs. 92.5%, 210 of 227) and for MRSA (94.9%, 75 of 79, vs. 91.8%, 56 of 61). The rates of AEs, serious AEs, deaths, and discontinuations because of AEs were similar for ceftaroline and vancomycin-aztreonam. The most common AEs for ceftaroline and vancomycin-aztreonam were nausea (5.7% vs. 4.6%), headache (5.1% vs. 3.7%), and pruritus (3.1% vs. 8.4%).
CONCLUSION: Ceftaroline had high clinical cure and microbiologic success rates; it was also efficacious against MRSA and other common cSSSI pathogens and well tolerated. Ceftaroline has the potential to provide a monotherapy alternative for treatment of cSSSI.
Presented at the 48th Interscience Conference on Antimicrobial Agents and Chemotherapy/Infectious Diseases Society of America, 46th Annual Meeting, Washington, DC, October 25–28, 2008.

117. Prior vancomycin exposure and its impact on vancomycin MIC in patients with MRSA pneumonia. *Jack Brown, Pharm.D., M.S., BCPS,*[1] Kristen Brown, MSN,[2] Elizabeth Dodds Ashley, Pharm.D., MHS, BCPS,[2] Robert Betts, M.D.,[2] Fred Doloresco, Pharm.D., M.S.,[1] Smita Kothari, Ph.D., MBA, RPh[3]; (1) State University of New York at Buffalo, Buffalo, NY; (2) University of Rochester Medical Center, Rochester, NY; (3) Astellas Pharma, Deerfield, IL
PURPOSE: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of pneumonia in hospitalized patients. Several analyses have found prior vancomycin an independent risk factor for increased MIC. To our knowledge, no study to date has quantitatively investigated the effects of previous vancomycin on MIC in patients with MRSA pneumonia.
METHODS: We performed a retrospective analysis of patients treated for microbiologically confirmed MRSA pneumonia from July 1, 2006, to June 30, 2008. A sample size of 25 in each group is required to determine whether prior vancomycin exposure in patients with MRSA pneumonia results in an increase in vancomycin MICs compared with those without previous vancomycin. Data collected included clinical, microbiologic, acuity, and treatment information for patients exclusively treated at our institution. Treatment information included dose, frequency, and duration of each previous inpatient and outpatient vancomycin within the previous 3 years. Vancomycin MIC was performed using E-test. Univariate and regression models were performed.
RESULTS: A total of 50 patients were identified, 25 with varying degrees of prior vancomycin and 25 without prior vancomycin within the past 3 years. On univariate analysis, patients with more than 10 and less than 25 g of prior vancomycin compared with

patients without prior vancomycin were statistically similar in age, gender, and length of hospitalization. Patients with more than 10 and more than 25 g of vancomycin did have higher median APACHE II scores (13 vs. 9, p=0.005 and 15 vs. 9, p=0.003) and more vancomycin MICs of 2 (46% vs. 5%, p=0.002; and 71% vs. 5%, p=0.0001). On multivariate analysis, the only significant predictor of vancomycin MICs of 2 was more than 10 g of vancomycin within the past 3 years (p=0.01).
CONCLUSION: Patients with MRSA pneumonia receiving more than 10 g of vancomycin in the past 3 years have a higher likelihood of vancomycin MIC equal to 2. There appears to be a predictable relationship with prior vancomycin and increased vancomycin MIC in this population.

118. Assessing the impact of an antimicrobial allergy label in the medical record on patient's clinical course. Gaurav Deshpande, Doctoral Candidate,[1] *Lisa Charneski, Pharm.D., BCPS*,[2] Sheila Weiss, Ph.D.,[1] Angela Wilks, Ph.D.[3]; (1) Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD; (2) Department of Pharmacy Practice and Science, University of Maryland School of Pharmacy, Rockville, MD; (3) Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, MD
PURPOSE: To determine whether patients carrying a label of "allergy" to an antimicrobial have worse clinical outcomes compared with patients who do not have this label.
METHODS: The study population is nonsurgical inpatients, 20 years and older, who received an antimicrobial prescription from August 1, 2007, to July 31, 2008. The groups were patients with no allergy label versus patients with an antimicrobial allergy label. Patient demographics and outcomes were compared, including number of days spent in ICU, length of stay (LOS), readmission within 4 weeks of discharge, number of antibiotics ordered, and death. Basic frequencies, *t*-tests, and χ^2 tests were calculated.
RESULTS: Total number of patients was 25,444, 8.5% (2172) with an allergy label. The mean age (allergy group 56.04 years versus nonallergy group 52.41 years; p<0.0001) and gender (allergy group about 65% female vs. nonallergy group about 51% female; p<0.0001) distribution was significantly different between the groups. Patients with an allergy label fared worse based on the number of days spent in the ICU (1.59 vs. 0.75 days; p<0.0001), the average number of antibiotics prescribed (1.5 vs. 0.88 orders; p<0.0001), and risk of death (RR = 1.84; 95% CI: 1.44–2.24) In contrast, LOS was higher among patients without an allergy label (3.89 vs. 1.89 days; p<0.0001), and the RR for readmission was 0.79 (95% CI: 0.75–0.84). Outcomes were significantly different among the groups.
CONCLUSION: We anticipated that having a label of allergy would result in worse outcomes for patients carrying that label. This was supported by significant differences in days spent in the ICU and risk of death but did not hold true for readmission and LOS. Further analysis will be conducted to detect the effect of confounding variables.

119E. Bactericidal activity of ceftaroline combined with NXL-104 against critical targeted organisms possessing various resistance mechanisms. Helio S. Sader, M.D., Ph.D.,[1] Gregory Williams, M.D.,[2] Ian Critchley, Ph.D.,[2] *Joseph Laudano, Pharm.D.*,[3] Ronald N. Jones, M.D.[1]; (1) JMI Laboratories, North Liberty, IA; (2) Cerexa, Inc., Oakland, CA; (3) Forest Research Institute, Jersey City, NJ
PURPOSE: Ceftaroline (CPT), a broad-spectrum cephalosporin with gram-positive activity (including anti-MRSA), was tested in combination with NXL-104 (NXL), a potent inhibitor of AmpC, ESBL, and KPC β-lactamases (βL) against a selected group of characterized *Enterobacteriaceae* (ENT).
METHODS: Six βL-producing ENTs (CMY-2, derepressed AmpC, CTX-M-15, KPC-2 and -3, and a KPC-cured with SHV-27) and one wild-type strain were tested. MIC and MBC were assessed according to Clinical and Laboratory Standards Institute (CLSI) guidelines in Mueller-Hinton broth with or without 10% human serum (HS). Time-kill analysis used CPT, CPT/NXL combinations (fixed 4 mg/mL [CPT/NXL4] and 2:1 ratio), and NXL alone at 1 times, 2 times, 4 times, and 8 times the MIC. Expression of βL genes was determined by quantitative real-time PCR. Plasmid curing was performed by culturing isolates with DNA intercalating compounds.
RESULTS: CPT and NXL MBCs were generally elevated, with MBC/MIC ratios of 2–32 among βL-producing strains, whereas CPT/NXL4 had low MICs and MBC/MIC ratios at 1 or 2. Ten percent HS did not adversely influence CPT or CPT/NXL MIC or MBC values. βL-producing ENT had CPT/NXL4 MICs at 1/4 µg/mL and MBC/MIC of 1 or 2 (one strain). NXL showed direct antimicrobial activity (MIC, 8–16 mg/mL) against wild-type and four of six βL-producing strains. Time-kill analysis detected rapid bactericidal action of CPT/NXL combinations at 2 times the MIC, with some strains having highest enzyme expression showing regrowth at 4–12 hours at 1 times the MIC. The KPC-cured strain was killed rapidly by CPT at 2 times the MIC.
CONCLUSION: NXL demonstrated a remarkably wide and potent βL inhibitory potency against contemporary isolates producing clinically important βL. These results should be used to optimize CPT/NXL dosing regimens.
To be presented at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, CA, September 12–15, 2009.

120. Methicillin-resistant *Staphylococcus aureus* (MRSA) strain characteristics predictive of mortality in bloodstream infections. *Paulina Deming, Pharm.D.*, Brian Werth, Pharm.D. Candidate, Melinda Montoya, Pharm.D. Candidate, Chris Werth, Pharm.D., Jora Sliwinski, Pharm.D. Candidate, George Sakoulas, M.D., Steve Young, Ph.D., Renee-Claude Mercier, Pharm.D.; University of New Mexico Health Sciences Center, Albuquerque, NM
PURPOSE: Various virulence factors and increased minimum inhibitory concentrations (MICs) are associated with an increased risk of mortality in patients with MRSA infections. Hospital strain acquisition of virulence factors from community strains is of concern for increased mortality risk. This study aimed to identify patient- and strain-specific factors influencing patients' outcomes.
METHODS: Adults (18 years and older) with bloodstream MRSA infections admitted between January 2002 and March 2007 (n=85) were reviewed for demographic and hospital course data. Isolates were tested for Panton-Valentine leukocidin (PVL), *agr* functionality using delta hemolysin assays, strain relatedness by pulsed-field gel electrophoresis (PFGE), and vancomycin (VAN) MIC by Vitek and E-test.
RESULTS: Nineteen (22%) patients died of MRSA. Forty-six patients (54%) tested positive for PVL (USA100 n=3, USA300 n=42, USA500 n=1) with a range of MICs by E-test (MIC of 1 or less, n=8; MIC of 1.5, n=47; MIC of 2, n=29; MIC of 3, n=1) and Vitek (MIC of 1, n=83; MIC of 2, n=2). Ventilator use, intensive care unit (ICU) stay, and vancomycin MIC of 2 mg/L or more by Vitek were independently associated with mortality. Appropriateness of antimicrobial therapy, presence of PVL, vancomycin MIC by E-test, and risk factors for acquisition of MRSA were not predictive of mortality. Loss of *agr* function (absent delta hemolysin expression) showed a trend toward increased mortality (p=0.06). Strain distribution and *agr* functionality are shown below.

MRSA Strain	Deceased (n=19)		Not Deceased (n=66)	
	agr	*agr*	*agr*	*agr*
PFGE	Functional	Nonfunctional	Functional	Nonfunctional
USA100	4	5	16	4
USA200	0	0	3	0
USA300	8	1	33	2
USA400	1	0	0	0
USA500	0	0	1	0
Unique	0	0	6	1

CONCLUSION: Mortality risk in MRSA bacteremic patients is multifactorial. A strong association between mortality and MRSA virulence factors was not found in patients with MRSA bloodstream infections.

121. Evaluation of risk factors associated with invasive candidiasis in critically ill infants. *Mike K. Wang, Pharm.D.*,[1] Lupe Padilla, M.D.,[1] Tina Song, Pharm.D.,[1] Jennifer Le, Pharm.D., BCPS-ID[2]; (1) Miller

Children's Hospital, Long Beach, CA; (2) UCSD Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, CA

PURPOSE: Invasive candidiasis (IC) has been reported to occur in about 10% of very low birth weight (less than 1500 g) infants. Early detection of IC by identification of its risk factors is important in preventing morbidity and mortality. The primary objective was to evaluate the risk factors associated with the development of IC in critically ill infants.

METHODS: A case-control retrospective study was performed among infants admitted to the neonatal intensive care unit (NICU) at Miller Children's Hospital from January 1990 to December 2008. The sample size determined a priori was 150.

RESULTS: There were a total of 161 subjects, 103 cases and 58 controls. The mean gestational age and median birth weight for case versus control groups was 28.1 ± 4.4 vs. 28.0 ± 3.7 weeks and 954 (415–6191) versus 940 (568–3481) g, respectively. Demographics such as age, sex, weight, and underlying diseases were similar between the groups. Using multivariate logistic regression analysis, significant risk factors contributing to the development of IC were congenital heart disease (OR = 1.17; 95% CI: 1.05–1.81, p<0.001), total parenteral nutrition (OR = 1.02; 95% CI: 1.01–1.33, p<0.001), gastrointestinal/abdominal surgery (OR = 1.24; 95% CI: 1.06–2.29, p<0.001), and H_2-receptor antagonist use (OR = 1.43; 95% CI: 1.15–2.56, p<0.001). Length of hospital stay was significantly longer in the case vs. control groups (103 ± 63.2 vs. 66.3 ± 27.1 days, p<0.001). More patients died in the case group versus the control groups (13 vs. 2, p=0.082).

CONCLUSION: Several risk factors associated with the development of IC were identified. Prompt initiation of antifungal therapy in infants with these risk factors is important in successfully managing IC.

122. Mandatory MRSA surveillance and absence of reduction in MRSA infection rates. *Sheila K. Wang, Pharm.D.,*[1] Anne M. Sadofsky, Pharm.D., Candidate,[1] Marc Scheetz, Pharm.D., M.S., BCPS,[1] Thomas J. Reutzel, Ph.D., M.S., B.A.,[1] Meghana Aruru,[1] Bala N. Hota, M.D., MPH,[2] Kamal Singh, M.D.[3]; (1) Midwestern University, Chicago College of Pharmacy, Downers Grove, IL; (2) Stroger Hospital of Cook County/Rush University Medical Center, Chicago, IL; (3) Rush University Medical Center, Chicago, IL

PURPOSE: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections have been on the rise with at least a 60% increase during the past three decades in U.S. intensive care units. To reduce MRSA acquisition rates, the state of Illinois enacted legislation mandating active MRSA surveillance in intensive care unit and other high-risk patients. To assess the impact of mandatory MRSA surveillance at our institution, we determined the prevalence of MRSA cases before and after the implementation of routine MRSA screening.

METHOD: A retrospective observational study at a 613-bed academic medical center in Chicago. About 1007 MRSA cases from all sources hospital-wide from January 2006 to January 2009 were identified from the microbiology laboratory database. Routine nasal MRSA screening of high-risk patients using ChromAgar (BD-MRSA) was implemented at our institution on March 19, 2008. The prevalence of MRSA cases before (January 2006–February 2008) and after (March 2008–January 2009) implementation was determined by the number of MRSA cases per 1000 patient-days. We observed a significant change in MRSA prevalence, and a linear regression model was performed to assess the relationship between the prevalence of MRSA cases and routine MRSA screening during the study period.

RESULTS: A total of 824 MRSA cases met inclusion criteria. The average number of MRSA cases per 1000 patient-days in hospital-wide and intensive care unit patients before and after implementation was 2.52 versus 2.55 and 2.10 versus 2.50, respectively. No significant change was observed in the prevalence of MRSA infections in hospital-wide and intensive care unit patients as a result of routine MRSA surveillance (p>0.05).

CONCLUSIONS: Routine MRSA surveillance did not produce a significant decrease in the number of MRSA cases. Data collection continues to provide further insight into the true effects of routine MRSA surveillance at our institution.

123E. Erroneous reporting of extended-spectrum β-lactamase producers from Vitek2 and BD Phoenix automated systems. *Natalie Boyd, Pharm.D., M.S.,*[1] Renee C. Mercier, Pharm.D.,[1] Clifford Gaylor, B.S.,[2] David S. Burgess, Pharm.D., FCCP,[3] Paul Schreckenberger, Ph.D.,[4] Steve Young, Ph.D.[2]; (1) University of New Mexico Health Sciences Center, Albuquerque, NM; (2) Tricore Reference Laboratories, Albuquerque, NM; (3) University of Texas Health Science Center San Antonio, San Antonio, TX; (4) University of Illinois Medical Center at Chicago, Chicago, IL

PURPOSE: Detection of extended-spectrum β-lactamase (ESBL) producers may be unreliable if K1 β-lactamase (K_1) or AmpC resistance is present in *Enterobacteriaceae* isolates. The purpose of this study was to evaluate the accuracy of Vitek2 (VTK2) and BD Phoenix (BDP) automated systems in reporting ESBLs as well as to determine the need for implementing a confirmatory modified double-disk diffusion method (MDDM).

METHODS: Thirty-six clinical isolates were obtained, which included 15 *Escherichia coli*, 7 *Klebsiella oxytoca*, 4 *Enterobacter* spp., 4 *Proteus mirabilis*, 3 *Klebsiella pneumoniae*, and one each of *Citrobacter freundii*, *Morganella morganii,* and *Serratia marcescens*. Automated susceptibility testing was performed with VTK2, using the AST GN13 card, and BDP, using the NMIC/ID 132 panel. The MDDM, which consists of 10 antibiotic disks, was used for ESBL confirmatory testing (CLSI M100-S19) and phenotypic detection of K_1 and AmpC resistance.

RESULTS: ESBL confirmatory testing detected 14 ESBLs and 22 non-ESBLs. Thirteen non-ESBLs were reported as positives with VTK2 and nine with BDP. Sensitivity was 87% for both VTK and BDP, but specificity was 40.9% for VTK2 and 59% for BDP. MDDM detected K_1 resistance for seven non-ESBLs. All of these strains were reported as ESBLs with VTK2 and six of them by BDP. MDDM also detected AmpC resistance for two false-positive ESBLs.

CONCLUSION: False-positive ESBLs may be reported by VTK2 and BDP. Implementation of phenotypic testing, such as MDDM, should be considered on strains testing ESBL positive to prevent erroneous reporting by automated systems.

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124. Successful treatment of vancomycin-resistant *Enterococcus faecium* meningitis with high-dose daptomycin. *P. Brandon Bookstaver, Pharm.D., BCPS, AAHIVE,*[1] Celeste N. Rudisill, Pharm.D.,[1] Mohammed Hashem, Pharm.D., Candidate,[1] Phillip Yeon, M.D.[2]; (1) South Carolina College of Pharmacy-USC Campus, Columbia, SC; (2) Palmetto Health Richland, Columbia, SC

PURPOSE: To report a case of severe meningitis secondary to vancomycin-resistant *Enterococcus faecium* (VRE) successfully treated with high-dose daptomycin.

METHODS: Literature review suggests this is the first reported case of VRE meningitis treated successfully with daptomycin. A retrospective chart review of the patient data was conducted spanning the 6 weeks of hospitalization. Concurrent cerebrospinal fluid (CSF) and serum daptomycin concentrations were obtained during therapy.

RESULTS: We report a case of a 78-year-old man who presented to the emergency department with fever and altered mental status change after incision and drainage of a paraspinal abscess secondary to laminectomy and decompression of the lumbar spine. The patient was initiated on ceftriaxone, piperacillin-tazobactam, and vancomycin with a working diagnosis of sepsis with disseminated intravascular coagulation. A lumbar puncture (LP) performed 1 week into antibiotic therapy with no clinical resolution suggested bacterial meningitis. The CSF culture results revealed VRE, susceptible only to chloramphenicol, streptomycin, gentamicin, and daptomycin (MIC was 3 µg/mL by E-test). Previous antibiotic therapy was discontinued, and daptomycin 640 mg (9 mg/kg) and gentamicin 450 mg (6.5 mg/kg) intravenously daily were initiated. Gentamicin was discontinued after 9 days of therapy. On day 16, daptomycin was decreased to 420 mg intravenously every 48 hours because of acute kidney injury and continued for 30 days. Steady-state daptomycin serum and CSF concentrations were 20.39 and 0.86 µg/mL, respectively. Creatine phosphokinase levels remained normal throughout therapy. Subsequent LP results were benign, and

blood and CSF cultures were negative. The patient was discharged with clinical resolution after a 42-day hospitalization.
CONCLUSION: The use of high-dose daptomycin for VRE meningitis in the patient of our study was safe and efficacious. Daptomycin penetration into the CSF was around 5% after 8 days of therapy. Future studies should focus on efficacy and toxicity with the clinical use of high-dose daptomycin.

125E. Misidentification of *Klebsiella pneumoniae* carbapenemases as extended spectrum β-lactamase producers by automated testing instruments. *Natalie Boyd, Pharm.D., M.S.,*[1] Renee C. Mercier, Pharm.D.,[1] David S. Burgess, Pharm.D., FCCP,[2] Paul Schreckenberger, Ph.D.,[3] Kamal Singh, M.D.[4]; (1) University of New Mexico Health Sciences Center, Albuquerque, NM; (2) University of Texas Health Science Center San Antonio, San Antonio, TX; (3) University of Illinois Medical Center at Chicago, Chicago, IL; (4) Rush University Medical Center, Chicago, IL
PURPOSE: *Klebsiella pneumonia* carbapenemase (KPC)-positive isolates can evade detection with automated susceptibility testing and be misinterpreted as extended-spectrum b-lactamase (ESBL) producers. The purpose of this study was to determine the necessity of incorporating routine manual phenotypic testing with automated systems for identifying KPCs.
METHODS: Thirty *K. pneumoniae* clinical isolates suspected of carbapenemase activity were obtained. Automated susceptibility testing was performed with Vitek2 (VTK2), using the AST GN13 card, and BD Phoenix (BDP), using the NMIC/ID 132 panel. The modified double-disk diffusion method (MDDM), which consists of 10 antibiotic disks, was used for ESBL confirmatory testing (CLSI M100-S19) and ertapenem (ERT) and imipenem (IMP) susceptibilities. Meropenem (MER) was included in VTK2 and BDP, but not MDDM, and IMP was not available for VTK2. The presence of KPCs was confirmed by PCR for blaKPC and modified Hodge testing (MHT).
RESULTS: BlaKPC was detected in 27 of 30 isolates tested. Twenty-six of these isolates were positive using the MHT. ERT activity was the most predictive of the carbapenems for the presence of KPCs. Of the 27 KPC-positive isolates, ERT was resistant in 89% with MDDM and in 100% with both BDP and VTK2. IMP activity, however, was a poor marker for the presence of KPC. Resistance to IMP was 30% for BDP and 40% for MDDM. ESBL activity was detected in 18 KPC isolates (66.7%). BDP reported all isolates (100%) as ESBLs, whereas only one ESBL strain (3.7%) was reported by VTK2.
CONCLUSION: KPCs can be undetected or misinterpreted as ESBLs by automated systems. Routine phenotypic testing, such as MHT, should be performed on ERT-resistant *K. pneumoniae* isolates and should be considered for ESBL-positive isolates.
Presented at 49th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 12–15, 2009.

126. In vitro activity of carbapenems (CARBs) alone and in combination with amikacin (AMK) against extended-spectrum β-lactamase (ESBL)-producing bacteria with reduced CARB susceptibility (S). *Jennifer Le, Pharm.D., BCPS-ID,*[1] Ronald N. Jones, M.D.,[2] Mariana Castanheira, Ph.D.,[2] Warunee Srisupha-olarn, Pharm.D.,[3] David S. Burgess, Pharm.D., FCCP[3]; (1) University of California San Diego, Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, CA; (2) JMI Laboratories, North Liberty, IA; (3) University of Texas Health Science Center, San Antonio, TX
PURPOSE: Although CARBs are the primary treatment strategy for invasive infections caused by ESBL bacteria, case reports of these pathogens with reduced CARB-S have emerged. One potential treatment modality is to optimize the use of anti-infectives with combination therapy. We evaluated the activity of CARBs alone and in combination with AMK against these clinical isolates.
METHODS: Susceptibility testing was performed by the CLSI broth microdilution method. ESBL confirmation used clavulanate inhibition, and carbapenemase screening applied the modified Hodge test (MHT). Isolates were tested by PCR for ESBL-, carbapenemase-, and plasmidic (p) AmpC-encoding genes. Time-kill studies evaluated ertapenem (ETP), imipenem (IMI), meropenem (MER), and amikacin (AMK) against four nonduplicate clinical isolates of *K. pneumoniae* (KPN) with varying susceptibility patterns.
RESULTS: All isolates showed elevated cephalosporin MICs (ceftriaxone and/or ceftazidime MIC, 8 µg/mL or greater), but only two displayed an ESBL confirmatory test. The MIC range and percent susceptible were as follows: ETP (0.5 to more than 8; 50%), IMI (0.25 to more than 8; 75%), MER (0.119 to more than 8; 50%), and AMK (1 to more than 32; 50%). One KPN isolate was resistant to CARBs (MIC, more than 8 µg/mL) and harbored bla_{KPC-2}. All strains harbored SHV- and 3 TEM-encoding genes. Of the nonconfirmed ESBLs, one DHA-like and one KPC (positive MHT) with CTX-M–like ESBL were detected. For monotherapy, ETP and IMI were unable to maintain bactericidal activity for 24 hours against any of the isolates; whereas MER was bactericidal against three isolates, and AMK was bactericidal against two susceptible isolates. For combination therapy, MER plus AMK was bactericidal against all four isolates; IMI plus AMK against only two isolates; and ETP plus AMK against one isolate; however, the addition of AMK enhanced the in vitro killing activity of all CARBs.
CONCLUSION: The addition of AMK to CARBs, particularly MER, enhanced bactericidal activity against KPN with and without reduced susceptibility to CARB.

Managed Care

127. Blood pressure control after conversion of high dose felodipine/nifedipine to amlodipine. *Jessica L. Milchak, Pharm.D.*, Roberta L. Shanahan, Pharm.D., Julia A. Kelleher, Pharm.D., Jane Kerzee, Pharm.D.; Kaiser Foundation of Colorado, Longmont, CO
PURPOSE: Therapeutic conversions are frequently undertaken by health care organizations such as Kaiser Permanente (KP) to allow cost-savings capitalization. KP patients taking felodipine or nifedipine, including those taking high doses, were switched to amlodipine after it became the preferred formulary calcium channel blocker (CCB). Small studies have demonstrated improvement in blood pressure (BP) control in converting patients on high-dose CCB to combination therapy; however, there are few data demonstrating how high-dose felodipine, such as 20 mg/day, compares with amlodipine 10 mg/day. The objectives of this study were to 1) successfully convert patients on high-dose felodipine-nifedipine to amlodipine and 2) ensure continued BP control postconversion.
METHODS: This initiative targeted 7313 members taking felodipine or nifedipine. Patients taking felodipine less than 10 mg and nifedipine 90 mg were automatically converted to equivalent-dose amlodipine by KP outpatient pharmacies. The remaining 196 members were identified on high doses of these medications, with 175 patients taking more than 10 mg of felodipine and 21 taking nifedipine more than 90 mg daily. These patients were referred to clinical pharmacy specialists (CPSs) to assist with individualized conversions of BP medications. To optimize BP control, CPSs recommended conversions and additions/changes to antihypertensive regimen, and they actively monitored BP. BP measurements were obtained through chart review at baseline and 8 months postconversion.
RESULTS: One hundred ninety-one patients were converted to amlodipine. For all patients, at baseline, 38.8% were controlled to goal (less than 140/90 mm Hg or less than 130/80 mm Hg for patients with diabetes/CKD) compared with 70.4% after conversion, $p<0.001$. Systolic BP was significantly lower after conversion: 138.0 mm Hg versus 131.4 mm Hg, $p<0.001$. Diastolic BP was also significantly lower after conversion: 73.5 versus 73.3 mm Hg, $p<0.001$.
CONCLUSIONS: Most patients were successfully converted to the formulary-preferred CCB (amlodipine). Significant improvement in overall BP control rate and reduction in BP were demonstrated. Clinical pharmacists play a valuable role in therapeutically converting challenging cases.

Medication Safety

128. Patient safety initiative for patients on concomitant amiodarone and simvastatin therapy. Sahar Karimi, Pharm.D.,

Cherylyn Beckey, Pharm.D., *David Parra, Pharm.D.*, Augustus R. Hough, Pharm.D.; West Palm Beach Veterans Affairs Medical Center, West Palm Beach, FL

BACKGROUND: In 2002, amiodarone and simvastatin labeling was revised to include an increased risk of rhabdomyolysis when used together; however, the U.S. Food and Drug Administration continued to receive reports of rhabdomyolysis with this combination, and it reissued a statement warning against concomitant amiodarone and simvastatin in doses exceeding 20 mg/day.

PURPOSE: Assess the prevalence of the above combination and the frequency of additional risk factors for myopathy and implement a conversion protocol to alternative statins for patients receiving this combination.

METHODS: A retrospective review of patients on the above combination was conducted. Data collected included demographics, duration of therapy, and risk factors for myopathy. Patients taking simvastatin 40 mg/day were converted to pravastatin 80 mg/day if they were within 10% of their low-density lipoprotein goal. Otherwise, they were converted to rosuvastatin 5–10 mg/day based on renal function.

RESULTS: Ninety-two patients were receiving the above combination for an average of 43 months. Sixty patients were converted to rosuvastatin and 11 patients to pravastatin; 21 patients were converted outside the protocol. Additional risk factors for myopathy included the following: age older than 80 years (43%; 40 of 92), female sex (1%; 1 of 92), hypothyroidism (32%; 29 of 92), renal insufficiency (12%; 11 of 92), diabetes (36%; 33 of 92), and use of medications that increase the risk of myopathy (gemfibrozil [3%; 3 of 92], nicotinic acid [20%; 18 of 92], macrolides [4%; 4 of 92], verapamil [1%; 1 of 92], and diltiazem [3%; 3 of 92]). There were no statistically significant changes in the lipid or hepatic panels from baseline in patients converted according to the protocol.

CONCLUSIONS: In our population, patients on the above combination often have additional risk factors for myopathy. The conversion protocol implemented was not only feasible, but also safe and effective. Our findings underscore the need for health care systems to critically assess the use rates of such combinations and consider initiatives to minimize this risk.

129. A retrospective evaluation of the safety of desmopressin as a hemostatic agent in renally impaired patients. *Jeanne J. Ventura, Pharm.D.*, Maria K. Stubbs, RPh, Chai L. Low, Pharm.D.; Veterans Affairs San Diego Healthcare System, San Diego, CA

PURPOSE: This study aimed to investigate whether renal function correlated with the incidence of severe hyponatremia and seizures when intravenous desmopressin (DDAVP) was used as a hemostatic agent in renally impaired patients.

METHODS: Retrospective, single-center study assessing patients who had received single intravenous doses of DDAVP from July 2003 to June 2008. Patients with a history of SIADH, seizures, or preexisting hyponatremia were excluded. Laboratory data including serum creatinine, estimated glomerular filtration rate, and serum sodium at baseline and up to 3 days post-DDAVP were required for inclusion in the analysis. Any reported incidence of seizures was documented. Patients were stratified according to the KDOQI stages of kidney disease and analyzed for changes from baseline characteristics. Between-group analysis was evaluated using a Fisher exact test.

RESULTS: Sixty-two patients received a total of 75 intravenous doses of DDAVP during the 5-year review period. The average age was 65.2 ± 12.5 years, and most of the patients (61) were men. DDAVP at 0.3 µg/kg was used. Most of the patients (66%) were in stage IV–V CKD. There was no incidence of severe hyponatremia (serum Na less than 130 mEq/L). One seizure event occurred, but it was associated with alcohol withdrawal. There was no significant difference between CKD stages and changes in laboratory values from baseline.

CONCLUSIONS: This study suggests that single hemostatic doses of intravenous DDAVP appear safe without risk of hyponatremia and seizure in patients with varying degrees of renal impairment. The package insert statement indicating the contraindication for use in renally impaired patients may not be applicable when DDAVP is used as a single dose for hemostasis.

130. Investigation of the implementation of an anticoagulation protocol. *Andrew J. Crannage, Pharm.D.*, Julie A. Murphy, Pharm.D.; St. Louis College of Pharmacy and St. John's Mercy Medical Center, St. Louis, MO

PURPOSE: The objective of this study was to determine the impact of the implementation of a hospital anticoagulation protocol on adherence to standards of care for dosing and monitoring of unfractionated heparin (UFH) and low-molecular-weight heparin for the treatment of venous thromboembolism (VTE), pulmonary embolism (PE), and/or acute coronary syndrome (ACS).

METHODS: Patients 18 years and older with a primary diagnosis of VTE, PE, and/or ACS treated with UFH and/or enoxaparin were included. Data including primary diagnosis, anticoagulant treatment and dosing, patient height and weight, serum creatinine, complete blood cell count, and partial thromboplastin time (aPTT) were collected on patients admitted to St. John's Mercy Medical Center during February 2008 (preimplementation) and February 2009 (postimplementation).

RESULTS: Forty-six patients (UFH, n=16; enoxaparin, n=30) were included in the preimplementation group, and 25 patients (UFH, n=9; enoxaparin, n=16) were included in the postimplementation group. Forty-six percent of patients were dosed properly throughout the hospital visit in the preimplementation group (UFH, 38%; enoxaparin, 50%) compared with 76% of patients in the postimplementation group (UFH, 56%; enoxaparin, 88%), (p=0.023). Fifty-four percent of patients were monitored properly in the preimplementation group (UFH, 31%; enoxaparin, 67%) compared with 68% of patients in the postimplementation group (UFH, 56%; enoxaparin, 75%) (p=0.318).

CONCLUSIONS: Standardizing dosing with an anticoagulation protocol significantly increased proper dosing of anticoagulant therapy. Standardizing monitoring with an anticoagulation protocol did not significantly improve proper monitoring of anticoagulant therapy. A lack of understanding of the need for baseline laboratory data contributes to improper anticoagulant monitoring. Variable aPTT monitoring frequency, dependent on previous results, and the necessity for multiple venous blood draws per day contribute to the difficulty in properly monitoring UFH. An approach that includes significant educational strategies regarding standards associated with anticoagulant therapy is necessary to optimize patient care.

131. Persistence of antibodies to the topical hemostat bovine thrombin. *C. Duane Randleman, M.D.*,[1] Neil K. Singla, M.D.,[2] Kenneth L. Renkens Jr., M.D.,[3] John Pribble, Pharm.D.,[4] Allan Alexander, M.D.[4]; (1) Cardio Thoracic Surgeons, PC, Birmingham, AL; (2) Lotus Clinical Research, Inc., Pasadena, CA; (3) Indiana Spine Group, Indianapolis, IN; (4) ZymoGenetics, Inc., Seattle, WA

PURPOSE: In two recent prospective clinical trials, antibodies to bovine thrombin were present at study entry in 5% of the patients (10 of 200) in a general surgical population (study 1) and in 15.6% of the patients (32 of 205) with histories of surgical procedures in which exposure to bovine thrombin was documented or highly likely (study 2). Re-exposure to bovine thrombin-containing preparations is contraindicated in patients with these antibodies. There is no readily available test for antibodies to bovine thrombin; thus, it is important for clinicians to understand whether these antibodies persist after exposure because they can be associated with immune-mediated coagulopathies. We characterized one aspect of immune sensitization, the persistence of circulating antibodies to the topical hemostat bovine thrombin.

METHODS: The length of time since the most recent previous surgical procedure with documented or highly likely use of bovine thrombin was determined for 204 patients enrolled in a recent clinical trial (study 2; completed in 2008). The presence or absence of antibodies to bovine thrombin was determined for each patient at study entry. Antibody data were sorted on the basis of time since prior exposure to bovine thrombin and were grouped by 1-year intervals. The proportion of patients with antibodies to bovine thrombin and 95% confidence interval (CI) were determined for each interval; this provided an estimate for antibody persistence.

RESULTS: Antibodies to bovine thrombin were detected in 21% of patients (23 of 111; 95% CI: 14–29) within 1 year since prior surgery, 7% of patients (3 of 44; 95% CI: 2–19) within 1–2 years

since prior surgery, 16% of patients (5 of 31; 95% CI: 7–33) within 2-3 years since prior surgery, and 6% of patients (1 of 18; 95% CI: 0–28) within 3–4 years since prior surgery.
CONCLUSIONS: The proportion of patients with antibodies to bovine thrombin ranged from 6% to 21% across the 4-year postsurgery window. Clinicians should be aware that antibodies to bovine thrombin products might persist for years after exposure.

132. Prevalence of medication sharing and use of "left over" medications in an inner city urban population. *Nima M. Patel, Pharm.D., BCPS,*[1] Lawrence Ward, M.D.[2]; (1) Temple University School of Pharmacy, Philadelphia, PA; (2) Temple University School of Medicine, Philadelphia, PA
PURPOSE: To describe the extent of medication sharing and use of "leftover" medications that occurs in an inner-city urban population without the supervision of a health care provider.
METHODS: Prospective one-on-one interviews were conducted at Temple University Hospital. Patients were excluded for inability to understand English, altered mental status, or medical instability. Survey questions included demographic data, social history, chronic pain history, and psychiatric disorders. Patients were asked about use of leftover medications from a previous prescription and any use of prescription drugs that were not prescribed to the individual. If the participant stated "yes" to the question, they were prompted to recall the indication and particular medication.
RESULTS: Eight hundred five individuals were approached, and 643 agreed to participate, yielding a response rate of 80%. Patients' age ranged from 18 to 92 years, with 59% female. The sample was primarily African American (75.4%). Thirty percent had less than a high school education, and 89.5% had health insurance. Overall, 23.7% reported using leftover medications from a prior prescription, and 18.1% reported using a prescription medication that was not originally written for them (medication sharing). A significant portion in the leftover medication group (67.1%) and medication sharing group (81.9%) reported using one medication. The top three indications for use of leftover medications were pain (35.5%), infection (31.6%), and cardiovascular disease (8.5%). In the medication sharing group, the most frequently reported reason for use by indication was pain (66.4%), mood (12.9%), and infection/cardiovascular disease (10.4%). About 44% in the leftover medication group and 25.9% in the medication sharing group were unable to identify the exact medication taken.
CONCLUSION: Pharmacists should be aware that use of leftover medications and medication sharing are common behavior patterns. This behavior can lead to unanticipated adverse reactions, drug-drug interactions, antibiotic resistance, and addiction or misuse.

133. Evaluation of incorporating trigger tool into daily pharmacy monitoring for increased detection and reporting of medication related harm. *Christine B. Rualo, Pharm.D.,*[1] Danny Vu, Pharm.D.,[1] Ronald Floyd, Pharm.D.,[2] Grant Lum, Pharm.D.[1]; (1) Sharp Chula Vista Medical Center, Chula Vista, CA; (2) Sharp Mary Birch Hospital for Women, San Diego, CA
PURPOSE: The purpose of this study was to determine the impact of pharmacist monitoring of adverse drug events (ADEs) associated with designated trigger medications to decrease the recurrence of adverse events.
METHODS: Trigger events (TEs) were reviewed between January 1, 2008, and March 31, 2008, and between January 1, 2009, and March 31, 2009. Each TE was evaluated by pharmacists for evidence of ADE occurrence that reached the patient and required intervention to preclude harm and those that contributed to/resulted in temporary/permanent harm/death. ADEs were categorized on the basis of the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) index. Trigger medications monitored were as follows: dextrose 50%, glucose gel, glucagon; vitamin K; naloxone; flumazenil; sodium polystyrene; protamine; diphenhydramine; diphenoxylate-tropine; and loperamide. TEs were documented using a trigger tool adapted from the Institute for Healthcare Improvement (IHI). Primary outcome measures included incidence and characteristics of ADEs reported and identified with the trigger tool. Data were expressed as occurrences and analyzed using χ^2.
RESULTS: Two hundred thirty-five TEs retrospectively and 301 TEs prospectively were evaluated. Incidence of TEs associated retrospectively and prospectively with potential ADEs, 12.3% and 13.3%; reported ADEs, 3.4% and 82.5% ($p<0.05$). Incidence of TEs associated with reported ADEs retrospectively and prospectively: ADEs not reported and should have been reported: 96.6% and 17.5% ($p<0.05$); preventable reported ADEs: 3.4% and 72.7% ($p<0.05$); nonpreventable reported ADEs: 0% and 27.3% ($p<0.05$). Characteristics of prospective TEs: 80% non-ADEs, 6% not determined, 2% not reported, and 11% ADEs reported (as categorized by the NCC MERP index: 1% C, 6% D, 2% E, 2% F).
CONCLUSION: Incorporating a trigger tool into pharmacy daily monitoring increased reporting and detection of potential ADEs. Benefits of the trigger tool include capability of involving multidisciplinary monitoring, providing a consistent method to monitor ADEs, and identifying process improvements to prevent recurrences of medication-related harm.

Nephrology

134. γ-glutamyl transpeptidase expression and activity in human kidney tissue. *Stacy Shord, Pharm.D., BCOP*, Shitalben R. Patel, M.S.; University of Illinois at Chicago College of Pharmacy, Chicago, IL
PURPOSE: More blacks may develop nephrotoxicity compared with whites after cisplatin. γ-glutamyl transpeptidase (GGT) helps catabolize cisplatin to a nephrotoxic thiol in the kidney, and this enzyme appears to play a pivotal role in the development of nephrotoxicity; however, the expression and activity of this enzyme has not been characterized in the human kidney. Therefore, we measured the expression and activity of GGT in the human kidney.
METHODS: Cadaveric human kidney tissue was obtained from the Cooperative Human Tissue Network. Total RNA was extracted from homogenized tissue (MagMax kit, Ambion) and reverse transcribed (High Capacity cDNA reverse transcription kit, Applied Biosystems). Messenger RNA levels were measured using custom TaqMan probes specific for the three splice variants of the 5′-untranslated region of *GGT*. Specific activity was measured using spectrophotometry (Catachem) and was confirmed by the inhibitor acivicin 500 µM.
RESULTS: Human kidney tissue was obtained from 10 white and 9 black donors (8 female, 10 male, 1 unknown) ranging in age from 2 to 88 years. Messenger RNA levels normalized to β-actin were 15.7 ± 19.3 type A, 1.5 ± 3.1 type B, and 2.9 ± 3.4 type C (mean ± SD). Expression varied 32-fold (type A), 17-fold (type B), and 70-fold (type C). Activity was 2986 ± 1427 U/mg of protein and varied 9-fold. Activity was negatively correlated with the ratio of mRNA levels of type B to type C ($r = -0.47$, $p=0.04$). Messenger RNA levels and activity did not differ on the basis of age, gender, or race.
CONCLUSIONS: Type A mRNA levels were the dominant splice variant expressed in human kidney. Messenger RNA levels and activity did not differ on the basis of age, race, or gender in our sample. Relative mRNA levels of the splice variants may be predictive of activity. Laboratory studies to examine the relationship between cisplatin toxicity in human kidney cells and expression and activity of the splice variants are being completed.

135. Vancomycin clearance during modeled slow low efficiency dialysis. *Mariann D. Churchwell, Pharm.D.*; University of Toledo College of Pharmacy, Toledo, OH
PURPOSE: Slow low-efficiency dialysis (SLED) is frequently used in critically ill patients unable to tolerate intermittent hemodialysis (IHD) by using blood (Qb) and dialysate flow rates (Qd) slower than IHD. Very few reports exist to guide drug dosing in patients receiving SLED; therefore, this study was designed to determine vancomycin clearance during modeled SLED therapy.
METHODS: Vancomycin transmembrane clearance (CLt) was assessed with a single-pass bovine blood in vitro SLED model with a high-flux cellulose triacetate hemodialyzer (Electra 150, Baxter) at a Qb of 200 mL/minute and a Qd of 9 and 12 L/hour. Prefilter blood and spent dialysate samples were obtained from ports on the extracorporeal circuit at 15, 30, 45, 60, 90, and 120 minutes after the initiation of SLED and repeated 6 times with new disposable

components. Sample concentrations were determined by a Fluorescence Polarization Immunoassay using a TDx (Abbott Diagnostics) analyzer.
RESULTS: The mean CLt mL/minute (±SD) at 9 L/hour was 59.6 (9.1), 59.3 (11.8), 64.6 (16.4), and 74.9 (19.6), and for 12 L/hour, the mean CLt mL/minute (±SD) was 58.8 (5.9), 63.3 (9.8), 75.2 (14.1), and 71.9 (30.7) at 15, 30, 45, and 60 minutes. Multiple concentrations were below the level of detection (0.00–100 µg/mL) for samples obtained at 90 and 120 minutes in both arms, resulting in an indeterminate CLt. Comparison of 9- and 12-L/hour arms at similar time points (Student t-test unequal variance) showed no significant difference in CLt between Qd. Vancomycin CLt at 9 L/hour (150 mL/minute) was about 40%–50% of Qd, indicating a substantial removal of vancomycin by this in vitro SLED model.
CONCLUSION: Overall, the results of this in vitro SLED model showed a substantial vancomycin CLt, which may lead to subtherapeutic vancomycin concentrations. Vancomycin serum concentration should be monitored closely in patients receiving concomitant therapy with SLED.

Neurology

136. A clinical pharmacology study to determine the selective and non-selective doses of rasagiline, a monoamine oxidase type B inhibitor. *Jack J. Chen, Pharm.D.,*[1] Liat Adar, Ph.D.,[2] Tamar Goren, Ph.D.,[2] Nissim Sasson, M.A.,[2] Yoni Weiss, M.D., MBA[2]; (1) Loma Linda University, Loma Linda, CA; (2) Teva Pharmaceutical Industries Ltd., Netanya, Israel
PURPOSE: To assess tyramine sensitivity and MAO-B selectivity associated with rasagiline.
BACKGROUND: Rasagiline inhibits MAO-B and is indicated for the treatment of Parkinson disease (PD) with doses of up to 1 mg/day. The dose at which rasagiline retains selectivity for MAO-B has not been fully characterized.
METHODS: Randomized, placebo-controlled, phase I study incorporating positive and comparator controls in healthy subjects. Subjects received run-in tyramine HCl (TYR) challenge tests with escalating doses (5–800 mg) for up to 10 days, followed by study drug for 14 days (except as noted): phenelzine (positive control, 15 mg 3 times/day), rasagiline (1, 2, 4, or 6 mg once daily), rasagiline 2 mg once daily (14 and 30 days), or selegiline (comparator, 5 mg twice daily), followed by TYR rechallenge with escalating doses up to 11 days. During both challenges, TYR dose was increased daily until systolic blood pressure increased by 30 mm Hg for three consecutive measurements over 10 minutes (TYR30). With the exception of phenelzine and rasagiline 30 days, all groups also included matching placebo subjects. Primary outcome measure was the ratio of TYR30 in the run-in period (no MAO-I) to TYR30 with MAO-I. Blood was sampled for rasagiline, tyramine, and dihydroxyphenylglycol (DHPG, an index of MAO-A inhibition).
RESULTS: One hundred forty-nine subjects completed the study. Mean age was 58 ± 8 years. The TYR30 ratios (geometric mean) were as follows:

Phenelzine, 45 mg/day (17.32) (n=15)
Selegiline, 10 mg/day (2.47) (n=15)
Rasagiline, 1 mg/day (2.03) (n=15)
Rasagiline, 2 mg/day, 14 days (3.33) (n=13)
Rasagiline, 2 mg/day, 30 days (2.45) (n=14)
Rasagiline, 4 mg/day (4.50) (n=17)
Rasagiline, 6 mg/day (5.10) (n=13)
Pooled matching placebo (1.50) (n=38)
[excludes placebo 30 days, n=9]

A decrease in mean DHPG plasma concentration (indicating inhibition of MAO-A) was observed for phenelzine, selegiline, and rasagiline 4 and 6 mg/day.
CONCLUSIONS: Rasagiline 1 mg/day (maximum recommended dose) demonstrates selectivity for inhibition of MAO-B. Selectivity is attenuated at doses of 4 mg/day or more.

137. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) treatment with immune globulin intravenous, 10% caprylate/chromatography purified (IGIV-C): summary of a randomized placebo-controlled study. *Peter Donofrio, M.D.,*[1] Vera Bril, M.D.,[2] Marinos C. Dalakas, M.D.,[3] Chunqin Deng, Ph.D.,[4] Kim Hanna, M.S.,[4] Hans-Peter Hartung, M.D.,[5] Richard A.C. Hughes, M.D.,[6] Norman Latov, M.D.,[7] Ingemar S.J. Merkies, M.D.,[8] Pieter A. van Doorn, M.D.[8]; (1) Department of Neurology, Vanderbilt University, Nashville, TN; (2) Division of Neurology, University Health Network, Toronto, Ontario, Canada; (3) Clinical Neuroscience, Imperial College, London, United Kingdom; (4) Talecris Biotherapeutics, Research Triangle Park, NC; (5) Department of Neurology, Heinrich Heine University, Düesseldorf, Germany; (6) Department of Clinical Neuroscience, King's College and Guy's Hospital, London, United Kingdom; (7) Peripheral Neuropathy Center, Cornell University, New York, NY; (8) Department of Neurology, Erasmus MC, Rotterdam, Netherlands
PURPOSE: To critically review short- and long-term benefits reported in the IGIV-C CIDP Efficacy (ICE) study.
METHODS: CIDP patients received IGIV-C (n=59) or placebo (n=58) at a 2-g/kg baseline loading dose followed by 1 g/kg every 3 weeks for up to 24 weeks (first period [FP]). Crossover to alternate treatment (crossover period [CP]) occurred if the adjusted inflammatory neuropathy cause and treatment (INCAT) score did not improve from baseline by one or more points by week 6 or deteriorated at any visit. Patients who responded and maintained a one- or more point improvement in INCAT score through week 24 during FP/CP were re-randomized to IGIV-C 1 g/kg or placebo every 3 weeks in a double-blind 24-week extension phase. Relapse was defined as a one-point or higher worsening in extension-phase baseline INCAT score.
RESULTS: At the end of FP, 54% (32 of 59) of IGIV-C patients and 21% (12 of 58) of placebo patients responded ($p<0.001$). Grip strength improved versus placebo for dominant (10.9-kPa difference; $p=0.0008$) and nondominant (8.6-kPa difference; $p=0.005$) hands. IGIV-C also improved Rotterdam Handicap Scale (RHS) score versus placebo (3.4-point difference; $p=0.001$). Greater improvements in SF-36 were observed with IGIV-C, with physical component summary reaching significance (4.4-point difference; $p=0.020$). Significant improvements were also observed for multiple nerve conduction assessments. Of 57 patients entering extension phase who responded to IGIV-C in FP/CP, 31 were re-randomized to continue IGIV-C, and 26 were randomized to placebo. The extension-phase relapse rate was 13% with IGIV-C versus 42% with placebo ($p=0.012$). Continued IGIV-C for 24 weeks better maintained FP/CP grip strength improvements, and RHS and SF-36 were generally improved/maintained. IGIV-C loading/maintenance doses were safe and well tolerated.
CONCLUSIONS: IGIV-C every 3 weeks significantly improves short- and long-term disability and quality of life. Data support the continued benefit of IGIV-C as a first-line acute and maintenance therapy for CIDP management.

138. Open-label naturalistic study of pregabalin for cervical dystonia and other hyperkinetic movement disorders (HMDs): effectiveness and tolerability. *Jack J. Chen, Pharm.D.,*[1] Michelle Prideaux, Pharm.D.,[2] David M. Swope, M.D.[1]; [1]Loma Linda University, Loma Linda, CA; [2]Loma Linda University Medical Center, Loma Linda, CA
PURPOSE: Within the CNS, pregabalin attenuates the release of glutamate, norepinephrine, and substance P. Pregabalin also increases neuronal GABA concentrations. The pathophysiology of cervical dystonia (CD) and other HMDs is not well elucidated, but it may involve excessive glutamate activity. Pregabalin provides antiglutamate and pro-GABA activity and may be effective for HMDs. This study evaluates the effectiveness and tolerability of pregabalin for the treatment of CD and other HMDs.
METHODS: The study was conducted under an open-label, naturalistic manner in a movement disorders clinic. Records of patients 18 years and older who received pregabalin for HMDs were analyzed. A movement disorder specialist using standard neurologic examination and patient interview assessed the effectiveness and tolerability of pregabalin qualitatively. Only patients meeting the criteria of one or more follow-up assessments were included.
RESULTS: Forty-eight patients met the inclusion criteria (18 men, 30 women; mean age, 63.7 years; range, 31–88 years). All patients

were suboptimally responsive to their current therapeutic regimen. Before initiation of pregabalin, the mean number of concurrent HMD-specific medications (including botulinum toxin) was 2.5 (range, 1–5). Effectiveness and tolerability of adjunctive pregabalin for various HMDs are presented. The most treatment-responsive HMD was CD plus head tremor (CD+HT; mean age, 65.6 years; mean duration of follow-up, 60 weeks (4–159 weeks); mean pregabalin dose, 165.3 mg/day (150–225 mg), with improvement of HT in 71.4%. In the CD+HT group, discontinuation because of adverse effects occurred in three patients (21.4%). The most common adverse effect across all groups was somnolence.
CONCLUSIONS: Pregabalin appears to be more effective for management of CD+HT compared with other HMDs. A prospective, controlled study is warranted to further evaluate efficacy and tolerability in patients with CD+HT.

139E. Mortality after intracerebral hemorrhage is associated with renal dysfunction. *Denise H. Rhoney, Pharm.D.*,[1] Dennis Parker, Pharm.D.,[1] Scott Millis, Ph.D.,[2] Peter Whittaker, Ph.D.[3]; (1) Wayne State University, Detroit, MI; (2) Rehabilitation Institute of Michigan, Detroit, MI; (3) Wayne State University School of Medicine, Cardiovascular Research Institute and Department of Emergency Medicine, Detroit, MI
PURPOSE: Recent studies have demonstrated renal dysfunction's adverse effect on outcome after vascular disease. The relationship between compromised renal function and outcome after intracerebral hemorrhage (ICH) is ill defined. We sought to determine the relationship between in-hospital mortality after ICH and renal dysfunction evaluated by admission estimated glomerular filtration rate (eGFR) and the occurrence of an in-hospital increase in serum creatinine (SCr) of 0.3 mg/dL.
METHODS: We performed a retrospective chart review from 101 consecutive ICH patients admitted from January 2006 to May 2008. eGFR was calculated using the Modification of Diet in Renal Disease and Cockcroft-Gault equations.
RESULTS: The patients were 62% male, 59 ± 1 years of age, with 23 ± 5 mL of ICH volume (48% lobar). Patients who survived had a higher admission eGFR than those who died (89+/4 vs. 59+/6 mL/minute; $p<0.001$). eGFR increased on the first day in both groups, probably because of rehydration; however, only the survival group showed an increase on day 2 ($p<0.05$). Univariate analysis indicated that in-hospital death was associated with the presence of intraventricular hemorrhage, ICH volume, age, eGFR less than 90 mL/minute, and admission values of glucose, Glasgow Coma Scale, SCr, and blood urea nitrogen ($p<0.05$). After controlling for confounding variables, multiple logistic regressions revealed that admission eGFR was an independent predictor of death. Overall, the mortality was 31%; however, the mortality was higher in patients with an eGFR less than 90 mL/minute (40% vs. 16%; $p=0.014$) – this was the case no matter which formula was used. Moreover, for each 10-mL/minute decrease in eGFR, there was a 22% increase in the odds of death. In contrast, the occurrence of a 0.3-mg/dL increase in SCr did not differ between groups ($p=0.20$).
CONCLUSIONS: Renal dysfunction, assessed by admission eGFR but not by SCr increase during hospital stay, was an independent predictor of in-hospital mortality. Our findings suggest that renal function can help stratify risk in hemorrhagic stroke patients.
Presented at International Stroke Conference, San Diego, CA, February 18–20, 2009.

Nutrition

140. Eicosapentaenoic acid attenuates bile acid induced hepatocellular injury by reducing apoptosis and inflammation. *Emma M. Tillman, Pharm.D.*, Brian L. Neudeck, Pharm.D., Richard A. Helms, Pharm.D., Dennis D. Black, M.D.; University of Tennessee Health Science Center, Memphis, TN
PURPOSE: Parenteral nutrition (PN)-associated liver disease (PNALD) occurs in patients receiving long-term PN and may progress from cholestasis to liver cirrhosis, hepatic failure, and death. Recent clinical studies in infants with PNALD have demonstrated improvement and even reversal of PNALD with omega-3 fatty acid supplementation, although the mechanism of action is not well understood and is likely multifactorial. The aim of these studies was to determine whether a specific fish oil–derived omega-3 polyunsaturated fatty acid, eicosapentaenoic acid (EPA), attenuates hepatocellular injury induced by the bile acid and chenodeoxycholic acid (CDCA), with a focus on apoptosis and inflammation.
METHODS: Cultured HepG2 cells were treated with 200 µM CDCA in the presence and absence of 10 µM EPA. Controls included cells incubated with vehicle alone (EtOH) and EPA alone. Apoptosis was evaluated after 24 hours using visual assessment of cellular apoptosis by staining with ethidium bromide (EB) and acridine orange (AO) dyes with fluorescent microscopy. After 2 hours of incubation, pro-inflammatory cytokines (IL-1, IL-6) were evaluated using quantitative real-time RT-PCR.
RESULTS: Apoptosis in HepG2 cells was induced by incubation with CDCA, as demonstrated by nuclear EB/AO staining, and was reduced by coincubation with EPA. There was a 1.7- and 8-fold increase in expression of IL-1 and IL-6 mRNA levels, respectively, when incubated with CDCA alone, compared with a 13% and 47% attenuation of these increases, respectively, when incubated with both CDCA and EPA ($p=0.009$).
CONCLUSION: Bile acid–induced hepatocellular injury is associated with both release of inflammatory mediators and apoptosis. Both of these processes are reduced in the presence of EPA. These data support the therapeutic use of EPA in the prevention and treatment of PNALD.

Oncology

141. Pharmacoeconomics of pharmacogenetics of pediatric cancer patients: case study on 6-mercaptopurine. Ehab Moussa, student,[1] Ahmed Gad, student,[1] *Sherif Kamal, BSC*[2]; (1) Ain Shams University, Cairo, Egypt; (2) Children Cancer Hospital Cairo, Cairo, Egypt
PURPOSE: To study the clinical and pharmacoeconomic effectiveness of applying a combined phenotyping/genotyping approach to screen acute lymphocytic leukemia patients for hereditary thiopurine methyl transferase abnormalities to predict and prevent the acute hematologic toxicities that might take place on administration of 6-mercaptopurine (6-MP).
METHODS: In our study, we screened nine white pediatric patients with acute lymphocytic leukemia at the children's cancer hospital (CCH). We correlated the protocol with the therapeutic drug monitoring reports and the hematologic laboratory results in the same period. We outlined the approximate cost of anti-infective therapy per week in the hospital and the cost of phenotyping and genotyping procedures; we also checked the availability of all equipment, materials, and experiences required to smoothly introduce the approach to the hospital.
RESULTS: Of nine patients, one patient showed severe life-threatening neutropenia and persistent high fever during the consolidation phase of the protocol. This patient is apparently an intermediate to poor 6-MP metabolizer. The average cost of anti-infective therapy in the hospital per week for the average-weight child ranges from L.E. 2023 to L.E. 4000; however, the phenotyping technique costs no more than L.E. 100, and the cost of the genotyping technique is around L.E. 500, given that its cost is decreasing gradually.
CONCLUSIONS: The application of phenotyping screening using the HPLC-UV system to screen patients admitted to the CCH, followed by genotyping, to the patients who show susceptibility to being poor or intermediate metabolizers of 6-MP and hence susceptible to developing severe neutropenia accompanied by possible nosocomial infections, proves to be an effective primary prevention tool. From the pharmacoeconomic point of view, the cost of controlling neutropenia and handling fever by anti-infective therapy is higher than the cost of screening patients, in addition to the advantage of patients' adherence. Based on these results, we recommend this approach to be applied in the hospital.

142. Risk of skeletal-related events in patients with prostate cancer treated with pamidronate or zoledronic acid. *Michele M. Spence, Ph.D.*,[1] Rita L. Hui, Pharm.D., M.S.,[2] Jim Chan, Pharm.D., Ph.D.,[2] Joanne E. Schottinger, M.D.[3]; (1) Kaiser Permanente,

Downey, CA; (2) Kaiser Permanente, Oakland, CA; (3) Kaiser Permanente, Pasadena, CA

PURPOSE: This study estimates the risk of developing a skeletal-related event (SRE) among men with metastatic prostate cancer after being treated with either pamidronate or zoledronic acid.

METHODS: This was a retrospective cohort study using data from Kaiser Permanente's Southern California region. The cohort included men given a diagnosis of prostate cancer from 1998 to 2004 with at least one infusion of either pamidronate or zoledronic acid after cancer diagnosis. We included patients 18 years and older and enrolled with a drug benefit for at least 1 year before diagnosis. We excluded patients receiving both drugs and those with documented SRE before diagnosis. The primary outcome of SRE was defined using diagnosis codes for fractures, spinal cord compression, radiation to bone, and hypercalcemia of malignancy. Secondary outcome was deterioration in renal function based on serum creatinine laboratory results. Logistic regression was used to predict SRE risk of pamidronate compared with zoledronic acid, adjusting for the following covariates: age, medical center, time since diagnosis, number of doses, previous SRE before first dose, and chemotherapy. The proportion of patients with renal function deterioration was analyzed by χ^2 tests.

RESULTS: The cohort included 118 patients treated with pamidronate and 274 with zoledronic acid. Results showed no significant difference in risk of SRE for pamidronate versus zoledronic acid (OR = 0.99; 95% CI: 0.59–1.68). No difference in renal function deterioration was found (χ^2 test = 2.08; p=0.15).

CONCLUSIONS: For patients with prostate cancer, the choice between these two bisphosphonates must be balanced between the shorter infusion times of zoledronic acid versus its increased costs. We did not find evidence for a difference in outcomes; therefore, pamidronate is an effective choice where clinic capacity permits.

143E. Effect of chemotherapy-induced nausea and vomiting on clinical oncology practice in the United States. *Laura Menditto, MBA, MPH,*[1] Amin Haiderali, MBBS, MBA, MPH,[2] Etta Fanning, M.D., Ph.D., MPH,[3] Margaret Good, Ph.D.,[4] April Teitelbaum, M.D., M.S., FACP,[5] Jessica Wegner, B.A.[4]; [1]GlaxoSmithKline, Philadelphia, PA; [2]GlaxoSmithKline, Collegeville, PA; [3]GlaxoSmithKline, Shavano Park, TX; [4]i3 Innovus, Eden Prairie, MN; [5]i3 Research, San Diego, CA

PURPOSE: Despite guidelines for aggressive prevention of chemotherapy-induced nausea and vomiting (CINV), CINV remains a significant problem for patients undergoing chemotherapy. The objective of this study was to examine the clinical burden and economic impact of CINV on clinical practices in the United States.

METHODS: This was an observational study of patients undergoing the first cycle of highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy (MEC) from September 2007 to April 2008. Patients maintained personal diaries of their nausea and vomiting experience (severity, frequency) and use of any health care resources. Patients completed the Functional Living Index-Emesis (FLIE) on days 1/6 and the modified Work Productivity and Assessment Inventory – N/V (WPAI-NV) – on day 6. Descriptive analysis was conducted, with stratification by chemotherapy emetogenicity and symptom severity. Multivariate techniques tested for differences in health-related quality of life and direct/total costs of CINV management.

RESULTS: Patients (n=192) from 46 office-based oncology practices enrolled, and 178 patients (MEC: n=125; HEC: n=53) completed 90% or more of diary items. Patients treated with HEC (n=35 [66%]) and MEC (n=69 [55%]) reported delayed CINV, and six (11%) HEC patients and eight (6%) MEC patients reported a health care visit for CINV during the 5 days after chemotherapy. Use was greater for those with delayed CINV. Patients reported taking fewer prophylactic medications (especially on days 1–3) than prescribed and often required rescue medications. Total costs (direct and indirect) during the 5-day period were $779/patient. Total costs varied significantly with nausea severity: $675 (no nausea) through $1072 (severe nausea). More than 108 (90%) of the individuals reported no CINV, and 36% of the patients reported that CINV (p=0.0001) affected their daily activities.

CONCLUSION: Although CINV has improved, nausea and vomiting remain a severe adverse effect of chemotherapy. This negatively affects daily activities, work attendance, and productivity and burdens the health care system.

To be presented at the Academy of Managed Care Pharmacy, San Antonio, TX, 2009 Educational Conference, October 7–9, 2009.

144. Evaluation of two closed system transfer devices in an outpatient community cancer center. *Andrea Ledford, Pharm.D., BCOP*, Pius Maliakal, Pharm.D., Ph.D., Tom L. Rogers, Pharm.D., BCPS, Marie Mackey, BSN, RN; M.D. Anderson Cancer Center–Orlando, Orlando, FL

PURPOSE: Exposure to cytotoxic agents from leakage or spills is a major occupational concern for oncologic personnel. This study evaluated the effectiveness of the ICU medical closed system compared with the Phaseal closed system transfer device in preventing contamination on work surfaces in the outpatient oncology pharmacy department and patient treatment areas.

METHODS: Before the trial, all study areas were thoroughly cleaned with Surface Safe. Swipe samples were analyzed for fluorouracil, cyclophosphamide, methotrexate, carboplatin, and cisplatin by GS/MS. The trial design established 2-week testing periods for each system. The Phaseal system was evaluated first, followed by a second decontamination with Surface Safe. The ICU medical system was then evaluated using the same procedure. Blinded control samples of each test agent were admixed in fixed doses in a designated BSC using both closed system devices during each study period.

RESULTS: In the chemo-admixture room, 22% of the Phaseal trial samples demonstrated lower levels of surface contamination, whereas 44% of the ICU trial samples showed lower levels of contamination. At the same time, 33% of samples from both systems showed product equivalence. In the treatment areas, the terminal Phaseal injector connection to the injection port was not consistently used, but the complete ICU medical system was used with a 70% lower level detection rate.

CONCLUSIONS: The blinded evaluation of both ICU medical and Phaseal devices, using controlled admixtures, demonstrated that the products are generally equivalent, with nondetectable levels for fluorouracil, cyclophosphamide, and methotrexate. Cyclophosphamide and platinum agents were detected most often. In the pharmacy area, both closed system transfer devices when used in combination with daily Surface Safe treatment provided equivalent control of surface contamination.

Ophthalmology

145E. The ocular comfort and safety of the novel anti-histamine bepotastine besilate ophthalmic solution 1.5% in a healthy pediatric population. Eugene E. Protzko, M.D.,[1] Paul J. Gomes, M.D.,[2] *Jon I. Williams, Ph.D.,*[3] James A. Gow, M.D.,[3] Timothy R. McNamara, Pharm.D.[3]; (1) Seidenberg-Protzko Eye Associates, Bel Air, MD; (2) ORA Clinical Research & Development, Inc., North Andover, MA; (3) ISTA Pharmaceuticals, Inc., Irvine, CA

PURPOSE: To evaluate the ocular comfort and safety of the investigational product bepotastine besilate ophthalmic solution 1.5% dosed twice daily for 6 weeks in a healthy pediatric population.

METHODS: The clinical trial was a multicenter, randomized, double-masked, placebo-controlled, parallel-group 6-week safety study involving four study visits with two treatment groups, bepotastine besilate ophthalmic solution 1.5% and placebo. Pediatric subjects as young as 3 years represented about 15% (127 of 861) of the enrolled subjects. Investigational products were dosed twice daily, and dosing adherence was monitored with dosing diaries. After test drop instillation for each eye at visits 2 and 3, the overall comfort of the investigational product was graded using a quantitative scale (0–3 units, with half-unit increments allowed): 0 = comfortable, discomfort absent; 1 = generally comfortable, mild discomfort; 2 = some discomfort, but tolerable, moderate comfort; and 3 = severely uncomfortable or intolerable.

RESULTS: All enrolled pediatric subjects completed the clinical trial. A comparison with two-sided statistical t-tests after 1 week

(visit 2) and 3 weeks (visit 3) of ophthalmic dosing demonstrated there was no clinically or statistically significant difference in the ocular comfort of bepotastine besilate ophthalmic solution 1.5% and placebo, either immediately after or 5 minutes after instillation. The frequency of total adverse events with bepotastine besilate ophthalmic solution 1.5% in all pediatric subjects was similar to placebo. No severe adverse events were reported during the clinical trial.
CONCLUSIONS: Bepotastine besilate ophthalmic solution 1.5% dosed twice daily for 6 weeks was safe and well tolerated in a healthy pediatric population.
Presented at the Proceedings of the Annual American Academy of Allergy and Asthma Immunology (AAAAI) Meeting, Washington, DC, March 13–17, 2009.

146E. Bepotastine besilate ophthalmic solution reduces nasal symptoms in the conjunctival allergen challenge (CAC) clinical model. Gail L. Torkildsen, M.D.,[1] Paul J. Gomes, M.D.,[1] Jon I. Williams, Ph.D.,[2] *James A. Gow, M.D.,*[2] Mark B. Abelson, M.D.,[1] Timothy R. McNamara, Pharm.D.[2]; [1]ORA Clinical Research & Development, Inc., North Andover, MA; [2]ISTA Pharmaceuticals, Inc., Irvine, CA
PURPOSE: To establish the efficacy of BEPO (bepotastine besilate ophthalmic solution) 1.0% and 1.5%, investigational antihistamine eye drops, compared with placebo in reducing total nonocular symptoms, nasal congestion, and rhinorrhea using the CAC clinical model of allergic conjunctivitis.
METHODS: Single-center, double-masked, randomized (1:1), placebo-controlled, 7-week CAC clinical trial. Eligible subjects were assigned randomly to BEPO 1.0% (n=36), BEPO 1.5% (n=35), or placebo (n=36).
RESULTS: BEPO 1.0% achieved statistical significance 15 minutes ($p<0.002$) and 8 hours ($p<0.001$) after dosing compared with placebo for reducing total nonocular symptom scores. BEPO 1.0% was clinically superior to placebo also for reducing nasal congestion 15 minutes ($p<0.001$) after dosing. BEPO 1.5% was clinically superior to placebo 8 hours after dosing for reducing rhinorrhea ($p<0.001$). Subjects withdrawn included BEPO 1.0% = 0; BEPO 1.5% = 3 (nonadherence [2] and unacceptable baseline ocular itching and redness [1]); and placebo group = 1 (nonadherence). Additional visits were not needed for any enrolled subjects.
CONCLUSIONS: After ophthalmic dosing, BEPO 1.0% reduced total nonocular symptom scores at 15 minutes and 8 hours, BEPO 1.0% reduced nasal congestion at 15 minutes, and BEPO 1.5% reduced rhinorrhea at 8 hours. These clinical results support twice-daily dosing for either BEPO 1.0% or 1.5% formulation.
Presented at Annual Western Society of Allergy and Asthma Immunology (WSAAI) Meeting, Maui, HI, January 25–29, 2009.

147E. Bepotastine besilate ophthalmic solution 1% reduces ear or palate pruritus with rapid onset in a clinical model of allergic conjunctivitis. *Gail L. Torkildsen, M.D.,*[1] Paul J. Gomes, M.D.,[1] Jon I. Williams, Ph.D.,[2] James A. Gow, M.D.,[2] Mark B. Abelson, M.D.,[1] Timothy R. McNamara, Pharm.D.[2]; (1) ORA Clinical Research & Development, Inc., North Andover, MA; (2) ISTA Pharmaceuticals, Inc., Irvine, CA
PURPOSE: To establish the efficacy and safety of bepotastine besilate ophthalmic solution 1%, an investigational antihistamine eye drop, compared with placebo in reducing ear or palate pruritus using the conjunctival allergen challenge (CAC) clinical model of allergic conjunctivitis at 15 minutes after ophthalmic dosing.
METHODS: Single-center, double-masked, randomized, placebo-controlled, 7-week clinical trial using the CAC model of allergic conjunctivitis. The clinical trial was approved by an institutional review board (IRB). Eligible subjects were assigned randomly to either bepotastine besilate ophthalmic solution 1% (n=36) or placebo (n=36).
RESULTS: Bepotastine besilate ophthalmic solution 1% was clinically superior to placebo ($p\leq0.001$) at all observation time points 15 minutes after dosing for reducing CAC-induced ocular itching, with no incidence of treatment-emergent ocular adverse events. Clinical superiority was defined as clinical and statistical significance according to predetermined criteria, including recognition of the need for statistical multiplicity corrections because of the unique clinical trial design. One subject in the placebo treatment group was withdrawn because of nonadherence. No subjects were withdrawn from the bepotastine besilate ophthalmic solution 1% treatment group during the clinical trial. Additional follow-up visits were not needed for any of the enrolled subjects.
CONCLUSIONS: Bepotastine besilate ophthalmic solution 1% was clinically superior to placebo in reducing ear or palate pruritus in the CAC model of allergic conjunctivitis at 15 minutes after ophthalmic dosing. The positive result strongly suggests that bepotastine besilate ophthalmic solution 1% may provide rapid relief from the symptom of ear or palate pruritus associated with allergic conjunctivitis.
Presented at the American College of Allergy, Asthma and Immunology, Seattle, WA, November 6–11, 2008.

Other

148. Recombinant human hyaluronidase-facilitated subcutaneous fluid administration techniques. *George Harb, M.D., MPH*; Baxter Healthcare Corporation, New Providence, NJ
PURPOSE: The Increased Flow Utilizing Subcutaneously Enabled Administration Technique (INFUSE AT) study evaluated recombinant human hyaluronidase (rHuPH20)-facilitated subcutaneous fluid administration techniques.
METHODS: In a randomized, parallel group, open-label trial, one of nine subcutaneous infusion techniques was assigned to healthy adult volunteers. Variations included Smith's Medical JELCO catheter gauge, catheter material, and securement method; one group used a Medtronic Sof-set Ultimate QR subcutaneous button. One milliliter of rHuPH20 (150 U) was administered subcutaneously in the anterior thigh by infusion set, followed by 1000 mL of lactated Ringer solution delivered subcutaneously by a Baxter COLLEAGUE Single Channel Volumetric Infusion Pump, Model CXE 2M9161, over 7–10 hours at 200 mL/hour for 2 hours and then at 125 mL/hour. Technical challenge (TC) assessments included catheter kinking; catheter dislodgement/pullout; and infusion pump alert/failure. Ease-of-use assessments included time for catheter placement; number of needle insertion attempts; and flow-rate reductions/interruptions. Safety and tolerability assessments included infusion-site reactions and adverse events (AEs).
RESULTS: One hundred volunteers (mean age, 34.5 years) were enrolled. TCs were reported in 21 subjects; the proportion with one or more TCs was comparable across treatment groups. Median time from infusion start to first TC report was 1.3–5.2 hours. Pump alert was the most frequent TC (9%–27% of treatment groups). Median time to catheter placement was 9–48.5 seconds. Successful subcutaneous access was achieved on the first attempt in all but two subjects (each required two attempts). TCs resulted in flow interruptions in 20 subjects and flow reduction in 1 subject. Mean interruption duration was 1–6.5 minutes. One or more AEs were reported in 46%–91% of subjects. Except in two subjects reporting moderate to severe AEs, AEs were mild. One serious AE (ureteral calculus) was not considered drug related.
CONCLUSIONS: TCs were comparable across administration techniques.

Pain Management/Analgesia

149E. Methylnaltrexone for the treatment of postoperative ileus: combined safety analysis from two phase 3 studies. *Seth Schulman, M.D.*, Evan Tzanis, M.D., Bruce Randazzo, M.D.; Wyeth Pharmaceuticals, Inc., Collegeville, PA
PURPOSE: Postoperative ileus (POI), a common complication of abdominal surgery, causes pain and nausea. Opioid administration for pain relief is believed to contribute to POI. Methylnaltrexone, a selective mu-opioid receptor antagonist, decreases the constipating effects of opioids without affecting central analgesia. Subcutaneous methylnaltrexone (0.15 mg/kg) significantly improves laxation in patients with advanced illness and opioid-induced constipation. We

report the combined safety analysis of two double-blind, placebo-controlled phase 3 studies evaluating the use of intravenous methylnaltrexone administered every 6 hours in patients with POI.
METHODS: Patients who met inclusion/exclusion criteria had segmental colectomy under general anesthesia by open laparotomy. Laparoscopic surgery was excluded. After surgery, patients who met requirements for continuation were randomly assigned (1:1:1 ratio) to intravenous methylnaltrexone 12 or 24 mg or placebo. All patients were placed on opioids by patient-controlled analgesia pump. Study drug dosing began within 90 minutes after the end of surgery; then, it was repeated every 6 hours until 24 hours after the return of bowel function (tolerance of clear liquids and bowel movement), patient discharge, or completion of the 10-day treatment period. Adverse events (AEs), vital signs, electrocardiograms (ECGs), and laboratory assessments were collected at various times to assess safety.
RESULTS: Combined safety population was composed of 1048 patients. Neither study showed significant improvement in time to GI recovery with methylnaltrexone. Overall, 6.2% withdrew because of AEs (5.1% and 6.8% with methylnaltrexone 12 and 24 mg, respectively; 6.6% with placebo). The most common treatment-emergent AEs were nausea, pyrexia, and vomiting. Incidence of AEs and serious AEs was similar between the methylnaltrexone and placebo groups. No changes that were considered clinically significant occurred during the study in laboratory parameters, vital signs, or ECGs.
CONCLUSIONS: Although it did not demonstrate efficacy for POI, intravenous methylnaltrexone at doses as high as 24 mg every 6 hours was generally well tolerated in postcolectomy patients.
Presented at Digestive Disease Week® 2009, Chicago, IL, May 30–June 4, 2009.

150E. Adherence of and fentanyl absorption from fentanyl buccal soluble film (FBSF) under various administration conditions. *Niraj Vasisht, Ph.D.,*[1] Jeffrey G. Stark, Ph.D.,[2] Andrew L. Finn, Pharm.D.,[1] Larry N. Gever, Pharm.D.[3]; (1) BioDelivery Sciences International, Inc., Raleigh, NC; (2) CEDRA Corporation, Austin, TX; (3) Meda Pharmaceuticals, Inc., Somerset, NJ
PURPOSE: The BioErodible MucoAdhesive (BEMA) drug delivery system is a small, bilayered, water-soluble, polymer film that adheres to the buccal mucosa and rapidly delivers medication into the systemic circulation. The objectives of this study were to evaluate the absorption of fentanyl from FBSF under various conditions and examine the adherence of FBSF to the buccal mucosa.
METHODS: Six healthy volunteers participated in an open-label, five-period, Latin-square, crossover study. Transmucosal fentanyl absorption of FBSF (400 µg) was assessed after the consumption of hot tea or the application of a warm heating pad to the cheek before and during administration. Buccal mucosa adhesion of FBSF was assessed using a placebo film. Fentanyl absorption after transdermal application of FBSF (1200 µg) was assessed by application of the moistened film to the forearm under an occlusive dressing.
RESULTS: Consumption of hot liquid or application of an external heating pad did not meaningfully increase the speed (median T_{first} 10.2 minutes and T_{max} 2 hours, for all three conditions) or extent (mean $AUC_{0–12}$, 3.7, 4.0, and 4.4 hour·ng/mL for hot liquid, heating pad, and no heat, respectively) of fentanyl absorption from the FBSF unit. Five of the six subjects could remove the placebo film within 2 minutes of initial buccal application; however, only three (60%) of these subjects could reapply the film. Removal was not possible beyond 5 minutes in any subject. Plasma fentanyl concentrations were undetectable for at least 2 hours after transdermal application.
CONCLUSIONS: These results demonstrate that FBSF absorption is not meaningfully altered when subjects drink hot liquids or apply external heat during buccal administration. In addition, FBSF cannot readily be removed from or reapplied to the buccal mucosa. Transdermal absorption of fentanyl from the FBSF unit is substantially slower than transmucosal absorption.
Presented at American Society of Regional Anesthesia and Pain Medicine Annual Pain Medicine Meeting and Workshops 2008.

151E. Fentanyl buccal soluble film (FBSF) offers high absolute bioavailability and demonstrates faster absorption and greater exposure to fentanyl oral transmucosal fentanyl citrate (OTFC). *Niraj Vasisht, Ph.D.,*[1] Jeffrey G. Stark, Ph.D.,[2] Andrew L. Finn, Pharm.D.,[1] Larry N. Gever, Pharm.D.[3]; (1) BioDelivery Sciences International, Inc., Raleigh, NC; (2) CEDRA Corporation, Austin, TX; (3) Meda Pharmaceuticals, Inc., Somerset, NJ
PURPOSE: FBSF consists of a small, bilayered, water-soluble polymer film (BioErodible MucoAdhesive [BEMA]) that adheres to the buccal mucosa and rapidly delivers fentanyl into the systemic circulation. The objectives of these studies were to 1) understand the differences in the PK of fentanyl from the BEMA delivery system compared with oral transmucosal fentanyl citrate (OTFC); 2) evaluate the effect of system pH on the absorption of fentanyl from the BEMA system; 3) determine the absolute bioavailability of fentanyl from the BEMA delivery system; 4) determine the percentage of fentanyl dose that is absorbed through the buccal mucosa; and 5) compare the fentanyl plasma concentration profile after multiple BEMA films with an equivalent dose administered as a single film.
METHODS: In an open-label, four-period, crossover study (FEN-107), 12 healthy volunteers received single 800-µg doses of three FBSF formulations (pH 6.0, 7.25, and 8.5) and OTFC at 48-hour intervals. In another four-period crossover study (FEN-114), 12 healthy volunteers received single fentanyl doses (200 µg intravenously, 800 µg orally, and one 800-µg dose and four 200-µg FBSF doses) 72 hours apart. Serial blood samples were collected for 48 hours after each dose.
RESULTS: The FBSF formulations provided faster absorption, higher maximum plasma concentrations, and greater systemic fentanyl exposure compared with OTFC; FBSF pH 7.25 offered the best profile with a 62% higher C_{max} and 46% higher AUC_{0-24}. Absolute bioavailability of fentanyl was 71% for both single (800 µg) and multiunit (4 × 200 µg) FBSF; the two regimens were bioequivalent based on C_{max} and AUC. An estimated 51% of the FBSF dose was absorbed buccally.
CONCLUSIONS: Plasma fentanyl concentrations were greater and observed earlier with FBSF than with OTFC. FBSF delivers a high percentage of the fentanyl dose through the buccal mucosa, resulting in high absolute bioavailability.
Presented at World Institute of Pain 5th World Pain Congress, New York, NY, March 13–16, 2009.

152. A retrospective review of the effect of fentanyl patch on postoperative pain management in orthopedic surgery. *Sandy R. Liu, Pharm.D.*, Jeff Nemeth, Pharm.D., MPA, CACP; Englewood Hospital and Medical Center, Englewood, NJ
PURPOSE: This retrospective review investigated the effect of preoperative fentanyl patch administration on postoperative 72-hour cumulative opioid use, pain score, and adverse effects. The study also evaluated the extent of fentanyl patch documentation in patient chart.
METHODS: Medical records of total hip or knee arthroplasty cases from February 2006 to March 2009 were reviewed. The comparison group included patients who received standard postoperative patient-controlled-anesthesia (PCA) and oral opioid regimens; the fentanyl group included those who received an additional fentanyl patch 25 µg/hour preoperatively. Within the postoperative 72-hour period, data on daily opioid use, total morphine PCA use, pain score (0–10), adverse reactions, and fentanyl patch documentation were collected.
RESULTS: Fifty-four patients were reviewed. Average 72-hour cumulative opioid use (in morphine equivalents) was 87.5 mg in the fentanyl group (n=25) and 85.2 mg in the comparison group (n=29). The fentanyl group used 49.5 mg of morphine PCA on average, compared with 44.7 mg used by the comparison group. The fentanyl group had higher pain scores (fentanyl group, 4.6; comparison group, 4.1) and more nausea and vomiting (fentanyl group, 67%; comparison group, 36%). Respiratory depression occurred in three patients from the comparison group. The site of patch application was documented in four charts, but none had documentation regarding daily checks and removal of the patch.
CONCLUSIONS: The study found no reduction in postoperative

opioid use when patients are given a fentanyl patch preoperatively. Considering the adverse effects associated with the fentanyl patch, its utility in the surgical setting remains unclear; however, there is a need for standardized documentation of application site, daily checks, and removal of the patch.

Pediatrics

153E. The safety of the anti-histamine bepotastine besilate ophthalmic solution in a healthy pediatric population from ten to seventeen years of age. Eugene E. Protzko, M.D.,[1] Jon I. Williams, Ph.D.,[2] *James A. Gow, M.D.,*[2] Paul J. Gomes, M.D.,[3] Mark B. Abelson, M.D.,[3] Timothy R. McNamara, Pharm.D.[2]; (1) Seidenberg-Protzko Eye Associates, Bel Air, MD; (2) ISTA Pharmaceuticals, Inc., Irvine, CA; (3) ORA Clinical Research & Development, Inc., North Andover, MA

PURPOSE: Bepotastine besilate ophthalmic solution 1.5% is an antiallergic medication under investigation in the United States with selective histamine H_1 receptor antagonistic action, stabilization of mast cell function, and inhibitory action on eosinophilic infiltration to inflammatory sites. The purpose of this clinical trial was to evaluate the safety of bepotastine besilate ophthalmic solution 1.5% dosed twice daily in a healthy pediatric population from age 10 to 17 years.

METHODS: The clinical trial randomization was at a ratio of 2:1 (active to vehicle). The clinical trial was a multicenter, randomized, masked, 6-week safety study involving four study visits with two treatment groups, bepotastine besilate ophthalmic solution 1.5% and placebo. Pediatric subjects as young as 3 years represented around 15% of the 861 enrolled subjects. Both investigational products were dosed twice daily, and dosing adherence was monitored with dosing diaries. The number of healthy subjects from 10 to 17 years old was distributed between bepotastine ophthalmic solution 1.5% (n=40) and placebo (n=15).

RESULTS: All enrolled pediatric subjects completed the study. The frequency of total adverse events (22.5% for bepotastine besilate ophthalmic solution 1.5%, 20.0% for placebo) and the absolute incidence of ocular adverse events (one bepotastine besilate ophthalmic solution 1.5% subject, two placebo subjects) in subjects from 10 to 17 years old were similar for both treatment groups. There also was no difference between treatment groups in this age range in IOP ($p>0.65$), visual acuity ($p>0.73$), or comfort ($p>0.48$). No severe adverse events were reported during the clinical trial.

CONCLUSIONS: Bepotastine besilate ophthalmic solution 1.5% dosed twice daily for 6 weeks was safe with minimal adverse events in a healthy pediatric population from 10 to 17 years old.

Presented at Proceedings of the 81st Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, Ft. Lauderdale, FL, May 3–7, 2009.

154E. Recombinant human hyaluronidase-facilitated subcutaneous versus intravenous fluid administration for rehydration of infants and children. *George Maher, D.O., FAAP, FACOP, CPI,*[1] Sharon E. Mace, M.D., FACEP, FAAP,[2] Barry Hahn, M.D., FACEP,[3] George Harb, M.D., MPH[4]; (1) Memorial Children's Hospital, South Bend, IN; (2) Cleveland Clinic, Cleveland, OH; (3) Staten Island University Hospital, Staten Island, NY; (4) Baxter Healthcare Corporation, New Providence, NJ

PURPOSE: The Increased Flow Utilizing Subcutaneously Enabled Pediatric Rehydration Study II (INFUSE II) compares efficacy and safety of recombinant human hyaluronidase (rHuPH20)-facilitated subcutaneous fluid administration with the intravenous route in infants and children with mild to moderate dehydration.

METHODS: In this phase 4, open-label, randomized, stratified study, patients are children (aged 1 month to less than 3 years) with mild to moderate dehydration (Gorelick scores 1–6). Patients are randomized to receive rehydration therapy—20 mL/kg of isotonic fluid over 1 hour and additional fluid as needed until deemed clinically rehydrated up to 72 hours—by rHuPH20-facilitated subcutaneous or intravenous administration. One milliliter (150 U) of rHuPH20 is administered subcutaneously, immediately followed by subcutaneous isotonic fluids. The primary study end point is total fluid volume administered at a single infusion site. Secondary end points include percent successfully hydrated, total volume infused, and safety and provider ease of use assessments.

RESULTS: Interim analysis was conducted on 41 patients (mean age, 1.6 years). Baseline Gorelick score indicated mild dehydration in 45% versus 71% and moderate in 55% versus 29% in subcutaneous versus intravenous groups, respectively. Least-squares mean (SD) for total volume, adjusted for infusion duration, was 466 (176.1) mL for subcutaneous versus 429 (175.9) mL for intravenous. Mean total volume (standard deviation [SD]) infused subcutaneously at a single site was 329.4 (216.7) mL versus 560.2 (799.4) mL intravenously. At discharge, more patients were successfully rehydrated by rHuPH20-facilitated subcutaneous (95%) versus intravenous (67%). Both routes of infusion were generally well tolerated; 100% of providers considered subcutaneous administration easy to use versus 67% intravenous.

CONCLUSIONS: Interim results suggest rHuPH20-facilitated subcutaneous infusion is safe and well tolerated, resulting in a higher percentage of patients successfully rehydrated versus intravenous infusion.

The abstract will be presented at the following meetings: ACEP (American College of Emergency Physicians) Boston, MA, October 5–8, 2009; ENA Emergency Nurses Association, Baltimore, MD, October 7–10, 2009.

155E. Association between recent and future asthma exacerbations in pediatric patients with severe or difficult-to-treat asthma. *Tmirah Haselkorn, Ph.D.,*[1] Jim E. Fish, M.D.,[1] Marc Massanari, Pharm.D.[2]; (1) Genentech, Inc., South San Francisco, CA; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ

PURPOSE: To investigate whether pediatric patients with severe or difficult-to-treat asthma with a recent severe asthma exacerbation (RSE) are at risk of future severe exacerbations (FSEs).

METHODS: Pediatric patients (age, 6–11 years) in the TENOR 3-year observational study were assessed. An RSE was defined as either an overnight hospitalization or emergency department (ED) visit in the 3 months before baseline; an FSE was defined as an overnight hospitalization, ED visit, or death between month 6 and month 36 visits. A secondary analysis examined steroid bursts as an independent predictor and outcome. Generalized estimating equations repeated-measures logistic regression models were used to assess risk of future exacerbations adjusting for demographics, clinical variables, asthma severity, and control.

RESULTS: Compared with patients without an RSE, patients with an RSE were more than 3 times (OR = 3.8, 95% CI: 2.7, 5.4) more likely to experience an FSE. The association persisted after adjusting for demographic and clinical variables (OR = 3.1, 95% CI: 2.2, 4.4), asthma severity (OR = 3.4, 95% CI: 2.4, 4.8), and asthma control (OR = 4.5, 95% CI: 3.1, 7.0). Patients with a recent steroid burst were more than 2 times (OR = 2.8, 95% CI: 2.2, 3.7) more likely to experience a future steroid burst after adjusting for demographic and clinical variables (OR = 2.6, 95% CI: 2.0, 3.4).

CONCLUSIONS: RSEs are an independent predictor of FSEs in pediatric patients with severe or difficult-to-treat asthma and should be considered during clinical assessment. Physician awareness of patients' recent exacerbation status and response to the occurrence can reduce the risk of repeat episodes.

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156E. Add-on omalizumab significantly reduces exacerbation rates in children with inadequately controlled moderate-severe allergic (IgE-mediated) asthma. *Henry Milgrom, M.D.,*[1] Richard L. Wasserman, M.D., Ph.D.,[2] Angel Fowler-Taylor, M.D.,[3] Carlos Fernandez Vidaurre, M.D.,[3] M. Blogg, M.D.,[4] Howard Fox, M.D.[4]; (1) University of Colorado Health Sciences Center, Denver, CO; (2) Dallas Allergy Immunology, Dallas, TX; (3) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (4) Novartis Horsham Research Centre, Horsham, United Kingdom

PURPOSE: Omalizumab (OMA) is currently approved for the treatment of adults and adolescents (12 years and older) with uncontrolled moderate-severe allergic (IgE mediated) asthma. This

large Phase III clinical trial examined the efficacy of OMA in children with inadequately controlled moderate-severe allergic (IgE mediated) asthma.
METHODS: A randomized, double-blind, placebo (PBO)-controlled study enrolled children (6–11 years) with perennial allergen sensitivity and inadequately controlled moderate-severe (NHLBI 1997, NAEPP 2002) asthma despite use of maintenance inhaled corticosteroids (ICS; fluticasone 200 µg/day or more or equivalent) with or without other controller medications. Children received add-on OMA (75–375 mg subcutaneously every 2 or every 4 weeks) or PBO for 52 weeks (24-week fixed-steroid phase and then a 28-week adjustable-steroid phase). The rate of clinically significant asthma exacerbations (worsening of symptoms requiring doubling of baseline ICS dose and/or systemic steroids for 3 days or more) over 24 and 52 weeks was analyzed.
RESULTS: Six hundred twenty-seven patients were randomized, and 576 patients met efficacy evaluation criteria (OMA, n=384; PBO, n=192). Mean baseline ICS dose was 515 µg/day of fluticasone. Compared with PBO, OMA reduced the exacerbation rate per treatment period by 31% during the 24-week fixed-steroid phase (0.45 vs. 0.64, RR [95% CI] 0.69 [0.53, 0.90], p=0.007) and by 43% during the 52-week treatment phase (0.78 vs. 1.36, RR [95% CI] 0.57 [0.45, 0.73], p<0.001).
CONCLUSIONS: Add-on OMA reduces the rate of clinically significant asthma exacerbations in children (6–12 years old) with inadequately controlled allergic (IgE mediated) asthma despite ICS. This exacerbation reduction is consistent with previous studies in adolescents/adults.
Milgrom H, Fink J, Fowler-Taylor A, et al. Safety of omalizumab in children with inadequately controlled moderate-to-severe allergic (IgE-mediated) asthma. Poster presented at American Thoracic Society (ATS) International Conference, San Diego, CA, May 15–20, 2009.

157. Pharmacokinetic and therapeutic evaluation of two doses of aminophylline administered as multiple intermittent infusions to Iranian premature neonates. *Afsaneh Vazin, Pharm.D.,*[1] Mohammad Moslehi, Pharm.D.,[1] Mehrdad Hamidi, Ph.D.,[1] Narjes Phishva, M.D.[2]; (1) Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran; (2) Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
PURPOSE: Pharmacokinetic parameters of theophylline in Iranian premature neonates and their relationship with clinical response.
METHODS: Sixty-eight patients were included once a decision to administer aminophylline was made. All patients received 5 mg/kg as the loading dose. They were then divided randomly into two groups; the first group received 1 mg/kg of aminophylline, and the second group received 2 mg/kg every 8 hours. One blood sample was taken just before the 11th dose.
RESULTS: Clinical response did not show a significant difference between the two groups. The length of hospitalization in the second group (2 mg/kg/8 hours) was less than in first group.
CONCLUSIONS: Based on clinical and pharmacokinetic results, both dosing regimens could be administered in Iranian neonates safely; however, the single advantage of the 2-mg/kg every-8-hour administration is its shorter length of hospitalization.

158. Duration of neonatal ICU stay does not increase with longer phototherapy for hyperbilirubinemia within three weeks. *Zon-Min Lee Sr., master*; Department of Pharmacy, Chang Gung Memorial Hospital, Kaohsiung, Kaohsiung, Taiwan
PURPOSE: Neonatal hyperbilirubinemia can be physiologic and pathologic and frequently is a consequence of faster erythrocyte (RBC) hemolysis. If jaundice persists beyond age 3 weeks, measurement of total and direct-reacting bilirubin is mandatory to distinguish pathologic conditions; however, whether longer phototherapy for less than 3 weeks is related to duration of ICU stay caused by more severe disease is still unknown.
METHODS: To determine whether longer phototherapy for hyperbilirubinemia leads to longer neonatal ICU stay because of physiologic and pathologic causes. A total of 375 neonates undergoing phototherapy for less than 3 weeks were included in this study, beginning December 1, 2007, and going to May 31, 2009; birth weight ranged from 605 to 4150 g. Neonates were divided into three groups (less than 1500 g: 78 [20.8%] of 375 neonates; 1501–2500 g: 186 [49.6%] of 375; more than 2500 g: 111 [29.6%] of 375).
RESULTS: The results showed no significant relationship between length of phototherapy and duration of ICU stay, p=0.453 (partial correlation).
CONCLUSION: Longer use of phototherapy for neonatal hyperbilirubinemia for less than 3 weeks is not necessarily caused by more severe diseases, leading to longer neonatal ICU stay.

Pharmacoeconomics/Outcomes

159. Economic impact of immune mediated coagulopathy in the post-operative patient. *M. Scot Maxon, Pharm.D.*, Gerald Engley, Pharm.D., Karen Wisont, M.S., Tony Russell, Ph.D.; ZymoGenetics, Seattle, WA
PURPOSE: Bovine thrombin–containing topical hemostatic preparations have occasionally been associated with immune-mediated coagulopathy (IMC) after patient exposure; however, the costs associated with IMC have not been previously described. The objectives of this study were to identify quantifiable cost drivers in the relevant published literature and construct an incremental cost model to estimate the economic impact of a case of bovine thrombin–associated IMC.
METHODS: A MEDLINE search was conducted to identify case reports describing bovine thrombin–associated IMC published between 1989 and 2008. Medical resources used to manage IMC-associated sequelae were identified. When available, quantifiable resource use data were extracted from the literature. Patient cases were classified as "nonbleeding" or "bleeding" to better categorize the range of resources used. Median costs for resources commonly used to manage IMC were determined using published cost data. The incremental cost for nonbleeding and bleeding patients was estimated from a summation of the median quantifiable cost drivers.
RESULTS: A total of 27 published reports representing 46 patient cases met the inclusion criteria. Of these reports, 29 cases (14 nonbleeding, 15 bleeding) included quantitative information on health care resources used to manage IMC. Commonly described cost drivers included extended length of stay, blood product transfusion, and drug therapy (e.g., intravenous immune globulin). The estimated incremental costs of managing IMC were $54,666 (range, $16,111–121,558) and $93,961 (range, $36,276–154,802) for nonbleeding and bleeding patients, respectively.
CONCLUSIONS: The economic impact of bovine thrombin–associated IMC may vary significantly based on the wide range of clinical manifestations. Despite the variation in associated sequelae, IMC may result in extensive resource use and therefore increased cost for a given patient and to a health care system.

160E. Clinical and economic outcomes in cancer chemotherapy patients initiated on erythropoietic stimulating agents (ESAs) at hemoglobin (Hb) levels < 10 g/dL. Tanya Burton, Ph.D.,[1] Kay Larholt, ScD,[1] Elizabeth Apgar, MPH,[1] Chris L. Pashos, Ph.D.,[1] *R. Scott McKenzie, M.D.,*[2] Catherine T. Piech, MBA[2]; (1) Abt Bio-Pharma Solutions, Inc., Lexington, MA; (2) Centocor Ortho Biotech Services, LLC, Horsham, PA
PURPOSE: Recent changes to ESA prescribing information recommend initiation at hemoglobin concentrations less than 10 g/dL in patients undergoing cancer chemotherapy. Real-world clinical and economic outcomes data associated with this initiation range for the two FDA-approved ESAs for this population (epoetin alfa [EPO] and darbepoetin alfa [DARB]) are sparse.
METHODS: Data collected between December 2003 and September 2008 from 61 U.S. oncology clinics from the Dosing and Outcomes Study of Erythropoietic Stimulating Therapies (D.O.S.E.) registry were assessed. Patients were included if they were initiated on ESAs at baseline (BL) hemoglobin less than 10 g/dL, age 18 years and older, and received two or more doses of either EPO or DARB. Outcomes assessed included transfusion use, cumulative ESA doses, dose ratio (cumulative dose EPO:DARB) and ESA cost (based on

cumulative ESA dose and December 2008 wholesale acquisition cost: EPO $13.77/1000 U, DARB $4.818/µg).
RESULTS: Five hundred forty-five patients (237 EPO, 308 DARB) were included. BL characteristics were similar between treatment groups with respect to age, weight, cancer type, and hemoglobin. The mean administered dose was 42,610 U in the EPO group and 259 µg in the DARB group with treatment intervals of 11.6 and 19.4 days, respectively. Mean treatment duration was similar between groups (about 65 days, p=0.34). The proportion of patients transfused was similar between groups (about 30%, p=0.70). Mean cumulative administered dose was 318,918 U for EPO and 1261 µg for DARB, corresponding to a dose ratio of 253:1 (U EPO:µg DARB). ESA cost was significantly lower in the EPO group compared with the DARB group (EPO, $4392; DARB, $6075; p<0.001).
CONCLUSIONS: In patients undergoing cancer chemotherapy with hemoglobin values less than 10 g/dL before ESA initiation, transfusion use was similar between groups; however, ESA costs were 28% lower in the EPO group than in the DARB group. These ESA-associated outcomes and cost data are informative to stakeholders treating patients undergoing cancer chemotherapy.
Abstract published in Value in Health 2009;12:A37 (Abstr PCN7). Poster presented at the International Society for Pharmacoeconomics and Outcomes Research 14th Annual International Meeting, Orlando, FL, May 16–20, 2009.

161. Relationship between daily dosing frequency, compliance, and healthcare resource utilization: evidence from the treatment of chronic obstructive pulmonary disease (COPD). Edmond L. Toy, Ph.D.,[1] Nicolas U. Beaulieu, M.A.,[2] Joshua M. McHale, MPH,[2] Timothy R. Welland, B.A.,[1] Craig A. Plauschinat, Pharm.D., MPH,[3] Andrine Swensen, Ph.D., M.S.,[3] *Mei-Sheng Duh, MPH, ScD*[2]; (1) Analysis Group, Inc., Lakewood, CO; (2) Analysis Group, Inc., Boston, MA; (3) Novartis Pharmaceuticals Corporation, East Hanover, NJ
PURPOSE: To assess the relationship between daily dosing frequency (DDF) of COPD pharmacotherapies and treatment adherence and to estimate the effect of adherence on health care resource use.
METHODS: Patients with COPD were identified (ICD-9 491.XX, 492.XX, 493.2X, and 496.XX) using an administrative claims database covering 8 million privately insured lives (1999–2006). Patients were stratified on the basis of the recommended DDF (once daily, twice daily, 3 times/day, or 4 times/day) of their first COPD drug claim (index) post-COPD diagnosis. Continuous enrollment was required for 6 months before and 12 months after the index date. Comparisons of baseline demographics between groups were conducted using the Wilcoxon test for continuous outcomes and the χ^2 test for categoric outcomes. Adherence was measured using proportion of days covered (PDC). Health care resource use outcomes included inpatient days and medical visits (inpatient, outpatient, and emergency department). A multivariate negative binomial regression model assessed the relationship between adherence and 1-year health care resource use controlling for demographics, comorbidities, and baseline health care resource use.
RESULTS: Sample sizes ranged from 3678 (once daily) to 25,011 (twice daily). Adherence was strongly correlated with dosing frequency: PDCs for once-daily, twice-daily, 3 times/day, and 4 times/day patients were 43.3%, 37.0%, 30.2%, and 23.0%, respectively (p<0.001 for comparisons between QD and other dosing categories). Multivariate analysis showed that 1-year adherence was strongly correlated with health care resource use. For 1000 patients with COPD, a 5-percentage point increase in PDC reduced the number of inpatient visits by 30, hospital inpatient days by 190 days, and emergency department visits by 10; the estimated number of outpatient visits increased by 30 (p<0.001 for all comparisons).
CONCLUSIONS: Patients with COPD who initiated treatment with QD dosing had significantly higher adherence than those with more frequent dosing. Patients with higher adherence incurred less hospital- and emergency department–related health care resource use.

162. A cost-efficacy analysis of certolizumab and infliximab in the treatment of rheumatoid arthritis. *Boxiong Tang, M.D., Ph.D.*, Chureen T. Carter, Pharm.D., M.S., R. Scott McKenzie, M.D., Catherine T. Piech, MBA; Centocor Ortho Biotech Services, LLC, Horsham, PA
PURPOSE: To estimate and compare the cost-efficacy of antitumor necrosis factors certolizumab pegol (CTP) and infliximab (IFX), both combined with methotrexate (MTX), in the treatment of rheumatoid arthritis (RA).
METHODS: Control (MTX)-adjusted mean changes in erosion score (ES), joint space narrowing (JSN) score, and total Sharp score (TSS) from baseline to 12 months were used as efficacy measures. Annual costs were calculated based on May 2009 Wholesale Acquisition Cost and labeled dosing. CTP costs were based on 15 injections of 400 mg (assuming week 0, 2, and 4 loading doses and maintenance dosing of 400 mg every 4 weeks). No infusion costs were included for CTP. IFX cost was calculated based on initial dosing of 3 mg/kg for a 75-kg patient with eight infusions per year (assuming week 0, 2, and 6 loading doses with every-8-week maintenance infusions, dose increase to 5 mg/kg after 6 months, vial wastage, and infusion fees of $203/infusion). Cost of adverse events was not included in the analysis. Cost-efficacy ratio (CER) was defined as the annual treatment costs divided by gains in efficacy at 1 year, indicating the cost/unit end point improved.
RESULTS: Patient demographics were similar between the two clinical trials included in the analyses. The annual treatment costs of CTP and IFX were $21,510 and $18,557, respectively. The control-adjusted mean changes from baseline in ES, JSN, and TSS were –1.4, –1.0, and –2.4 for CTP and –3.80, –1.80, and –5.70 for IFX. The CERs were $15,364 (ES), $21,510 (JSN), and $8962 (TSS) for CTP and $4883 (ES), $10,309 (JSN), and $3255 (TSS) for IFX.
CONCLUSIONS: IFX had lower cost-efficacy ratios for improvements in ES, JSN, and TSS compared with CTP in the treatment of RA. Cost-effectiveness in clinical practice will depend on real-world use and the effectiveness achieved.

163E. Compliance, persistence, and outcomes in patients with Alzheimer disease treated with oral cholinesterase inhibitors. Francis Vekeman, M.A.,[1] Francois Laliberte, M.A.,[1] Kristijian Kahler, Ph.D., RPh,[2] Nikita Mode-Patel, Pharm.D.,[2] *Amit S. Kulkarni, Ph.D.,*[2] Mei Sheng Duh, MPH, ScD,[3] Patrick Lefebvre, M.A.[1]; (1) Groupe d'analyse, Ltée, Montreal, Quebec, Canada; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) Analysis Group, Inc., Boston, MA
PURPOSE: This study quantifies adherence and persistence rates of oral cholinesterase inhibitors (ChEIs) in patients with Alzheimer disease (AD) and assesses the health care cost associated with adherence to oral ChEIs.
METHODS: The MedStat MarketScan health insurance claims database from January 2004 to June 2008 was used. Patients with 9 or more months of continuous insurance coverage, newly initiated on oral ChEI (no use in prior 6 months), 3 or more months of follow-up, and one or more diagnosis of AD were included. Adherence was estimated using the medication possession ratio (MPR), calculated as the number of days of therapy divided by the observation period for each patient. Persistence was defined as continuous drug use without a gap of 30 days or more between medication refills at any time after treatment initiation. Proportion of adherent patients (MPR of 0.8 or more) and Kaplan-Meier rates of persistence were reported. Health care costs, stratified into outpatient, inpatient, and pharmacy costs, were assessed for adherent versus nonadherent patients during the first year of follow-up.
RESULTS: Of the 17,717 study patients, mean age was 81.0 years, and patients were observed for 546 days on average. Mean (SD) treatment exposure was 408 (347) days. During the first year of follow-up, mean (median) MPR and proportion of adherent patients were 0.67 (0.80) and 49.9%, respectively. Kaplan-Meier rates of persistence after 3, 6, 12, and 24 months of therapy were 66.5%, 52.6%, 36.1%, and 19.7%, respectively. Mean total health care costs were significantly lower by $2252 (14.6%; $13,218 vs. $15,470, p<0.0001) in adherent versus nonadherent patients (outpatient and inpatient services: $7420 vs. $11.771, p<0.0001; pharmacy costs: $5798 vs. $3699, p<0.0001, respectively).

CONCLUSIONS: Based on real-world data from a large cohort of AD patients initiated on ChEI, only 36% were persistent on therapy after the first year after ChEI treatment initiation. Adherence was associated with lower health care costs during the same period.
Accepted for presentation as poster at the International Conference on Alzheimer's Disease (ICAD), Vienna, Austria, July 11–16, 2009. Accepted for presentation as poster at the American Neurological Association 134th Annual Meeting, Baltimore, MD, October 2009.

164E. Emergent use of antipsychotic drugs in patients with Alzheimer's disease treated with rivastigmine versus donepezil: evidence from health claims data. Douglas Scharre, M.D., CMD,[1] Francis Vekeman, M.A.,[2] Patrick Lefebvre, M.A.,[2] Kristijian Kahler, Ph.D., RPh,[3] Nikita Mode-Patel, Pharm.D.,[3] *Amit S. Kulkarni, Ph.D.,*[3] Mei Sheng Duh, MPH, ScD[4]; (1) Ohio State University, Department of Neurology, Columbus, OH; (2) Groupe d'analyse, Montreal, Quebec, Canada; (3) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (4) Analysis Group, Inc., Boston, MA
PURPOSE: This study investigated whether treatment with rivastigmine was associated with less use of antipsychotics compared with treatment with donepezil.
METHODS: Combined claims analysis from the MedStat MarketScan database, January 2004–December 2006, and the Ingenix Impact National Managed Care database, October 2002–September 2007, was conducted. Patients included had continuous insurance coverage, had one or more diagnoses of AD or dementia with Lewy bodies (ICD-9 331.0, 331.82, 290.0-290.3, 294.10-294.11), and were newly initiated on either rivastigmine or donepezil after the first AD claim. Patients using memantine or receiving antipsychotics in the time interval of 180 days or more before and 14 days after the first rivastigmine or donepezil drug dispensing were excluded. Both Kaplan-Meier (KM) and multivariate Cox regression analyses were conducted to compare the time to first antipsychotic drug dispensing between the rivastigmine and donepezil groups.
RESULTS: A total of 966 patients receiving rivastigmine and 12,845 patients receiving donepezil formed the study population. The donepezil group had a greater proportion of women (60.0% vs. 54.7%; p=0.0011). The KM analysis showed that 64 (6.6%) rivastigmine and 994 (7.7%) donepezil patients received antipsychotic medications (log-rank p=0.1932). Multivariate adjustment showed that rivastigmine was associated with a statistically significant reduction in emergent use of antipsychotic drugs by 26% relative to donepezil (hazard ratio, 0.74; p=0.0496). Patients receiving effective doses of either drug had lower risk of antipsychotic use (hazard ratio, rivastigmine: 0.49; donepezil: 0.66). Older age, lower drug dose, and baseline depression and neuropsychiatric symptoms were associated with significantly increased likelihood of antipsychotic drug use.
CONCLUSIONS: Based on real-world data from a large cohort of antipsychotic-naïve patients with AD, rivastigmine was found to be associated with a significant reduction in the emergent use of antipsychotic drugs, compared with donepezil.
Presented as a poster at the Academy of Managed Care Pharmacy 21st Annual Meeting and Showcase, Orlando, FL, April 15–18, 2009.

165. Adherence to aliskiren in a real-world environment. Feng Zeng, Ph.D.,[1] Kristin Hanson, Pharm.D.,[2] Sara Gao, Ph.D.,[1] Bimal V. Patel, Pharm.D., M.S.,[1] *Helen Lau, M.S.*[2]; (1) MedImpact Healthcare Systems, San Diego, CA; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ
PURPOSE: Adherence to medications is important to achieve blood pressure control. Objectives were to evaluate adherence to aliskiren in a real-world environment.
METHODS: A retrospective data analysis was conducted using data from a national pharmacy benefit management company. Patients included in the study were 18 years or older, had two or more claims for aliskiren, and were continuously enrolled in the same health plan 12 months or more before and 12 months or more after initiating aliskiren between April 2007 and October 2008. Adherence was evaluated using a medication possession ratio (MPR) calculated as the total days of supply for all claims, excluding the last claim filled, divided by the number of days between the first and last claims. Patients with an MPR of 0.8 or more were considered adherent. A logistic regression evaluated factors that influence adherence to aliskiren. Covariates included age, sex, comorbidities, geographic region, copay, insurance type, and antihypertensive use the previous year.
RESULTS: A total of 1329 patients (52.3% female) were identified with mean age of 63.5 years (SD, 13.1). On average, patients received 2.8 antihypertensive medication classes (SD = 1.6) the year before initiating aliskiren, with 77.6% of patients using two or more antihypertensive classes. A total of 967 patients (72.9%) were adherent. Regression results showed that, compared with patients with low copays ($0–$5; n=260), patients with higher copays ($50 or above; n=111) were less adherent to aliskiren (OR = 0.26; p<0.001). Patients aged 40–49 years (n=139) were also less adherent relative to those 80 years and older (n=169) (OR = 0.60; p=0.024). Patients who used antidepressants (n=278) were relatively less adherent (OR = 0.65, p=0.003), whereas patients receiving dyslipidemia medications (n=779) were more adherent (OR = 1.31; p=0.034) with aliskiren.
CONCLUSIONS: Most patients receiving aliskiren were adherent; however, copay was an important factor affecting adherence to therapy. Additional research is needed to understand the clinical implications of these observations.

166. Risk of osteoporotic fracture and warfarin exposure: a case-control study. *Kristine B. Ebright, Pharm.D., BCPS*, Michele Spence, Ph.D.; Kaiser Permanente Drug Information Services, Downey, CA
PURPOSE: This study compared the risk of first osteoporotic fracture by warfarin use.
METHODS: A retrospective case-control study of Kaiser Permanente, Southern California patients 50 years and older using data from electronic databases from 2003 to 2007 was performed. Within the base population, cases were identified using ICD9 codes for new osteoporotic fracture (index date) and were matched to controls in a 1:4 ratio. Cases and controls were matched by age and gender and had to be alive and enrolled on the index date. Conditional logistic regression was performed to calculate the odds ratio of osteoporotic fracture risk by warfarin exposure. Short-term warfarin exposure was defined as total days' supply of 90 days or more and less than 1 year before index date. Long-term exposure was defined as total days' supply of 1 year or more before the index date. Odds ratios were adjusted for medications and disease states associated with an impact on fracture risk.
RESULTS: A total of 11,283 cases and 37,307 controls were identified. The odds ratio of patients with short-term warfarin exposure was 1.21 (95% CI: 1.00–1.47; p=0.06) compared with patients without a history of warfarin exposure. The odds ratio of patients with long-term warfarin exposure was 1.19 (95% CI: 1.02–1.40; p=0.03) compared with patients without a history of warfarin exposure.
CONCLUSIONS: This retrospective case-control study provides evidence that use of warfarin for 1 year or more in patients 50 years and older is associated with an increased risk of osteoporotic fracture compared with those without a history of warfarin use. Prior studies demonstrated similar conclusions. These results have the potential to positively affect patient care and highlight an association between a medication not usually associated with fractures and osteoporotic fracture risk.

167. Blood-stream infections and their attributable length of stay: does delivery of parenteral nutrition via multi-chamber bag have any impact?
Todd W. Canada, Pharm.D., BCNSP,[1] Robin S. Turpin, Ph.D.,[2] Katie Williams, MPH,[3] Shane Scott, Pharm.D.[2]; (1) University of Texas M.D. Anderson Cancer Center, Houston, TX; (2) Baxter Healthcare, Deerfield, IL; (3) United BioSource, Lexington, MA
PURPOSE: Bloodstream infections (BSIs) with parenteral nutrition (PN) are reportedly 7.2–39%, and BSI-attributable length of stay (LOS) ranges from 6.1 to 13.5 days. Our objective was to compare BSI rates and LOS for patients receiving PN by conventional compounding (COM) versus multichambered bag (MCB).

METHODS: A retrospective analysis of adult patients (18–89 years; n=68,984) in Premier's U.S. database (196 hospitals) receiving PN between January 2005 and December 2007 was conducted. Patients received MCB (two-chamber bag with dextrose/amino acids; fat emulsion and micronutrients added separately; n=4669) or COM PN (n=64,315). Logistic regression examined the impact of hospital and patient characteristics (age, diagnosis, comorbidities, surgeries, ICU stay, and PN days) on BSI rates determined from ICD-9 coding. Linear regression estimated BSI-attributable LOS.
RESULTS: Most PN patients were surgical (85.7%) and older than 55 years (73.3%). COM PN patients were more likely to have longer mean ICU (6.3 vs. 3.4) and hospital LOS (19.1 vs. 15 days) while receiving more days of PN (8.1 vs. 5.3) compared with MCB ($p<0.001$). The unadjusted BSI rate was 52% higher for COM than for MCB PN (26.6% vs. 17.5%). Using logistic regression, the adjusted BSI rate was 26% higher for COM versus MCB PN (25.9% vs. 20.6%; OR = 1.35; 95% CI: 1.25–1.45). BSI-attributable LOS was 6.0 days longer ($p<0.001$).
CONCLUSIONS: Compounded PN had a higher BSI rate and longer LOS than MCB PN, possibly from greater patient acuity. After accounting for baseline variables, the adjusted BSI rate was significantly lower for MCB than for COM PN, with attributable LOS shortened by 6 days.

168. Adherence and persistence of antiplatelet therapy following ischemic stroke/TIA hospitalization. *Karina L. Berenson, MPH*, Elisabetta Malangone, M.S., Lee Stern, M.S., Roman Casiano, M.S.; Analytica International, New York, NY
PURPOSE: Evaluate use patterns of oral antiplatelet (clopidogrel or aspirin-dipyridamole ER) therapy and discontinuation after hospitalization for acute ischemic stroke (AIS)/transient ischemic attack (TIA) in a cohort of U.S. managed care patients.
METHODS: This retrospective cohort study used the claims data of patients with an initial hospitalization for AIS or TIA (defined by the following inpatient ICD-9 codes: 433.x1, 434.01, 434.11, 434.91, 436.xx, or 435.x) in PharMetrics, a large U.S. database of nationally representative managed care plans (1995–2008). Patients with a claim for clopidogrel or aspirin-dipyridamole ER after the hospitalization were identified. The mean and median medication possession ratio (MPR) and time to therapy discontinuation were computed. Multivariate models identified predictors of discontinuation of therapy while controlling for follow-up time.
RESULTS: Of the total 163,493 AIS/TIA patients identified, 29,397 (18%) had an antiplatelet prescription claim after discharge from the AIS/TIA hospitalization. Univariate analyses demonstrated that the population was highly adherent (MPR: mean, 0.9; median, 1.0). More than 50% of patients had an overall days' supply less than 6 months (clopidogrel: median, 180 days; aspirin-dipyridamole ER: median, 120 days). Multivariate analyses controlling for demographics and clinical characteristics demonstrated that patients initially treated with aspirin-dipyridamole ER after the AIS/TIA hospitalization were 30% more likely to discontinue treatment compared with those initially treated with clopidogrel (HR 1.32, [1.27, 1.37]).
CONCLUSION: Patients prescribed antiplatelet therapy after an AIS/TIA hospitalization have a high level of adherence to therapy; however, most do not continue therapy beyond 6 months. Patients initially treated with clopidogrel after the AIS/TIA hospitalization were more likely to continue treatment compared with those initially treated with aspirin-dipyridamole ER. Further research should examine reasons for antiplatelet discontinuation in this population and its impact on costs and outcomes.

169. Acquired coagulopathy in post-surgical patients: a pilot study to determine the impact on clinical and economic outcomes. *Emily Beth Devine, Pharm.D., Ph.D., MBA*,[1] Lingtak-Neander Chan, Pharm.D., BCNSP,[1] Joseph Babigumira, M.S., MBChB,[1] Henry Kao, Pharm.D.,[1] Troy Drysdale, Pharm.D.,[1] Dominic F. Reilly, M.D.,[2] Marguerite J. McNeely, M.D., MPH,[2] Sean D. Sullivan, Ph.D.[1]; (1) University of Washington, Department of Pharmacy, Seattle, WA; (2) University of Washington Department of Medicine, Seattle, WA
PURPOSE: This was a pilot study to 1) determine the clinical characteristics and outcomes of hospitalized surgical patients who developed coagulopathy and 2) assess resource use and the incremental cost associated with postoperative coagulopathy.
METHODS: Case-control design involving five categories of major surgical procedures (abdominal, cardiovascular, neurosurgery, orthopedic, and spine) performed in a 6-month period at a university-affiliated hospital. Coagulopathy was defined as two consecutive postoperative prothrombin time values or as activated thromboplastin time values 20% above upper normal limits without other established causes. Exclusion criteria were documented clotting factor disorders, cardiac arrest requiring cardiopulmonary resuscitation, coagulopathy developing within 72 hours of therapeutic hypothermia, or receiving treatment doses of antithrombotic therapy. Matched controls were identified using the ICD-9 codes of the index surgeries and demographics of case patients. Data collected included clinical characteristics and outcomes, management of coagulopathy, resource use, hospital costs, and Medicare-based physician reimbursements.
RESULTS: A total of 4784 patients underwent a qualifying index surgery. After applying inclusion/exclusion criteria, 23 confirmed cases of postoperative coagulopathy and 23 matched controls were identified. Patients with coagulopathy were more likely to require admission to the intensive care unit (ICU) (95% vs. 78%) and experienced longer median ICU and overall hospital length-of-stay (9 vs. 3 days and 26 vs. 7 days, respectively). Hospital mortality rate was higher in cases (21.7% vs. 0%). Average hospital cost per case was 2.5 times higher for cases than for controls ($108,723 vs. $43,616). Average physician reimbursement was 2.8 times higher for cases than for controls ($2686 vs. $937).
CONCLUSION: Postoperative coagulopathy was associated with prolonged ICU and hospital stay and decreased survival. Costs of caring for these cases were 2.5 times higher than for controls. Future research should include identifying risk factors and specific clinical indicators that may prevent this costly complication.

170. Cost and effectiveness analysis of rate versus rhythm control of atrial fibrillation in patients with heart failure. *Alexandra Perez, Pharm.D.*,[1] Daniel Touchette, Pharm.D., M.A.,[2] Robert J. DiDomenico, Pharm.D.,[2] Surrey M. Walton, Ph.D.[2]; (1) Nova Southeastern University, Ft. Lauderdale, FL; (2) University of Illinois at Chicago, Chicago, IL
PURPOSE: Coexistence of atrial fibrillation (AF) and heart failure (HF) has been shown to produce a worse prognosis than either condition alone. Rate control and rhythm control are two common treatment options; however, the relative cost-effectiveness of these options in this population is not known. The objective was to compare costs and effects of rate versus rhythm control of AF in HF.
METHODS: A Markov model was created to evaluate the cost-effectiveness of rate and rhythm control in a simulated cohort aged 65 with persistent/paroxysmal AF and HF or left ventricular dysfunction. Costs were measured in 2008 U.S. dollars and clinical outcomes in life-years, taking the third-party payer perspective (5% annual discount rate). Economic outcomes of interest were drug acquisition, AF and HF hospitalization, and severe adverse effect costs. Costs and transition probabilities were obtained from the most rigorous studies available (predefined criteria) identified in MEDLINE and EMBASE searches and references of published manuscripts. When cost data were not available from the literature, the Healthcare Cost and Utilization Project database was used. Initial treatment with rate-controlling drugs, followed by rhythm-controlling agents or ablation, was compared with initial treatment with rhythm-controlling agents followed by rate-controlling drugs or ablation. Crossover between rate- and rhythm-controlling drugs within strategies occurred if treatment failure, AF hospitalization, or severe adverse effects triggered discontinuation of the drugs. A probabilistic sensitivity analysis was also conducted.
RESULTS: In the base-case analysis, the average life expectancy per patient was 4.88 life-years for both strategies; the incremental lifetime cost of rhythm versus rate control as initial treatment was $6920 ($29,589 vs. $22,669 per patient per year). The same results were observed in the probabilistic sensitivity analysis.
CONCLUSION: Based on this cost and effectiveness analysis, rate control should be the initial treatment of AF in this population.

Pharmacoepidemiology

171. Differences in predictors of elevated vancomycin MIC among patients with MSSA and MRSA infections. *S. Lena Kang-Birken, Pharm.D.*; Santa Barbara Cottage Hospital, Santa Barbara, CA

PURPOSE: Recent emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) in community settings has driven vancomycin use. Consequently, there has been a surge of MRSA strains with increasing MICs of vancomycin (2 mg/L or more). Unfortunately, methicillin-sensitive *S. aureus* (MSSA) strains are beginning to show this trend. To date, predictors of elevated vancomycin MICs among MRSA infections have not been compared with those of MSSA-infected patients with high vancomycin MICs. The objectives were to describe the characteristics of patients infected with *S. aureus* with elevated vancomycin MICs and to compare the risk factors among patients with MRSA and MSSA infections.

METHODS: Electronic medical records were used to identify patients with positive *S. aureus* cultures between January 1, 2007, and December 31, 2008. Only patients with elevated vancomycin MICs (1.5 mg/L or more) were included in the data collection including demographics, comorbid conditions, hospitalization within 3 months, vancomycin exposure within the past 30 days, and microbiologic data. A Fisher exact test was performed to compare the predictive parameters between MSSA and MRSA groups. Multivariate analysis was performed to identify independent predictors.

RESULTS: Of the 1265 MSSA isolates, 17 (1.34%) exhibited elevated vancomycin MICs. In comparison, 51 (6.1%) isolates of 836 MRSA isolates exhibited vancomycin MICs of 1.5 mg/L or greater.

Parameters (%)	MSSA (n=17)	MRSA (n=51)
Age > 75 years	5 (29.4)	12 (23.5)
Comorbidities	10 (58.8)	36 (70.6)
History of hospitalization	4 (23.5)	37 (72.5)*
Prior vancomycin exposure	0 (0)	19 (37.2)*
CrCl < 30 mL/minute	2 (11.8)	24 (47.1)*
Dialysis	0 (0)	12 (23.5)*
Community acquired	8 (47.1)	26 (51.0)
Intensive care unit	4 (23.5)	10 (19.6)

*Statistically significant: p<0.05.

CONCLUSIONS: Elevated MICs of vancomycin were documented among MSSA and MRSA infections during 2007–2008. Recent hospitalization and vancomycin use, renal impairment, and dialysis were strong predictors of MRSA isolates with elevated vancomycin MICs in comparison to MSSA isolates.

Pharmacogenomics/Pharmacogenetics

172. UGT2B7 and ABCC2 polymorphisms modify mycophenolic acid pharmacokinetics in islet transplant patients: a preliminary report. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAHS,*[1] Marie-Odile Benoit-Biancamano, DMV, M.S., Ph.D. Candidate,[2] Lillian S.L. Ting, Ph.D., M.S., B.S.,[3] Mai Al-Khatib, M.S., BS(Pharm),[4] R. Jean Shapiro, M.D., FRCPC,[5] Nilufar Partovi, Pharm.D., BS(Pharm),[6] Chantal Guillemette, Ph.D.[7]; (1) University of British Columbia, Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada; (2) CHUQ Research Centre, Laval University, Quebec City, Quebec, Canada; (3) University of British Columbia, Vancouver, British Columbia, Canada; (4) University of British Columbia, Vancouver, British Columbia, Canada; (5) University of British Columbia, Vancouver General Hospital, Vancouver, British Columbia, Canada; (6) University of British Columbia and Vancouver General Hospital, Vancouver, British Columbia, Canada; (7) CHUL Research Center, Laval University, Quebec City, Quebec, Canada

PURPOSE: Mycophenolic acid (MPA) is the active moiety of mycophenolate mofetil (MMF), an immunosuppressant commonly used in transplantation. Metabolism of MPA to the phenolic (MPAG) and acyl (AcMPAG) glucuronides is mediated by UDP-glucuronosyltransferase enzymes (UGTs); multidrug resistance–associated protein 2 (MRP2/*ABCC2*) is also involved in the disposition of MPA. Although studied in other populations, to our knowledge, the contribution of *UGT* and *ABCC2* genetic polymorphisms to pharmacokinetic variability has not been investigated in islet transplant patients. Thus, the purpose of this preliminary study was to characterize *UGT* and *ABCC2* polymorphisms and their contribution to MPA pharmacokinetics in islet transplant recipients.

METHODS: Sixteen stable islet transplant recipients on steady-state MMF were recruited for a 12-hour pharmacokinetic analysis. MPA and its metabolites were quantified by high-performance liquid chromatography coupled with ultraviolet detection. Patients' genetic status was determined by direct sequencing of polymerase chain reaction products. The contribution of genetic and other factors (age, sex, albumin, and serum creatinine) was analyzed by stepwise multiple regression.

RESULTS: Despite the small number of patients, marked interindividual variability was observed in the exposure (AUC 0–12 hours) and MPA (range, 15.1–118.1 µg/hour/mL) and its metabolites, MPAG (220–2395 µg/hour/mL) and AcMPAG (0.5–20.4 µg/hour/mL). *UGT2B7**2/*2 (H268Y) patients presented a 70% increased exposure to MPAG (p=0.0482); this genetic variation contributed to 21% of the interpatient variability in MPAG AUC; age contributed to 47% of the variability. In addition, *ABCC2* codon 417 had a significant impact on AcMPAG exposure (p=0.0093) with a 64% contribution to interpatient variability in AcMPAG AUC; specifically, AcMPAG AUC was 6.4 ± 7.0 µg/hour/mL (A carriers) versus 3.9 ± 5.4 µg•hour/mL (GG carriers).

CONCLUSIONS: Significant variation of pharmacokinetic parameters for MPA and its metabolites is observed for islet transplant patients. Although preliminary data support genetic effects on MPA pharmacokinetics, future larger pharmacogenetic studies in relation to pharmacokinetics and clinical outcomes are warranted.

173. Pharmacogenetics of mycophenolate and UGT and ABCC2 polymorphisms in thoracic transplant recipients. Lillian S.L. Ting, Ph.D., M.S., B.S.,[1] Marie-Odile Benoit-Biancamano, DMV, M.S., Ph.D. Candidate,[2] Olivier Bernard, M.S., BS(Pharm),[3] K. Wayne Riggs, BS(Pharm), Ph.D.,[1] Chantal Guillemette, Ph.D.,[3] *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAHS*[4]; (1) University of British Columbia, Vancouver, British Columbia, Canada; (2) CHUQ Research Centre, Laval University, Quebec City, Quebec, Canada; (3) CHUL Research Center, Laval University, Quebec City, Quebec, Canada; (4) University of British Columbia, Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada

PURPOSE: Mycophenolic acid (MPA), the active metabolite of mycophenolate mofetil (MMF), is known for its wide interpatient variability in pharmacokinetics. Metabolism of MPA to the phenolic (MPAG) and acyl (AcMPAG) glucuronides is mediated by UGT enzymes, and multidrug resistance–associated protein 2 (MRP2/*ABCC2*) is also involved in their disposition. The purpose of this study was to assess contribution of *UGT* and *ABCC2* genetics to MPA pharmacokinetics (by multivariate analysis) and investigate the association of MPA pharmacokinetic parameters with clinical outcomes (using a Fisher exact test) in thoracic transplant recipients.

METHODS: After written informed consent and a steady-state MMF dose, 12-hour serial blood samples were obtained from 32 heart and 36 lung transplant recipients. Concentrations of MPA, free MPA, MPAG, and AcMPAG were determined by a validated high-performance liquid chromatography method with ultraviolet detection, and conventional dose-normalized pharmacokinetic parameters were determined by noncompartmental methods. Patient charts were reviewed for occurrences of rejection, infection, anemia, leucopenia, and gastrointestinal toxicities. More than 40 genetic polymorphisms in *UGT1A8, UGT1A9*, *UGT2B7*, and *ABCC2* genes were assessed by direct sequencing of polymerase chain reactions.

RESULTS: Substantially lower MPA pharmacokinetic exposure was observed in lung transplant recipients (compared with heart) and in patients taking cyclosporine (compared with tacrolimus). There was wide interpatient variability of MPA, MPAG, and AcMPAG pharmacokinetics, with coefficients of variation more than 50%. For

both transplant groups, comedication (cyclosporine) was associated with lower MPA C_{min}; *UGT2B7* variants 802T (*2a) and -138A (*2g) markedly modified AcMPAG exposure. High AcMPAG exposure (more than 50 µg/hour/mL) was associated with occurrences of infection and rejection, and high AcMPAG/MPA metabolic ratio (more than 2) was associated with occurrences of infection, anemia, and leucopenia.
CONCLUSIONS: *UGT2B7* is a promising gene candidate that may influence MPA pharmacokinetics clinically; however, larger clinical pharmacogenetic studies in thoracic transplant subpopulations are warranted to corroborate the role of AcMPAG and *UGT2B7* variants in optimizing mycophenolate therapy.

174. A survey on warfarin pharmacogenetic testing among anticoagulation providers. *Jaekyu Shin, Pharm.D.*, Maha Kadafour, Pharm.D., Roshanak Haugh, Pharm.D., Monica Posin, Pharm.D., Steven Kayser, Pharm.D.; University of California San Francisco, San Francisco, CA
PURPOSE: Pharmacogenetic testing of *CYP2C9* and *VKORC1* is recommended by the U.S. Food and Drug Administration to identify patients who may require lower initial warfarin doses. Anticoagulation providers are the primary users of the available tests, but their perception and knowledge of warfarin pharmacogenetic testing as well as barriers to testing are unknown. Our study was designed to 1) assess anticoagulation providers' perception and knowledge of warfarin pharmacogenetic testing and 2) identify barriers to using it in their clinical practice.
METHODS: An online survey was conducted of anticoagulation providers in North America. The survey consisted of 25 questions including 5 perception and 5 knowledge questions about warfarin pharmacogenetic testing. Participants were also asked to rank the three most significant barriers to implementing testing in their clinical practice. Correlation between sums of the perception and the knowledge scores was assessed by the Pearson correlation test. Logistic regression was used to identify variables that predict providers' accuracy of interpretation of test results.
RESULTS: Four hundred forty-eight anticoagulation providers participated in the survey. More than 60% were pharmacists. More than 40% of participants were undecided about the potential clinical benefits of warfarin pharmacogenetic testing. On average, providers correctly answered two of five knowledge questions. Sum of the knowledge score was uncorrelated with sum of the perception score. Self-confidence in interpreting test results was significantly associated with accuracy of the interpretation of the test results. The top three barriers to warfarin pharmacogenetic testing are inadequate literature evidence, impracticality of the testing (unavailability and turnaround time), and unproven applicability.
CONCLUSIONS: Our study suggests inadequate literature evidence influences anticoagulation providers' perceptions and use of warfarin pharmacogenetic testing in clinical practice. In addition, provider education on warfarin pharmacogenetics may be necessary for more widespread clinical use of the testing.

175. Apolipoprotein E genotype influences time to stable warfarin dosing in African Americans. *Christopher P. Butler, Pharm.D.,*[1] Shitalben R. Patel, M.S.,[1] Taimour Y. Langaee, Ph.D.,[2] Edith A. Nutescu, Pharm.D.,[1] Nancy L. Shapiro, Pharm.D.,[1] Larisa H. Cavallari, Pharm.D.[1]; (1) University of Illinois at Chicago, Chicago, IL; (2) University of Florida, Gainesville, FL
PURPOSE: We sought to determine whether the cytochrome P450 2C9 (*CYP2C9*), vitamin K oxidoreductase complex 1 (*VKORC1*), or apolipoprotein E genotypes (*APOEs)* influence time to reach stable warfarin dose in African Americans.
METHODS: A total of 75 warfarin-treated African Americans for whom data were available at the time of warfarin initiation were enrolled. A genetic sample and information on warfarin dose and INR values at each anticoagulation visit after warfarin initiation were collected. The association between genotype and time to reach stable dose, defined as the time to first INR that was within therapeutic range and remained in therapeutic range for 2 consecutive clinic visits, was examined.
RESULTS: Only three patients carried a *CYP2C9* variant; thus, no further analysis was done with the *CYP2C9* genotype. Most patients required 3 months or longer to reach stable dose. Twenty-nine percent of patients required longer than 6 months to reach stable dosing. Both *VKORC1* and *APOE* genotype frequencies were compared between patients reaching a stable dose within 90 days and those requiring longer than 90 days, as shown in the table.

Genotype	Time to stable dose < 90 days (n=35)	Time to stable dose > 90 days (n=40)
VKORC1 –1639AG	0.20	0.125
VKORC1 –1639GG	0.80	0.875
APOE ε3/ε3	0.31	0.625
APOE ε2 or ε4	0.69	0.375

The *VKORC1* genotype was not associated with time to stable dose; however, the *APOE* ε3/ε3 genotype was associated with longer time to reach stable dose (p<0.01).
CONCLUSIONS: Individuals with the wild-type *APOE* ε3/ε3 genotype required longer to reach stable dose than patients with a variant ε2 or ε4 allele. Given the associations between *APOE* genotype and hepatic uptake of vitamin K, our data suggest that patients with the *APOE* ε3/ε3 genotype are more susceptible to anticoagulation instability during warfarin initiation, possibly because of dietary changes.

176. Cyclooxygenase-2 and endothelial nitric oxide synthase polymorphisms and endothelial function in coronary artery disease patients. *Kyle J. Ellis, Pharm.D.,*[1] Almasa Bass, Pharm.D.,[1] Katherine N. Theken, Pharm.D.,[1] Melissa Caughey, RVT,[2] Lauranell H. Burch, Ph.D.,[3] Nancy J. Brown, M.D.,[4] Darryl C. Zeldin, M.D.,[3] 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-Chapel Hill, Chapel Hill, NC; (2) School of Medicine, UNC-Chapel Hill, Chapel Hill, NC; (3) National Institute of Environmental Health Sciences, Research Triangle Park, NC; (4) School of Medicine, Vanderbilt University, Nashville, TN
PURPOSE: Cyclooxygenase (COX)-derived prostaglandins and nitric oxide (NO) regulate endothelial function. Endothelial dysfunction contributes to the progression of coronary artery disease (CAD). Peripheral arterial tonometry (PAT) is an emerging, automated method that assesses endothelial function in the fingertip. It can be conducted by pharmacists; however, the pathways that regulate this phenotypic measure remain poorly defined. We evaluated whether polymorphisms in COX-2 (*PTGS2:* -765G>C) and endothelial NO synthase (*NOS3:* -786T>C, Glu298Asp) were associated with PAT in patients with CAD.
METHODS: Forty-eight patients with 50% or more stenosis in one or more major epicardial coronary arteries were studied for 60 ± 27 (mean ± SD) days after cardiac catheterization after fasting overnight and withholding morning medications. After induction of reactive hyperemia by suprasystolic forearm cuff occlusion for 5 minutes, digital pulse volume amplitude was measured using the EndoPAT2000 device and expressed relative to baseline (PAT-ratio). Associations between PAT-ratio and genotype were evaluated by regression.
RESULTS: Subjects were 57 ± 9 years old, 69% men, and 81% white. Sixty-seven percent had undergone revascularization; 50%, 85%, and 92% were receiving ACE inhibitors, b-blockers, and statins, respectively. The PAT-ratio was significantly lower in variant *PTGS2* -765C allele carriers (n=18, 1.51 ± 0.58) compared with wild-type G/G individuals (n=29, 1.98 ± 0.88) (p=0.044). Similar results were observed when the analysis was limited to whites (1.33 ± 0.46 [n=12] vs. 1.87 ± 0.72 [n=26], respectively; p=0.013). The PAT-ratio was significantly lower in variant *NOS3* -786C allele carriers (n=24, 1.50 ± 0.59) compared with wild-type T/T individuals (n=23, 2.04 ± 0.91) (p=0.032); however, no significant difference was observed in the white-only analysis (p=0.175). The *NOS3* Glu298Asp genotype was not associated with the PAT-ratio (p=0.368).
CONCLUSIONS: These results suggest that genetic variation in *PTGS2* and *NOS3* may be associated with PAT measures of endothelial function in patients with CAD despite standard therapy. Additional studies are needed to confirm these associations in larger populations and to determine whether therapeutic modulation of these pathways alters the PAT-ratio.

Pharmacokinetics/Pharmacodynamics/Drug

177. The effect of serum albumin on methotrexate level variability and methotrexate toxicity. *Sherif Kamal, BSC*; Children Cancer Hospital Cairo, Cairo, Egypt

PURPOSE: Among pediatric oncology patients receiving high-dose methotrexate, does the serum albumin have a prognosis about the toxicity and can serum albumin explain the variability in the pharmacokinetics of methotrexate in the same patient in different courses?

METHODS: Retrospective study of patients receiving high-dose methotrexate (HDMTX). Hypoalbuminemia was classified as mild (2.5–3.5 g/dL) and severe (less than 2.5 g/dL). Methotrexate toxicity is defined as 24-hour level more than 10 µmol and 44- to 48-hour levels more than 1 µmol. The MTX levels were compared in the different courses for the same/different patients and correlated with the serum albumin concentration. Nonparametric Spearman rank correlation analysis was applied for the analysis of the correlation between MTX level and serum albumin.

RESULTS: A total of 455 samples were taken from 130 patients, in whom toxic levels were shown in 12 (8%) of 135, 6 (8.9%) of 76, and 31 (12.7%) of 244 samples from patients with osteosarcoma (OS), non-Hodgkin lymphoma (NHL), and acute lymphoblastic lymphoma (ALL), respectively. In patients with ALL, the samples showing toxic levels were 12 (38.7%) of 31 from low-risk patients and 19 (61.3%) of 31 from standard- and high-risk patients.

The mean (+SD) serum albumin concentration for all patients (except OS) was 3.2 + 0.9 g/dL. Patients with a serum albumin concentration less than 2.5 g/dL had a mean MTX level of 1.6 ± 0.19 µmol/L compared with patients with serum albumin concentrations between 2.5 and 3.5 g/dL, who had a mean MTX level of 0.8 ± 0.4 µmol/L, and patients with serum albumin concentrations greater than 3.5 g/dL had a mean MTX level of 0.41 ± 0.05 µmol/L. The nonparametric Spearman rank correlation analysis showed a correlation between decreased albumin level and increased MTX level, which may indicate toxicity.

CONCLUSIONS: The serum albumin concentration can explain the variability in PK parameters in different courses. Albumin is now routinely ordered for all patients receiving HDMTX, and pharmacists monitor the levels, giving recommendations based on the levels and putting the albumin level into consideration.

178. Pharmacokinetics of mycophenolate and its glucuronidated metabolites in stable islet transplant recipients. Mai Al-Khatib, MS(Pharm), BS(Pharm),[1] R. Jean Shapiro, M.D., FRCPC,[2] Nilufar Partovi, Pharm.D., BS(Pharm),[3] Lillian S.L. Ting, Ph.D., M.S., B.S.,[1] *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAHS*[4]; (1) University of British Columbia, Vancouver, British Columbia, Canada; (2) University of British Columbia, Vancouver General Hospital, Vancouver, British Columbia; (3) University of British Columbia and Vancouver General Hospital, Vancouver, British Columbia, Canada; (4) University of British Columbia, Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada

PURPOSE: The purpose of this study was to characterize the pharmacokinetics of mycophenolic acid (MPA) and its glucuronidated metabolites, MPAG (phenolic-glucuronide) and AcMPAG (acyl-glucuronide), in stable islet transplant recipients.

METHODS: Sixteen subjects were enrolled 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. MPA, MPAG, and AcMPAG concentrations were measured by a validated high-performance liquid chromatography (HPLC) method with ultraviolet detection, and pharmacokinetic parameters were analyzed by conventional noncompartmental modeling.

RESULTS: (Data are in mean ± SD.) Subjects included 11 females and 5 males who had received 2.7 ± 0.8 islet transplants by the study date. Days after the last transplant ranged from 16 to 2006. Age was 50 ± 8 years, and weight was 64 ± 11 kg. Serum albumin concentration was 4.2 ± 0.3 g/dL, and serum creatinine was 1.1 ± 0.4 µmol/L. All patients were also on tacrolimus-based steroid-free immunosuppressant regimens. MMF dosage ranged from 1 to 2 g/day (25.4 ± 6.1 mg/kg/day). Pharmacokinetic parameters for MPA were as follows: area-under-the-curve [AUC(0-12h)] 42.9 ± 21.6 µg/hour/mL; dose-normalized AUC(0-12h) 52.9 ± 25.4 µg/hour/mL; maximal concentration (C_{max}) 13.0 ± 6.2 µg/mL; time to C_{max} (t_{max}) 1.2 ± 0.4 hours; minimum concentration (C_{min}) 1.4 ± 1.0 µg/mL; and MPA free fraction 1.2% ± 1.0%. AUC ratios of MPAG to MPA and AcMPAG to MPA were 17.8 ± 12.4 and 0.1 ± 0.1, 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. There was large interpatient variability in all pharmacokinetic parameters of MPA, MPAG, and AcMPAG. Factors such as concomitant medication, disease state, patient demographics, and lifestyle as well as genetic polymorphisms may all play a role in explaining and predicting this variability and should be the aim of future studies in this field.

179. The effect of ethanol on oral cocaine pharmacokinetics reveals an unrecognized class of clinical ethanol-drug interactions. *S. Casey Laizure, Pharm.D.*, Robert B. Parker, Pharm.D.; University of Tennessee Department of Clinical Pharmacy, Memphis, TN

PURPOSE: It is well accepted that ethanol decreases the clearance of cocaine by inhibiting the hydrolysis of cocaine to benzoylecgonine and ecgonine methyl ester by carboxylesterases, and there is a large body of literature describing this interaction as it pertains to the abuse of cocaine. In this study, we describe the effect of intravenous ethanol on the pharmacokinetics of cocaine after intravenous and oral administration in the dog. The intent is to determine the effect of ethanol on drug hydrolysis using cocaine metabolism as a surrogate marker of carboxylesterase activity.

METHODS: Five dogs were administered intravenous cocaine alone, intravenous cocaine after ethanol, oral cocaine alone, and oral cocaine after ethanol on separate study days in a repeated-measures design. Cocaine, benzoylecgonine, and cocaethylene serum concentrations were determined by HPLC.

RESULTS: Cocaine had poor systemic bioavailability with a dose-adjusted cocaine AUC about 5.5-fold higher after intravenous compared with oral administration. The coadministration of ethanol and cocaine resulted in a 23.5% decrease in the clearance of intravenous cocaine and a 300% increase in the bioavailability of oral cocaine. Cocaine behaves like a classic high extraction drug, which undergoes extensive first-pass metabolism in the gut and liver by two carboxylesterases (CES1 and CES2) that are profoundly inhibited by ethanol.

CONCLUSIONS: These data suggest that ethanol has the potential to inhibit the hydrolysis of other drug compounds that are subject to hydrolysis by carboxylesterases. Indeed, there are numerous commonly prescribed therapeutic agents with carboxylesterase-dependent first-pass metabolism including enalapril, lovastatin, clopidogrel, irinotecan, and oseltamivir that may interact with ethanol. The consumption of ethanol with these drugs is likely to alter their effectiveness. The actual clinical significance of interactions between ethanol and commonly prescribed drugs that undergo first-pass metabolism by carboxylesterases is unknown because they have not been studied.

180. Outcomes of the implementation of an area under the curve/minimum inhibitory concentration vancomycin nomogram. *Cristy L. Pounders, Pharm.D.*,[1] Sarah J. Hollis, Pharm.D.,[2] Elizabeth L. Michalets, Pharm.D., BCPS, CPP,[2] John D. Phillips, Pharm.D.,[2] Susan E. Sutherland, Ph.D.[2]; (1) Methodist University Hospital, Memphis, TN; (2) Mission Hospitals, Asheville, NC

PURPOSE: Published studies and a 2009 consensus statement suggest a vancomycin AUC_{24}/MIC of 400 or more is associated with improved clinical outcomes. The objectives of this study were to evaluate clinical outcomes, safety, and cost of a vancomycin AUC_{24}/MIC dosing nomogram (ND) compared with a control group using traditional dosing (TD).

METHODS: A retrospective comparison study between ND patients from November 2007 to March 2009 and TD patients from November 2005 to October 2007 was conducted. Patients 18 years and older, weighing 50–150 kg, with a creatinine clearance of 30

mL/minute or more and a pharmacy consult for vancomycin dosing who received 3 days or more of vancomycin therapy were included. Efficacy was measured by change in the modified clinical pneumonia score from day 1 to therapy end.

RESULTS: Sixty-seven ND patients and 66 TD patients met inclusion criteria. Mean AUC_{24}/MIC was 504 ± 158 for ND versus 383 ± 208 for TD. Of the 46 patients with a respiratory tract infection, 26% ND and 67% TD had troughs less than 15 µg/mL (p=0.16). Mean trough levels (µg/mL) were 20.7 ± 10.8 in the ND patients compared with 13.2 ± 8.6 in the TD patients. Mean improvement in pneumonia score from day 1 to therapy end was –0.9 ± 3.7 in the ND versus –0.4 ± 2.8 in the TD. Sixteen patients in each group (23.9% ND vs. 24.6% TD) experienced an increase of 20% or more in serum creatinine from day 1 to therapy end. The mean monitoring cost was less in the ND compared with the TD ($89 vs. $150) because of fewer vancomycin levels per patient.

CONCLUSIONS: Dosing using an AUC_{24}/MIC nomogram was more likely to achieve the targeted AUC_{24}/MIC of 400 or more and trough of 15 µg/mL or more with a similar change in serum creatinine compared with TD. A trend toward improvement in the pneumonia score with less costly monitoring was observed. Further research evaluating the efficacy of the AUC_{24}/MIC nomogram is needed.

181E. A population pharmacokinetic analysis for aripiprazole in children and adolescents ages 10–17. Sarah Marston, Ph.D.,[1] Robert L. Findling, M.D.,[2] Suresh Mallikaarjun, Ph.D.,[1] Taro Iwamoto, Ph.D.,[3] William Carson, M.D.,[3] Andrei Pikalov, M.D., Ph.D.,[4] *Carlos Rojas-Fernandez, Pharm.D., BCPP,*[5] Quynh-Van Tran, Pharm.D., BCPP[4]; (1) Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD; (2) University Hospitals Case Medical Center, Cleveland, OH; (3) Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ; (4) Otsuka America Pharmaceutical, Inc., Rockville, MD; (5) Bristol-Myers Squibb, Plainsboro, NJ

PURPOSE: The objectives of this population pharmacokinetics (PK) analysis were to describe the PK of aripiprazole in the pediatric population (10–17 years) and to investigate the impact of covariates such as size and age on the clearance (Cl) and volume of distribution (Vd).

METHODS: Population pharmacokinetic (PK) data were collected in 343 pediatric patients and were analyzed using nonlinear mixed-effects modeling by standard methods.

Models with both size-independent and allometrically scaled Cl/F and V/F parameters were investigated, and several body size metrics were evaluated at baseline such as lean body weight (LBW).

RESULTS: The pharmacokinetics of aripiprazole were best described by a one-compartment allometrically scaled model. The relationship of Cl/F and V/F with respect to body size is shown below.

$$Cl/F = Cl/F_{TV}(LBW_i/LBW_{ref})^{0.75}$$
$$V/F = (V/F)_{TV}\,(Wt_i/Wt_{ref})^{1.0}$$

Typical values (95% CI) given the reference covariates (70-kg weight and 50-kg lean body mass) in pediatric patients (10–17 years) for CL/F, V/F, and ka were 3.44 (3.26, 3.63) L/hour, 255 (231, 283) L, and 1.67 (0.748, 4.28) $hour^{-1}$, respectively. Typical values in adults for Cl/F, V/F, and ka were 3.81 L/hour, 293 L, and 1.06 $hour^{-1}$, respectively.

The pharmacokinetic of aripiprazole was linear with respect to dose, and no significant effects owing to age, gender, race, or study population were identified.

CONCLUSIONS: The relationship of Cl/F and V/F were best described by classic allometric scaling.

Aripiprazole pharmacokinetics in pediatric patients appeared to be similar to adults based on an informal comparison with a historical adult population PK analysis. No clinically meaningful differences in PK parameters were identified to suggest dose adjustment is necessary for pediatric patients aged 10–17 years based on age and weight.

Presented at the Annual Meeting of the College of Psychiatric and Neurologic Pharmacists (CPNP), Jacksonville, FL, April 19–22, 2009. Presented at the 64th Annual Meeting of Society of Biological Psychiatry (SOBP) in Vancouver, British Columbia, Canada, May 14–16, 2009.

182E. Pharmacokinetics of doripenem in subjects with varying degrees of renal impairment. Iolanda Cirillo, M.S., *Nicole Vaccaro, B.S.*, Hong Tian, Ph.D., Bibiana Castaneda-Ruiz, M.D., Kenneth Turner, Ph.D., Rebecca Redman, M.D.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ

PURPOSE: To determine the pharmacokinetics of a single intravenous 500-mg dose of doripenem, a broad-spectrum carbapenem antibiotic, in subjects with normal renal function (NRF) and in those with varying degrees of renal impairment (RI). Safety and tolerability were also assessed.

METHODS: In study 1, subjects with mild (n=6; creatinine clearance [CrCl] 51–79 mL/minute), moderate (n=6; 31–50 mL/minute), severe (n=6; 30 mL/minute or less) RI, subjects with end-stage renal disease (ESRD) (n=6) undergoing hemodialysis, and healthy subjects with NRF matched by age, weight, and gender to RI categories (n=8; CrCl, 80 mL/minute or more) received a single doripenem 500-mg 30-minute intravenous infusion. Subjects with ESRD received doripenem either before or after hemodialysis. In study 2, NRF subjects (n=6) and ESRD subjects (n=6) matched by age and weight received a single doripenem 500-mg 1-hour intravenous infusion. ESRD subjects received doripenem before and after hemodialysis on two separate occasions. Doripenem and doripenem-M-1 (inactive metabolite assessed only in study 2) plasma concentrations were determined by liquid chromatography/tandem mass spectrometry.

RESULTS: Study 1: Doripenem half-life in NRF subjects was 1 hour and increased with decreasing renal function to 4.6 hours in subjects with severe RI. Exposure to doripenem was 1.6-, 2.8-, and 5.1-fold higher in subjects with mild, moderate, and severe RI, respectively, compared with NRF subjects. Study 2: Doripenem exposure was increased 3.3 (predialysis) and 7.7 (postdialysis) times in ESRD versus NRF subjects, similar to results obtained in ESRD subjects in study 1. Retention of doripenem-M-1 in plasma was observed. Hemodialysis removed about 52% of the administered dose as doripenem (46%) and doripenem-M-1. No serious adverse events occurred.

CONCLUSIONS: Exposure to doripenem increased with RI. Both doripenem and doripenem-M-1 were removed by hemodialysis. A single 500-mg dose of doripenem was safe and well tolerated.

Poster presented at the 48th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Infectious Diseases Society of America (IDSA) 46th Annual Meeting, Washington, DC, October 25–28, 2008.

183E. Effects of age and gender on doripenem pharmacokinetics. Kenneth Turner, Ph.D., Iolanda Cirillo, M.S., *Nicole Vaccaro, B.S.,* Bhavna Solanki, Ph.D., Rebecca Redman, M.D.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ

PURPOSE: To evaluate the effects of age and gender on the pharmacokinetics (PK) of the broad-spectrum carbapenem antibiotic doripenem. Safety and tolerability also were assessed.

METHODS: Twenty-four healthy nonelderly (n=6 M, 6 F; aged 18–29 years) and elderly (n=6 M, 6 F; aged 66–84 years) subjects with normal renal function received a single 1-hour intravenous infusion of doripenem 500 mg. Nonelderly males and females were matched to mean body weight (±20%) of their respective elderly gender group; six elderly subjects (n=3 M, 3 F) were older than 75 years. Blood and urine PK samples were collected for 24 hours postdose. Plasma and urine concentrations of doripenem and doripenem-M-1 (inactive metabolite) were quantified by LC/MS/MS. Analysis of variance models were used to evaluate the effects of age and gender on PK parameters (C_{max}, AUC).

RESULTS: The age effect was statistically significant for doripenem C_{max} ($p<0.05$) and AUCs ($p<0.0001$); the gender effect was not statistically significant for either parameter. DOR C_{max}, AUC, and $t_{1/2}$ were increased by 23%, 49%, and 53% in the elderly. Doripenem CL and CL_R were about 30% lower in the elderly, similar to the observed reduction in creatinine clearance (CL_{CR}). Nonrenal clearance of doripenem (CL_{NR}) was 40% lower in the elderly. Small

differences in doripenem C_{max} and AUCs (less than 15%) were seen between males and females. No serious adverse events (AEs) or discontinuations because of AEs occurred.
CONCLUSIONS: The increase in doripenem exposure in the elderly was primarily owing to an age-related decline in renal function and, to a lesser extent, an age-related reduction in CL_{NR}. The small difference in exposure between males and females was not clinically important. No dosage adjustment is recommended in elderly subjects with normal renal function or on the basis of gender. Doripenem 500 mg was safe and well tolerated.
Poster presented at American College of Clinical Pharmacology's 37th Annual Meeting, Philadelphia, PA, September 14–16, 2008.

184E. Pharmacokinetics of doripenem 1g administered over 4 hours in patients with ventilator associated pneumonia. *Nicole Vaccaro, B.S.*, Rebecca Redman, M.D., Iolanda Cirillo, M.S.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ
PURPOSE: Doripenem (DORI), a broad-spectrum carbapenem antibiotic, administered as a 1-g 4-hour infusion may be a treatment option for patients with serious nosocomial infections caused by pathogens with higher DORI MICs. The pharmacokinetics (PK) after multiple, intravenous 1-g doses of DORI in patients with ventilator-associated pneumonia (VAP) were characterized, and the time above threshold MICs (%T greater than MIC) was estimated.
METHODS: PK samples were collected at specified times relative to the morning doripenem infusion on day 2, 3, or 4 from subjects with VAP after DORI 1 g was administered over 4 hours every 8 hours. DORI concentrations in plasma were determined by LC-MS/MS and steady-state PK parameters were calculated by noncompartmental techniques.
RESULTS: Mean DORI AUC in patients with VAP (n=19) was about 70 µg/hour/mL, similar to systemic exposures observed historically in healthy subjects at the same doripenem dose. DORI concentrations were maintained above the MIC thresholds of 4, 8, and 16 µg/mL for about 75%, about 47%, and about 13% of an 8-hour dosing interval, respectively. Mean DORI half-life (about 3 hours) was longer than observed in healthy subjects (1 hour), and mean DORI volume of distribution (about 40 L) was greater than observed in healthy subjects (18 L).
CONCLUSIONS: Similar systemic exposures were achieved in subjects with VAP compared with healthy subjects after DORI 1 g. Some differences in disposition pharmacokinetics were noted. Assuming a MIC_{90} of 4 µg/mL for DORI against *P. aeruginosa*, a VAP pathogen, the %T greater than MIC for subjects in this study was greater than 70% of the dosing interval. Interpretations are limited by the small sample size.
Poster presented at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, CA, September 12–15, 2009.

185E. Pharmacokinetics of doripenem in chronic HD subjects during CRRT. Iolanda Cirillo, M.S., *Nicole Vaccaro, B.S.*, Rosemary Evans, M.D., Rebecca Redman, M.D.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ
PURPOSE: The pharmacokinetics (PK) of a single intravenous 500-mg dose of doripenem (DORI), a broad-spectrum carbapenem antibiotic, in chronic hemodialysis (HD) subjects undergoing a 12-hour continuous renal replacement therapy session (CRRT) were determined and compared with healthy volunteers (HVs). Safety and tolerability were also assessed.
METHODS: Chronic HD subjects receiving CRRT (n=12) and HVs with normal renal function matched by age and weight received a single 500-mg 1-hour intravenous DORI infusion. CRRT subjects received DORI about 1 hour after the start of CRRT (either continuous venovenous hemofiltration [CVVH] or continuous venovenous hemodiafiltration [CVVHDF]). Serial blood and dialysis effluent samples were collected for DORI and M1 (inactive metabolite) concentration measurement by LC-MS/MS.
RESULTS: The DORI elimination half-life was around 4 times longer for subjects on CRRT compared with HV. Exposure to DORI and M1 was around 3- and 5-fold greater for subjects on CRRT compared with HV, respectively. The mean sieving coefficients (CVVH) and saturation coefficients (CVVHDF) were above 0.6 for DORI and M1, indicating that they pass through the CRRT filter membrane. The percent excreted into effluent (Ae_{CRRT}) during the 12-hour dialysis period was around 27.5% and 14.1% for DORI and 5% and 6% for M1 in CVVH and CVVHDF, respectively. The CL of DORI by CRRT was around 1.4 and 0.79 L/hour in CVVH and CVVHDF, respectively. The recovery of drug in the dialysis effluent was lower than expected based on the almost 90% reduction in DORI plasma concentrations from the end of the DORI infusion to the end of CRRT. No serious adverse events occurred.
CONCLUSIONS: The recovery of drug in effluent and reduction of plasma concentrations indicate that CVVH and CVVHDF are effective at filtering DORI from the plasma. A single 500-mg dose of DORI was safe and well tolerated.
Poster presented at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, CA, September 12–15, 2009.

186E. Pharmacokinetics of doripenem in adults with cystic fibrosis. Iolanda Cirillo, M.S.,[1] *Nicole Vaccaro, B.S.*,[1] Rosemary Evans, M.D.,[1] Rebecca Redman, M.D.,[1] Gregory L. Kearns, Pharm.D., Ph.D.[2]; (1) Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ; (2) Children's Mercy Hospitals and Clinics, Kansas City, MO
PURPOSE: Doripenem (DORI), an expanded-spectrum carbapenem, has an antimicrobial profile that could be useful in treating pulmonary exacerbations in cystic fibrosis (CF). Differences in the disposition of other antimicrobials in patients with and without CF mandated a pharmacokinetic (PK) study of DORI in patients with CF.
METHODS: PK data were available from nine adults (45–66 kg) receiving a single sequential 1- and 2-g intravenous DORI dose administered over 4 hours separated by a washout period. Blood samples and quantitative urine samples were obtained up to 24 hours postdose. DORI and its M1 metabolite were quantitated from samples by LC-MS/MS, and PK parameters were calculated by noncompartmental techniques. Tolerability was also assessed.
RESULTS: PK parameters (mean ± SD) for DORI after the 1- and 2-g doses, respectively, were as follows: AUC_{∞} = 80.3 ± 24.9 versus 171.0 ± 49.3 µg/hour/mL; C_{max} = 20.0 ± 5.62 versus 43.2 ± 13.9 µg/mL; elimination $t_{½}$ = 1.0 ± 0.27 versus 1.11 ± 1.3 hours; Vd_{ss}= 19.5 ± 8.1 versus 20.4 ± 7.3 L; and total plasma CL= 13.5 ± 3.4 versus 12.6 ± 3.6 L. The extent of DORI urinary excretion was similar between the 1-g dose (58.6% ± 15.8%) and the 2-g dose (67.3% ± 9.9%). No difference was observed when weight-adjusted Vd_{ss} and CL were compared between the 1- and 2-g doses. DORI PK in subjects with CF were comparable to those from a previous study conducted in adults without the disease.
CONCLUSIONS: Over a 1- to 2-g dose range, the PK of DORI in adults with CF appears to be dose-proportionate for exposure and dose-independent with respect to Vd_{ss}, CL, and extent of renal excretion. In adults, CF per se does not seem to alter the PK of DORI.
Assuming a MIC of 4 µg/mL for DORI against *P. aeruginosa*, a pathogen that CF subjects may become chronically infected with, the T greater than MIC in this study was more than 5 hours for both doripenem doses (67% of the dosing interval for 1 g; 83% of the dosing interval for 2 g). Doripenem was well tolerated.
Poster presented at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, CA, September 12–15, 2009.

187E. The influence of CYP3A5 and MDR1 (ABCB1) polymorphisms on the pharmacokinetics of tacrolimus in patients with rheumatoid arthritis and lupus nephritis. *Tomonori Nakamura, Ph.D.*,[1] Yuko Okada, Ph.D.,[2] Keiju Hiromura, M.D., Ph.D.,[1] Yoshihisa Nojima, M.D., Ph.D.,[1] Katsunori Nakamura, Ph.D.,[1] Koujirou Yamamoto, Ph.D.[1]; (1) Gunma University Graduate School of Medicine, Maebshi, Japan; (2) Takasaki University of Health and Welfare, Faculty of Pharmacy, Takasaki, Japan
PURPOSE: Tacrolimus (TAC) is a substrate for cytochrome P450

(CYP) 3A5 and P-glycoprotein encoded by *CYP3A5* and MDR1 (*ABCB1*), respectively, having multiple single nucleotide polymorphisms. In this study, we genotyped CYP3A5 A6986G (*CYP3A5*3*), MDR1 G2677(A/T), and C3435T polymorphisms and investigated the effect of these polymorphisms on the pharmacokinetics of TAC in patients with rheumatoid arthritis (RA) and lupus nephritis (LN).

METHODS: Thirty-six consecutive recipients (RA, n=20; LN, n=16) were enrolled in this study. The patients received oral TAC at a dose of 3 mg or less once daily after the evening meal. Whole blood concentrations of TAC 12 hours after administration per dose (C/D) were measured by semiautomated microparticle enzyme immunoassay. The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and direct sequence methods were used for genotyping the *CYP3A5* and *MDR1* polymorphisms, respectively.

RESULTS: The C/D values (ng/mL per mg/kg) were significantly lower in the patients with *CYP3A5*1* than *CYP3A5*3/*3* (Kruskal-Wallis test, p=0.0007). The *MDR1* polymorphism was not associated with any pharmacokinetic parameters. The C/D value of TAC in female patients younger than 50 years was significantly lower than in those older than 50 years. In male patients, the significant difference might not be detected between younger and older than 50 years.

CONCLUSIONS: RA and LN patients with the *CYP3A5*1* allele required a higher daily TAC dose compared with those with the *CYP3A5*3/*3* genotype to maintain the target 12-hour concentration, suggesting that this polymorphism is useful for determining the appropriate dose of TAC. In addition, it is suggested that the consideration of sex difference and age is necessary for the medication of TAC.

Presented at 3rd Asian Pacific Regional ISSX Meeting, Bangkok, Thailand, May 10–12, 2009.

188E. Efficacy and safety of desvenlafaxine 50 and 100 mg/d in the treatment of major depressive disorder: results from 2 placebo-controlled studies. *Michael Liebowitz, M.D.,*[1] Stuart Montgomery, M.D., FRCPsych,[2] Patrice Boyer, M.D., Ph.D.,[3] Amy Manley, M.S.,[4] Sudharshan Padmanabhan, Ph.D.,[4] Jean-Michel Germain, Ph.D.,[5] Claudine Brisard, M.D.,[5] Karen Tourian, M.D.[5]; (1) Columbia University, New York, NY; (2) Imperial College School of Medicine, London, United Kingdom; (3) University of Ottawa, Ontario, ON, Canada; (4) Wyeth Research, Collegeville, PA; (5) Wyeth Research France, Paris, France

PURPOSE: To assess the efficacy and safety of 50- and 100-mg/day doses of the serotonin-norepinephrine reuptake inhibitor (SNRI) desvenlafaxine (administered as desvenlafaxine succinate) in the treatment of major depressive disorder (MDD).

METHODS: Two identically designed, multicenter, randomized, double-blind, placebo-controlled studies were conducted. One study took place in the United States, and the other study was international (INT; European Union and South Africa). Participants were 18 years or older and met criteria for MDD per the *Diagnostic and Statistical Manual of Mental Disorders,* fourth edition, with a 17-item Hamilton Rating Scale for Depression ($HAM\text{-}D_{17}$) total score of 20 or more at screening and baseline. Patients were randomly assigned to treatment groups, which included desvenlafaxine 50 mg/day, desvenlafaxine 100 mg/day, or placebo. Treatment was administered for 8 weeks (including a 1-week, 50-mg/day titration period for the 100-mg/day group). The primary efficacy variable was change from baseline on the $HAM\text{-}D_{17}$ at the final on-therapy evaluation. Analysis of covariance model was used for the efficacy analysis.

RESULTS: In the U.S. study (n=447), compared with placebo, a significant difference was observed in the adjusted mean change from baseline on the $HAM\text{-}D_{17}$ in the 50-mg/day group (–11.5 vs. –9.5; p=0.018), although no significant difference was observed in the 100-mg/day group. In the INT study (n=483), there was a significantly greater improvement on this same measure for both desvenlafaxine groups (50 mg: –13.2; p=0.002; 100 mg: –13.7; p<0.001) compared with placebo (–10.7). Each dose of desvenlafaxine was generally well tolerated, and adverse events were consistent with the SNRI class.

CONCLUSIONS: These results demonstrate the efficacy of desvenlafaxine 50 and 100 mg/day in the treatment of MDD.

Funding: Wyeth Research

Presented at the International Society for Affective Disorders, Brisbane, Australia, February 28–March 2, 2009. Presented at the College of Psychiatric & Neurologic Pharmacists Meeting, Jacksonville, FL, April 19–22, 2009.

189E. Venlafaxine efficacy varies with CYP2D6 phenotype in patients treated for depression. *Kasia Lobello, M.D.,*[1] Christine Guico-Pabia, M.D., MBA, MPH,[1] Qin Jiang, M.S.,[1] Alice Nichols, Ph.D.,[1] Sheldon Preskorn, M.D.[2]; (1) Wyeth Research, Collegeville, PA; (2) Clinical Research Institute, Wichita, KS

PURPOSE: Venlafaxine (VEN) is primarily metabolized by *CYP2D6* into *O*-desmethylvenlafaxine (ODV). Individuals can be broadly classified as poor metabolizers (PMs) or extensive metabolizers (EMs) based on *CYP2D6* activity. This analysis examines the relative efficacy of VEN in patients with major depressive disorder (MDD) classified as EMs versus PMs based on the plasma ODV-to-VEN ratio (ODV/VEN) after VEN administration.

METHODS: Data from four double-blind, placebo-controlled efficacy studies of patients with MDD were pooled to assess VEN efficacy in VEN-treated EMs and PMs versus placebo. In those studies, blood samples were taken, and plasma concentrations of VEN and ODV were determined to calculate ODV/VEN. Depression rating scale scores and remission rates (17-item Hamilton Rating Scale for Depression [$HAM\text{-}D_{17}$] score of 7 or less) were compared for EMs and PMs, classified based on ODV/VEN versus placebo using t-tests and the Fisher exact test, respectively. Distributions of percent improvement in $HAM\text{-}D_{17}$ scores were compared for VEN-treated EMs and PMs versus placebo by the Cochran-Mantel-Haenszel test.

RESULTS: VEN-treated MDD patients, both EMs (n=415) and PMs (n=49), had significantly improved depression rating scale scores compared with placebo-treated patients (n=372; p≤0.04). Compared with PMs, VEN-treated EMs had significantly greater change from baseline on four of five depression rating scales (p-values of 0.020 or less). For VEN-treated EMs, but not PMs, remission rate (EM, 41.4%; PM, 28.6%; placebo, 20.8%) and distribution of percent improvement in $HAM\text{-}D_{17}$ scores were significantly different from placebo (p-values less than 0.001). Discontinuation rates did not differ significantly between EMs and PMs.

CONCLUSION: VEN treatment in EMs was associated with greater efficacy in MDD on virtually all measures compared with PMs, with no significant tolerability differences.

Funding: Wyeth Research

Presented at the 2009 New Clinical Drug Evaluation Unit Annual Meeting, Hollywood, FL, June 29–July 2, 2009.

190E. Assessing the pharmacokinetics of venlafaxine ER 75 mg and desvenlafaxine 50 mg in CYP2D6 extensive and poor metabolizers. *Cecelia Kane, M.D.,*[1] Alice Nichols, Ph.D.,[1] Kristen Focht, MBA,[1] Qin Jiang, M.S.,[1] Sheldon Preskorn, M.D.,[2] Ted Burczynski, Ph.D.[1]; (1) Wyeth Research, Collegeville, PA; (2) Clinical Research Institute, Wichita, KS

PURPOSE: *CYP2D6* metabolic polymorphisms have been shown to decrease plasma concentrations of certain antidepressant medications. This study was conducted to evaluate the impact of *CYP2D6* extensive (EM) or poor metabolizer (PM) genotypes on the pharmacokinetics of single doses of venlafaxine extended release (ER) and desvenlafaxine (administered as desvenlafaxine succinate) in healthy adults.

METHODS: In this open-label, crossover study, subjects were administered, in randomized sequences, single doses of venlafaxine ER 75 mg and desvenlafaxine 50 mg. *CYP2D6* genotyping was performed using internally developed and commercially available assays. Arithmetic means for area under the plasma concentration-versus-time curve (AUC) and peak plasma concentration (C_{max}) were calculated. Comparisons between EMs and PMs were made using a two-tailed Wilcoxon exact test.

RESULTS: No carryover effect was observed between treatment sequence groups. For subjects receiving desvenlafaxine 50 mg, the

differences between PMs (n=7) and EMs (n=7) in desvenlafaxine AUC (17% higher) and C_{max} (24% higher) were not significant; however, for subjects receiving venlafaxine ER 75 mg, the AUC and C_{max} of desvenlafaxine were 181% and 264% higher, respectively, in EMs compared with PMs ($p \leq 0.001$). For subjects receiving venlafaxine ER 75 mg, the AUC and C_{max} of venlafaxine increased 490% and 165%, respectively, for PMs compared with EMs ($p<0.001$). In addition, the ratio of desvenlafaxine to venlafaxine on AUC and C_{max} for subjects receiving venlafaxine ER 75 mg were higher for EMs (7.5 and 4.0) than for PMs (0.5 and 0.4; $p \leq 0.001$ for both comparisons).
CONCLUSION: The pharmacokinetics of desvenlafaxine 50 mg were not significantly affected by *CYP2D6* polymorphisms, whereas PMs receiving venlafaxine ER 75 mg had significantly lower desvenlafaxine plasma concentrations compared with EMs.
Funding: Supported by Wyeth Research
Presented at the American Psychiatric Association, San Francisco, CA, May 16–21, 2009. Presented at the 2009 Royal Australian & New Zealand College of Psychiatrists, Adelaide, Australia, May 24–28, 2009.

191E. An open-label pharmacokinetic, safety, and tolerability study of single intravenous doses of ceftaroline in subjects with normal renal function or severe renal impairment. *Todd Riccobene, Ph.D.*,[1] Joseph Laudano, Pharm.D.,[1] Ed Fang, M.D.,[2] Dirk Thye, M.D.[2]; (1) Forest Research Institute, Jersey City, NJ; (2) Cerexa, Inc., Oakland, CA
PURPOSE: Ceftaroline is a novel, parenteral, broad-spectrum cephalosporin that exhibits 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. This study evaluated the pharmacokinetic (PK) profile, safety, and tolerability of a single intravenous dose of ceftaroline in subjects with severe renal impairment or normal renal function.
METHODS: Twelve adults (six with severe renal impairment [creatinine clearance (CrCL) 30 mL/minute or less, and six with normal renal function [CrCL more than 80 mL/minute]) received one dose of ceftaroline 400 mg intravenously over 1 hour. Plasma and urine samples were analyzed for ceftaroline using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Adverse events were monitored, and physical examination findings, vital signs, laboratory tests, and electrocardiograms (ECGs) were recorded at baseline and throughout the study.
RESULTS: The AUC was 115% greater, and the $t_{1/2}$ was longer for ceftaroline in subjects with severe renal impairment. The C_{max} of ceftaroline was 21% greater, and CL, CL_r, and Ae_{0-t} were less (decreases of 53%, 66%, and 84%, respectively) in subjects with severe renal impairment. The T_{max} for ceftaroline was comparable between groups. A significant relationship existed between ceftaroline CL and CrCL. Ceftaroline was well tolerated in both groups. No clinically meaningful changes in laboratory parameters, ECGs, or vital signs were observed.
CONCLUSION: PK parameters for a single dose of ceftaroline were altered in adults with severe renal impairment, resulting in a longer $t_{1/2}$ and greater systemic exposure. Dose adjustment should be considered in patients with severe renal impairment. These data will be used in population PK analyses and simulations to explore target attainment (%T greater than MIC) for different dose regimens in subjects with CrCL less than 30 mL/minute.
Presented at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy/Infectious Diseases Society of America 47th Annual Meeting, San Francisco, CA, September 12–15, 2009.

192E. Accelerator mass spectrometry in neonatal clinical research. *Le T. Vuong, Ph.D.*,[1] Pete Lohstroh, Ph.D.,[1] Stephen Dueker, Ph.D.,[1] Arlin Blood, Ph.D.,[2] Herbert Vasquez, M.D.[2]; (1) Vitalea Science, Inc., Davis, CA; (2) Loma Linda University Children's Hospital, Loma Linda, CA
PURPOSE: Pharmaceutical and nutritive interventions can be used as rapid, nonsurgical responses for neonatal disease; however, the neonatal patient is far from being a small, uncommunicative replicate of the adult counterpart on whom most pharmaceutical and nutritional research is focused. As a result, there is a critical lack of pediatric and particularly neonatal drug research. The consequences of this knowledge gap are the off-label use of medications and lack of therapies with proven efficacy for many indications unique to the infant.
METHODS: The "single-drop" analytic capability of accelerator mass spectrometry (AMS) for quantifying 14C-labeled compounds enables clinical study designs (e.g., microdose, phase I microtrace) that use levels of labeled drug that are at minimal risk and are therefore appropriate for studies of neonatal patients. AMS can be used to quantify the concentration of subtherapeutic doses of 14C-labeled compounds in as little as a few microliters of biologic specimens, such as blood obtained by heel prick or urine collected urethrally or directly from a diaper.
RESULTS: A proof-of-concept study of ursodiol (Actigal) in infants using AMS for bioanalysis is under way at the Neonatal Intensive Care Unit of Loma Linda University Children's Hospital. The primary objective of the study is to determine the pharmacokinetic (PK) parameters and dose proportionality of orally administered ursodiol, an endogenous produced compound used to treat infant cholestasis, a common disease in premature infants receiving total parenteral nutrition; however, there is no available newborn PK information.
CONCLUSION: We report the methods used and preliminary data of the first two neonates receiving doses of 1, 3.3, and 10 nCi (37, 120, and 370 Bq) of labeled ursodiol.
Presented at International Isotope Society Meeting 2009.

Prescription Error

193. Detection of prescription errors by a unit-based clinical pharmacist in a nephrology ward. *Ghazal Vessal, Pharm.D., Ph.D.*; Shiraz University of Medical Sciences, Shiraz, Iran
PURPOSE: To determine the impact of a clinical pharmacist on the detection and prevention of prescription errors at the nephrology ward of a referral hospital.
METHODS: During a 4-month period, a clinical pharmacist was assigned to review medication order sheets and drug orders 3 times weekly at the nephrology ward. In addition to the chart review, the clinical pharmacist participated in medical rounds once weekly. The occurrence of prescribing errors and related harm was determined on hospitalized patients in this ward during the 4-month period. When an error was detected, intervention was made after agreement of the attending physician.
RESULTS: Seventy-six patient charts were reviewed during the 4-month period. A total of 818 medications were ordered in these patients. Eighty-four prescribing errors were detected in 46 hospital admissions. The mean age of the patients was 47.7 ± 17.2. Fifty-five percent were male, and 45% were female. Different types of prescribing errors and their frequencies were as follows: wrong frequency (37.2%), wrong drug selection (19.8%), overdose (12.8%), failure to discontinue (10.5%), failure to order (7%), underdose (3.5%), wrong time (3.5%), monitoring (3.5%), wrong route (1.2%), and drug interaction (1.2%). The attending physician agreed to 96.5% of the prescription errors detected, and interventions were made. Although 89.5% of the detected errors caused no harm, four (4.7%) of the errors increased the need for monitoring, two (2.3%) increased length of stay, and two (2.3%) led to permanent patient harm.
CONCLUSIONS: There are few clinical pharmacists working in Iran. This study shows that the presence of a clinical pharmacist in the nephrology ward helps in the early detection of prescription errors and therefore the prevention of negative consequences owing to drug administration.

Psychiatry

194. Factors associated with initial choice of atypical antipsychotics. *Rita Hui, Pharm.D., M.S.*,[1] James Chan, Pharm.D., Ph.D.,[1] Michele M. Spence, Ph.D.,[2] Deborah R. Kubota, Pharm.D.,[2] David R. Chandler, M.D.,[3] Paul Wilson, M.D.[4]; (1) Kaiser Permanente Medical Care

Program, Oakland, CA; (2) Kaiser Permanente, Downey, CA; (3) Southern California Permanente Medical Group, Santa Ana, CA; (4) The Permanente Medical Group, Redwood City, CA

PURPOSE: This study aimed to identify patient- and prescriber-specific factors associated with the initial choice of atypical antipsychotics (AAPs).

METHODS: This was a retrospective cohort study using data from the Kaiser Permanente Medical Program at Northern California. The cohort included patients initiated on any of the five common AAPs (aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone) during 2001–2007. Patients were naïve to these AAPs for 6 months before the study. They were enrolled with a drug benefit 6 months before and 6 months after treatment initiation. Logistic regression was used to predict the initial choice of AAP, adjusting for patient- and prescriber-specific factors. Patient-specific factors included age, sex, psychiatric diseases (e.g., schizophrenia, bipolar disorder, depression, anxiety), other comorbid diseases (e.g., diabetes, cardiovascular diseases), and concomitant medications that might interact with AAPs (e.g., anxiolytics, hypnotics, QT prolonging agents). Prescriber-specific factors included specialty and prescribing history of AAP in the prior year.

RESULTS: The cohort included 52,679 patients. The mean age was 49.5 ± 24.6 years, and 58% were female. Patients younger than 18 were more likely to be prescribed an AAP by a psychiatrist than were adults (84% vs. 62% p<0.001). Physicians' prescribing history of the same AAP was the best predictor of initial AAP (aripiprazole OR = 6.6 [CI: 5.7–7.6), olanzapine OR = 2.6 [CI: 2.5–2.7], quetiapine OR = 3.6 [CI: 3.4–3.8], risperidone OR = 2.7 [CI 2.6–2.9], and ziprasidone OR = 3.3 (CI: 2.1–5.1)]. Children (younger than 13 years) were more likely to receive risperidone than other AAPs (OR = 3.9; CI: 3.5–4.3). Patients with schizophrenia were more likely to receive risperidone (OR = 1.7; CI: 1.5–2.1) or ziprasidone (OR = 2.4; CI: 1.6–3.7).

CONCLUSIONS: Physicians' initial choice of AAP was based on past individual preference for a specific AAP, rather than patient-specific factors. This effect was consistent across all AAPs.

195. Evaluation of the inhibitory effects of duloxetine compared to escitalopram on norepinephrine uptake in healthy subjects. *Jill Chappell, Pharm.D.,*[1] Graeme Eisenhofer, Ph.D.,[2] Harry Haber, MPH,[3] Mary Pat Knadler, Ph.D.,[1] D. Richard Lachno, DPhil,[4] Evelyn Lobo, Ph.D.,[1] Ryan Wright, Ph.D.,[1] Beth A. Pangallo, RN[1]; (1) Eli Lilly and Company, Indianapolis, IN; (2) Universitätsklinikum Carl Gustav Carus, Dresden, Germany; (3) i3 Statprobe, Inc., Ann Arbor, MI; (4) Lilly UK, Windlesham, Surrey, United Kingdom

PURPOSE: To determine the extent of neuronal norepinephrine (NE) uptake inhibition by duloxetine at an approved 60-mg/day dose.

METHODS: This was a randomized, placebo-controlled, single-blind, two-period crossover study of healthy subjects. In part A, 32 subjects 50–65 years old were randomly assigned to receive duloxetine 60 mg/day or escitalopram 20 mg/day for 11 days, to reach steady state for both drugs, and then to receive tapered doses for 4 days in each period. In Part B, 11 subjects aged 18–65 years were to receive duloxetine 60 mg once daily for 11 days and then tapered doses for 4 days. Plasma concentrations of NE and its metabolite, 3,4-dihydroxyphenylglycol (DHPG), were measured in supine and upright positions in part A. Plasma and cerebral spinal fluid (CSF) NE and DHPG concentrations were measured at multiple time points in part B. In a post hoc analysis, the ratio of supine to upright changes in plasma concentrations of DHPG to NE (ΔDHPG/ΔNE) was analyzed in comparison to baseline (average of day 1 in each period) using a mixed-effect analysis of variance model.

RESULTS: On day 11, the plasma ΔDHPG/ΔNE ratio for both duloxetine (0.270 ± 0.040; p<0.0001) and escitalopram (0.624 ± 0.058; p=0.03) was reduced compared with baseline (0.779 ± 0.055); plasma NE uptake inhibition for duloxetine (62.9%) was greater than for escitalopram (25.2%; p<0.0001). In part B, the maximal reduction in plasma DHPG occurred at the time of maximal duloxetine concentration at steady state (6 hours). Duloxetine reduced CSF DHPG concentrations across time points by up to 30% (90% CI: 21%–39%) compared with baseline but did not affect CSF NE. New safety findings were not observed.

CONCLUSIONS: The greater neuronal NE uptake inhibition by duloxetine compared with escitalopram measured in plasma and the DHPG reduction measured in CSF compared with baseline support an effect of duloxetine at an approved 60-mg/day dose on NE uptake.

196E. Response and symptomatic remission in a long-term trial of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder. *Keva Gwin, Pharm.D.,*[1] Joel Young, M.D.,[2] Greg Mattingly, M.D.,[3] Richard H. Weisler, M.D.,[4] Liza Squires, M.D.,[1] Ben Adeyi, M.S.,[1] Bryan Dirks, M.D.,[1] Thomas Babcock, D.O.,[1] Brian Scheckner, Pharm.D.[1]; (1) Shire Development Inc., Wayne, PA; (2) Rochester Center for Behavioral Medicine, Rochester Hills, MI; (3) Washington University, St. Charles, MO; (4) Duke University Medical School and University of North Carolina College of Medicine, Durham and Chapel Hill, NC

PURPOSE: To evaluate response and symptomatic remission in adults with attention-deficit/hyperactivity disorder (ADHD) in a long-term trial of lisdexamfetamine dimesylate (LDX) treatment.

METHODS: This open-label, single-arm study enrolled adults (aged 18–55 years) with a diagnosis of ADHD. LDX treatment began at 30 mg/day. At weekly visits 2–5 (weeks 1–4), the dose was increased or decreased in 20-mg increments until an optimal dose between 30 and 70 mg/day was attained. The maintenance phase continued for an additional 11 months. Primary and secondary efficacy measures were the ADHD Rating Scale Version IV (ADHD-RS-IV) with adult ADHD prompts and the Clinical Global Impressions-Improvement (CGI-I) scale, respectively. Response was defined as a reduction in ADHD-RS-IV score of 30% or more and a CGI-I score of 2 or less relative to the baseline score of the preceding double-blind study. Symptomatic remission was defined as an ADHD-RS-IV total score of 18 or less.

RESULTS: The study enrolled 349 subjects; 191 completed the study. The mean (SD) ADHD-RS-IV change from baseline score in the intent-to-treat population (n=345) was -24.8 (11.7), p<0.0001 at end point. Of subjects who entered the maintenance phase (n=327), criteria for response were met by 95.7% and symptomatic remission by 85.0% at any point in the study. Of those who had response at visit 5, 75.2% maintained their response through the maintenance phase. Of those in remission at visit 5, 65.7% remained in remission through maintenance. Median time to first remission was 22 days. Common adverse events included upper respiratory tract infection, insomnia, headache, dry mouth, and decreased appetite.

CONCLUSIONS: Long-term treatment with LDX resulted in significant improvement in ADHD symptoms in adults, with a majority achieving sustained response and symptomatic remission over 11 months of follow-up. Symptomatic remission provides clinicians with an additional measure of response to treatment.

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197. Evaluating the frequency of as-needed dosing for anxiety/agitation in smoking versus non-smoking patients with schizophrenia. *G.S. Shankar, M.S., Pharm.D., PhC, BCPP, CG*; Western University of Health Sciences, Pomona, CA

Evaluating the frequency of as-needed dosing for anxiety/agitation in smoking versus nonsmoking patients with schizophrenia.

PURPOSE: Using as-needed doses of medication for these anxiety/agitation symptoms is a frequent practice in psychiatric inpatient units. Frequent use of as-needed medications has also been associated with depression, incontinency, and hip fracture that will eventually increase treatment difficulties for both caregivers and patients. Smoking is very common in patients with schizophrenia, and the authors wanted to study the impact of smoking on the use of as-needed medications and anxiety episodes.

METHODS: This retrospective and longitudinal chart review study over 3 months was conducted from December 2008 to February 2009. Inclusion criteria were 1) a diagnosis of schizophrenia, 2) age between 18 and 60 years, (3) both male and female, (4) both smoker and nonsmoker, (5) length of stay in facility for at least 3

months, and (6) good health. Exclusion criteria were as follows: 1) a diagnosis other than schizophrenia, 2) length of stay in facility for less than 3 months, and 3) in bad health.
RESULTS: During the 3-month study period, the nursing staff gave 28 smokers a total of 619 as-needed medications for anxiety/agitation, which gave the 10 nonsmokers a total of 122 as-needed medications for anxiety/agitation. The average for smokers and nonsmokers who were given as-needed medications was 22.11 versus 12.20.
CONCLUSIONS: One assumption is that the episodes of anxiety or agitation, together with the use of as-needed medication, should be the same as for schizophrenic patients who smoke; however, this study produced results different from those expected. It was statistically significant that more as-needed medication was given in the smoker group, 22.11, versus the nonsmoker group, 12.2.

198. Evaluation of paliperidone in improving positive symptoms and negative symptoms in an inpatient psychiatric facility. *Amy Montes, Pharm.D.,*[1] Jose Rey, Pharm.D., BCPP[2]; (1) Broward General Medical Center/Nova Southeastern University College of Pharmacy, Ft. Lauderdale, FL; (2) Nova Southeastern University College of Pharmacy/South Florida State Hospital (GeoCare Inc.), Ft. Lauderdale, FL
PURPOSE: The main goal of this study was to evaluate the efficacy of paliperidone in an inpatient clinical setting while comparing the improvements in positive and negative symptoms specific to schizophrenia. This evaluation will help determine if paliperidone treatment is equally effective in both symptom clusters. To evaluate these outcomes, the 24-item Brief Psychiatric Rating Scale (BPRS) will be used.
METHODS: Medical records of 73 psychiatric inpatients treated with paliperidone were reviewed. Psychiatrist-rated BPRS scores were completed prior; at 1 month, 3 months, and 6 months; and last recorded scores to paliperidone treatment were analyzed.
RESULTS: The negative symptom cluster of the 24-item BPRS (blunted affect, emotional withdrawal, and motor retardation) showed an average of 3.7% decrease with no statistical significance; however, 32% (n=23) of the patients did have a 20% or greater improvement in negative symptoms. The positive symptom cluster (hostility, grandiosity, hallucinations, excitement, suspiciousness, and conceptual disorganization) had a 16.7% decrease, from baseline to last recorded, and overall showed a statistical significance in both the one- and two-tailed paired t-test (p=0.0026 and p=0.0053, respectively), with 41% (n=30) of patients having a 20% or greater reduction in positive symptoms.
CONCLUSION: Paliperidone demonstrated a significant reduction in the positive symptoms of schizophrenia but demonstrated no statistical significance in reducing the negative symptoms in the severely mentally ill and inpatient population.

199. Non-continuous use of antidepressant treatment in adults with major depressive disorders—a retrospective cohort study. *Chui Ping Lee, Pharm.D.,*[1] Winnie W.Y. Yau, BPharm,[2] Grace M.C. Chan, Ph.D.,[2] Y.K. Wing, Ph.D.,[3] Marco H.B. Lam, M.D.,[4] Wei Lin, M.D.,[4] Joyce Lam, M.D.[4]; (1) School of Pharmacy, The Chinese University of Hong Kong, Hong Kong; (2) Pharmacy Department, Prince of Wales Hospital, Shatin, Hong Kong; (3) Department of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong., Shatin, Hong Kong; (4) Department of Psychiatry, Prince of Wales Hospital, Shatin, Hong Kong
PURPOSE: Depression is a prevalent and recurrent illness that requires at least 6 months of antidepressant treatment; however, noncontinuous antidepressant use is frequently detected in practice. This retrospective cohort study aimed to investigate the rate of noncontinuous use of antidepressant treatment in adult outpatients and the factors associated.
METHODS: Eligible patients were identified through the electronic patient records of a large academic hospital in Hong Kong. Patients were included if they were attending the psychiatry outpatient clinic in 2007 and had an antidepressant newly dispensed. Patients with a diagnosis of psychosis were excluded. Primary outcome was the rate of noncontinuous antidepressant use within 6 months of therapy, which is defined as a gap of more than 15 days in antidepressant prescription dispensing record. Secondary outcomes include the factors associated with noncontinuous antidepressant use, including the rate of subsequent depression relapse. Univariate analyses including χ^2 test, two independent sample *t*-tests, and Mann-Whitney test were used for comparisons between groups where appropriate. Stepwise logistic regression analysis was used to assess the associations.
RESULTS: One hundred eighty-nine subjects were included in this study. Forty-six percent of them were noncontinuous users with an 8-fold increase (OR = 8.421, 95% CI: 3.303–21.467) in the risks of relapse depressive episodes within 1 year after treatment initiation. Perceptions of stigma about depression (p=0.004), residency in public housing estate (p=0.025), and infrequent follow-ups (p=0.006) were three factors significantly associated with noncontinuous antidepressant use. Other factors include adverse effects experienced, lack of knowledge about the importance of regular follow-ups, and regular antidepressant use.
CONCLUSIONS: Noncontinuous antidepressant use is common and associated with a high rate of relapse. To achieve a better prognosis, a collaborative approach that targets patient education and enhances follow-up adherence is worth exploring.

200. Analysis of cardiovascular risk within a mental health population. *Nancy K. Bell, Pharm.D.*, Susannah E. Moroney, Pharm.D.; Pfizer Global Medical, West Des Moines, IA
PURPOSE: Cardiovascular (CV) disease is the leading cause of U.S. deaths. Mental health patients have CV mortality rates double the general population because of multiple factors including lifestyle, poor diet, tobacco use, and medication therapy. The main objective of this analysis was to evaluate metabolic monitoring and CV risk in patients receiving atypical antipsychotics.
METHODS: Using a cross-sectional, descriptive design, HIPAA-compliant data were collected between August and December 2008 on mental health patients older than 18 years at sites in Iowa and Wisconsin. Self-administered questionnaires and medical records were used to collect demographics and metabolic findings. Descriptive and statistical analyses, including t-tests, were used to compare sample findings with NHANES 1999–2002 survey results (p<0.05 was statistically significant).
RESULTS: On average, patients (n=299) were 45.2 years old, 95% white, and 42% male. Compared with national statistics, patients had greater smoking rates (46.5% vs. 20.8%; p<0.0001) and a higher prevalence of diabetes (17.7% vs. 10.7%; p<0.003), and they were more likely to be overweight (78.6% vs. 65.2%; p<0.0001) and obese (52.0% vs. 30.5%; p<0.0001). Patients had similar rates of hypertension or were taking blood pressure medications (32.8% vs. 30.1%; p=NS) but had lower rates of hypercholesteremia (11.4% vs. 17.3%; p=0.024) compared with national statistics.
CONCLUSION: This sample purposefully contained patients who received CV-related laboratory work through their mental health care provider. Significant modifiable CV risk factors exist in this patient population, including a large prevalence of obesity, diabetes, hypertension, and smoking. CV-related monitoring of patients receiving atypical antipsychotics as well as coordinated care between primary care and mental health providers is essential to improve CV risk factors in this patient population.

201. Evaluation of treatment in schizoaffective disorder at an inpatient psychiatric facility: a comparison of single versus combination antipsychotic therapy with or without adjunctive mood stabilizer. *Tatiana Yero, Pharm.D.*, Jose A. Rey, Pharm.D., BCPP; Nova Southeastern University College of Pharmacy/South Florida State Hospital (GEOCare, Inc.), Ft. Lauderdale, FL
PURPOSE: Mood stabilizers (MSs) are a common addition to antipsychotic therapy in patients with schizoaffective disorder (SD), however, minimal evidence exists to support the use of this treatment approach. The purpose of this study was to evaluate whether combination antipsychotic therapy (CAT) improved clinical outcomes more than single antipsychotic therapy (SAT) and to determine whether adding an MS provided significant improvement in this population.

METHODS: This retrospective evaluation was approved by the institutional review board. Subjects were selected from an inpatient psychiatric hospital. To be included, subjects must have had a current primary diagnosis of SD and at least one antipsychotic as part of their treatment regimen. In addition, subjects must have had scores on different scales (Brief Psychiatric Rating Scale [BPRS], Global Assessment of Function [GAF], Functional Assessment Rating Scale [FARS], and Abnormal Involuntary Movement Scale [AIMS]). Subjects were divided into groups based on medications received. Admission and current scores from each group were compared. A p-value less than 0.05 indicated statistical significance using paired and unpaired t-tests.
RESULTS: Forty-five patients met inclusion criteria. When analyzing average BPRS, GAF, and FARS scores, the SAT plus MS group significantly improved from admission to current in both BPRS and FARS (BPRS: 58.29 vs. 46.29, p=0.015; FARS: 108.94 vs. 78.18, p=0.006), and the CAT plus MS group significantly improved on the FARS score (98.83 vs. 83.33, p=0.023). The other groups showed improvement across all scales but did not meet statistical significance. AIMS scores showed no significant differences in any group.
CONCLUSIONS: This evaluation demonstrated that subjects receiving SAT plus MS had significantly improved outcomes. AIMS scores did not increase significantly, despite some subjects receiving CAT. Further studies should be conducted evaluating the clinical impact of adding MS to antipsychotic regimens in SD.

202E. Evaluation of treatment and clinical outcomes of schizoaffective disorder in an inpatient psychiatric facility. *Tatiana Yero, Pharm.D.*, Jose A. Rey, Pharm.D., BCPP; Nova Southeastern University College of Pharmacy/South Florida State Hospital (GEOCare, Inc.), Ft. Lauderdale, FL
PURPOSE: Clinicians currently treat patients with schizoaffective disorder (SD) using different drug combinations with limited data to guide their selection. The purpose of this study was to determine whether the current treatments used are effective, as evidenced in certain clinical outcomes, and whether any particular treatment regimen has a more favorable outcome.
METHODS: This retrospective evaluation was approved by the institutional review board. Subjects were selected from an inpatient psychiatric hospital for study inclusion based on data collected. To be included, patients must have received a current primary diagnosis of SD, with medication regimens and dosages recorded. In addition, subjects must have had scores on different scales (BPRS, GAF, FARS, and AIMS) reported. Subjects were then grouped based on medication regimen (single antipsychotic therapy [SAT] or combination antipsychotic therapy [CAT]). Admission and current scores from scales were compared. A p-value less than 0.05 indicated statistical significance using paired and unpaired t-tests.
RESULTS: Forty-five patients met inclusion criteria. Only subjects on SAT demonstrated statistically significant differences between admission and current scores on BPRS, FARS, and GAF scales (BPRS: 54.61 vs. 45.39, p=0.0098; FARS: 105.82 vs. 82.25, p=0.0031; GAF: 31.52 vs. 36.8, p=0.0199). AIMS scores showed no significant differences in any group. Effects of the presence of selected adjunctive medications were also assessed, and no statistically significant improvement was found from admission to current scores in any group.
CONCLUSION: Efficacy measures indicated significant differences favoring SAT compared with CAT, even when groups were comparable at admission. This indicates that no efficacy advantage exists in using CAT over SAT. Adjunctive therapy appeared to have no significant effect on outcomes in this evaluation. Further studies must be conducted to determine the appropriateness of SAT versus CAT and the use of adjunctive therapies in SD patients.
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203. Comparison of scoring methods for cognitive screens used to predict patient accuracy in filling a pillbox. *Katherine J. Anderson, Pharm.D.,*[1] Julie C. Kissack, Pharm.D.,[1] Richard E. Remington, M.S.[2]; (1) Harding University, Searcy, AR; (2) Quantified Inc., Boise, ID
PURPOSE: An efficient screening method is needed to assess patients at risk of pillbox organizational skill deficits. This study compares two pillbox scoring methods: the Pill Count (PC) and the Pillbox Fill Assessment (PBF). Mini-Mental Status Examination (MMSE) and Mini-Cog, and new cognitive screens, Medication Transfer Screen (MTS), MMSE+MTS (Medi-Mental), and Mini-Cog+MTS (Medi-Cog), were evaluated for ability to predict patient pillbox fill score.
METHODS: Fifty-three subjects, with an average age of 62.5 years, underwent cognitive screening, and mistakes were documented to generate accuracy scores; 80% was required for a passing score. Pearson correlation was used to evaluate cognitive screens predictive of pillbox loading accuracy as measured by PBF and PC methods.
RESULTS: Pass rates were 45% and 53% for the PBF and PC, respectively. The PBF scoring system was determined to be more rigorous because it failed five additional patients and provided additional information regarding mistakes the patient made during pillbox loading. Cognitive screen score correlations with the PC and PBF, respectively, were the MMSE 0.394 and 0.443, Mini-Cog 0.564 and 0.563, MTS 0.570 and 0.577, Medi-Mental 0.575 and 0.593, and Medi-Cog 0.709 and 0.713 (p<0.01 for all).
CONCLUSION: Medi-Cog (Mini-Cog plus MTS) scores correlated most closely with patient pillbox assessment scores as measured by both PC and PBF methods (0.709) and (0.713), respectively. The PBF proved a more rigorous scoring method and provided information regarding mistakes made during pillbox organization. Further study may prove cognitive assessments beneficial for screening patients at risk of pillbox mismanagement and offer measures for quantifying cognitive decline.

204. Quality of depression care in Kentucky. *Sheila R. Botts, Pharm.D., BCPP,*[1] Gao Liu, Ph.D., Candidate,[2] Joseph Conigliaro, M.D.,[3] Jeffrey Talbert, Ph.D.[1]; (1) University of Kentucky College of Pharmacy, Lexington, KY; (2) University of Kentucky, Lexington, KY; (3) University of Kentucky HealthCare, Lexington, KY
PURPOSE: To determine the extent of guideline-concordant depression care and identify variables associated with receipt of quality care.
METHODS: Retrospective evaluation using a large administrative claims database. Subjects included Kentucky Medicaid enrollees with a new (index) episode of depression and 12 months of continuous eligibility from January 2000 to December 2008. Guideline-concordant care was defined as 1) receipt of an antidepressant within the first 84 days and a medication possession ratio of more than 80% during the first 6 months or 2) receipt of psychotherapy within 30 days of the index episode and at least two treatments within 84 days. Explanatory variables included subject demographics, care setting and location, comorbidity, rural index, and Appalachian county designation.
RESULTS: Of the 49,301 depression episodes evaluated, 45% of the subjects resided in rural Appalachian counties. Twenty-five percent of the subjects received an antidepressant; 3.5% had adequate supply of medication during the first 6 months. Sixteen percent of the subjects received adequate psychotherapy. Treatment at a community mental health center increased the odds of receiving psychotherapy (OR = 2.1, SE = 0.05, p<0.001) and decreased the odds of adequate antidepressant treatment (OR = 0.87, SE = 0.05, p<0.01). Follow-up visits increased the odds of receiving adequate antidepressant treatment (OR = 1.47, SE = 0.076, p<0.001), as did comorbid diabetes (OR = 1.29, SE = 0.10, p<0.001). Appalachian residents were less likely to receive psychotherapy (OR = 0.91, SE = 0.03, p<0.008) and just as likely to receive medication as non-Appalachian residents.
CONCLUSION: Less than one in five Medicaid enrollees received adequate treatment of depression. Treatment at CMHC was associated with greater receipt of psychotherapy but less medication interventions. Consistent with other literature, comorbid diabetes and follow-up care increased adequate antidepressant treatment.

Sleep Disorders

205. Comparison between armodafinil and modafinil for the treatment of excessive sleepiness associated with shift work disorder, treated obstructive sleep apnea, or narcolepsy using pharmacokinetic/pharmacodynamic models. *Mona Darwish, Ph.D.,*[1] Lauren S. Young, B.S.,[1] Mary Kirby, M.S.,[1] Farkad Ezzet, Ph.D., M.S.[2]; (1) Clinical Pharmacology Department, Cephalon, Inc., Frazer, PA; (2) Strategic Consulting Services, Pharsight Corporation, Mountain View, CA

PURPOSE: Using a pharmacokinetic/pharmacodynamic model, we assessed potential benefits of armodafinil 200 mg compared with modafinil 200 mg on the basis of pharmacokinetic characteristics in patients with excessive sleepiness (ES) associated with shift work disorder (SWD), treated obstructive sleep apnea (OSA), or narcolepsy.

METHODS: Randomized, double-blind, placebo-controlled studies of either armodafinil or modafinil in patients with ES associated with SWD, treated OSA, or narcolepsy were combined and used to determine the relationship of concentration to effect using a multiple-component, nonlinear, mixed-effect model (NONMEM). Concentration was estimated from pooled pharmacokinetic data for each drug. The pharmacodynamic effect was calculated from pooled Maintenance of Wakefulness Test data. Three separate models were determined for each indication—SWD, OSA, and narcolepsy.

RESULTS: Mean (observed) response matched the model prediction (fit) for all treatments for all three indications, suggesting the models were appropriate. Under the assumption that armodafinil and modafinil were equally potent, the pharmacokinetic/pharmacodynamic models indicated that plasma drug concentrations producing 50% of maximal drug effect (EC_{50}) of both drugs were 4.6 µg/mL for patients with SWD, 8.4 µg/mL for patients with treated OSA, and 9.8 µg/mL for patients with narcolepsy. In patients with SWD, armodafinil provides plasma concentrations sufficient to produce EC_{40} or more for 12 hours, compared with only 7 hours with modafinil. In the treated OSA and narcolepsy patient populations, armodafinil maintained 30% or more of maximal effect for 12 hours, compared with only 6 or 5 hours, respectively, with modafinil.

CONCLUSIONS: The models indicated that patients with ES associated with narcolepsy or treated OSA required a higher plasma drug concentration to achieve EC_{50} compared with those with SWD. Armodafinil 200 mg may provide greater improvement in wakefulness throughout the day, especially at later times, compared with modafinil 200 mg in patients with ES associated with SWD, treated OSA, or narcolepsy.

Transplant/Immunology

206. Limited sampling strategies for mycophenolic acid area under the concentration-time curve in islet transplant recipients. Mai Al-Khatib, MS(Pharm), BS(Pharm),[1] R. Jean Shapiro, M.D., FRCPC,[2] Nilufar Partovi, Pharm.D., BS(Pharm),[3] Lillian S.L. Ting, Ph.D., M.S., B.S.,[1] Marc Levine, Ph.D.,[1] *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAHS*[4]; (1) University of British Columbia, Vancouver, British Columbia, Canada; (2) University of British Columbia, Vancouver General Hospital, Vancouver, British Columbia, Canada; (3) University of British Columbia and Vancouver General Hospital, Vancouver, British Columbia, Canada; (4) University of British Columbia, Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada

PURPOSE: The purpose of this study was to define optimal limited sampling strategies (LSSs) for mycophenolic acid (MPA) monitoring and to test their predictive performance in islet transplant recipients.

METHODS: After written informed consent and on administration of a steady-state morning mycophenolate mofetil dose, blood samples were collected at 0, 0.3, 0.6, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 hours from 16 stable islet transplant recipients. MPA concentrations were measured by a validated high-performance liquid chromatography method with ultraviolet detection and pharmacokinetic parameters analyzed by noncompartmental modeling. All 16 patients' profiles were used to develop the LSSs by multiple regression analysis. Potential LSSs were restricted to ones having $r^2 \geq 0.90$ and three or fewer time points within the first 4 hours postdose. Resulting equations were validated for their predictive performance using the jackknife method, with acceptable criteria for bias and precision preset to within 15%. In addition, 15 published LSSs (in the renal transplant population) were tested in the islet transplant patients.

RESULTS: One two-concentration and four three-concentration LSSs met preset criteria and had conventional sampling times:

- AUC = 1.783 + 1.248C1 + 0.888C2 + 8.027C4 (r^2=0.98, bias = –3.09%, precision = 9.53%)
- AUC = 2.778 + 1.413C1 + 0.963C3 + 7.511C4 (r^2=0.97, bias = –3.22%, precision = 11.02%)
- AUC = 1.448 + 1.239C1 + 0.271C1.5 + 9.108C4 (r^2=0.96, bias = –1.90%, precision = 11.46)
- AUC = 1.410 – 0.259C0 + 1.443C1 + 9.622C4 (r^2=0.96, bias = –2.68%, precision = 11.53%)
- AUC = 1.547 + 1.417C1 + 9.448C4 (r^2=0.96, bias = –2.46%, precision = 11.14%)

As expected, none of the other published LSSs in the renal transplant population met the preset criteria for bias and precision.

CONCLUSIONS: To our knowledge, these are the first precise and accurate LSSs for predicting MPA AUC developed specifically for islet transplant recipients. The LSS we recommend is the one using two concentrations: AUC = 1.547 + 1.417C1 + 9.448C4. This equation is convenient and clinically feasible. Other islet transplant centers may wish to validate our equation in their population or use our study template as a guide to develop accurate and precise LSSs specific to their own patient population.

207. Limited sampling strategies for predicting mycophenolate area-under-the-curve in thoracic transplant recipients. Lillian S.L. Ting, Ph.D., M.S., B.S.,[1] Nilufar Partovi, Pharm.D., BSc(Pharm),[2] Robert D. Levy, M.D., FRCPC,[3] Andrew P. Ignaszewski, M.D., FRCPC,[4] *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP, FCAHS*[5]; (1) University of British Columbia, Vancouver, British Columbia, Canada; (2) University of British Columbia and Vancouver General Hospital, Vancouver, British Columbia, Canada; (3) University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, British Columbia, Canada; (4) University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, British Columbia, Canada; (5) University of British Columbia, Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada

PURPOSE: To establish clinically convenient mycophenolate limited sampling strategies (LSSs) for heart and lung transplant populations and evaluate predictive performance of published LSSs in our heart transplant population.

METHODS: Twelve-hour pharmacokinetic data from 64 thoracic transplant recipients were used to develop separate LSSs in heart and lung groups (by multiple regression analysis). Only concentrations taken on or before 2 hours postdose were considered clinically convenient LSSs. A maximum of three concentrations were used. Seventeen and 16 patient profiles from heart and lung transplant groups, respectively, were randomly assigned as the index groups, with remaining patients serving as the validation group (16 and 15 heart and lung, respectively). Concentration and area-under-the-curve (AUC) were log transformed to normalize the data. Predictive performances of eight published LSSs for heart transplants were also evaluated in all heart transplant recipients (n=33). Acceptable bias and precision were deemed to be around 15%.

RESULTS: No LSS from the heart transplant group satisfied the predefined criteria for an acceptable LSS. The best LSSs for both transplant populations were developed from the lung transplant group data; equations (log C1.5,C2) and (log C0,C1.5) were the best candidates for the heart and lung transplant populations, respectively:

- log AUC = 0.1817 log C1.5 + 0.4994 log C2 + 1.1132; r^2=0.804, %bias = –3.30%, and %precision = 11.12%
- log AUC = 0.1677 log C0 + 0.5657 log C1.5 + 1.0830; r^2 = 0.806, %bias = 4.71%, and %precision = 11.79%

The predictive performance of eight published LSS equations in the heart transplant population yielded less optimal results; %bias and %precision ranged from 6.50% to 30.62% and from 20.44% to 68.00%, respectively.
CONCLUSIONS: Minimally biased, highly precise, and convenient LSSs for predicting MPA exposure were developed in lung transplant recipients; these LSSs also performed well when applied to the heart transplant population, whereas other published LSSs developed in heart transplant recipients yielded less optimal results when applied to our population. LSSs, which appear to be center-specific, should be revalidated before use.

208E. Persistence of influenza antibody seroprotection in lung transplant patients over five seasons. *Mary S. Hayney, Pharm.D., MPH*, John J.M. Moran, B.S., Allyson J. Darga, undergraduate, Kalynn A. Rohde, undergraduate, Michael J. Faber, Pharm.D. student; University of Wisconsin, Madison, WI
PURPOSE: Immunization policy-making bodies advised against immunizing too early before the influenza season because vaccine-specific antibody may wane before the end of the influenza season. This recommendation was based on only a small amount of data in very frail, elderly individuals. Lung transplant patients are included in the group of high-risk patients for whom this recommendation has been made. We hypothesized that immunosuppressed lung transplant patients would maintain protective concentrations of influenza antigen-specific antibodies between seasons.
METHODS: As part of a planned 5-year study of influenza vaccine antibody responses in lung transplant patients, we measured influenza antibody concentrations by hemagglutination inhibition assay before influenza immunization annually. The fraction of lung transplant patients who maintained seroprotective levels (more than 40 hemagglutination units) about 12 months from the last season immunization was calculated. Response rates in lung transplant patients were compared with healthy individuals and those waiting for lung transplantation.
RESULTS: Most lung transplant patients maintained seroprotective influenza antigen-specific antibody concentrations for about 12 months after immunization. Seroprotection rates varied greatly with influenza antigens—healthy, 10%–100%; pretransplant, 38%–90%; transplant, 22%–94%—and were similar when groups were compared. The transplant group had a statistically significantly lower response rate than healthy and pretransplant to A/H1N1 influenza in 2006 (73% vs. 100% vs. 90%; p<0.03).
CONCLUSION: Seroprotective influenza antibody concentrations are maintained at very high rates among immunosuppressed lung transplant patients. Antibody measurements during influenza season are required to consider expanding the time frame in which influenza vaccines may be administered to patients with high-risk conditions such as immunosuppression.
Presented at the Twelfth Annual Conference on Vaccine Research, Baltimore, MD, April 27–29, 2009.

209. Evaluation of pre- and post-transplant glycemic control measures and association with outcomes in liver transplant recipients. *Alison P. Healey, Pharm.D.*,[1] Nick Parrish, Pharm.D.[2]; (1) University Hospital: Health Alliance of Greater Cincinnati: Department of Pharmacy, Cincinnati, OH; (2) University of Cincinnati College of Pharmacy, Division of Pharmacy Practice, Cincinnati, OH
PURPOSE: Based on recent guidelines advocating the need for more stringent glycemic control, we hypothesized that 85% of glucose readings in liver transplant patients would be "at goal" across posttransplant environments.
METHODS: We retrospectively evaluated the level of inpatient and outpatient glycemic control and the incidence of transplant-related outcomes in patients who received a liver transplant (LTX) between 2005 and 2007. Inclusion criteria were adult primary LTX and deceased donor LTX without combined organs. Patients who died within 6 months after LTX were excluded. Patients were classified into one of four groups: 1) pre-LTX diabetes mellitus (DM); 2) sustained NODM (greater than or equal to 6 months); 3) transitory NODM (greater than or equal to 1 month to less than 6 months); or 4) normal: (no DM either pre- or post-LTX). Patients were observed for 1 year posttransplant.
RESULTS: Ninety-eight patients met inclusion criteria. Overall mean percentage of patient-days at goal was 73% with a trend toward improvement from 2005 (69%) to 2007 (80%); p=0.041. When analyzed by DM status, the poorest control was observed in the pre-LTX DM patients, both in the outpatient setting and overall. Similar trends were seen in mean glucoses both by transplant year and DM status. By year, guideline adherence was consistently achieved, although more patients were counseled in 2007. By DM status, incidence of wound infections was highest in the transitory NODM group.
CONCLUSION: Although improvement was shown, we did not attain 85% of glucose readings at goal. Glycemic control and guideline adherence improved from 2005 to 2007. Standardization of inpatient and outpatient processes and customization of pre-DM LTX patient management may improve outcomes.

Urology

210E. Assessment of cardiovascular (CV) comorbidity in patients with overactive bladder (OAB). Jaewhan Kim, Ph.D.,[1] Carl Asche, Ph.D.,[1] Kristijian Kahler, RPh, Ph.D.,[2] *Amit S. Kulkarni, Ph.D.,*[2] Karl-Eric Andersson, M.D., Ph.D.[3]; (1) Pharmacotherapy Outcomes Research Center, Salt Lake City, UT; (2) Novartis Pharmaceuticals Corporation, East Hanover, NJ; (3) Wake Forest University, Winston-Salem, NC
PURPOSE: Antimuscarinic drugs used in OAB potentially increase heart rate (HR). Elevated HR is linked to mortality and CV events in patients with CV comorbidities. This is a concern for OAB patients because autonomic imbalance associated with OAB may increase the likelihood of CV comorbidities.
OBJECTIVE: To determine the proportion of OAB patients potentially at risk of adverse events by assessing preexisting CV comorbidity.
METHODS: This retrospective cohort study used the GE Centricity EMR database. Patients with OAB were identified by ICD-9 codes or a prescription between January 1, 1996, and March 30, 2007, for an OAB antimuscarinic agent. Patients with OAB with 13 months of continuous eligibility pre- and postindex date formed the OAB cohort. Based on the presence of pharmacy claim for OAB antimuscarinic agents, the OAB cohort was stratified as treated or untreated. A random sample of age- and gender-matched patients with no diagnosis of OAB, urinary bladder dysfunction, or pharmacy claim for OAB antimuscarinic agent formed a non-OAB control cohort. For 6 months before OAB diagnosis/treatment, CV comorbidity as measured by biologic measures, CV diagnoses, and CV concomitant drugs was assessed across the cohorts using t-tests or χ^2 tests as appropriate.
RESULTS: Patients with OAB (n=41,440; 83.6% women; median age, 65 years) compared with patients without OAB (n=77,272; 83.2% women; median age, 64 years) were more likely to have CV comorbidities (57.6% vs. 44.6%; p<0.001), higher HR (80 beats/minute) (31.4% vs. 19.9%; p<0.001), and use of CV medications (57.1% vs. 38.8%; p<0.001). In treated versus untreated patients with OAB, CV comorbidities (58.8% vs. 53.7%; p<0.001), proportion with higher HR (32.3% vs. 27.6%; p<0.001), and use of CV medications (60.7% vs. 42.4%; p<0.001) differed.
CONCLUSIONS: Preexisting CV comorbidities were more prevalent in patients with OAB than in patients without OAB and in those receiving antimuscarinic treatment than in patients not receiving treatment.
Presented at International Society for Pharmacoeconomics and Outcomes Research 14th Annual International Meeting, Orlando, FL, May 16–20, 2009.

211E. Pharmacokinetics and safety of silodosin in subjects with moderate liver dysfunction. *Lawrence A. Hill, Pharm.D., RPh,* Weining Volinn, M.S., Gary Hoel, RPh, Ph.D.; Watson Laboratories, Salt Lake City, UT
PURPOSE: Silodosin, a selective β-blocker, rapidly improves urinary symptoms in patients with benign prostatic hyperplasia, and

it is well tolerated. The pharmacokinetics (PK) and safety of silodosin in subjects with moderate liver dysfunction (LD) were studied.
METHODS: In this open-label crossover study, 18 men (white; 47–68 years) were enrolled, 9 with moderate liver dysfunction (Child-Pugh score 7–9) and 9 weight- and age-matched controls. Subjects received a single dose of silodosin 4 mg on day 1 of a 7-day period and a single dose of silodosin 8 mg on day 1 of the consecutive 7-day period. Plasma PK and adverse events (AEs) were evaluated daily; urinary elimination PK was evaluated for 48 hours postdose in the 8-mg dosing period only.
RESULTS: Indocyanine green tests confirmed a significant degree of LD in eight subjects. C_{max} and AUC (0–72) values for total (bound and unbound) silodosin and its two primary metabolites, KMD-3213G and KMD-3293, were lower slightly in LD than in control subjects. The ratios of AUC(0–72) and C_{max} for LD versus control subjects (LD:control) were 0.7 for silodosin 4 mg and 0.8 for silodosin 8 mg. For the two main metabolites of silodosin, LD-to-control ratios of AUC (0–72) and C_{max} ranged from 0.5 to 0.7. Compared with controls, LD subjects had slightly higher C_{max} and AUC (0–72) values for unbound silodosin (LD:control subjects, 1.0–1.3) and a wider range of values for unbound metabolites (LD:control subjects, 0.2–0.9). Renal clearance of all moieties was higher in LD than in controls. All (10) AEs were mild; 6 were treatment related. Two LD subjects had treatment-related orthostatic hypotension.
CONCLUSIONS: The PK of silodosin and its primary metabolites was changed only slightly in subjects with moderate LD. Silodosin was safe and well tolerated in all subjects.
Published in Hill LA, Volinn W, Hoel G. Pharmacokinetics of silodosin and its primary metabolites in subjects with moderate liver dysfunction. Clin Pharmacol Ther 2009;85(Suppl 1):S71.

CLINICAL PHARMACY FORUM

ADR/Drug Interactions

212. Evaluation of medication errors via a computerized physician order entry system in an inpatient renal transplant unit. *Kwaku Marfo, Pharm.D.*, Daniel Garcia, Pharm.D., Saira Khalique, Pharm.D., Amy Lu, M.D., Karen Berger, B.A.; Montefiore Medical Center, Bronx, NY
PURPOSE: Medication errors are a prime concern for all in health care. It is estimated that between 44,000 and 98,000 Americans die of medical errors each year in hospitals and that as many as 40% of these deaths could have been prevented. The use of information technologies in drug prescribing and administration has received considerable attention in recent years with the hope of decreasing medication errors and thereby improving patient safety. Because of the complexity of drug regimens in renal transplant patients, the occurrence of medication errors is inevitable even with a well-adopted CPOE system. Our objective was to quantify medication error type and frequency in an inpatient renal transplant unit.
METHODS: Systematic evaluation of all medication errors during an initial 10-day audit and a 28-day follow-up audit in an inpatient renal transplant unit. Each error was concurrently evaluated for potential to result in adverse patient consequences (category), error type, and associated medication class.
RESULTS: A total of 103 clinically significant medication errors were detected during the 10-day audit (43 errors) and 28-day audit (60 errors) periods. The most common errors were wrong medication dose ordered and wrong time of drug administration. Thirty-six of 66 prescribing/ordering errors reached the patient.
CONCLUSIONS: Even with the use of a computerized physician order entry system in an inpatient renal transplant unit, postkidney transplant patients are at risk of adverse outcomes caused by medication errors. The risk is attributed to the complexity of drug therapy regimens. Although half of the errors were caught before they reached the patient, these near misses illustrate the potential for future errors.

Adult Medicine

213. The impact of glucose control in non-intensive care hospitalized patients: a retrospective review. *Laura Labbe, Pharm.D.,*[1] Sue Kim, Pharm.D., BCPS,[1] Schmidt Justin, Pharm.D., BCPS,[1] Todd Lee, Pharm.D., Ph.D.[2]; (1) Edward Hines Jr. VA Hospital, Hines, IL; (2) Edward Hines Jr. VA Hospital, Hines, IL
PURPOSE: Glucose control affects clinically meaningful outcomes in the critical care setting including length of stay, morbidity, and mortality; however, glucose goals are not aggressively sought in the nonintensive care unit (ICU) setting. An examination of optimal glucose control in the non-ICU setting is warranted.
METHODS: A retrospective chart review of patients admitted to the general medicine service at Edward Hines Jr. VA Hospital was conducted. Patient charts were randomly selected using computer-generated numbers and accessed by the computerized patient record system (CPRS). Two groups of patients were compared: those with hyperglycemia and those without. The primary outcome was the hospital length of stay (LOS). Secondary outcomes included mortality, transfer to ICU, antibiotic use, and troponin elevation.
RESULTS: The differences in a majority of baseline characteristics were not statistically significant between groups. There was, however, a difference in mean age. The average LOS in the controlled glucose group was 4.3 days compared with 5.7 days in the uncontrolled glucose group (p=0.135). After adjusting for baseline characteristics, controlled glucose was associated with a 1.79-day reduction in LOS compared with uncontrolled glucose (p=0.057). The difference in antibiotic initiation was statistically significant between groups; 29 patients in the controlled glucose group versus 42 in the uncontrolled glucose group required antibiotics (p=0.02). Differences in mortality, discharge to ICU, troponin concentrations, and hypoglycemic events were not statistically significant between groups.
CONCLUSION: Controlled glucose in non-ICU hospitalized patients at Hines VA Hospital was associated with a 1.79-day reduction in LOS compared with uncontrolled glucose. This reduction approached, but did not achieve, statistical significance.

Ambulatory Care

214. Evaluation of hypertension management in patients treated in the pharmacist-run outpatient pharmacotherapy clinics at Grady Health System. *Crystal M. Calloway, Pharm.D.,*[1] Akilah Strawder, Pharm.D.,[1] Nurcan Ilksoy, M.D.[2]; (1) Grady Health System, Atlanta, GA; (2) Emory University School of Medicine, Atlanta, GA
PURPOSE: To assess the impact of clinical pharmacists' interventions on assisting patients and their primary care providers (PCPs) in achieving Joint National Committee (JNC 7) blood pressure (BP) goals in a large, urban teaching institution.
METHODS: This IRB-approved study was a retrospective chart review of patients seen in the pharmacist-run outpatient clinics at Grady Health System (GHS) from July 1, 2007, to July 1, 2008. Patients were included if they had two or more consecutive visits to any of the pharmacist-run clinics, a documented diagnosis of hypertension (HTN), and a documented referral to the pharmacotherapy clinics for HTN management. Patients were excluded if their medication therapy was changed by an outside provider between visits to the pharmacotherapy clinics.
RESULTS: A total of 51 patients were included in the study. Twenty-three (45%) of the 51 patients were at their JNC 7 BP goal at their last visit in the pharmacy clinic. Twenty-two (43%) of the 51 patients were at their JNC 7 BP goal at their first follow-up visit with the PCP after being discharged from the pharmacy clinic. Patients experienced a median reduction in systolic BP (SBP) from baseline to last pharmacy clinic visit of 17 mm Hg (10.9% SBP reduction) and a median reduction in diastolic BP (DBP) from baseline to last pharmacy clinic visit of 8 mm Hg (10% DBP reduction). The median reduction in SBP from baseline to the follow-up visit with the PCP after being discharged from the pharmacy clinic was 15 mm Hg (9.7% SBP reduction); the median reduction in DBP from baseline to the follow-up PCP visit was 0 mm Hg (0% DBP reduction).

CONCLUSIONS: Pharmacists' interventions were effective in helping almost half of the patients studied reach their JNC 7 BP goals. Patients experienced clinically significant BP reductions because of pharmacists' interventions in the pharmacotherapy clinics.

215. Diabetic nephropathy guideline adherence among family medicine physicians. Ashley Trull, Pharm.D.,[1] *Renee M. DeHart, Pharm.D.*[2]; (1) Samford University McWhorter School of Pharmacy, Birmingham, AL; (2) University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR

PURPOSE: The American Diabetes Association (ADA) publishes guidelines regarding diabetic nephropathy screening and treatment. Despite a wealth of literature to support them, guideline adherence is historically poor. This study provides an updated examination of screening and treatment trends among family medicine physicians.

METHODS: After IRB approval, data were collected by chart audit of patients with diabetes at a family medicine program of 19 physicians. The primary end point was the percentage of patients screened per ADA guidelines the previous year. Secondary end points were changes in therapy after screening and subgroup comparisons based on age, gender, race, and presence of hypertension, heart failure (HF), or chronic kidney disease (CKD).

RESULTS: Data from 254 patients were reviewed. Seventy-two patients (28.5%) were screened the previous year. Of these, 65 (89.0%) were screened using the spot collection method, whereas 8 (11.0%) were screened by 24-hour urine collection. The only characteristic found to be predictive of screening was the absence of HF. Patients without HF were significantly more likely to be screened (31% vs. 14% for HF negative, p=0.046). Screening rates did not differ based on the presence of hypertension (29% vs. 22% nonhypertensive, p=0.44), gender (20% male vs. 32% female, p=0.08), presence of CKD (27% vs. 29%, p=0.85), age younger than 50 years (26% vs. 30% for age older than 50, p=0.64), or race (45% for blacks vs. 41% other races, p=0.57). Regarding anti-angiotensin use, 227 patients (89.7%) were prescribed an ACE inhibitor or ARB; 32 (43.8%) screened patients had evidence of micro- or macroalbuminuria. All 32 screened patients were prescribed anti-angiotensin therapy by the time of data collection. Six (18.8%) were prescribed a change in anti-angiotensin therapy after testing.

CONCLUSIONS: The screening rate of 28.5% is well below optimal. The only factor predictive of screening was the absence of HF. Screening for nephropathy led to alterations in therapy in a subset of patients.

216. Pharmacist medication reconciliation in a primary care setting. *Autumn L. Runyon, Pharm.D.,*[1] Kevin J. Lynch, Pharm.D., BCPS,[2] Christine Tumis, Pharm.D.,[3] Suzanne Higginbotham, Pharm.D.,[1] Hildegarde J. Berdine, Pharm.D., BCPS[4]; (1) Duquesne University, Mylan School of Pharmacy, Pittsburgh, PA; (2) Pfizer, Inc., Upper St. Clair, PA; (3) Duquesne University, Pittsburgh, PA; (4) Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA

PURPOSE: Medication reconciliation is recognized as a critical patient safety initiative, with the Joint Commission requiring organizations to "accurately and completely reconcile medications across the continuum of care." Although research has demonstrated the importance of medication reconciliation in the hospital setting, little information exists to describe the current state of medication reconciliation in an outpatient primary care setting. This study seeks to describe the types and causes of discrepancies between patient-reported medications and medications listed in the medical chart as identified during pharmacist medication reconciliation.

METHODS: An observational case-series design was used. Participants were recruited from a primary care clinic and a physician office practice. Patient interviews were conducted on-site by pharmacists before the scheduled physician visit. The patient interview gathered demographic variables, medication name, dose, regimen, and indication. Patient-reported medications were compared with data collected from the charted medication list to identify discrepancies between the patient chart and self-reported medications. Discrepancies identified were categorized and coded by "Discrepancy Type" and "Discrepancy Reason(s)."

RESULTS: Descriptive analysis and statistics will be used. Demographic variables and frequency of discrepancies will be collected and reported. The types and reasons for discrepancies will also be collected and described. All results will be presented at the ACCP Annual Meeting in October 2009.

CONCLUSIONS: Medication reconciliation is necessary along the continuum of care because discrepancies exist between charted medication lists and actual medications being taken by the patient. Pharmacists are able to identify and correct discrepancies between charted medications and patient-reported medications.

217. Development of a clinical pharmacy services provider network for homeless patients. *Leticia R. Moczygemba, Pharm.D., Ph.D.,*[1] Gary R. Matzke, Pharm.D.,[1] Sharon B.S. Gatewood, Pharm.D.,[1] Akash Alexander, Pharm.D.,[1] Amy Kennedy, Pharm.D.,[1] Robert D. Osborn, MSW,[2] Jean-Venable R. Goode, Pharm.D.,[1] Dianne Reynolds-Cane, M.D.[2]; (1) Virginia Commonwealth University School of Pharmacy, Richmond, VA; (2) Daily Planet, Inc., Richmond, VA

PURPOSE: To enhance the continuity of clinical pharmacy services at transition points of care through the development of a provider network.

METHODS: The Daily Planet, Inc., a Health Care for the Homeless Clinic, and the Virginia Commonwealth University School of Pharmacy (VCU SOP) through their collaborative care provision to homeless mental health patients have identified many barriers to optimal medication use. Homeless patients have high rates of mental and physical health problems and substance abuse, which are exacerbated by living on the streets and in shelters. In addition, homeless patients often experience transitions of care, such as emergency department visits or incarcerations, which may lead to medication errors and gaps in medication use for chronic diseases. Disruptions in patients' medication regimens decrease medication adherence and can lead to poor health outcomes. Therefore, the Daily Planet and VCU SOP providers proposed a plan to enhance the communication and quality of care with community providers. The first step in this process was to create a Clinical Pharmacy Services Provider Network (CPSPN) to minimize medication errors and gaps in medication use during transitions of care. The CPSPN currently has four additional partners, VCU Health System Outpatient Pharmacy, VCU Health System Emergency Department, and two community pharmacies, all of which have enthusiastically endorsed the mission to coordinate clinical pharmacy services with an initial focus on medication reconciliation.

RESULTS: Initial funding for this CPSPN initiative has been received from the VCU Council for Community Engagement. This pilot project will test the utility of the network's foundational electronic tool for coordinating medication reconciliation between the Daily Planet-VCU team and community providers.

CONCLUSION: The CPSPN concept has been implemented, and further expansion to additional partners, which includes inpatient treatment and correctional facilities, is planned. The initial results of the pilot project will be available in fall 2009.

218. Implementation and results of a pharmacist-led hypertension clinic. *Kimberly L. Liang, Pharm.D.*, Daniel F. Seidensticker, M.D., Christopher B. Haas, D.O.; Naval Medical Center San Diego, San Diego, CA

PURPOSE: The Naval Medical Center Hypertension Clinic was developed in mid-2007 and after protocol approval by the Pharmacy & Therapeutics Committee, begun in late 2007. The protocol is based on current JNC VII Hypertension Guidelines, and the medications used are in accordance with the Department of Defense formulary.

Patients are initially evaluated and treated by their primary cardiologist and then referred to the Hypertension Clinic. The pharmacist performs continuing evaluation and treatment delivery, including medication initiation or adjustments and appropriate consults to other services, and then reports the patient's progress to the referring physician for review and final approval.

The purpose of this poster is to present observational data from our Hypertension Clinic collected from late 2007 to early 2009

regarding the success of achieving blood pressure goals in a diverse patient population under the care of a pharmacist with cardiologist supervision.
METHODS: The population includes active duty members from any military branch and their dependents and retirees and their dependents. Ages range from 19 to 92 years. Patients can have isolated hypertension but many are classified as having resistant hypertension, making management more complicated.
RESULTS: One hundred fifty patients were referred to the clinic, 60 of whom were not at goal on their initial visit with the pharmacist. Each of them had at least one subsequent visit to the clinic. Of these 60 patients, 73.3% (n=44) were at their goal within 6 months according to the applicable JNC-VII guidelines; 16.7% (n=10) were not at goal but had improvement in their blood pressure; 10% (n=6) had no improvement.
CONCLUSIONS: Results show that an intensive Hypertension Clinic operated by a pharmacist with cardiologist supervision can greatly improve blood pressure control in a diverse population compared with the generalized national average reported by JNC VII of 34% of patients controlled to less than 140/90 mm Hg.

219. Clinical pharmacist impact on lowering hemoglobin A1c in patients with diabetes. *Kevin J. Bacigalupo, Pharm.D.*, Frank J. Svete, Pharm.D., BCPS, Todd Lee, Ph.D., Pharm.D.; Edward Hines Jr.; VA Hospital, Hines, IL
PURPOSE: The purpose of this research was to evaluate the impact of clinical pharmacist–managed clinics compared with standard care for patients with diabetes in a VA setting using improvement in hemoglobin A1c as the primary outcome.
METHODS: This was a retrospective chart review of 279 patients identified as taking either oral antihyperglycemic medications or insulin with a documented hemoglobin A1c of more than 9% within 1 year of November 21, 2007. Patients' records were reviewed for pertinent demographic data, laboratory data, visit information, and objective screening and medication parameters. Data for all primary and secondary end points were evaluated at baseline and at 12 months from baseline using the last measure carried forward method.
RESULTS: Patients whose treatment was managed by clinical pharmacists had a greater mean A1c reduction than those receiving standard care (1.9% vs. 1.3%, p=0.036). There was a larger percentage of patients with treatment managed by clinical pharmacists who received appropriate antiplatelet therapy (84% vs. 74%, p=0.031), who were using insulin (84% vs. 62%, p<0.001), and who had appropriate urine microalbumin screenings (84% vs. 71%, p=0.008). The average number of per patient clinic visits where diabetes was addressed was also higher in the pharmacist group (8.1 vs. 4.5, p<0.001).
CONCLUSION: Patients with diabetes receiving care from the clinical pharmacist group saw a significant mean hemoglobin A1c reduction compared with those receiving standard care. Patients were also more likely to receive appropriate antiplatelet therapy, insulin treatment, and urine microalbumin screenings. These findings confirm the need and the benefit for clinical pharmacists to assist with diabetes management in the primary care setting.

220. Evaluation of the therapeutic use and monitoring of outpatient amiodarone therapy in a Veterans Administration population. *Erika J. Briegel, Pharm.D.*, Arthur L. Allen, Pharm.D., CACP, Scott E. Mambourg, Pharm.D., BCPS, William F. Graettinger, M.D., FACC; Veterans Administration Sierra Nevada Health Care System, Reno, NV
PURPOSE: An initial review of ambulatory care patients receiving amiodarone at the Sierra Nevada Health Care System demonstrated poor adherence with recommended monitoring parameters and a need to readdress appropriateness of therapy based on indication. This study examined the impact of a pharmacist-driven program designed to ensure appropriate indication for and monitoring of amiodarone therapy versus usual care.
METHODS: Medical records of 157 patients receiving outpatient amiodarone from May to October 2008 were reviewed. Documentation included indication for amiodarone therapy, presence or absence of a thyroid panel, liver panel, and ECG in the preceding 6 months and presence or absence of chest radiography in the past year. Providers were alerted about potential amiodarone-related adverse effects. If patients were found to have deficiencies in recommended monitoring, laboratory and imaging studies were ordered by the clinical pharmacist for review by the provider. Patients who were eligible for discontinuation of rhythm control strategy were reviewed with cardiology, and if appropriate, a rate control strategy replaced rhythm control with amiodarone.
RESULTS: After review, 114 patients were eligible for the study. Complete adherence with recommended monitoring was present in 17% (19 of 114) of patients. Adherence with individual tests was as follows: thyroid panel, 44.7%; liver panel, 51.8%; ECG, 30.7%; and chest radiography, 48.7%. After intervention by the clinical pharmacist, complete adherence with recommended drug monitoring parameters was achieved in 100% of patients. Of patients initially thought to be eligible for discontinuation (32 of 114), 16 continued therapy, 2 continued therapy with a reduced dose, 10 discontinued therapy, and 4 have pending test results.
CONCLUSIONS: Pharmacist involvement in amiodarone therapy allows greater adherence with recommended monitoring for adverse effects. In addition, the burden of monitoring and risk of toxicity may be eliminated altogether if amiodarone is actively pursued for discontinuation when found to be ineffective.

221. Development of a Comprehensive Clinical Pharmacy Service (CCPS) practice model in a health care for the homeless clinic. *Jean-Venable R. Goode, Pharm.D.,*[1] Amy K. Kennedy, Pharm.D.,[1] Leticia R. Moczygemba, Pharm.D., Ph.D.,[1] Sharon B.S. Gatewood, Pharm.D.,[1] Akash J. Alexander, Pharm.D.,[1] Robert D. Osborn, MSW,[2] Gary R. Matzke, Pharm.D.,[1] Dianne Reynolds-Cane, M.D.[2]; (1) Virginia Commonwealth University School of Pharmacy, Richmond, VA; (2) Daily Planet, Inc., Richmond, VA
PURPOSE: To develop a Comprehensive Clinical Pharmacy Service (CCPS) practice model to increase the availability and scope of clinical pharmacy services for underserved patients who receive their primary care at the Daily Planet, Inc., a federally qualified Health Care for the Homeless (HCH) clinic.
METHODS: The CCPS practice model was developed to improve medication outcomes in an underserved homeless population. The CCPS incorporates the following five components: 1) medication therapy management (MTM); 2) disease state management (DSM); 3) health education; 4) drug information; and 5) interprofessional and community integration and coordination of care. The foundation of CCPS is MTM, and all patients will receive a yearly session to identify and resolve drug-related problems. Four clinical pharmacists will also provide DSM, which will initially focus on the management of diabetes mellitus, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, and obesity, for patients who meet national eligibility guidelines for each disease state. Education, which promotes healthy living and foundational disease management principles, will be provided by print materials, by video, and during pharmacist-directed individual or group sessions. Pharmacists will also serve as a drug information resource for clinic patients and providers. Finally, the pharmacists will facilitate coordination of care with community partners such as local pharmacies, emergency departments, and jails. An electronic medical record will be used to document all CCPS activities. The CCPS practice model will be implemented in July 2009 and is a dramatic expansion of clinical pharmacy services provided since 2005.
RESULTS: The staff and physicians of the HCH clinic have enthusiastically endorsed the CCPS to provide clinical pharmacy services for this high-risk patient population.
CONCLUSION: It is hoped that the CCPS will serve as a model for the provision of clinical pharmacy services in an underserved population in the greater Richmond community.

222. Relationship between medication intolerance and achieving therapeutic goals for hypertension, diabetes, and hyperlipidemia. *Julianna M. Kula, Pharm.D.,*[1] James D. Hoehns, Pharm.D.,[2] Michelle L. Graham, M.D.,[1] John E. Sutherland, M.D.,[1] Robert Greenwood, RPh,[3] Erin E. Thatcher, B.A., Biochemistry[4]; (1) NEIFPC, Waterloo,

IA; (2) University of Iowa College of Pharmacy/Northeast Iowa Family Practice Center, Waterloo, IA; (3) Greenwood Pharmacy, Waterloo, IA; (4) University of Iowa, Iowa City, IA

PURPOSE: Experiencing a medication intolerance may lead to a delay in a patient's ability to achieve a therapeutic goal in the short term; however, there is little evidence relating how drug intolerance affects a patient's eventual ability to meet his/her therapeutic goal in clinical practice. The objective of this study was to determine the association of drug intolerance with the ability of patients with hypertension, diabetes, or hyperlipidemia to reach their therapeutic goals.

METHODS: An electronic medical record (EMR) was used to identify active patients with hypertension, diabetes, or hyperlipidemia within our clinic. The EMR for these patients was reviewed for all recorded drug intolerances. For each drug intolerance, the therapeutic class of drug involved and frequency were collected. Patients were assessed to see whether they were at their therapeutic goal for each disease state (hypertension, diabetes, or hyperlipidemia). For each disease state, drug intolerances related to that condition and drug intolerances overall were evaluated for their association with achieving therapeutic goals.

RESULTS: There were 1680 patients identified with one or more conditions (diabetes, n=415; hypertension, n=1288; and hyperlipidemia, n=1323). One or more drug intolerances of any medication type were observed in 49.5% of the patients. Drug intolerances specific to their condition were observed in 2.5%, 6.1%, and 5.7% of patients with diabetes, hypertension, and hyperlipidemia, respectively. Patients with an intolerance to a disease-specific medication were less likely to achieve therapeutic goals than those without such an intolerance: diabetes (12.5% vs. 66.7%, p=0.001); hypertension (61.1% vs. 71.2%, p=0.07), and hyperlipidemia (56.7% vs. 68.3%, p=0.061). The frequency of nondisease-specific medication intolerances was not related to ability to achieve therapeutic goal.

CONCLUSION: Patients with intolerance to a medication specific for diabetes, hypertension, or hyperlipidemia were less likely to reach their respective therapeutic goal. Such patients may warrant additional attention to ensure optimal care.

223. Pharmacist-physician collaboration to improve hyperlipidemia treatment among diabetic patients. Doug Hansen, Pharm.D.,[1] Chris Accola, Pharm.D., PA-C,[1] *James D. Hoehns, Pharm.D.*,[2] John E. Sutherland, M.D.[1]; (1) Northeast Iowa Family Practice Center, Waterloo, IA; (2) University of Iowa College of Pharmacy/Northeast Iowa Family Practice Center, Waterloo, IA

PURPOSE: Patients with diabetes are at elevated risk of cardiovascular events and warrant special consideration and effort for treatment of risk factors such as hyperlipidemia. The National Cholesterol Education Program (NCEP) recommends an LDL goal of less than 100 mg/dL for individuals with diabetes. The purpose of this quality improvement project was to characterize adherence to NCEP guidelines among patients with diabetes at the Northeast Iowa Family Practice Center (NEIFPC) as well as to evaluate whether a pharmacy student–initiated action plan would help improve the frequency with which patients with diabetes attain their LDL goal.

METHODS: The electronic medical record at NEIFPC was queried to identify active patients with diabetes. Information for each patient was collected regarding recent LDL values, current and past hyperlipidemia treatment, drug intolerances, and previous physician actions. For patients not achieving their LDL goal, an individualized hyperlipidemia treatment plan was initiated by the pharmacy student and suggested to the physician. A pre-post comparison was performed to evaluate the primary outcome of patients achieving an LDL goal of less than 100 mg/dL after 4 months.

RESULTS: Of the 362 patients identified with diabetes, 246 (68.0%) were already at the LDL goal of less than 100 mg/dL, and 79.6% were taking lipid medication. There were 116 patients not at LDL goal who were the focus of this intervention. Their baseline mean LDL was 123 (±24), and 69% were on lipid medication. Pharmacy students made therapeutic recommendations to the primary physician for 80 patients. After 4 months, the most recent mean LDL (n=116) was 113 (±33) (p=0.002), and 28 (24.1%) of 116 were at LDL goal (p<0.001).

CONCLUSION: This quality improvement project, which was patient-specific and initiated by pharmacy students, resulted in a significant improvement in hyperlipidemia care among patients with diabetes.

224. Establishment of a pharmacist-managed pharmacotherapy clinic. *Heidi M. Wood, Pharm.D.*, Erica F. Pearce, Pharm.D., Kathleen E. Horner, Pharm.D., BCPS, Deanna L. McDanel, Pharm.D., BCPS, Ryan B. Jacobsen, Pharm.D., BCPS, Lisa A. Mascardo, Pharm.D.; University of Iowa Hospitals and Clinics, Iowa City, IA

PURPOSE: The clinical and economic impact pharmacists can have on achieving therapeutic outcomes through specialized disease state management programs has been recognized, and the provision of direct patient care by pharmacists has increased as a result. Most states have legislation in place that allows pharmacists to collaborate with physicians and enhance patient care through the use of collaborative practice agreements (CPAs). The purpose of this project was to establish a referral-based, pharmacist-managed pharmacotherapy clinic at the University of Iowa Hospitals and Clinics (UIHC).

METHODS: The development phase of the clinic included identifying disease states most in need of additional management, writing and receiving approval of CPAs, formulating policies and procedures, establishing a referral process, investigating the process for billing and reimbursement for clinical services, and educating referring providers about this new clinic. Initial services provided by the clinic included management of hypertension, dyslipidemia, and type 2 diabetes mellitus.

RESULTS: The following clinic development steps are complete: protocols for collaboration and corresponding polices and procedures for each of the managed disease states were approved by the institution's Pharmacy & Therapeutics Subcommittee, a patient referral system was launched, a billing method for clinic services was established, and physicians were familiarized with this new service. Referrals are being received from physicians, and patients are being scheduled for an initial clinic visit.

CONCLUSION: At this time, the pharmacist-managed pharmacotherapy clinic is fully established, and it is accepting patient referrals. In addition to providing this clinical service, data will be collected to evaluate outcomes of the clinic, including achievement of therapeutic targets, economic outcomes, and physician and patient perceptions.

Antimicrobial Stewardship

225. Impact of pharmacists on the management of *Clostridium difficile* associated disease in a community hospital. *Janice R. McDonough, Pharm.D.*, Kenneth R. Eugenio, Pharm.D., Robert A. Motha, RPh, MBA; St. Luke's Hospital, New Bedford, MA

PURPOSE: *Clostridium difficile*–associated disease (CDAD) is often complicated by significant morbidity and mortality. Across a broad array of disease states, pharmacists have been shown to improve patient care. We sought to determine the impact of pharmacists on the care of patients with CDAD in a 390-bed community, nonteaching hospital.

METHODS: Thirty-nine inpatients, with 45 documented episodes of CDAD, were retrospectively reviewed from October 2008 to January 2009 and served as the control group. The pharmacy intervention group consisted of 25 patients with CDAD prospectively identified and observed by a pharmacist between February 2009 and May 2009. Patients' medical history, age, serum creatinine, white blood cell count, number of CDAD occurrences, appropriateness of CDAD treatment (i.e., evidence based), severity of illness, length of stay, and outcome were documented.

RESULTS: Appropriate evidence-based treatment of CDAD occurred in 72% of the patients retrospectively reviewed. The all-cause mortality rate for this group was 30%; attributable mortality was not established. Pharmacy interventions resulted in evidence-based treatment for 88% of the patients with an all-cause mortality rate of 4%. Patients not meeting preestablished treatment guidelines included two patients with significant clinical improvement on metronidazole, despite meeting criteria for vancomycin, and one

patient taking vancomycin for an initial episode of mild CDAD secondary to a physician preferring to avoid a significant drug interaction with warfarin.
CONCLUSIONS: This study demonstrated that 28% of the patients in our facility were not optimally treated before pharmacy intervention. A pharmacist had a substantial impact on the treatment and outcomes of patients with CDAD. Pharmacists can improve prescribing practices and outcomes by assisting with the implementation of evidence-based treatment recommendations. Automated alerting methodologies are currently being evaluated to broaden the impact of this effort to involve all pharmacists in our hospital.

Cardiovascular

226. Utilization of acute coronary syndrome secondary prevention pharmacotherapy at discharge. *Lana Y.H. Lai, Pharmacy,*[1] L.L. Tiong, Pharmacy,[2] Yanti N. Sani, Pharmacy,[3] Alan Y.Y. Fong, Cardiology,[4] M.A. Kamarunnesa, Pharmacy,[5] S.A.R. Sameerah, Pharmacy,[6] Kh. Sim, Cardiology[4]; (1) Department of Pharmacy, Sibu Hospital, Sibu, Malaysia; (2) Department of Pharmacy, Sarawak General Hospital, Kuching, Malaysia; (3) Clinical Research Center, Kuching, Malaysia; (4) Department of Cardiology, Sarawak General Hospital, Kuching, Malaysia; (5) Department of Pharmacy, Serdang Hospital, Serdang, Malaysia; (6) Pharmaceutical Services Division, Ministry of Health, Kuala Lumpur, Malaysia
PURPOSE: To investigate the use of secondary prevention pharmacotherapy prescribed at discharge in patients with ACS and to evaluate its relevance with clinical or laboratory parameters.
METHODS: A prospective cross-sectional audit was conducted at 15 Ministry of Health hospitals in Malaysia. Six hundred seven patients, discharged with a principal diagnosis of ACS between December 2008 and January 2009, enrolled. This study focused on the use of antiplatelets, b-blockers, inhibitors/angiotensin receptor blockers (ACE-I/ARBs), and statins. Data were obtained from case notes, discharge summaries, and prescriptions. SPSS version 16.0 was used for analysis.
RESULTS: Aspirin was the most commonly prescribed antiplatelet (90.8%), followed by clopidogrel (71.7%); 69.0% of patients with ACS received dual antiplatelet therapy (DAP), the predominant combination being aspirin and clopidogrel. Eighty-five percent of STEMI patients received DAP compared with 63.7% of UA/NSTEMI patients. Statins were commonly prescribed (96.2%), particularly lovastatin, simvastatin, and atorvastatin (45.9%, 45.7%, and 8.0%), respectively. Choice of statin prescribed was closely associated with admission serum lower density lipoprotein-cholesterol (LDL-C) concentration. Mean LDL-C for the lovastatin group was 2.75 (SD 1.30) for simvastatin, 3.51 (SD 1.42); and for atorvastatin, 3.59 (SD 1.82). A total of 73.6% of patients were prescribed b-blockers (BB), with metoprolol most commonly prescribed (62.8%). Carvedilol and bisoprolol prescriptions were relatively less (10.8% and 23.8%, respectively). A total of 89.5% of patients prescribed BBs had preserved left ventricular systolic function by echocardiography (LVEF of 40% or more); 73.1% of patients were prescribed ACE-I/ARB. In the latter group, 46.2% had diabetes, and 10.6% had an LVEF less than 40%. Perindopril was the most commonly prescribed drug in this category (81.5%).
CONCLUSIONS: There is good use to evidence-based ACS secondary prevention pharmacotherapy in public hospitals of a developing country. Clinical pharmacists will have an increasing role in the translation of evidence-based guidelines to direct patient care.

227. Cost minimization analysis with tirofiban and eptifibatide in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Regan M. Healy, Pharm.D.*, Matthew W. Call, Pharm.D., Curtis J. McEntire, B.S., Kathryn D. Mathews, Pharm.D., BCPS; Intermountain Medical Center, Murray, UT
PURPOSE: Glycoprotein IIb/IIIa inhibitors (GPIs) have an established role in the management of therapy for patients experiencing acute coronary syndrome (ACS). Within the class 2 small molecule agents, tirofiban and eptifibatide share similar pharmacodynamic and pharmacokinetic properties. Recent investigation of high-bolus dosing (HBD) of tirofiban appears favorable when evaluated in platelet and clinical studies specifically in patients undergoing percutaneous coronary intervention (PCI). We sought to perform a cost analysis with the intent to pursue an agent demonstrating the best market value for the Intermountain Healthcare System.
METHODS: This cost-minimization analysis compared the total use cost of tirofiban versus eptifibatide. The study comparison integrated variables contributing to cost fluctuations. Variables included HBD, weight-based dosing, various infusion durations, and nursing administration fees. These variables were incorporated into the final cost per patient as well.
RESULTS: After data collection and comparison, evidence of the financial benefit of tirofiban was confirmed. For Intermountain Healthcare, the expense decrease was estimated at 52% with an annual savings of $812,000. Presentation of a formulary conversion proposal is planned for the Pharmacy & Therapeutics Committee meeting in August 2009.
CONCLUSION: Tirofiban is an acceptable alternative to eptifibatide in patients with ACS undergoing PCI. Systemwide formulary conversion to tirofiban will result in significant cost savings for Intermountain Healthcare.

228. Evaluation of blood pressure in hypertensive patients following formulary conversion in angiotensin receptor blocker. *Tripti Kurup, Pharm.D.*, Christina W. Rivers, Pharm.D., BCPS, Todd Lee, Pharm.D., Ph.D.; Edward Hines Jr. VA Hospital, Hines, IL
PURPOSE: In June 2005, the VA formulary angiotensin II receptor blocker (ARB) changed from candesartan to losartan or valsartan. Patients with heart failure were converted to valsartan, and patients with other indications were converted to losartan. The purpose of this study was to determine whether blood pressure was maintained in hypertensive patients who were converted to losartan.
METHODS: This was a retrospective chart review evaluating 95 hypertensive patients who were switched from candesartan to losartan at Edward Hines Jr. VA Hospital over a period of 6 months before and 6 months after the conversion. Subjects were evaluated for the following: two to four most recent blood pressure readings 6 months before and after the conversion, serum creatinine, serum potassium, adverse effects, changes in ARB dosing, and changes in other antihypertensive medications.
RESULTS: The change in systolic blood pressure after the conversion was –1.56 (p=0.28) and –1.27 in diastolic blood pressure (p=0.15). The mean serum creatinine concentration was 1.59 mg/dL before and 1.61 mg/dL after the conversion (p=0.55). The mean potassium concentration was 4.6 mEq/L before and 4.5 mEq/L after the conversion (p=0.06). Ten patients required losartan dose adjustments because of unchanged but elevated blood pressure, elevation in blood pressure, or elevated blood pressure because of change in diuretic dose. Postconversion, there was an increased use of β-blockers (p=0.01) and α-blockers (p=0.01). Doses for other antihypertensive medications were increased in 17.89% of the patients preconversion versus 16.84% of the patients postconversion (p=0.83). Similarly, doses of these medications were decreased in 3.16% of the patients preconversion versus 2.11% of the patients postconversion (p=0.66).
CONCLUSIONS: There was no statistically significant difference detected in blood pressure after the candesartan to losartan conversion. Based on this retrospective review, blood pressure is maintained after formulary ARB conversion.

Clinical Administration

229. Development and implementation of a method for characterizing clinical pharmacy services. *Haitham W. Tuffaha, MBA, M.S., BCOP*, Sara Koopmans, Pharm.D.; King Hussein Cancer Center, Amman, Jordan
PURPOSE: Develop and implement a method to describe clinical pharmacy services. A standard characterization of services in different settings facilitates benchmarking and informs services development.
METHODS: A set of quantifiable parameters to describe clinical

pharmacy activities and the associated medication use was proposed based on previous work and was validated by peer review. For implementation, clinical pharmacy interventions for six wards at the King Hussein Cancer Center in 2008 were prospectively documented, and the number of patients and medications dispensed for the same period were obtained from the admission office and pharmacy database, respectively.
RESULTS: The method comprises several parameters covering four main aspects: 1) number of interventions, 2) type of interventions, 3) number of unit doses dispensed, and 4) number needed to intervene (NNI), which is the number of unit doses dispensed for one intervention to occur. A total of 8980 interventions were recorded for 6500 patients. Interventions were highest in the pediatric oncology and intensive care unit (ICU) with 2696 (30%) and 2001 (22%), respectively, followed by medical oncology, 1654 (18%); bone marrow transplant (BMT), 1036 (12%); hospice, 844 (9%); and surgery, 749 (8%). Interventions per patient were BMT 6.5, ICU 6.4, hospice 2.2, pediatric oncology 1.7, medical oncology 0.9, and surgery 0.3. Main intervention categories for all services were as follows: therapeutic 3055 (34%), safety 2196 (25%), clarifications 1584 (18%), education 925 (10%), quality assurance 481 (5%), and intravenous to oral 311 (4%). The number of doses dispensed per patient was BMT 382, hospice 149, ICU 132, medical oncology 79, pediatric oncology 62, and surgery 36. Finally, NNI was as follows: ICU 21, pediatric oncology 36, BMT 59, hospice 66, medical oncology 91, and surgery 104.
CONCLUSIONS: A method for characterizing clinical pharmacy services has been developed and used to compare different clinical settings. Further research is warranted to refine and validate the parameters proposed.

230. A randomized double-blind (withdrawal) phase 3 study to evaluate the efficacy and tolerability of pancrease-MT capsules compared with placebo in the treatment of subjects with cystic fibrosis-dependent exocrine pancreatic insufficiency. *Gerhard J. Leitz, M.D., Ph.D.*, Andrew Mulberg, M.D., Silber Steven, M.D.; Johnson & Johnson Pharmaceutical Research & Development, LLC, Titusville, FL
PURPOSE: The primary objective of the study was to evaluate the efficacy and tolerability of PANCREASE-MT capsules (MT 10.5 or MT 21).
METHODS: After screening, subjects entered an open-label, run-in phase during which a high-fat diet was initiated, and current pancreatic enzyme therapy was replaced by PANCREASE-MT. When an optimal PANCREASE-MT dose was reached and the high-fat diet was maintained for at least 3 days, subjects underwent the first 72-hour stool collection period to determine the open-label treatment coefficient of fat absorption (CFA). Subjects with a CFA of 80% or more were randomized into the double-blind withdrawal phase to continue either on PANCREASE-MT or matching placebo. After a minimum of 24 hours in the double-blind phase, a repeat 72-hour stool collection was performed to determine the CFA of the double-blind phase.
RESULTS: Forty-nine subjects entered the open-label, run-in phase, and 40 subjects (14 adolescents 12 to less than 18 years old; 26 adults 18 years and older to 60 years) were randomized into the double-blind withdrawal phase. The mean CFA from open-label phase to the end of double-blind phase decreased slightly by 1.4% (88.2%–86.8%) in subjects who continued to receive PANCREASE-MT compared with a decrease by 34.1% (90.5% down to 56.4%) in subjects receiving placebo (between-group difference $p<0.001$). Marked improvements were also noted in the clinical signs and symptoms of EPI (20% vs. 55%), stool consistency, and CGI scores. All treatment emergent adverse events were mild to moderate in severity and occurred less frequently in the PANCREASE-MT group (40% vs. 60%). The most common adverse events were gastrointestinal disorders including abdominal pain, diarrhea, flatulence, and abnormal feces.
CONCLUSION: PANCREASE-MT compared with placebo significantly improved fat and protein absorption that was accompanied by marked improvements in EPI symptoms, stool consistency, and CGI scores. No unexpected adverse events were reported in this population of patients with CF.

231. Financial justification of a clinical pharmacist anticoagulation service at Intermountain Medical Center. *Nannette M. Berensen, Pharm.D., MBA, BCPS,*[1] Missy Skelton Duke, Pharm.D.,[2] Jeff A. Jensen, MBA,[1] Bruce E. Leavitt, Pharm.D., BCPS,[1] Jeffery L. Olson, Pharm.D., BCPS,[1] Russell K. Hulse, MBA[1]; (1) Intermountain Medical Center, Murray, UT; (2) Intermountain Healthcare, Salt Lake City, UT
PURPOSE: Anticoagulants are one of the top five medication classes associated with patient safety incidents. A risk-reduction strategy recommended by The Joint Commission is to implement a pharmacist-managed anticoagulation service. The purpose of this project was to provide the financial justification for funding the development and implementation of a pharmacist-driven anticoagulation service for patients who require chronic anticoagulation.
METHODS: The clinical pharmacist anticoagulation service (CPAS) began at Intermountain Medical Center (IMC) in January 2009. CPAS was originally created to manage patients' acute anticoagulation needs. At about the same time, IMC acquired two cardiology clinics, and it was discovered that around 650 patients would require chronic anticoagulation management. Although it was recognized that the clinical pharmacists had the core competencies to manage the patients' chronic anticoagulation needs, the resources (e.g., point-of-care testing devices, office space, automated voice response system, telephones, computers, decision-support software, additional personnel) would have to be approved and funded before the care for these patients could be assumed. Pro forma projections and a net present value analysis were performed to provide the financial justification to get the project approved. Revenue projections were based on expected laboratory charges, initial patient visits, return patient visits, and remote management encounters. Expenses were analyzed based on one-time expenses, ongoing expenses, and personnel.
RESULTS: The net present value was calculated to be $428,079, and the benefit-cost ratio was 22.78. For the period 2010–2015, the excess of revenue over expenses is projected to be about $110,000 annually. Because of the relatively small amount of capital required for this project, the return of investment was calculated to be 2277%. The project was approved and funded. CPAS began managing the therapy of patients who required chronic anticoagulation in July 2009.
CONCLUSIONS: Financial modeling using standard business methodology is an effective mechanism for getting projects approved.

Community Pharmacy Practice

232. Status of immunization certification among community pharmacists in Alabama. Marilyn Brown, Pharm.D.,[1] *Renee M. DeHart, Pharm.D.*[2]; (1) Samford University McWhorter School of Pharmacy, Birmingham, AL; (2) University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR
PURPOSE: Pharmacists are uniquely positioned to help increase immunization rates and reduce vaccine-preventable disease. In addition to being easily accessible, pharmacists provide extended availability hours; however, there has been little state-specific research on community pharmacists' immunization practices and attitudes. The primary objective of this study was to collect such information among Alabama pharmacists.
METHODS: After IRB approval, 425 surveys were mailed to randomly selected Alabama community pharmacists. Subgroup comparisons of certification rates based on practice setting and gender were completed. Responses of immunization- versus nonimmunization-certified pharmacists were also compared. Ordinal and continuous data were analyzed by χ^2 and *t*-test, respectively.
RESULTS: A total of 170 surveys were received (response rate, 42.6%). Eighty-six respondents (50.6%) indicated they were immunization certified. Of those, 37.2% were certified while in school, 67.4% host immunization days, and 79.1% immunize patients. The respondents who provided immunizations each immunized an average of more than 300 patients per flu season. Of those not currently certified, 59.5% indicated an interest in becoming certified. No statistically significant differences in

certification rates were found based on gender (p=0.52) or practice setting (p=0.65). Desire to improve public health, increased convenience, and patient cost savings were identified as the most important reasons for becoming certified. Time constraints, liability coverage, and reimbursement were the factors perceived as most problematic. No statistically significant differences were found between immunization-certified and noncertified pharmacists with respect to immunization barriers for pharmacists.
CONCLUSIONS: More than half of the Alabama community pharmacists surveyed are involved in the roles of immunization advocacy outlined by APhA: educator, facilitator, or immunizer. Certification rates were not associated with practice setting, indicating similar interest in immunizations regardless of practice site. Desire to improve public health, increased patient convenience, and patient cost savings were the most important drivers for immunization certification.

233. Implementation of a community-based medication therapy management model in the underserved Mississippi Delta. *Leigh Ann Ross, Pharm.D., BCPS*, Lauren S. Bloodworth, Pharm.D., BCPS, Katie S. McClendon, Pharm.D., BCPS, James J. Pitcock, Pharm.D., BCPS, Margaret B. Pitcock, Pharm.D., BCPS, Michael Warren, Pharm.D.; University of Mississippi School of Pharmacy, Jackson, MS
PURPOSE: To provide a description of the challenges encountered, successes achieved, and preliminary results in the first year of a multiyear implementation of a community-based pharmacy services model to improve medication use in an underserved region.
METHODS: Pharmacist medication therapy management (MTM) interventions are provided in seven community pharmacies in three Mississippi Delta counties. The targeted counties have a large racial and ethnic minority population with significant risk factors for poor disease outcomes and disparities in access to quality health care services. MTM services are targeted for the Medicaid population. Services are provided in both chain and independent pharmacies. School of Pharmacy faculty who are trained in disease management provide specialized, disease-specific MTM services in asthma and diabetes one-half day per week in the pharmacies. The interventions are focused on patient self-education and medication recommendations to primary care providers. Enrolled patients complete a survey at baseline and 6 months. Patient assessment at each visit includes measurement of blood pressure, weight, body mass index, lipid panel, and hemoglobin A1c. Computer software was developed to document patient encounters.
RESULTS: Fifty patients have been enrolled, and recruitment is ongoing. Clinical and humanistic outcomes are being evaluated. Patient self-reported data will be compared with prescription refill data to determine medication adherence. Evaluation will include an assessment of barriers encountered, incentives for partnerships, and successful communication strategies. Interviews with participating pharmacists are being conducted to determine areas for improvement in year 2 of implementation.
CONCLUSIONS: Pharmacists are uniquely trained to provide direct patient care services that improve medication use outcomes, control of disease, and prevention of complications from chronic disease. Community pharmacies are accessible, especially in underserved regions. Successful implementation of a pharmacy MTM model in community pharmacies in these underserved areas will provide a strategy to increase access to quality care.

Critical Care

234. Development and implementation of a heparin-induced thrombocytopenia pathway in a trauma intensive care unit. *Kathryn A. Connor, Pharm.D.*, G. Christopher Wood, Pharm.D., Martin A. Croce, M.D., Joseph M. Swanson, Pharm.D., Bradley A. Boucher, Pharm.D., Timothy C. Fabian, M.D.; Regional Medical Center at Memphis/The University of Tennessee Health Science Center, Memphis, TN
PURPOSE: Thrombocytopenia is common in critically ill patients, with an incidence of up to 40%; however, there is a lack of evidence regarding HIT in trauma patients and no unified approach to managing HIT in our trauma intensive care unit (TICU). A systematic evaluation of thrombocytopenia is essential to correctly diagnose and manage HIT. A TICU HIT clinical pathway was developed at a regional level 1 trauma center to provide guidance and a standardized approach to diagnosing and treating HIT.
METHODS: An extensive literature search of thrombocytopenia and HIT in critically ill trauma patients was performed, including the databases MEDLINE, EMBASE, and PubMed. A preliminary 1-month audit was conducted to characterize the incidence and severity of thrombocytopenia in all patients admitted to the TICU in January 2009. A cost analysis was performed to determine the most cost-efficient pharmacotherapy and diagnostic methods to include in the pathway. The departments of clinical pharmacy and surgery collaborated to develop a TICU HIT clinical pathway.
RESULTS: Lepirudin was chosen as the primary agent mainly because of cost, which was 4-fold less than that of argatroban per day of HIT treatment. Initial and confirmatory HIT diagnostic laboratory tests would cost about $366 per patient who qualified for the pathway. Twelve (21%) of 56 patients experienced thrombocytopenia, defined as a decrease in platelets greater than 50% of baseline value within 5–14 days of beginning unfractionated or low-molecular-weight heparin. One patient (1.8%), who met inclusion criteria for the HIT pathway, was later found to be HIT antibody negative.
CONCLUSIONS: The TICU HIT clinical pathway addresses an important clinical problem; it is expected to help standardize the management of HIT and decrease costs. Implementation and education efforts are ongoing. A postimplementation study would be helpful to compare HIT management using the pathway to baseline data.

235. Evaluation of process defects associated with delayed antibiotic administration in patients with severe sepsis and septic shock at a large academic teaching institution. *Garrett E. Schramm, Pharm.D.,*[1] Kylian S. Kirkham, Pharm.D.,[2] Maria I. Rudis, Pharm.D.,[1] Bekele Afessa, M.D.[1]; (1) Mayo Clinic, Rochester, Rochester, MN; (2) North Dakota State University College of Pharmacy, Fargo, ND
PURPOSE: The Institute for Healthcare Improvement and the Surviving Sepsis Campaign guidelines recommend that empiric antibiotics be administered to patients within 3 hours of severe sepsis or septic shock onset in the ED or within 1 hour for floor or ICU patients. The objective of this study was to identify defects in antibiotic delivery to improve the overall processes of care involved in severe sepsis and/or septic shock.
METHODS: Prospective, observational study of patients admitted to a medical ICU at Mayo Clinic (Rochester, Minnesota) who met established criteria for severe sepsis or septic shock between January 1, 2008, and June 1, 2009, and failed to meet established criteria for timely antibiotic therapy. Antibiotic defects were categorized into components of the medication use process. Data are expressed as the most common defect as well as those that most significantly contributed to the delay in antibiotic delivery.
RESULTS: Of the 555 patients screened, 48 (8.6%) met the criteria for delayed antibiotic administration (median, 197 minutes; interquartile range, 120–423). Original patient admission locations included 8 (16.7%) directly admitted to the ICU from an outside institution, 24 (50.0%) from the ED, and 16 (33.3%) from the floor or within the ICU. The defect with the largest attributable time delay was the failure to recognize severe sepsis or septic shock, accounting for 65.4% of the time lapse (median, 129 minutes; interquartile range, 52–395). The second most attributable delay occurred between pharmacy processing and antibiotic administration, accounting for 28.6% of the time lapse (median, 52 minutes; interquartile range, 26–81).
CONCLUSIONS: Delays in identification of severe sepsis or septic shock account for most of the antibiotic defects in this cohort. Further educational efforts are under way to improve early recognition and to prevent progression of sepsis to severe sepsis.

236. High-dose ciprofloxacin for *Enterobacter aerogenes* lumbar osteomyelitis in an obese critically ill patient receiving continuous renal replacement therapy: a case report. *Theresa R. Utrup,*

Pharm.D.,[1] Eric W. Mueller, Pharm.D.,[2] Daniel P. Healy, Pharm.D.,[3] Rachael A. Calcutt, M.D.,[3] John D. Peterson, D.O.,[3] William E. Hurford, M.D.[3]; (1) The University Hospital, Cincinnati, OH; (2) Department of Pharmacy Services, The University Hospital and Division of Pharmacy Practice, University of Cincinnati, Cincinnati, OH; (3) University of Cincinnati, Cincinnati, OH

PURPOSE: Few data exist to guide appropriate antibiotic dosing in critically ill obese patients receiving continuous venovenous hemodiafiltration. We present a case of an obese, critically ill, multiple-trauma patient who received high-dose ciprofloxacin for lumbar spine osteomyelitis after spinal fixation.
METHODS: Pharmacokinetic analysis and chart review.
RESULTS: Pharmacokinetic and pharmacodynamic profiles were determined for ciprofloxacin 800 mg intravenously every 12 hours in a class 3 extreme obesity (185 kg; body mass index = 53.7), critically ill, trauma patient with *Enterobacter aerogenes* (ciprofloxacin minimum inhibitory concentration [MIC] of 1 µg/mL or less) lumbar spine osteomyelitis receiving continuous venovenous hemodiafiltration (CVVHDF). Steady-state ciprofloxacin plasma concentrations measured on treatment day 11 revealed plasma areas under the curve (AUCs)-to-MIC ratios more than 125 and plasma peak-to-MIC ratios more than 8 across organism MICs of 1 µg/mL or less. Estimated ciprofloxacin bone concentrations (published reports suggest 35%–48% of plasma concentration) for this dosage met these pharmacodynamic targets for organism MICs of 0.5 µg/mL or less. Lumbar spine cultures on day 24 of ciprofloxacin therapy demonstrated no growth coinciding with overall improvement of the invasive wound. A week later, however, the patient developed worsening septic shock and died secondary to an unrelated occult subdiaphragmatic abscess.
CONCLUSIONS: Critically ill, obese patients with deep-seated infection receiving CVVHDF likely require ciprofloxacin dosages greater than 400–800 mg/day to achieve optimal pharmacodynamic targets.

Drug Information

237. Impact of seamless care at a traumatology ward. *Charlotte Delobel, Pharm.D.*,[1] Sarah Mertens, Pharm.D.,[1] Verdonk René, M.D., Ph.D.,[2] Hugo Robays, Pharm.D.[1]; (1) Ghent University Hospital, Pharmacy Department, Ghent, Belgium; (2) Ghent University Hospital, Department of Orthopaedic Surgery and Traumatology, Ghent, Belgium

PURPOSE: Lack of communication of pertinent drug information between the hospital and primary caregivers is a source of adverse drug events.
The objective of this project was to investigate if a clinical pharmacist (CP) could contribute to optimizing the process of seamless care.
METHODS: At the traumatology ward during 2 consecutive months, a CP – compared at the time of admission the standard reconciliation of drug history by caregivers (physicians, nurses) with reconciliation by a CP – evaluated during the hospital stay the therapy in accordance with local guidelines and recommended adaptations on the occasion of ward rounds – informed the patient at the time of discharge and provided recommendations to general practitioners (GPs).
RESULTS: Admission: 161 drug histories (588 drugs) were registered; 288 discrepancies were found (22.3% omitted drugs, 9.5% incorrect drugs, 3.2% incorrect dosages, 4.3% incorrect frequencies, 13.1% missing dosages, and 3.8% missing frequencies).
Hospital stay: 172 interventions with 80 pieces of advice for therapy modification, clarification of therapy, or increased monitoring. In 92 cases, information was supplied as an answer to a question of a physician (56.6%) or nurse (28.3%). The acceptance degree was 86%.
DISCHARGE: Ninety-seven patients were provided with a discharge medication list. Interviews with 30 GPs showed that 63.3% of patients consulted their GP, and 42.1% of them showed the medication list. All the GPs who were given the list were satisfied.
CONCLUSIONS: Drug histories were more accurate and complete when reconciled by a CP. With the cooperation of orthopedic surgeons, the quality of pharmacotherapy could be improved. The CP contributes to a more substantial information transfer to the GP, which leads to a higher satisfaction of the primary caregivers.

Drugs in Pregnancy

238. Assessment of pregnancy risk categorization for non–FDA approved medications available in Saudi Arabian market. *Sakra S. Balhareth, Pharm.D., B.S.,* Ahmed H. Aljedai, Pharm.D., MBA, BCPS, FCCP, Roa'a A. Algain, BSPharm; King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

PURPOSE: Many of the marketed medications in Europe and Japan are not currently approved by the U.S. Food and Drug Administration (FDA) and hence do not have pregnancy risk categorization. The objective of this study was to review and categorize the fetal risk associated with non–FDA-approved medications registered by the Saudi Arabian (SA) Ministry of Health using the FDA pregnancy risk categorization system.
METHODS: Non–FDA-approved medications were identified using the Saudi National Formulary according to an approved list of registered products in October 2007. One hundred nine medications were identified. Herbal products, withdrawn medications, or veterinary medicines were excluded. The search was performed using different databases and references (i.e., Electronic Medicines Compendium, Medicines and Healthcare Products Regulatory Agency, British National Formulary, International Lexi Drug Information Handbook, Micromedex, Middle East Drug Index, Australian Drug Evaluation Committee's Category, and MEDLINE). Any functional, anatomic birth defects or embryocidal-associated risk was considered for evaluation.
An algorithm illustrating the official FDA categorization group (A, B, C, D, and X) for fetal risk assessment was used by a panel of three pharmacists to assign pregnancy risk category for the studied medications.
RESULTS: Ninety-three medications were eligible for this evaluation. Seventy-four percent of the medications were assigned category risk C. Ten (11%) medications were assigned category risk D. Fourteen (15%) medications were assigned to category risk B. Only two medications were judged safe during pregnancy based on the available evidence and were assigned category risk A.
CONCLUSIONS: Our results showed comparable figures of pregnancy risk category to the currently FDA-approved medications. The inconsistency in defining the fetal risk category among different drug regulatory authorities would create confusion and affect the prescribing decision. We believe that standardization and inclusion of this information in medication package inserts is extremely important to all health care practitioners.

Education/Training

239. Collaboration between colleges of pharmacy and pharmaceutical industry: a unique relationship. *Colleen M. Moffitt, Pharm.D., M.S.*, Walter J. McClain, Pharm.D., BCPS, Scott E. Glosner, Pharm.D., BCPS, Shannon H. Goldwater, Pharm.D., BSPS, FASHP; Pfizer, New York, NY

PURPOSE: This survey was conducted to identify existing partnerships between industry pharmacists and colleges of pharmacy (COPs); identify industry educational opportunities; list barriers preventing industry pharmacists from precepting students/residents; share best practices; and identify partnership benefits for students/residents, COPs, and the pharmaceutical industry.
METHODS: Data were gathered by an online tool (*SurveyMonkey.com*). During spring 2009, 110 Pfizer medical outcomes specialists (MOS) were asked to report their current COP affiliations and activities. Data were downloaded into Microsoft Excel and Minitab 15 for analysis.
RESULTS: One hundred two MOS completed surveys (92.7% response rate). Response rate was equally distributed across the country. Currently, 62% of respondents hold faculty appointments at COPs, 63% precept students/residents, and 20% indicate a desire to precept students/residents. Other COP MOS activities include guest lecturing (67%), teaching a graded course (9%), and assisting

faculty in outcomes research projects (7%). Of the 38 MOS not currently precepting, 34 described specific barriers. Lack of time was identified as the primary reason (16%), followed by uncertainty about how (18%) and travel constraints (15%). MOS working with students/residents identified several benefits from participating in student-industry collaborations. Benefits to students/residents include exposure to developing and deploying data collection tools; writing, presenting, and analyzing data; introduction to industry opportunities; and varied practice settings. Student/resident involvement in industry rotations provide MOS colleagues with a perspective of current pharmacy practice patterns and highlight issues relevant in the delivery of health care. Most MOS preceptors indicated that data collection by students/residents, increased credibility, and enhanced customer dialog were beneficial to the MOS.
CONCLUSIONS: Relationships between COPs, students and residents, and industry pharmacists can be mutually beneficial, especially with the increasing number of new pharmacy schools. The partnership can expose students to alternative career paths and outcomes research. Industry pharmacists can also benefit through increased credibility, assistance with research projects, and enhanced dialog.

240. Longitudinal research experience during a first year PGY-1 residency program: accomplishments and future directions. *Michael L. Bentley, Pharm.D., FCCM,*[1] Wesley Blankenship, Pharm.D.,[2] Sheri Ober, Pharm.D., BCPS,[2] Megan Goodwin, Pharm.D., BCPS,[2] Corey Goodwin, Pharm.D., BCPS,[2] Jason Hoffman, Pharm.D., BCPS,[2] Amanda Hansen, Pharm.D.[2]; (1) Carilion Roanoke Memorial Hospital and Virginia Commonwealth University School of Pharmacy, Roanoke, VA; (2) Carilion Roanoke Memorial Hospital, Roanoke, VA
PURPOSE: The number of pharmacy students seeking postgraduate training grows each year. In addition, the number of hospital-based residencies seeking accreditation continues to increase. Establishing a structured, mentor-led research experience to meet standards and enhance the residency experience should be a priority for new programs.
METHODS: One year before the start of our program, a preceptor was given the task of developing a longitudinal research experience. Using accreditation standards and preceptor experiences, a plan was developed. It included recommendations from ASHP, project requirements, and a detailed timeline. Subsequently, a small group met to discuss the document and provide feedback. After the process was finalized, a "call" for proposals was sent to administrative and clinical staff. Projects consistent with medical center and department goals as well as feasible within 1 year were considered. Residents could suggest an alternative project if it met the same predefined criteria.
RESULTS: Projects were completed and presented at a regional residency conference. Although our program provided detailed guidance, we identified three areas that should be strengthened or developed:

1. Formal Project Advisory Committee (PAC):
   It was determined in the planning stages not to establish a PAC. By default, those initially agreeing to this format served in this role and provided invaluable guidance. We feel that a formal PAC would help define individual responsibilities, provide oversight, and serve as advocates for the residents.
2. Written Manuscript:
   The process for a formal manuscript was not well defined. We are in the process of developing a review series to discuss manuscript preparation and authorship.
3. Scheduled Discussions:
   In addition to manuscript preparation, educational discussions are being developed to include core research topics to broaden the resident's experience.

CONCLUSIONS: Although much was accomplished during our first year, we feel improvements in our structure will enhance the resident's experience.

241. Integration of human patient simulation mannequins into doctor of pharmacy curriculum. *Megan Willson, Pharm.D.*, Brenda S. Bray, BPharm, MPH, Colleen M. Terriff, Pharm.D., Mark W. Garrison, Pharm.D.; Washington State University College of Pharmacy, Spokane, WA
PURPOSE: To describe human patient simulation (HPS) and highlight our experiences using this sophisticated technology within our pharmacy curriculum at Washington State University (WSU). Examples of grading tools and preliminary data on student perceptions of learning by HPS will be shared.
METHODS: HPS, first adopted into the training of medical students, has now expanded to include nursing, pharmacy, and other health care professions. The College of Pharmacy at WSU purchased a HPS mannequin in 2007 to facilitate student learning through realistic patient care scenarios. Patient cases include acute coronary syndrome, community-acquired pneumonia, *Clostridium difficile* disease, and emergency preparedness. Students work in groups of three or four during the scenario to implement a therapeutic plan for the patient. Immediately after the simulation, the faculty facilitator conducts a debriefing session, which addresses key points. Communication efficiency, professional attitude, clinical skills and knowledge, error identification, and critical thinking are addressed by the facilitator using a detailed grading rubric.
RESULTS: During the past 3 years, five HPS cases have been used with third professional year student pharmacists. Each year, patient scenarios are updated, and grading rubrics are refined and improved. Based on formal course evaluations, students report positive attitudes toward HPS use.
CONCLUSIONS: Incorporating HPS into our pharmacy curriculum at WSU has been well received by students. Continued efforts are under way to validate our evaluation tool and formally assess the impact of HPS on enhancing clinical skills and knowledge. With increasing emphasis on patient safety, HSP provides an opportunity for students to actively participate in realistic patient care scenarios without concern for direct harm to patients.

242. Integration of pharmacy students into a population based care program to promote the Accreditation Council for Pharmacy Education (ACPE) requirements. *Kristin A. Tuiskula, Pharm.D.*, Abir O. Kanaan, Pharm.D.; Massachusetts College of Pharmacy and Health Sciences, Worcester, MA
PURPOSE: The Accreditation Council for Pharmacy Education (ACPE) requires students to acquire the ability to practice pharmacy independently upon graduation. Integrating students into pharmacy clinical services that promote population-based care programs can achieve such a requirement. An anticoagulation monitoring program was started at a 349-bed hospital to ensure proper prescribing and monitoring of anticoagulants. The objectives for this study were to determine whether students could be successfully integrated into an anticoagulation program and the degree to which students affect reporting of bleeding events.
METHODS: After training and education as part of a 1-week orientation, students monitored and assessed patients receiving anticoagulants as part of three 6-week internal medicine rotations. Responsibilities included 1) ensuring proper prescribing of enoxaparin and fondaparinux according to patient weight, creatinine clearance (CrCl), indications, and formulary restrictions; 2) monitoring platelet count in patients receiving enoxaparin and intravenous unfractionated heparin (UFH); 3) monitoring patients on warfarin; and 4) reporting bleeding events. Students performed the service twice weekly and were required to have their recommendations approved by a preceptor before making any interventions. Primary end points included the number of interventions made by students, the number of interventions accepted by physicians, and the number of bleeding events reported.
RESULTS: Ten students participated in this program. A total of 295 interventions were made; 55 were made by students, including the following: adjusting warfarin dose (8), discontinuing or adjusting fondaparinux because of CrCl (20) or weight (18), adjusting enoxaparin dose because of CrCl and indication (8), and discontinuing UFH because of thrombocytopenia (1). All interventions were accepted except for one. Bleeding events were increased; however, they are not reported because of hospital policy.
CONCLUSION: Students were successfully integrated into a

population-based care program as required by ACPE. This integration may be helpful in institutions, especially when resources are limited.

243. Development of online instruction for motivational interviewing. *Megan Willson, Pharm.D.*,[1] Michele A. Packard, Ph.D.,[2] Randall Smith, Ph.D.,[3] Janice Pringle, Ph.D.,[3] James Bennett, RPh[4]; (1) Washington State University Spokane, Spokane, WA; (2) Sage Institute, Boulder, CO; (3) University of Pittsburgh, Pittsburgh, PA; (4) James Bennett Apothecary, Corinth, MS

PURPOSE: The goal of this project was to develop an online course in facilitating patient behavioral change that is based in motivational interviewing to help health care practitioners improve patient health and health behavior outcomes. The module's design integrates motivational interviewing into traditional pharmacy patient counseling skills.

METHODS: DM Educate is an online comprehensive diabetes continuing education course that emphasizes a multidisciplinary approach to diabetes management for health professionals. Fourteen modules, created and presented by experts in the area of diabetes, provide the foundation for diabetes management. Behavior change and self-care are identified as key to successful diabetes management. Motivational interviewing is a well-studied counseling technique that is now being applied to health care to effect patient behavioral change. Currently, motivational interviewing courses are being taught as multiple-day on-site seminars; this creates difficulties in training multiple individuals and affordability. In light of this identified barrier, as a continuum of the DM Educate model, a group of pharmacists, pharmacy educators, a psychologist, the University of Pittsburgh Dean's Office, and a health services researcher gathered to design a module to teach motivational interviewing in a manner that integrates it with pharmacy patient counseling in an online format.

RESULTS: This online course will be designed to provide training in motivational interviewing through case vignettes. The case scenarios will depict difficult situations that a pharmacist/health care provider might encounter during patient interactions both during longer term counseling sessions and in over-the-counter dispensing encounters. They provide solutions through the integration of motivational interviewing principles. Together with the vignettes, the theoretical background and foundational concepts of motivational interviewing will be presented and reinforced.

CONCLUSION: Practitioners will be better prepared to care for their patients with diabetes when they are able to proficiently integrate motivational interviewing techniques into their patient counseling encounters. This online training course, which supports the acquisition of motivational interviewing skills, facilitates this goal.

Emergency Medicine

244. Clinical pharmacy services in the emergency department at a level II trauma center. *Bethany S. Delk, Pharm.D., BCPS*, Kelli O. Kirkpatrick, Pharm.D., Julie Applegate, Pharm.D., BCPS; Mission Hospitals, Asheville, NC

PURPOSE: This study assessed outcomes associated with the first year of pharmacy services provided by four pharmacists and six pharmacy technicians in the emergency department (ED) from January to December 2008.

METHODS: ED pharmacists documented interventions using an electronic clinical interventions database. The financial impact of the ED pharmacist-provided medication therapy outcomes was derived from a national benchmarking tool that includes a comprehensive database of more than 150 hospital comparison groups. Computerized reports summarizing order verification actions, pharmacy consults, completed medication histories, and documented clinical interventions were analyzed. Clinical intervention documentation rates were assessed.

RESULTS: There were 2057 clinical interventions and 34 physician-ordered pharmacy consults documented by ED pharmacists in 2008. The most prevalent interventions and consults included 471 (23%) code responses, 397 (19%) therapeutic recommendations, 344 (16%) medication histories, 345 (16%) order clarifications, and 207 (10%) drug information requests. These interventions and consults provided a cost avoidance of around $420,000. When surveyed, the ED pharmacists estimated that they documented only 40%–50% of their daily interventions. Between July and December 2008, the ED pharmacy technicians obtained medication histories and assisted physicians with medication reconciliation for 7179 patients. Data analysis on cost avoidance from technician-obtained medication histories is ongoing.

CONCLUSIONS: During the first year of practice, the ED pharmacists verified medication orders and provided point-of-care medication management, and pharmacy technicians obtained medication histories. These services resulted in significant cost avoidance despite incomplete documentation. The clinical role of the ED pharmacist is expanding, and cost avoidance is expected to increase.

245. Medication error reports in the emergency department: the impact of emergency medicine pharmacists. *Kyle A. Weant, Pharm.D.*, David A. Santrock Jr., Pharm.D., Roger L. Humphries, M.D., Kimberley B. Hite, Pharm.D., M.S., John A. Armitstead, M.S., RPh; University of Kentucky HealthCare, Lexington, KY

PURPOSE: Medication error reports (MERs) are underrepresented in health care because of time constraints, fear of punishment, and lack of appreciation for their importance. In 2006, the University of Kentucky began to implement clinical pharmacy services in the emergency department (ED). The primary objective of this study is to assess the impact of an emergency medicine (EM) clinical pharmacist on medication error capture rates in a level 1 trauma center.

METHODS: A retrospective analysis of ME reporting over three different periods was conducted: no EM pharmacist (September 1, 2005–February 28, 2006), one EM pharmacist (September 1, 2007–February 28, 2008), and two EM pharmacists (September 1, 2008–February 28, 2009). MEs are reported in an online database available to all health care personnel.

RESULTS: Overall, 497 MEs were reported in the ED, with pharmacy personnel capturing significantly more than other health care personnel (7% vs. 93%, $p<0.001$). The addition of one EM pharmacist increased the medication error capture rate by 2.9-fold, and the effect of two EM pharmacists increased this rate by 11.6-fold. Most of the errors documented (81%) were ordering errors, with deficits in performance and knowledge being the most common contributing factors. Of all MERs, 79% were prevented from reaching the patient. The characteristics of MERs did change, with more severe errors being captured with two pharmacists present (15% vs. 77%, $p<0.001$).

CONCLUSIONS: The presence of EM pharmacists has been shown to result in potential cost savings and reduce the rate of MEs that reach the patient. Their ability to identify potential errors and opportunities for process improvement compared with other health care professionals has not been previously reported. The implementation of EM clinical pharmacy services significantly increased the number of overall MEs captured as well as increased the documentation of more severe errors.

246. Increased communication improves timeliness of the medication use process. *Ming Poi, Pharm.D., Ph.D.*, Mary B. Shirk, Pharm.D., BCPS; The Ohio State University Medical Center, Columbus, OH

PURPOSE: To assess the impact of increased communication between pharmacy and emergency department (ED) nursing on the timeliness of the use process for nonautomated dispensing cabinet medications.

METHODS: Data were collected during 2-week periods in September 2007 (TP1) and June 2008 (TP2) to evaluate the electronic ED medication use process workflow using an observational retrospective design. Time intervals for each of five phases (prescribing, nurse notification, pharmacy notification, medication preparation and delivery, and administration) were collected for analysis. During TP2, pharmacy staff contacted the patient's primary nurse by telephone before medication delivery (pneumatic tube, ED personnel pickup, or pharmacy delivery). At

completion of TP2, a nursing survey was administered to assess satisfaction with pharmacy services and the process modification.
RESULTS: Randomly selected orders (n=221) were screened against inclusion/exclusion criteria to identify 70 per period. Medication types and routes of administration were similar between TP1 and TP2 (t-test and Fisher exact test). Eighty-seven percent of medications were delivered through a pneumatic tube in both study periods. Time differences between TP1 and TP2 for phases 1–4 were insignificant (p=0.64, 0.08, 0.85, 0.22). Time between delivery and administration was significantly reduced (58 ± 65 to 27 ± 25 minutes, p=0.0003). Order to administration was reduced by 31% (86 ± 64 to 59 ± 36 minutes, p=0.0029). Direct communication perceptibly improved the nurse's workflow (mean, 4.5; median, 5.0; 1 = strongly disagree and 5 = strongly agree).
CONCLUSIONS: Timeliness to first medication has been shown to influence ED and hospital length of stay and patient outcomes. Our results demonstrate that increased communication between pharmacy and ED nursing significantly improved medication timeliness; this may be used to augment the ED medication use process.
References: Clark K, Brush NL. Patient flow in the emergency department: is timeliness to events related to length of hospital stay. J Nurs Care Qual 2007;22:85–91.

247. Impact of an emergency department antibiogram on outpatient treatment of urinary tract infections. *Eric H. Gilliam, Pharm.D.*, Kevin O. Rynn, Pharm.D., FCCP, DABAT; Rutgers University Ernest Mario School of Pharmacy, Piscataway, NJ; Robert Wood Johnson University Hospital Emergency Department, New Brunswick, NJ
PURPOSE: Pharmacists responsible for providing outpatient culture follow-up in the emergency department (ED) intended to improve patient care by educating providers regarding drug susceptibility of common bacterial pathogens. This study assessed a pharmacist-initiated education campaign that included distributing an ED-specific outpatient antibiogram. The primary outcome assessed was the rate of sensitive empiric therapy for urinary tract infections (UTIs) prescribed before patient discharge. Secondary outcomes included changes in antibiotic selection and need for patient follow-up.
METHODS: Urine cultures requiring follow-up were initially identified and documented daily by the ED pharmacists according to department policy. Culture and isolate data, treatment information, and follow-up actions were documented by the pharmacist on duty. Records created within the 3 months before and after the distribution of the antibiogram were reviewed retrospectively. Only the records for adult ED patients discharged directly from the ED were included for analysis.
RESULTS: A total of 146 records met inclusion criteria for review. After antibiogram distribution, the rate of sensitive empiric therapy prescribed on discharge increased from 40.2% to 43.8%. Furthermore, antibiotic selection changed, reflecting isolate sensitivity data: fluoroquinolone and trimethoprim-sulfamethoxazole use decreased from 62% to 50% and from 11% to 3.1%, respectively. Conversely, the use of first-generation cephalosporins and nitrofurantoin increased from 6.1% to 14.1% and from 6.1% to 9.4%, respectively. Among patients receiving treatment on discharge, the need for ED pharmacists to provide follow-up decreased from 25.7% to 18%.
CONCLUSION: By providing the ED culture follow-up service, clinical pharmacists can improve patient care, educate providers, and promote antibiotic stewardship in the outpatient community.

Family Medicine

248. Evaluation of beliefs about hypertension in a general population. *Sarah E. McBane, Pharm.D.,* Duke University and Campbell University, Durham, NC
PURPOSE: Hypertension affects millions of people in the United States, yet many do not reach their blood pressure goals. Existing data indicate that self-management skills improve chronic disease management. Knowledge, beliefs, and attitudes can be important contributors or barriers to successful self-management. This pilot study was designed to evaluate the knowledge and beliefs of the general public about hypertension.
METHODS: A convenience sample of 100 Duke Family Medicine patients completed an anonymous survey consisting of 16 true/false questions. Included subjects were 18 years and older and comfortable answering questions in English; they did not necessarily have hypertension. The questions addressed knowledge about the definition and complications of hypertension. Basic demographic data were collected. Descriptive statistics were performed on the data.
RESULTS: Surveyed subjects were similar to the general clinic population: 69% were women, 51% were African American, 55% were 45 years or older, and 51% had never had a diagnosis of hypertension. Seventy-nine percent of the subjects answered 13 or more questions correctly, and there were no differences in the number of correct answers by sex, age, race, or diagnosis of hypertension. The three most commonly missed questions addressed the fatality of hypertension, adverse effects of medications, and potential for curing hypertension.
CONCLUSIONS: Hypertension remains an important public health problem. Knowledge and beliefs about hypertension in this general clinic sample were more accurate than expected and consistent with current medical knowledge; however, this study evaluated only knowledge and beliefs, not actual patient behaviors. Further study is required to elucidate patient factors that may limit control of hypertension.

Health Services Research

249. Correlation between the use of gender and ethnicity specific teaching aids and patient acceptance rate of the pneumococcal vaccine in an inpatient setting. *Vicken Yaghdjian, Pharm.D.,*[1] Svetlana Simkhovich, Pharm.D.,[1] Igal Khorshidi, M.D.,[1] Keith Veltri, Pharm.D.[2]; (1) Montefiore Medical Center, Bronx, NY; (2) Touro College of Pharmacy, New York, NY
PURPOSE: *Staphylococcus pneumoniae* invasive infection causes an estimated 40,000 deaths annually in the United States. Despite these national statistics, the pneumococcal vaccine remains underused among certain racial/ethnic populations. The rates of vaccination against this infection in African American and Hispanic populations are significantly lower than those among whites. In an effort to increase vaccination rates in our medical institution, which serves a high number of racial minorities, a pharmacy-based immunization program using a clinical pharmacist to educate the patient directly at the bedside was developed in 2006.
METHODS: Analysis of the program during 2006–2007 depicted an overall average of 70% acceptance of patient subgroups that consented to pneumococcal vaccination. In this 4-week pilot study conducted in 2008, gender- and race-specific visual aids were used to increase overall acceptance rates. Identifying a correlation between vaccine acceptance and use of these educational tools among these minority groups was also studied. Our primary outcome was to detect a 10% increase in the overall acceptance rate. The secondary outcome was to detect an increase in individual subgroup acceptance rate by means of a gender- and race-specific tool.
RESULTS: The overall study group percentage of 81% met the target goal acceptance rate during this period. Moreover, the breakdown of each subgroup, 62% (8 of 13) of non-Hispanic blacks, 80% (28 of 35) of Hispanics, and 73% (19 of 26) of non-Hispanic whites depicted an overall increase in consent to the vaccine compared with the control group's 48% (12 of 25), 58.5% (21 of 36), and 54.5% (11 of 20).
CONCLUSIONS: Although this study was underpowered, the overall results were extremely promising. A follow-up evaluation with a power of 0.8 and a sample of 250 in each group will look at further validating this positive trend of higher acceptance rates among non-Hispanic blacks, Hispanics, and non-Hispanic white subgroups compared with the national average.

Hematology/Anticoagulation

250. A pilot study evaluating the impact and feasibility of a patient education and competency program for warfarin. *Lama H. Nazer, Pharm.D., BCPS*, Purvy Shah, Pharm.D., Briana Ballard, Pharm.D., Seth Roffler, Pharm.D.; Mount Sinai Hospital, Chicago, IL

PURPOSE: To evaluate the impact and feasibility of an education and competency program for patients receiving warfarin during their hospitalization.

METHODS: This was a 6-week prospective pilot study that included all hospitalized patients receiving warfarin. Patients with a medical condition that might interfere with their understanding and non–English-speaking patients were excluded. The program consisted of an education session and a follow-up session, both conducted during the patients' hospital stay. During the education session, the pharmacist assessed the patient's knowledge before and after by asking six predefined questions and counseled the patient about warfarin therapy. During the follow-up session, the patients' questions were addressed, and their knowledge was reassessed. If the patient answered at least five of the six questions correctly, he/she was considered competent. The impact of the program was assessed by comparing the competency before and after the education session as well as at the follow-up session. The feasibility of the program was assessed by determining the average time for the sessions and the number of patients who completed the program.

RESULTS: Forty-four patients received warfarin, 16 patients were excluded, 6 were discharged before assessment, 22 completed the first educational session, and 11 completed both sessions. Before the education session, 18% of the patients passed the warfarin competency, and 82% passed after the education and the follow-up sessions. The average time of the initial education session was 18 minutes (range, 5–30 minutes), and of the follow-up session, 7.6 minutes (range, 3–10 minutes).

CONCLUSIONS: The education and competency program had a positive impact on patients' warfarin competency. The average time required for the education and follow-up sessions appeared feasible. Additional strategies will be identified to ensure that all qualified patients undergo the two sessions of the warfarin education program before discharge.

251. Impact of a pharmacist-based monitoring program on warfarin therapy in home based primary care veterans. *Jennifer T. Selvage, Pharm.D.*, Liancy Gomez, Pharm.D., BCPS, Kavita Palla, Pharm.D., BCPS, Eunha Lai, Pharm.D., CACP, Todd Lee, Pharm.D., Ph.D.; Edward Hines Jr. VA Hospital, Hines, IL

PURPOSE: The purpose of this study was to evaluate the impact of a pharmacist-based monitoring program on warfarin therapy in home-based primary care (HPBC) veterans.

METHODS: A retrospective review of HBPC patients receiving warfarin during two time periods: the preintervention period (January 2005–October 2007) and after the implementation of a pharmacist-based monitoring program (November 2007–October 2008). The primary outcome was to compare the difference in the average proportion of therapeutic INR values per patient between the two groups. Secondary outcomes included documentation of adverse events and drug interactions, time until follow-up, time until INR documentation, dose changes, percentage of documented complete blood cell count (CBC) and urinalysis (UA), and number of different strengths of warfarin prescribed.

RESULTS: The average number of therapeutic INRs per patient in the preintervention group was 5.88 ± 1.92 versus 6.28 ± 1.42 in the pharmacist-monitored group (p=0.266). The average number of strengths of warfarin prescribed per patient was significantly lower in the pharmacist group (1.13 ± 0.34 vs. 1.67 ± 0.97; p<0.001). Documentation of CBC and UA was significantly higher during the pharmacist monitoring period (87% vs. 47.6%; p<0.001). There were 12 INRs without an associated therapeutic plan in the preintervention group versus none in the pharmacist group (p<0.001). There were no significant differences between groups for the remaining secondary outcomes.

CONCLUSION: Implementing a pharmacist-monitored anticoagulation program yielded a similar proportion of therapeutic INRs compared with the preintervention period. The pharmacist-monitored group had a greater percentage of documented CBC and UA, fewer strengths of warfarin prescribed per patient, and fewer undocumented therapeutic plans.

252E. Efficiency of an anticoagulation algorithm in patients undergoing intracardiac device implants. *Simon Tremblay, M.S., BPharm,* Marie Robitaille, M.S., BPharm, Lyne Vaillancourt, RN, Sylvia Audet, M.S., BPharm, Geneviève Cyr, M.S., BPharm, Martine Lacroix, M.S., BPharm, Nicolas Noël, M.S., BPharm, Denis Brouillette, BPharm, DPH, Angela Nguyen, M.S., BPharm, Bernard Thibault, M.D.; Montreal Heart Institute, Montreal, Quebec, Canada

PURPOSE: This study evaluated a new standardized algorithm for the management of oral anticoagulation (OAC) undergoing pacemaker or defibrillator implantation/replacement according to thromboembolic (TE) and hemorrhagic (H) risk.

METHODS: We developed an algorithm dividing patients into three groups according to TE and H risk. Patients had 1) their OAC discontinued 3 days before the intervention, 2) a targeted international normalized ratio (INR) of 2.0–2.5 for the intervention with subsequent heparin bridging if INR fell below 2.0, or 3) heparin bridging before and after the procedure. This algorithm was applied by a registered nurse and a pharmacist to 150 consecutive patients referred for cardiac device implantation/replacement and compared with 367 historic controls.

RESULTS: The algorithm reduced hospital stay by an average of 3 days per patient (3.1 ± 3.7 vs. 6.1 ± 10.4, p<0.001). Heparin use was also reduced in the experimental group (17% vs. 42%, p<0.001) because of the low use in the low TE risk group (1 of 90) and moderate use in higher TE risk patients (21 of 56). Heparin use resulted in an increased hospital stay in both groups (algorithm: 6.7 ± 5.3 vs. 2.4 ± 2.8 and controls: 9.4 ± 13.7 vs. 3.4 ± 5.7 days). No TE events occurred, and H complications were similar in both groups (6%).

CONCLUSION: A standardized OAC management algorithm for device implantation resulted in a reduced hospital stay and reduced heparin use with similar hemorrhagic events in both groups; however, applicability remains difficult, with 42% of patients at high risk of TE and H events having a subtherapeutic INR at hospital admission. Refining the algorithm for this category of patients could lead to a reduction in heparin use and H events.

Presented at the Heart Rhythm Society 2009 – 30th Annual Scientific Sessions, Boston, MA, May 13–16, 2009.

253. Clinical outcomes of a pharmacist-managed anticoagulation discharge process for the prophylaxis and treatment of venous thromboembolism. *Melissa A. Reger, Pharm.D.*, Jamie L. Chapman, Pharm.D., Eric W. Mueller, Pharm.D., Dave M. Lutomski, M.S.; Department of Pharmacy Services, The University Hospital and Division of Pharmacy Practice, University of Cincinnati, Cincinnati, OH

PURPOSE: Current evidence shows that outpatient treatment of venous thromboembolism (VTE) with low-molecular-weight heparin is a cost-effective and safe alternative to inpatient treatment with unfractionated heparin. This study evaluated the process, effectiveness, and safety of a long-standing pharmacist-driven anticoagulation discharge process.

METHODS: Any patient discharged from The University Hospital on an injectable anticoagulant between December 2008 and February 2009 was evaluated. The primary end point was the percentage of patients discharged on an injectable anticoagulant who were counseled by a pharmacist. Secondary end points included the duration of patient counseling and medication procurement; length of hospital stay for patients with a primary diagnosis of VTE; and VTE recurrence rates and bleeding events at 3 months.

RESULTS: Two hundred seven patients discharged on an injectable anticoagulant (3.4 discharges per day) were included. Pharmacist counseling was documented for 180 (87%) patients. Overall, pharmacists spent 37.6 ± 25.5 minutes per patient, including 19.4 ± 9.6 minutes for counseling and 19.7 ± 19.7 minutes for medication procurement; 150 (83%) patients required complete medication

procurement lasting 21.4 ± 19.6 minutes. The length of hospital stay for patients with a primary diagnosis of VTE was 3.2 ± 2.4 days. At 3 months, 5.3% and 15.9% of patients had a recurrent VTE or bleeding event, respectively, with a major bleed rate of 1.4%. Patients with major bleeding experienced intracranial hemorrhage (n=2) and gastrointestinal bleeding (n=1), all beyond the first 2 weeks after discharge.
CONCLUSIONS: Systemwide education is needed to ensure that all patients are counseled on their injectable anticoagulant before discharge. Continued evaluation of discharge criteria is encouraged to identify the most appropriate candidates to minimize recurrent VTE and bleeding events. Consideration should be given to outsourcing the procurement portion because this requires a significant amount of pharmacists' time.

Infectious Diseases

254. Development and implementation of Geisinger Medical Center's expanded Antimicrobial Stewardship Program. *Carolyn L. Villareal, Pharm.D., BCPS*, Dhuha A. Saber, Pharm.D., Kelly M. Bolesta, Pharm.D.; Geisinger Medical Center, Danville, PA
PURPOSE: Within the current Antimicrobial Stewardship (AMS) Program at Geisinger Medical Center (GMC), the infectious disease (ID) pharmacist provides daily reviews of patients' antimicrobial therapy. Specifically, the ID pharmacist reviews patients' antimicrobial therapy for appropriateness, documents the indication for the chosen antimicrobial therapy, and recommends alternative antimicrobial therapy or discontinuation of therapy. The goal of this project was to expand the clinical and pharmacoeconomic impact of the current AMS program through the use of a pharmacist-initiated automatic consult process.
METHODS: A policy and procedure was developed by the Antimicrobial Subcommittee. The policy gives the ID pharmacist responsibility to place mandatory ID consults based on the following criteria:

1. Restricted antimicrobial is continued beyond 48 hours without an appropriate documented indication
2. Systemic antifungal use, excluding oral fluconazole
3. Use of three or more antimicrobials
4. Use of oral vancomycin for treatment of *Clostridium difficile*

Consultation orders for patients who meet criteria are placed in the electronic medical record by the ID pharmacist and are accompanied by a simultaneous message alerting the primary service. The second phase of the project involved obtaining approval from necessary administrative committees as well as providing education to physicians and pharmacists.
RESULTS: In November 2008, the Pharmacy & Therapeutics Committee and Medical Executive Committee approved the policy. The program was implemented in January 2009 for adult patients and in April 2009 for pediatric patients. In 4 months, the ID pharmacist has placed about 140 consults for adult patients. The clinical impact includes improved acceptance of ID recommendations by the primary team and discontinuation of unnecessary antimicrobials.
CONCLUSIONS: The clinical impact of the pharmacist-initiated automatic consult process has begun to be observed. A research protocol is being developed to quantify the clinical and pharmacoeconomic impact of the expanded program.

255. Assessment of antimicrobial stewardship activities in a hospital network of smaller hospitals. *Rabiah Dys, Pharm.D.,*[1] Dimple Patel, Pharm.D.,[2] Jacques Landry, Pharm.D.,[1] Marvin Finnefrock, Pharm.D.,[3] Andrew Lowe, Pharm.D.[4]; (1) Comprehensive Pharmacy Services, Dracut, MA; (2) Comprehensive Pharmacy Services, Edison, NJ; (3) Comprehensive Pharmacy Services, Costa Mesa, CA; (4) Comprehensive Pharmacy Services, Colton, CA
PURPOSE: To evaluate the challenges and implement strategies to overcome barriers to successful antimicrobial stewardship in the smaller hospital and any hospital lacking specific infectious disease–trained practitioners.
METHODS: A cross-sectional survey was used to help a committee delineate priority areas for development around antimicrobial stewardship. The question domains included availability/reliability of ID resources within the hospital, microbiology laboratory interface and antibiogram development, National Patient Safety Goal 7, and issues around resistance and stewardship.
RESULTS: Nineteen clinical or operational pharmacist respondents participated in an 11-question survey. Of the 19 respondents, 5% indicated that no hospital-based ID coordinator or resource existed, whereas 16% and 11% indicated a physician or pharmacist resource. Fifty-seven percent (8 of 15) indicated no antimicrobial stewardship program was in place. Seventy-four percent (14 of 19) indicated they had an antibiogram, but only 14% (4 of 15) indicated that pharmacy provided input into the development or update of antibiogram. Only 21% (3 of 14) responded they were extremely familiar with microbiology laboratory methods around susceptibility, testing, and suppression. A gap analysis template was developed to aid in a more detailed hospital assessment. To date, five collaborative calls have been scheduled (four conducted) around National Patient Safety Goal 7 and the SHEA Compendium, Evidence-Based Approach to Obtaining Buy In from Administrators and Clinical Leadership, Antibiogram Development/Update/Analysis, and De-Escalation Strategies.
CONCLUSIONS: This baseline assessment confirmed the need for a more detailed assessment and provision of tangible approaches for the smaller hospital or limited-resource hospital in achieving stewardship activities around antimicrobial resistance.

256. Daptomycin for the treatment of gram-positive bacteremia: 5-year experience at a single center. *Corinne Chahine-Chakhtoura, Pharm.D., M.S., BCPS,*[1] Manisa Tanprayoon, Pharm.D., BCPS,[1] Darren Culshaw, Pharm.D.[2]; (1) St. Michael's Medical Center, Newark, NJ; (2) Cubist Pharmaceuticals, Lexington, MA
PURPOSE: To describe our clinical experience with daptomycin in the treatment of bacteremia using the data from the Cubicin Outcomes Registry and Experience (CORE) program.
METHODS: CORE is a retrospective, observational, multicenter study designed to describe the clinical use of daptomycin. Patients with bacteremia, excluding endocarditis or intracardiac foreign body infections, were assessed for baseline characteristics, pathogen types, and antibiotic dosing. All patients, starting in 2005, were evaluated for safety. Efficacy analyses were based on the evaluable population. Outcomes were assessed at the end of daptomycin therapy and classified into success (defined as cured or improved) or failure.
RESULTS: From 2004 to 2008, our institution enrolled 96 patients in the registry. Sixty-two of the 96 patients were evaluable for outcomes (53% females, 35% older than 65 years). Underlying diseases included hypertension (37%), diabetes (42%), chronic renal failure (29%), and heart failure (19%). Sixty-three percent of bacteremia cases were catheter related. A gram-positive pathogen was reported in 58 patients: 24% methicillin-resistant *Staphylococcus aureus* (MRSA), 31% coagulase-negative staphylococci, and 26% vancomycin-resistant enterococci (VRE). The median (range) daptomycin initial dose and duration of therapy was 6 mg/kg (3–8 mg/kg) and 8 days (1–45 days), respectively. Seventy percent of patients received a dose greater than 6 mg/kg. Patient outcomes were success 87% (cured 27%, improved 60%) and failure 13%. Successful therapy for patients with MRSA and VRE was 93% (14 of 15 patients) and 81% (13 of 16 patients), respectively. The median (range) response to therapy, reported in 35 patients, was 3 days (1–14 days). Four patients had five adverse events possibly related to daptomycin (four nonserious and one death in a patient with gram-negative sepsis).
CONCLUSION: In our institution, daptomycin has been shown to be an effective and well-tolerated antibiotic therapy in patients with gram-positive bacteremia.

Managed Care

257. Improving patient self-management of multiple sclerosis and medication management through a disease therapy management program. *Jennifer Shin, Pharm.D.*, Karen M. Stockl, Pharm.D., Sherry Gong, M.S., Ann S.M. Harada, Ph.D., MPH, Brian K. Solow,

M.D., FAAFP, Heidi C. Lew, Pharm.D.; Prescription Solutions, Irvine, CA

PURPOSE: To evaluate the impact of a specialty pharmacy–implemented disease therapy management (DTM) program for patients with multiple sclerosis (MS).

METHODS: Patients with MS enrolled in the DTM program received 1) pharmacist- or nurse-initiated telephone consultations on a monthly or bimonthly interval based on risk stratification, 2) personalized care plans, and 3) monthly educational mailings. DTM participants who were continuously eligible (n=156) were compared with two propensity score–matched control groups with MS: those using retail pharmacy (n=156) and those opting out of the specialty pharmacy's DTM program (n=156). The primary outcome examined was medication adherence and persistence to interferon-beta or glatiramer. Short Form (SF)-12, Work Productivity Activity Impairment (WPAI) questionnaire, and MS relapse rates were assessed at baseline (month 0) and month 6 among patients who completed the DTM program (n=283).

RESULTS: Medication adherence was significantly higher for DTM participants compared with retail pharmacy patients (0.92 vs. 0.86; p=0.0006) and similar compared with specialty pharmacy patients who opted not to receive DTM (0.92 vs. 0.90, p=0.23). Patients receiving DTM demonstrated significantly greater persistence (p<0.01) on therapy (220 days) compared with specialty pharmacy patients not receiving DTM (188 days) or retail pharmacy patients (177 days). Among patients receiving DTM, SF-12 and WPAI were not significantly changed from baseline to month 6; however, MS relapses were significantly reduced (14.0% of patients at baseline vs. 9.3% at month 6; p=0.03). At month 6, virtually all participants (97%) reported that the program was very or somewhat helpful in improving self-management of their health.

CONCLUSIONS: A specialty pharmacy MS DTM program focusing on medication management and patient education resulted in increased adherence and persistence to MS medications, fewer MS relapses, and improved self-management of their MS condition.

Medication Safety

258. Pharmacist intervention to improve prescribing near misses in emergency department. Chia-Ching Lin, M,[1] Hui-Ping Liu, M.S.,[1] You-Mei Lin, M,[2] *Hsiu-Yu Chien, M.S.*[2]; (1) Department of Pharmacy, Taipei Medical University-Shuang Ho Hospital, Jhonghe City, Taipei County, Taiwan; (2) 1. Taipei Medical University, 2. Department of Pharmacy, Taipei Medical University-Shuang Ho Hospital, Jhonghe City, Taipei County, Taiwan

PURPOSE: High-prescribing near-miss rate was noted in the emergency department of Taipei Medical University-Shuang Ho Hospital (TMU-SHH) from October 2008 to December 2008. To ensure medication safety and improve the quality of health care, pharmacists were actively involved in a series of improvement projects, and the impact of intervention on reducing the prescribing near-miss rate was also evaluated.

METHODS: The standard process plan-do-check-action (PDCA) cycle was applied on the issues of computerized physician order entry (CPOE) systems and personnel familiarity. We focused on these problems and carried out the following action plan to reduce the prescribing near-miss rate: 1) communicate with the physicians and computer programmers and then modify the CPOE systems, 2) share and discuss the near-miss information with physicians, 3) reinforce the identification of sound-alike or look-alike drugs, and 4) enhance the recruiting training. The rate of prescribing near misses was compared before and after the intervention.

RESULTS: After the PDCA cycle, the mean rate of prescribing near misses was decreased from 0.48% to 0.17%. The intervention we put forward was of statistical significance (t-test; p=0.0226; 95% CI: 0.28–0.68; 95% CI: 0.05–0.39, respectively).

CONCLUSIONS: Because errors in medication use contribute significantly to the morbidity and high costs of health care, it is our duty to continuously improve clinical quality to provide a patient-centered, high-quality, and safer medication system in TMU-SHH.

259. Evaluation of an innovative corrected QT (QTc) monitoring and intervention program: a pilot study. *Ederlyn Dia, Pharm.D.*, Judy Davidson, CNS, Zubair Nadiri, B.A., Stein Joseph, M.D., Harminder Sikand, Pharm.D.; Scripps Mercy Hospital, San Diego, CA

PURPOSE: Scripps Mercy Hospital currently uses continuous telemetry monitoring to determine risk of arrhythmias and prevent an adverse event. Measurement of the QT interval corrected for heart rate (QTc) provides with information on the risk of a malignant ventricular arrhythmia called torsades de pointes (TdP). Our goal is to describe the effect of a multidisciplinary QTc monitoring program on patient safety, identify possible etiologies of QTc prolongation, and help guide improvements in our QTc protocol.

METHODS: Telemetry-monitored patients with QTc prolongation were enrolled concurrently. A flow diagram was used by nurses, pharmacists, and physicians when a prolonged QTc was identified. Patient medical records were reviewed for baseline and daily QTc values, electrolyte status, and impact of current medications. Physician contact after assessment was initiated for all QTc values more than 450 milliseconds.

RESULTS: Seven hundred twenty-nine patients were monitored in a 6-week period; 45 had QTc prolongation, and 23 resulted in physician notification because of potential QTc-prolonging medications. Fifty percent were taking multiple QTc-prolonging medications. Three patients had medications discontinued, and three had medications changed. One in four patients had a treatment change because of the monitoring process, and three patients had nonsustained ventricular tachycardia. No patient died or had a code blue.

CONCLUSION: This is the first study to provide outcomes of a multidisciplinary QTc monitoring program. Protocol adherence and determining the etiology of QTc prolongation were challenging. Studies are needed to evaluate the outcomes of an automated QTc notification system versus the manual calculation and reporting process that we used. Future studies are needed in larger populations to analyze the effects of individual or combinations of medications to allow the development of risk mitigation strategies.

Neurology

260. Pharmacist role in improving rate and quality of stroke specific education given to stroke patients/caregivers: a pre and post-intervention comparison. *Paul Wohlt, Pharm.D., BCPS*, Vinnie Watkins, RN, Elizabeth McKnight, M.S., Dean Roller, M.D., John Zurasky, M.D.; Intermountain Medical Center, Murray, UT

PURPOSE: To improve the rate of education and documentation provided to stroke patients and their caregivers. Education provided to patients and/or family members should include 1) recognizing signs of stroke, 2) understanding the importance of calling 911 at the first sign of a stroke, 3) understanding personal modifiable stroke risk factors, and 4) teaching on medications prescribed.

METHODS: Before the intervention, an interdisciplinary team was assembled to evaluate the rate of stroke education and documentation provided to patients admitted to Intermountain Medical Center with a diagnosis of ischemic stroke. This team then identified processes aimed at improving the stroke education program. Pharmacy and nursing staff collaborated with the information technology department to create a computerized program capable of identifying inpatients with a diagnosis of ischemic stroke. The program became available for use on May 31, 2009. The pharmacist staffing the neuroscience critical care unit (NCCU) was designated to run this report daily. The NCCU pharmacist would then provide stroke education to the patient or assign this task to a pharmacy student, pharmacy resident, or nurse practitioner. In addition, a computerized charting program was updated to facilitate documentation of stroke education. The rate of stroke education documentation was reported at monthly administrative meetings. Differences in rates were evaluated using a Fisher exact test for equality of binomial proportions.

RESULTS: The percentage of comprehensive education given before interventions ranged from 15% to 84% with an overall rate of 51% (n=164). Percentages after May 31 ranged from 73% to 94% with an overall rate of 84% (n=241). The interventions resulted in a 33% increase in the rate of education provided (p=0.00, $\alpha = 0.05$).

CONCLUSIONS: Adherence, documentation, and specificity of education for stroke patients can be improved by standardizing electronic stroke education documentation, adding pharmacy leadership, and providing feedback.

Oncology

261. Quality improvement project for prophylaxis of deep vein thromboembolism in oncology patients in a community teaching hospital. *Dianne M. Brundage, Pharm.D.*, Rosaleen Duggan, RN, M.S., Andrea O'Hern, RN, Bethany Grommesh, M.D.; Methodist Hospital/Park Nicollet Health Services, Minneapolis, MN

PURPOSE: Prevention of deep vein thromboembolism (DVT) is necessary when cancer patients are hospitalized and inactive. The goal of this project was to use an interdisciplinary approach to decrease the incidence of DVT in hospitalized patients with cancer.
METHODS: Baseline data were collected from the claims data of ICD9 codes of hospitalized patients with cancer for 5 months. Presence of DVT during hospitalization was determined by claims data during the period of hospitalization. In addition, if oncology patients were readmitted during the next 48 hours after discharge for DVT, they were included as a case of DVT that should have been prevented. This unique order set for DVT prophylaxis was created to identify contraindications for anticoagulation, given that all oncology patients are at risk of DVT. Decentralized pharmacists checked risk factors for bleeding on the order set, which was to be signed by the physician. Nursing staff left daily progress notes regarding procedures scheduled and presence of DVT prophylaxis. Admission orders were changed to have patients perform ambulatory therapy 3 times daily to prevent DVT. After 6 months, claims data were reviewed in a manner similar to the baseline period.
RESULTS: During the baseline period, 12 patients developed DVT of 890 admissions for 592 patients, resulting in 20 DVTs per 1000 patients. During the follow-up period, 1 patient developed VTE of 813 admissions for 587 patients, resulting in 2 DVTs per 1000 patients.
CONCLUSIONS: An order set for DVT prophylaxis based on contraindications for anticoagulation significantly decreased DVT in hospitalized patients with cancer. A longer follow-up period is planned.

Pain Management/Analgesia

262E. Dose linearity, consistency, and predictability of plasma concentrations with fentanyl buccal soluble film (FBSF). *Niraj Vasisht, Ph.D.,*[1] Jeffrey G. Stark, Ph.D.,[2] Andrew L. Finn, Pharm.D.,[1] Larry N. Gever, Pharm.D.[3]; (1) BioDelivery Sciences International, Inc., Raleigh, NC; (2) CEDRA Corporation, Austin, TX; (3) Meda Pharmaceuticals, Inc., Somerset, NJ

PURPOSE: The BEMA (BioErodible MucoAdhesive) drug delivery system is a small, bilayered, water-soluble polymer film designed to deliver therapeutic systemic drug concentrations reliably and conveniently. Fentanyl is the initial product in the BEMA system. The objectives of these studies were to evaluate the dose linearity, consistency, and predictability of FBSF dosing.
METHODS: Three phase 1 studies were conducted in healthy volunteers to assess 1) dose linearity across a range of doses, 2) consistency of repeat-dose administration, and 3) predictability when dosing with a single-unit (1 × 800 µg) or multiple-unit (4 × 200 µg) regimen.
RESULTS: Mean C_{max} values for FBSF doses of 200, 600, and 1200 µg were 0.38, 1.16, and 2.19 ng/mL, and corresponding values for mean AUC_{inf} were 3.46, 11.72, and 20.43 ng/hour/mL, respectively. Two single 600-µg doses of FBSF administered 3 days apart in periods 1 and 2 produced almost identical mean C_{max} values (1.08 and 1.01 ng/mL) and $AUC_{0–12}$ values (6.3 and 6.2 ng/hour/mL). Three days later, application of three 600-µg doses of FBSF at 1-hour intervals in period 3 produced a proportional increase in peak plasma concentration and exposure compared with a single dose. Application of one 800-µg dose unit compared with four 200-µg dose units produced identical C_{max} (1.33 ng/mL) and almost identical AUC_{last} (11.4 vs. 11.7 ng/hour/mL).
CONCLUSIONS: Fentanyl plasma concentrations and exposure increase linearly across the 200- to 1200-µg FBSF dose range with highly consistent dose-to-dose exposure from FBSF. Fentanyl exposures after one 800-µg and four 200-µg dose units were bioequivalent, supporting the recommended titration process for FBSF. The predictability and consistency of plasma concentrations with FBSF is attributed to 1) the relationship between the fentanyl dose and the film's surface area and 2) the mucoadhesive properties of the delivery system that eliminate patient variability.
Presented at the American Academy of Pain Medicine 25th Annual Meeting, Honolulu, HI, January 28–31, 2009.

Pediatrics

263. Comparison of two different "potassium-cocktail" formulations used to lower serum potassium concentrations in neonates. *Tracy Sandritter, Pharm.D.*, Alex Oschman, Pharm.D., Susanne Liewer, Pharm.D., Howard Kilbride, M.D.; Children's Mercy Hospital, Kansas City, MO

PURPOSE: After a retrospective quality improvement project, modifications to a potassium-lowering cocktail were made because of hyperglycemia and acidosis. The purpose of this study was to determine whether modifications to the potassium cocktail formulation resulted in a decrease in hyperglycemia and acidosis.
METHODS: This was a retrospective cohort study of neonates with hyperkalemia receiving two different potassium cocktail formulations. Patients were divided into two groups based on the formulation of the potassium cocktail received (group 1, original; group 2, current). A power analysis was performed. Patients receiving the original formulation were matched 2:1 by gestational age and birth weight to patients receiving the modified formulation. Data collection included gestational age, weight, glucose, duration of infusion, serial serum electrolytes, time to first repeat potassium value, blood gasses, vital signs, urine output, and occurrence of arrhythmias. Demographic statistics and two-tailed t-tests were used. IRB approval was obtained.
RESULTS: Thirty-nine patients were eligible for participation in the study (n=13 group 1, n=26 group 2). Modifications made to the potassium cocktail formulation were sufficient to decrease the incidence of hyperglycemia from 76.9% to 21.7% (p=0.001). Mean glucose with the current formulation did not differ among the analyzed time points (p=0.329 and 0.809). The change in the sodium lactate content was not sufficient to decrease the incidence of acidosis during the infusion (76.9% vs. 68.2%, p=0.58). Mean pH measurements at the three time points were similar for both cocktail formulations. The mean decrease in serum potassium was similar between formulations (–1.37 mEq/L vs. –1.14 mEq/L, p=0.696). An increase in serum potassium monitoring 1 hour after initiation of the cocktail was not seen.
CONCLUSIONS: Additional modifications to the potassium cocktail are unwarranted. A recommendation was made to modify the ordering protocol to require a serum potassium concentration 1 hour postinitiation.

264. Pharmacist managed therapeutic drug monitoring (TDM) in pediatric cystic fibrosis (CF) patients. *Jeffrey J. Cies, Pharm.D., BCPS,*[1] Laurie Varlotta, M.D.[2]; (1) St. Christopher's Hospital for Children, Philadelphia, PA; (2) St. Christopher's Hospital for Children, Drexel University College of Medicine, Philadelphia, PA

PURPOSE: Patients with cystic fibrosis (CF) are often treated with aminoglycoside (AG) antibiotics during an infective pulmonary exacerbation caused by *Pseudomonas aeruginosa*. Achieving pharmacokinetic and pharmacodynamic (PK/PD) targets to improve outcomes and counteract increasing rates of resistance is paramount. The primary objective is to compare the number of pediatric CF patients achieving AG PK/PD targets when therapy is managed by a pharmacist compared with nonpharmacist practitioners. Secondary objectives include number of dosing adjustments, levels ordered, and drug waste and its related cost.
METHODS: This is a retrospective cohort study beginning January 1, 2007. Any CF patient receiving an AG and having two or more serum concentrations, which could be used to determine PK/PD

parameters, was included. To detect a 25% difference in the number of CF patients reaching AG PK/PD targets with an $\alpha = 0.05$ and a power of 80%, 40 treatment courses are required per group. A χ^2 test and Student *t*-test will be used to analyze nominal and continuous variables, respectively.
RESULTS: Baseline demographic data are similar between each group. So far, 29 patients, accounting for 52 courses of AG therapy, are in the pharmacist (P) group, and 22 patients, accounting for 42 courses, are in the nonpharmacist group (NP). Ninety-eight percent of patients in the P group reached AG PK/PD targets compared with 71% in the NP group ($p<0.001$, $\chi^2 = 13.8$). The P group was at goal in a mean of 1.98 days compared with 4.77 days in the NP group ($p<0.0001$). Data collection and analysis are ongoing.
CONCLUSION: Pharmacist-managed TDM resulted in a higher percentage of pediatric CF patients achieving AG PK/PD targets. Furthermore, patients in the P group attained AG PK/PD targets earlier, which could improve care and response to therapy and minimize costs related to dosage adjustments and drug wastage.

265. Cost-savings with palivizumab in a pediatric hospital. *Jeffrey J. Cies, Pharm.D., BCPS*; St. Christopher's Hospital for Children, Philadelphia, PA
PURPOSE: Bronchiolitis is a disorder most commonly caused in infants by viral lower respiratory tract infection (LRTI). The most common etiology is the respiratory syncytial virus (RSV), with the highest incidence of RSV infection occurring between December and March. The American Academy of Pediatric (AAP) guidelines for bronchiolitis state that clinicians may administer palivizumab prophylaxis to selected infants and children to prevent the acquisition of RSV bronchiolitis and hospital admission.
For the 2008 RSV season, the AAP criteria were distributed to prescribers promoting awareness of the approved indications for palivizumab. In addition, a twice-weekly batch compounding production process was implemented. The primary objective was to determine whether increased awareness and a batch-compounding process reduced expenses related to palivizumab therapy in the 2008 RSV season compared with the 2007 RSV season.
METHODS: This was a retrospective chart review from January 1, 2007, to April 30, 2009. Any patient who received a single dose of palivizumab was included. Patient charts were screened to determine whether one of the AAP recommendations for use was met. Pharmacy purchasing and dispensing records were used to determine the total number of palivizumab vials purchased and doses administered each season. A χ^2 test and Student *t*-test were used for nominal data and continuous data, respectively.
RESULTS: During the 2008 RSV season, 57 (93%) of 61 patients met AAP criteria compared with 52 (71%) of 73 patients in 2007 ($p<0.01$, $\chi^2 = 10.8$). The total cost of palivizumab during the 2008 season was $70,917.63 compared with $106,624.06 for the 2007 season, resulting in a cost savings of $35,706.43.
CONCLUSION: Promoting awareness and distributing the AAP recommendations hospital-wide decreased inappropriate use of palivizumab. Decreasing inappropriate use and a batch-compounding process reduced the overall purchase costs and waste related to palivizumab between the 2007 and 2008 RSV seasons.

Pharmacoeconomics/Outcomes

266. Continuous quality improvement of darbepoetin alfa (Aranesp)® injections administration order form (AAOF) to assure compliance with the 2007 updated CMS guidelines. *Stacy L. Yang, Pharm.D.*; Western University of Health Science, Monterey Park, CA
PURPOSE: To evaluate the effectiveness of a darbepoetin alfa (Aranesp) administration order form (AAOF) implemented at the Hematology Oncology Medical Group of Orange County, Inc., in improving adherence to the 2007 guidelines of the Centers of Medicare & Medicaid Services (CMS) and avoidance of reimbursement loss.
METHODS: Retrospective chart review at the medical office to include all the patients receiving darbepoetin alfa (EPO) for treatment of chemotherapy-induced anemia from May 1, 2008, to February 28, 2009, after implementation of the AAOF. Patient demographics, renal function, hemoglobin and hematocrit levels before chemotherapy and during the EPO treatment period, date of last dose of chemotherapy, initial and maintenance doses of EPO, dosing frequency, and duration of therapy for EPO were collected. Cost analysis was conducted to determine the projected reimbursement loss because of nonadherence to CMS guidelines. Comparative assessments were conducted using data before and after implementation of AAOF.
RESULTS: Fifty-three patients were included in the study. Sixty-six percent were women with breast cancer (35.8%), the most common type. Median age was 67 years, and median BMI was 25.1 kg/m^2. Inappropriate documentation of AAOF occurred in 19 of 53 subjects. Comparative nonadherence assessment using the Z proportion test was statistically significant ($p<0.0001$) in the areas of initial weight-based dose and dose frequency before and after implementation of AAOF, which is confirmed with the c2 association test. The absolute number in the area of inappropriate dose reduction and inappropriate dose escalation appeared to have been reduced. The cost benefit analysis showed about $72,611 annual avoidance of reimbursement loss.
CONCLUSIONS: The implementation of AAOF has statistically improved the adherence to EPO use according to the CMS guidelines in initial weight-based dose and the dose frequency ($p<0.0001$), leading to a projected avoidance of reimbursement loss by $72,611. Additional staff education may further improve the effectiveness of the AAOF.

267. Development and implementation of a STEP pharmacy. Janet D. Gaskins, M.S.,[1] *Darrell L. Willyard, Pharm.D.*,[1] Gena Dupus, Pharm.D., BCPS,[2] Tony Palmer, RPh, MBA,[2] Steven Meixel, M.D.[1]; (1) University of Oklahoma School of Community Medicine, Tulsa, OK; (2) University of Oklahoma College of Pharmacy, Tulsa, OK
PURPOSE: To develop and implement a STEP (safety, tolerability, efficacy, and price) pharmacy designed to provide evidence-based, low-cost medications and essential medication therapy management services (MTMS) to the uninsured populations of Tulsa.
METHODS: Collaboration between the University of Oklahoma Health Sciences Center–Tulsa and the St. John Health System Medical Access Program provided funding for a 20-hour per week STEP pharmacy pilot project including prescription services and MTMS. The primarily generic-only formulary was developed around four chronic diseases (asthma, diabetes, hypertension, and dyslipidemia) and evaluated with the STEP concept. With few exceptions, medications on the formulary cost $3 per 30-day supply.
RESULTS: Nine weeks of prescription services have provided 218 prescriptions for 93 unduplicated clients, with a refill rate of 20.4%. Diabetes (31.2%) and cardiovascular conditions (29.4%) accounted for 60.6% of prescriptions filled. Cost savings that potentially could save $6744 annually were demonstrated with a patient with diabetes and accomplished by substituting STEP-approved medications. Diabetes, hypertension, and dyslipidemia are the most common disease states identified for patients receiving MTMS. Educational handouts for diabetes and asthma, with consideration for health literacy, have been developed and distributed.
CONCLUSIONS: More than 18% of the adult Tulsa population is uninsured. The STEP pharmacy concept provides a cost-efficient approach to providing MTMS and medications to the underserved through the collaboration of academia and local philanthropic and charity organizations. Significant cost savings have been shown by therapeutic substitution of less expensive, evidence-based alternative medications. The unique, innovative mechanism of the STEP pharmacy meets community needs and allows patient adherence to medication regimens and receipt of counseling and education on disease management and lifestyle changes. We expect future data to show increased adherence because of MTMS and decreased medication expense. Although still in development, with appropriate resources, we believe the STEP pharmacy concept is sustainable and adaptable for various populations.

Pharmacogenomics/Pharmacogenetics

268. Evaluation of genetic and non-genetic factors on clinical response to clopidogrel (Plavix) after percutaneous coronary intervention in Iranian patients. *Soha Namazi, Pharm.D., Ph.D.*, Negar Azarpira, M.D., Pathologist, Andia Khalili, Pharm.D., Mohammadjavad Kojuri, M.D., Cardiologist; Shiraz University of Medical Sciences, Shiraz, Iran

PURPOSE: Subacute thrombosis is a major concern in patients undergoing percutaneous coronary intervention (PCI). Although treatment with clopidogrel and aspirin can reduce the risk of poststent thrombosis, 4%–30% of patients have shown inadequate response to clopidogrel. It is suggested that several genetic and nongenetic factors can be responsible for this problem. The aim of this study was to determine the role of two genetic factors (*P2Y12* and *CYP3A5*), demographic characteristics, and pathologic condition on clopidogrel response variability in patients after PCI.

METHODS: One hundred twelve patients who were candidates for elective PCI were enrolled in this study. All patients had received aspirin 80–325 mg daily for 1 week or more before PCI. Blood samples were taken from patients at baseline, 2 hours after taking a 600-mg loading dose of clopidogrel, and 24 hours and 30 days after PCI. Platelet aggregation was measured by the Turbidimetric aggregation assay with two different concentrations of two different agonist ADP (5 and 20 µM/mL) and arachidonic acid (500 and 5000 µg/mL). *CYP3A5* and *P2Y12* genotyping was performed by PCR-RFLP.

RESULTS: The statistic analysis revealed that maximal clopidogrel resistance occurred in 2 hours after taking clopidogrel; 25.9% of patients showed a low response to clopidogrel in this period. Although there were no significant associations between clopidogrel resistance and polymorphisms of *CYP3A5* and *P2Y12* ($p>0.05$), subjects who were expressers of *CYP3A5* genotypes had a greater inhibition of platelet aggregation. No significant associations were observed between nongenetic factors and clopidogrel resistance ($p>0.05$).

CONCLUSIONS: Our study showed that genetic and nongenetic factors had no significant effect on the antiplatelet activity of clopidogrel in an Iranian population. Further investigations to determine the effect of other probable factors (such as *CYP2C19*) on clopidogrel resistance are recommended.

Transplant/Immunology

269. Tolerability of de novo maintenance immunosuppressive therapy with sirolimus versus mycophenolic acid in combination with tacrolimus and prednisone renal transplant recipients. *Kwaku Marfo, Pharm.D.*, Julie Chen, Pharm.D., Javier Chapochnick, M.D.; Montefiore Medical Center, Bronx, NY

PURPOSE: Sirolimus is widely used in combination with other immunosuppressive agents to prevent graft rejection; however, the optimal time to initiate SRL therapy is still unclear because of potential toxicities such as prolonged wound healing, proteinuria, and thrombosis. The purpose of this retrospective review was to evaluate tolerability of tacrolimus-prednisone (FK/PRED) in combination with de novo sirolimus (SRL) versus mycophenolic acid (MPA) in renal transplant recipients.

METHODS: We retrospectively reviewed the medical records of 90 patients who underwent kidney transplantation at two different time points: 1) a cohort of 45 patients who received transplants between January 1 and June 30, 2007, and received SRL/FK/PRED and 2) a cohort of 45 patients who received transplants between January 1 and June 30, 2008, and received MMF/FK/PRED. The two groups were compared for rate of drug discontinuation, incidence of acute rejection, adverse effects (prolonged wound healing, lymphocele formation, infections, pneumonitis, thrombosis, dyslipidemia, and hyperglycemia), and renal function (serum creatinine and proteinuria).

RESULTS: Baseline demographics were similar between groups. At the end of 3 months, biopsy-confirmed acute rejection episodes (8.8% vs. 11.1%) and mean serum creatinine (1.7 ± 0.50 mg/dL vs. 1.5 ± 0.53 mg/dL) were similar (SRL vs. MMF group, respectively). There was a trend to higher blood concentrations of triglycerides (195 ± 100.3 mg/dL vs. 163 ± 85.8 mg/dL) and cholesterol (269 ± 457.5 mg/dL vs. 175 ± 29.8 mg/dL) in the SRL group; however, higher incidences of wound complications (14.6% vs. 9.8%) and pneumonia (7.1% vs. 9.8%) were observed in the MPA group. The SRL group had a drug discontinuation rate of 35.6% compared with 8.9% in the MPA group ($p=0.002$).

CONCLUSIONS: Both groups performed similarly, showing similar rates in acute rejections and serum creatinine at the end of 3 months; however, compared with the MPA group, there was a significantly higher drug discontinuation rate in the SRL group, with a trend toward higher incidence of lipid abnormalities.

RESIDENTS AND FELLOWS RESEARCH IN PROGRESS

Adult Medicine

270. Evaluation of vitamin K administration in a community hospital. *Deborah E. Wellington, Pharm.D.*, Janelle Berg, Pharm.D., BCPS, Estela Trimino, Pharm.D., BCPS; Mercy Hospital, Miami, FL

PURPOSE: To assess vitamin K administration at a community hospital for adherence to published guidelines and to compare the international normalized ratio (INR) reduction associated with different routes of administration.

METHODS: The medical records of all patients who received vitamin K between October and December 2008 were prospectively reviewed. The reason for reversal, dose, route, INR predose and 24 hours postdose, and warfarin dose and indication were collected and analyzed.

RESULTS: A total of 82 patients were given vitamin K: 43 (52%) subcutaneously, 19 (23%) intramuscularly, 18 (22%) orally, and 2 (2%) intravenously. Surprisingly, vitamin K was only used for treatment of excessive anticoagulation in 13 (16%) cases, yet it was administered to correct the INR before surgery in 43 (52%) of all cases. Of the 43 surgical patients, 21 (49%) received vitamin K to decrease the INR below 1.5. Twenty-two (51%) received vitamin K when the INR was already below the American College of Chest Physicians (ACCP) recommended target of 1.5. Twenty-three (54%) surgical patients received warfarin as a home medication, and only three (13%) were discharged with a therapeutic INR (2–3). Overall, oral administration of vitamin K produced a mean INR reduction of 66%, compared with 48% when administered by other routes ($p=0.03$).

CONCLUSION: This study suggests that vitamin K may be overused in the surgical population, possibly delaying time to reach therapeutic INR postsurgery. In addition, the INR reduction using oral vitamin K was greater than seen with other administration routes; oral administration may be underused in the treatment of excessive anticoagulation. These findings highlight the need for physician education emphasizing the safety and effectiveness of oral vitamin K as recommended by ACCP guidelines.

271. Heel ultrasonography in young healthy adults prescribed selective serotonin reuptake inhibitors. *Tara R. Loan, Pharm.D.,*[1] Charles F. Seifert, Pharm.D.[2]; (1) Texas Tech University Health Science Center School of Pharmacy, Lubbock, TX; (2) Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX

PURPOSE: To characterize the effect of SSRI use in adolescents and early adulthood on bone mineral density.

METHODS: A prospective review was conducted of patients who voluntarily responded to recruitment methods for the study. Inclusion criteria included young adults aged 18–25 years who were currently taking or had previously taken an SSRI for a minimum of 3 consecutive months. A subject interview was conducted of each patient to collect background information. Each patient's heel ultrasound was then measured by an ultrasonometer.

RESULTS: Complete data were collected on 52 patients. The median duration of SSRI use was 24 months. There was a significant negative correlation between SSRI duration and heel ultrasound T-score ($rs = -0.55$, $p<0.0001$). The median T-score was significantly lower in patients taking SSRIs longer than 24 months (0.3 vs. 0.9, $p=0.0036$).

CONCLUSIONS: Duration of SSRI use significantly correlates with heel ultrasound T-scores, implying a direct causal relationship with duration of SSRI use and worsening bone health.

272. Developing and implementing a pharmacist-led antimicrobial stewardship program (ASP) at a community hospital.

Deborah E. Wellington, Pharm.D., Janelle Berg, Pharm.D., BCPS; Mercy Hospital, Miami, FL

PURPOSE: Antimicrobial stewardship is a key component of preventing antimicrobial resistance in hospitals; recent guidelines call for an infectious disease (ID) physician and a clinical pharmacist with ID training as core members of an ASP. This study documented interventions made by a clinical pharmacist focused on one target antimicrobial to identify opportunities for improvement in antimicrobial use and to compare acceptance rates between traditional communication methods with direct prescriber feedback.

METHODS: All orders for piperacillin-tazobactam (Zosyn) were prospectively reviewed by a clinical pharmacist resident on a daily basis for 2 months. Baseline data were collected during an initial observation period, which was followed by a second phase in which recommendations were made by placement of nonpermanent chart note; finally, a third phase involved direct prescriber feedback with discussion.

RESULTS: Fifty-five interventions were documented; these included renal dose optimization, de-escalation of therapy, streamlining, intravenous-to-oral switch therapy, and dose optimization. Physician acceptance rates were high; 86% of recommendations made by placement of nonpermanent chart note were accepted compared with 88% acceptance of recommendations made directly to the prescriber. Cost savings associated with these interventions totaled $14,750, with projected annual savings of $176,700.

CONCLUSION: Allocating resources to a pharmacist-led ASP promotes appropriate antimicrobial use and reduces costs. Projected annual savings for one target antimicrobial at our institution would cover the salary of a dedicated full-time pharmacist and allow 5 hours/week physician involvement in stewardship efforts.

Ambulatory Care

273. Cost savings associated with pharmacist-assisted enrollment into prescription assistance programs. *Christine Tumis, Pharm.D.,*[1] Autumn L. Runyon, Pharm.D.,[2] Thomas J. Mattei, Pharm.D.[3]; (1) Duquesne University, Pittsburgh, PA; (2) Duquesne University, Mylan School of Pharmacy, Pittsburgh, PA; (3) Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA

PURPOSE: This study evaluated the cost savings of pharmacist-assisted enrollment into pharmaceutical manufacturer–sponsored prescription assistance programs (PAPs) in an ambulatory setting. The objectives of the study were to 1) identify the cost savings realized by using pharmacist-assisted enrollment into PAPs and 2) quantify the costs associated with missed opportunities of not using pharmacist-assisted PAPs.

METHODS: One hundred forty-eight enrollment applications for PAPs between March 1, 2008, and February 28, 2009, from a local free health care clinic were evaluated. Names of medications, quantity of drug, and number of refills were documented. The cost savings of using a pharmacist was calculated based on the Usual & Customary (U&C) charge for each of the medications applied for. The U&C charge, representing the "cash" price of each medication, was obtained from a local pharmacy. Using descriptive statistics, the U&C charges for all applications were totaled. The missed opportunity costs were calculated by totaling the clinic's charges for medications that could have been obtained by PAPs between March 1, 2008, and February 28, 2009.

RESULTS: The annual cost savings from implementing pharmacist-assisted PAPs totaled $182,791.81. The missed opportunity cost of not using the pharmacist-assisted PAP totaled $20,998.14.

CONCLUSION: The implementation of pharmacist-assisted enrollment into PAPs is an effective cost-saving mechanism for obtaining medications for indigent patients an ambulatory setting.

Cardiovascular

274. An evaluation of clopidogrel use after non-ST-elevation and ST-elevation acute coronary syndrome. *Shelley E. Snell, Pharm.D.,*[1] Jessica Starr, Pharm.D., BCPS[2]; (1) Princeton Baptist Medical Center, Birmingham, AL; (2) Auburn University Harrison School of Pharmacy, Birmingham, AL

PURPOSE: Clopidogrel is currently indicated for use after non–ST-segment elevation (NSTEMI) and ST-segment elevation (STEMI) myocardial infarction (MI) to decrease the rate of thrombotic complications and death. Premature discontinuation of clopidogrel therapy is the leading independent predictor for stent thrombosis, and it has been associated with recurrent MI and increased mortality. The purpose of this retrospective analysis was to determine whether clopidogrel therapy was initiated and continued after discharge in patients who experienced acute coronary syndrome.

METHODS: Medical records of patients hospitalized between October 2007 and October 2008 with a discharge diagnosis of NSTEMI and STEMI were reviewed. Specific parameters documented included the inpatient prescription of clopidogrel after diagnosis or inpatient procedure, outpatient prescription of clopidogrel at the time of discharge, and documentation of intended duration of clopidogrel therapy after hospital discharge.

RESULTS: Clopidogrel was prescribed in the hospital for 91% of the 95 patients studied, and 84% of patients received a prescription for clopidogrel on discharge. Of the 84% of patients who received clopidogrel at discharge, only 4% of the patients' medical records included documentation of how long clopidogrel therapy was to continue. No medical records reviewed included documentation that patients were verbally instructed on how long to continue clopidogrel.

CONCLUSIONS: Although clopidogrel was prescribed appropriately in most patients, there was still a small percentage of patients who did not receive clopidogrel after their acute coronary event. In addition, patients were not educated about the intended duration and importance of continuing clopidogrel after hospital discharge. The findings of this study will be used to educate physicians and medical residents on the importance of appropriate drug therapies after acute coronary syndrome.

275. Inappropriate digoxin use and patient outcomes. *Kathryn S. Voll, Pharm.D.,*[1] Jessina C. McGregor, Ph.D.,[2] Harleen Singh, Pharm.D.[3]; (1) Portland VA Medical Center, Portland, OR; (2) Oregon State University/Oregon Health & Science University College of Pharmacy, Portland, OR; (3) Oregon State University, College of Pharmacy, Portland, OR

PURPOSE: Digoxin has a narrow therapeutic range; therefore, toxicity can be observed at lower doses. Furthermore, renal insufficiency and electrolyte disturbances can predispose patients to digoxin toxicity. The objective of this study was to identify any inappropriate uses for digoxin and analyze associated outcomes such as all-cause hospitalization, digoxin toxicity, and death.

METHODS: A retrospective cohort study was conducted among adult veteran patients with heart failure (HF) and an original digoxin order between January 2006 and August 2008 at the Portland VAMC. Exclusion criteria included digoxin ordered by an outside provider, any missing data, and dialysis. The appropriateness of digoxin was assessed on the basis of indication, optimal titration of HF medications that improve mortality/morbidity, presence of HF symptoms, and contraindications. The frequency of hospitalization, toxicity, and 30-day mortality was assessed among appropriate and inappropriate digoxin groups.

RESULTS: Of the 58 patients included, 27 (46.6%) had digoxin inappropriately initiated. Among these patients, 100% had HF medications that were not appropriately titrated, 29.6% had no HF symptoms, and 3.7% had digoxin contraindications. One patient was hospitalized among the inappropriate digoxin group (3.7%) and zero patients among the appropriate group. One patient experienced documented digoxin toxicity among the appropriate digoxin group and none among the inappropriate group. No patients died within 30 days of digoxin initiation.

CONCLUSIONS: In this ongoing study, we observed that digoxin

was often initiated inappropriately, primarily because of a lack of optimally titrated HF medications. Hospitalization, toxicity, and death within 30 days of digoxin initiation were rare outcomes; thus, a larger study is needed to investigate the association with inappropriate digoxin initiation.

276. Heparin dosing nomograms in patients receiving mechanical circulatory assist devices. *Chaitali J. Desai, Pharm.D., BCPS,*[1] A. Janelle Hermosillo, Pharm.D.,[2] Brooke E. Baetz, Pharm.D., BCPS,[3] Andrew Peterson, Pharm.D.,[1] Mariell Jessup, M.D.,[4] Rohinton Morris, M.D.,[4] Sarah A. Spinler, Pharm.D., FCCP, BCPS[1]; (1) University of the Sciences in Philadelphia, Philadelphia, PA; (2) Lehigh Valley Health Network, Lehigh Valley, PA; (3) Penn Presbyterian Medical Center, Philadelphia, PA; (4) Hospital of the University of Pennsylvania, Philadelphia, PA

PURPOSE: Mechanical circulatory assist devices (MCADs) require anticoagulation, which is complicated by considerable concern for postoperative bleeding risks. There are very few data available for guidance on anticoagulation dosing in such patients.

METHODS: Prospective evaluation of early- and late-postoperative heparin dosing nomograms in patients receiving MCADs began in March 2009. Adult patients who met study criteria, with an implanted Thoratec PVADTM or Thoratec HeartMate II LVAD, receiving at least 2 days of anticoagulation using either the early or late heparin dosing nomogram and providing informed consent were enrolled. The primary objective was to evaluate the performance of these two nomograms by comparing the percentage of time spent within the nomogram-defined therapeutic range and number of heparin dosage adjustments to retrospective data collected from January 2006 to December 2007 before initiation of the nomograms. Up to eight anti-Xa levels were also collected and correlated with aPTT.

RESULTS: Six patients have been enrolled to date. Sixty-two percent of dosage adjustments were made using the nomogram. The percent time spent within the nomogram-defined therapeutic range was similar, 44% versus 48% in the historical group (mean difference, 0.04; 95% CI: –0.133 to 0.049), as was the mean number of dosage adjustments per day, 0.97 versus 1.2, respectively (mean difference, 0.23; 95% CI: –0.743 to 0.284). There were no bleeding or thrombotic events in the patients dosed by nomogram. The correlation between the aPTT and anti-Xa levels (n=30) was modest (r^2=0.39).

CONCLUSIONS: Additional education efforts are required regarding the use of the nomograms. Although there was no difference in time spent in therapeutic range between the two groups, there were no bleeding or thrombotic events reported in the nomogram group. Data from additional patients enrolled will be included.

277. Association between changes in NT-proBNP and clinical outcomes among chronic heart failure patients. *Rachael R. Allwine, Pharm.D.,*[1] Jessina C. McGregor, Ph.D.,[2] Harleen Singh, Pharm.D.[3]; (1) Portland VA Medical Center, Portland, OR; (2) Oregon State University/Oregon Health & Science University College of Pharmacy, Portland, OR; (3) Oregon State University, College of Pharmacy, Portland, OR

PURPOSE: Recent studies have suggested that N-terminal brain natriuretic peptide (NT-proBNP)-guided therapy may improve outcomes in patients with chronic heart failure (HF) compared with symptom-guided therapy. The objective of this study was to examine the association between change in NT-proBNP and risk of hospitalization and clinical outcomes in patients with HF.

METHODS: A retrospective cohort study was conducted among patients with HF between January 2006 and September 2008 at the Portland VAMC Heart Failure Clinic. Change in NT-proBNP was assessed as the difference between two NT-proBNP levels within 6 weeks. Patients were excluded if they were on dialysis or if they did not have two eligible NT-proBNP measurements. End points of interest were 1) 90-day all-cause mortality and hospitalization and 2) change in HF clinical signs and symptoms based on the Framingham risk criteria.

RESULTS: Of the 77 medical records reviewed, 39 met inclusion criteria. A nonsignificant association was observed between a reduction of at least 30% in NT-proBNP and 90-day hospitalization (odds ratio [OR] = 0.29, 95% confidence interval [CI]: 0.03–3.12) and between an increase in NT-proBNP of at least 30% and 90-day hospitalization (OR = 3.2, 95% CI: 0.52–19.84). There was no statistically significant association between change in NT-proBNP and clinical signs and symptoms.

CONCLUSION: This study suggests that reductions in NT-proBNP may be associated with reduced risk of 90-day hospitalization. This is an ongoing study, and continued data collection will assist in determining whether a statistically significant association exists between NT-proBNP and mortality, hospitalization, and clinical signs and symptoms.

Critical Care

278. Implementation of a real-time, computerized sepsis alerting system in non-ICU medicine patients. *Amber M. Sawyer, Pharm.D.,*[1] Eli N. Deal, Pharm.D.,[1] Andrew J. Labelle, M.D.,[2] Chad Witt, M.D.,[2] Steven W. Thiel, M.D.,[2] Richard M. Reichley, B.S.,[1] Scott T. Micek, Pharm.D.,[1] Marin H. Kollef, M.D.[2]; (1) Barnes-Jewish Hospital, St. Louis, MO; (2) Washington University School of Medicine, St. Louis, MO

PURPOSE: Patients developing sepsis on medicine wards may experience delays in initial fluid resuscitation and antibiotic administration, which could lead to ICU transfer and possibly increased hospital mortality. To improve early sepsis management, a real-time, computerized prediction tool (PT) using recursive partitioning regression tree analysis and an informatics-based alerting system was developed at Barnes-Jewish Hospital (BJH). The goal of the project was to evaluate whether implementation of the sepsis screening and alerting system facilitated early appropriate interventions and reduced sepsis-related morbidity and mortality.

METHODS: The study was designed as a before-after comparison with prospective, consecutive data collection. The before group (BG) consisted of 100 patients identified by the PT. The after group (AG) included 100 patients identified by the PT and had a real-time alert sent to a treating clinician by text page.

RESULTS: Of the 200 patients identified by the PT, 73 of 100 in the BG and 74 of 100 in the AG met sepsis criteria. After excluding patients without commitment to aggressive management, 64 patients in the BG and 66 patients in the AG were included. Baseline characteristics were similar between groups. Within 12 hours of the alert, the AG had more antibiotics prescribed and fluids administered versus the BG, with antibiotic escalation occurring in 28 versus 21 patients in the AG and BG, respectively. The AG also had a higher rate of ICU transfers as well as more transfers within 12 hours of the alert; however, no significant difference was found between groups for hospital LOS or hospital mortality.

CONCLUSION: The sepsis prediction tool developed at BJH is an effective method for early identification of non-ICU medicine patients with sepsis. Implementation of the PT by a real-time alerting system improved early interventions including antibiotic escalation and fluid resuscitation. Additional analysis of the PT is under way, and results are forthcoming.

Hematology/Anticoagulation

279. Impact of hospital guidelines on argatroban use in patients with suspected or confirmed heparin-induced thrombocytopenia: evaluation of clinical outcomes, adverse events and cost. *Snehal H. Bhatt, Pharm.D., BCPS*, Wendy T. Chen, Pharm.D., Katherine Cunningham, Pharm.D.; Beth Israel Deaconess Medical Center, Boston, MA

PURPOSE: Argatroban guidelines were implemented at Beth Israel Deaconess Medical Center (BIDMC) in 2007 to promote appropriate and safe use. The purpose of this study was to evaluate the impact of guideline implementation on argatroban use, duration of treatment, incidence of adverse effects and cost.

METHODS: A retrospective chart review was conducted to identify patients who received argatroban for more than 24 hours from January 2006 to January 2009. Patient demographics, pertinent clinical data, argatroban doses, timing of warfarin initiation and

doses used, aPTT and INR values therapy, and incidence of adverse events were collected. A 4-T's risk score for heparin-induced thrombocytopenia (HIT) was calculated for all patients. The primary analysis was to evaluate the impact of guideline implementation, determined by the number of patients receiving argatroban in accordance with BIDMC guidelines. Secondary analyses included the incidence of adverse effects and cost of argatroban therapy pre- and postguideline implementation.
RESULTS: One hundred sixty-three patients were included in the analysis. A greater proportion of patients in the postguideline group received argatroban in accordance with the institution guidelines (2008, 79%; 2007, 73%; vs. 2006, 60%; p<0.017). No significant difference in incidence of adverse events was observed between groups, whereas a significant cost reduction in argatroban purchases was noticed after the guideline implementation (2008, $316,000; 2007, $386,000; vs. 2006, $457,000), driven by a decrease in the number of patients prescribed argatroban (2008, 30 patients; 2007, 60 patients; vs. 2006, 70 patients). Most patients received argatroban for suspected HIT, as determined by patients' 4T risk scores (4.1 ± 2.2) and PF4-heparin–dependent antibody results. There were no differences in major bleeding, or treatment duration between groups.
CONCLUSION: Implementation of argatroban guidelines promotes appropriate patient selection and cost reduction. Continued emphasis on adherence to the guidelines is warranted.

Infectious Diseases

280. The effect of doxycycline on sputum biomarkers of inflammation and airway remodeling in patients with cystic fibrosis. *Heather M. Owens, Pharm.D., M.S.,* Ayana Boyd-King, M.D., Kamyar Afshar, M.D., Adupa Rao, M.D., Paul M. Beringer, Pharm.D.; University of Southern California, Los Angeles, CA
PURPOSE: Chronic *Pseudomonas aeruginosa* infection causes an inflammatory response in the airways of patients with CF. Accumulation of neutrophils and release of proteolytic enzymes (i.e., matrix metalloproteinase-9 [MMP-9]) cause airway destruction. We determined the effect of doxycycline on airway inflammation by measuring proteolytic enzyme levels (i.e., MMP-9) in induced sputum, correlated level changes with patient pulmonary function, and evaluated safety with short-term administration.
METHODS: A prospective, open-label, randomized, controlled study was conducted to determine effects of doxycycline on inflammatory biomarkers. Eight of 24 patients were stratified according to pulmonary function: mild (FEV_1 more than 70%) or moderate (FEV_1 40%–70%) and randomized in block to receive no drug, 40 mg, 100 mg, or 200 mg for 28 days. The first dose was administered intravenously. All subsequent doses were given orally. Induced sputum and spirometry were obtained during the 28-day treatment period and at a 2-week follow-up visit. MMP-9 levels in sputum were determined by ELISA. Additional sputum and blood biomarker analyses are planned.
RESULTS: Data for seven subjects taking doxycycline are presented. At baseline, mean FEV_1% was 78.2 (SEM = 8.3). At end of treatment, mean percent change in MMP-9 from baseline was 0.5 (SEM = 0.54), and mean FEV_1% was 80.1 (SEM = 9.2). Two weeks after doxycycline discontinuation, the mean percent change in MMP-9 from baseline was 9.5 (SEM = 8.5) and in FEV_1%, 83 (SEM = 14.5). The control patient has completed the study with percent change in MMP-9 from baseline of –0.19% and an FEV1% decrease from 96% to 91% at the end of the study period. No patients experienced significant adverse effects. One patient was removed from the study because of intolerance during the intravenous administration of doxycycline.
CONCLUSION: Preliminary results indicate no statistically significant differences in measures of airway inflammation or pulmonary function from baseline. Doxycycline was well tolerated by patients.

Pharmacokinetics/Pharmacodynamics/Drug

281. Pharmacodynamic evaluation of protein binding of antibiotics in critically ill patients. *Ashley D. Hall, Pharm.D.,*[1] Tyree H. Kiser, Pharm.D.,[2] Douglas N. Fish, Pharm.D.[2]; (1) University of Illinois Chicago College of Pharmacy, Chicago, IL; (2) University of Colorado School of Pharmacy, Aurora, CO
PURPOSE: The purpose of this study was to evaluate protein binding of levofloxacin in critically ill patients versus healthy patients. Pharmacodynamic properties related to potential alterations in the unbound fraction in critically ill patients versus historical values in normal volunteers were also evaluated.
METHODS: Blood samples were obtained from critically ill patients receiving levofloxacin. Selective-membrane centrifugation and high-performance liquid chromatography (HPLC) were used to separate and measure the total and free concentrations of antibiotics and calculate the percentage of protein binding. The probability of target attainment (PTA) for the ratio of free drug concentration to minimum inhibitory concentration (AUC_{free}:MIC) for *Streptococcus pneumoniae, Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* was determined using Monte Carlo simulation (Crystal Ball version 7, Decisioneering, Inc.). Target AUC_{free}:MIC ratios were 30 or greater for *S. pneumoniae* and 50 or greater for other organisms.
RESULTS: Analysis of levofloxacin samples in critically ill patients (n=20) determined an average protein binding of 17.2% ± 8.4% vs. 31.0 ± 7.8% in normal volunteers (p<0.0001). Protein binding at 2, 12, and 24 hours postdose was 20.2% ± 6.2%, 16.7% ± 8.9%, and 14.1% ± 9.2%, respectively. No association was found between plasma albumin concentrations and fraction of drug unbound (r^2=0.0048). There was a statistically significant (p<0.05) increase in PTA with protein-binding values in critically ill patients versus in normal volunteers for gram-negative isolates with MIC 0.5 µg/mL and gram-positive isolates at MIC 2 µg/mL for the 750- and 500-mg doses, but PTAs were otherwise not significantly different.
CONCLUSIONS: Critically ill patients demonstrated a significantly increased average levofloxacin fraction unbound, but it was highly variable among individuals. Occasionally, pharmacodynamic PTA was significantly increased in critically ill patients, but protein-binding differences would not be expected to contribute to improved clinical outcomes in most ICU organisms evaluated.

Transplant/Immunology

282. Implementing an adherence monitoring program in long-term kidney transplant recipients. *Trang Tran, Pharm.D.*, Jessica Lee, Pharm.D., Lannie Duong, Pharm.D., Ashley Feist, Pharm.D., BCPS, Linda Awdishu, Pharm.D., MAS; University of California–San Diego Medical Center, San Diego, CA
PURPOSE: Medication nonadherence is a major cause of graft loss after kidney transplantation. Therefore, frequent patient follow-up is necessary to achieve optimal results. In August 2008, we piloted an adherence monitoring program conducted by pharmacy residents and students. This program consisted of monthly telephone calls in which patients self-reported medication-taking behavior in a previously identified high-risk long-term kidney transplant population. The primary objective of this study was to determine the impact of the program on the achievement of target antirejection drug levels and serum creatinine (SCr). The secondary objective was to determine the impact of this program on the antirejection medication refill history.
METHODS: The results of the adherence monitoring program were retrospectively reviewed. SCr, immunosuppressant drug concentrations, and refill histories between the 6-month periods pre- and postadherence monitoring program were compared using ANCOVA, *t*-tests, and χ^2 analysis as appropriate.
RESULTS: Of the 48 patients enrolled in the program, 38 with complete data were included in the statistical analysis. The mean SCr levels pre- and postprogram intervention were 2.0 (95% CI: 1.6–2.3) versus 1.9 (95% CI: 1.6–2.2) (p=0.4). The achievement of target immunosuppressant concentrations pre- and postprogram intervention was 42% versus 53% (p=0.1). A multivariate analysis showed that African American patients (OR = 0.47, p=0.002) and elderly patients (OR = 0.99, p=0.04) were less likely to achieve target drug levels. Enrollment in the program showed a trend toward improvement in patients refilling antirejection medications

on time (OR = 1.31, p=0.07).
CONCLUSIONS: We were unable to find a statistically significant difference in our primary outcomes, likely because of the small sample size and short follow-up period; however, we did find a trend toward improved timeliness of refills. This program was easily implemented at our academic institution using pharmacy trainees. Future studies with larger sample sizes and longer follow-ups are warranted.

283. Retrospective assessment of risk factors for aspergillosis following cardiac transplantation: a case control study. *Abigail E. Miller, Pharm.D.*,[1] Patricia P. Chang, M.D., MHS,[1] Jo E. Rodgers, Pharm.D.[2]; (1) University of North Carolina Hospitals, Chapel Hill, NC; (2) University of North Carolina School of Pharmacy, Chapel Hill, NC
PURPOSE: Fungal infections are a significant cause of morbidity and mortality after solid organ transplantation. The most common fungal infections in cardiac transplant patients are caused by *Aspergillus* species. In recent years, the Cardiomyopathy and Cardiac Transplant service at the University of North Carolina Hospitals (UNCH) has perceived a rise in the incidence of aspergillosis in the cardiac transplant population. This retrospective case-control study was designed to identify probable risk factors for the development of aspergillosis in this patient population at our institution.
METHODS: The retrospective chart review included 23 cases of aspergillosis infection identified between 1986 and 2008 in cardiac transplant recipients. Two controls were randomly matched to each case within the same year of transplantation. All patients were at least 18 years old and underwent a single-organ heart transplantation at UNCH. Collected data in all subjects include demographics, transplant date, immunosuppressant regimen as well as opportunistic infection prophylaxis, rejection frequency and management, frequency of hospitalization, diabetes diagnosis, and laboratory parameters including renal function and serum albumin. Aspergillosis case data include hospitalization dates, survival, diagnosis source, *Aspergillus* type, and treatment. Data were collected for cases up to the date of aspergillosis diagnosis. Each matched control was observed for the equivalent number of days as the assigned case, or up to 1 year, whichever period was shorter. A t-test, χ^2, and linear regression were performed using SAS software (SAS Institute, Cary, NC).
RESULTS: Preliminary results suggest a mean time to aspergillosis diagnosis of 81 days (range, 7 days, 261 days). Age (case: 53.5 ± 9.5 years, 45.7 ± 14.2, p=0.03), mean prednisone dose (0.62 ± 0.56 mg/kg/day, 0.37 ± 0.20, p=0.058), and serum albumin (3.0 ± 0.71 g/dL, 3.2 ± 0.69, p=0.007) were associated with a higher risk of infection.
CONCLUSION: Conclusions will be confirmed with final analyses. Several additional end points and subgroup analyses will also be performed.

284. Retrospective evaluation of the efficacy and safety of a steroid withdrawal protocol in older kidney transplant recipients. *Kelly A. Cochran, Pharm.D.,*[1] David J. Thomsen, BSPharm,[1] Eric D. Whitaker, Pharm.D.,[1] Sarah B. Tierney, Pharm.D.,[1] Roberto S. Kalil, M.D.,[1] Sony Tuteja, Pharm.D., BCPS[2]; (1) University of Iowa Hospitals and Clinics, Iowa City, IA; (2) University of Iowa College of Pharmacy, Iowa City, IA
PURPOSE: The morbidities associated with the use of corticosteroids in immunosuppression regimens have prompted the implementation of steroid withdrawal protocols in older patients who are at high risk of steroid-induced adverse effects. This study evaluated the steroid withdrawal immunosuppression protocol used among University of Iowa Hospitals and Clinics (UIHC) kidney transplant recipients.
METHODS: This was a retrospective, single-center, chart analysis of 132 first-time kidney-only recipients of transplants between January 1, 2005, and December 31, 2007. Patients received methylprednisolone 500 mg intravenously × 1 and then underwent a rapid steroid taper, with steroids discontinued at postoperative day 6, tacrolimus or cyclosporine, and mycophenolate mofetil for rejection prophylaxis. Patients eligible for the steroid withdrawal protocol included the following: older than 55 years unless the donor is extended criteria or donation after cardiac death, preexisting comorbidities would be exacerbated with steroid use, or previous complications from steroid use, and history of kidney transplant, maintenance steroids for an underlying condition, or UIHC classification of immunologic high risk (panel reactive antibody more than 20% or two or more transplants) were exclusion factors. Data collection used the electronic medical record.
RESULTS: After applying inclusion and exclusion criteria, 23 patients were evaluated. Additional patients will undergo analysis. The steroid withdrawal immunosuppression protocol demonstrated 100% patient and graft survival with no rejection episodes. Thirteen percent of patients (n=3) failed to withdraw from steroids. Those successfully withdrawn from steroids demonstrated SCr 1.3 ± 0.3 mg/dL and 1.24 ± 0.3 mg/dL at 12 and 24 months, respectively. Ten patients required readmission to the hospital for bacterial infection and two for cytomegalovirus infection. The incidence of hypertension at 24 months declined by 9.1%.
CONCLUSIONS: The steroid withdrawal protocol used by UIHC provides effective immunosuppression for older kidney transplant recipients with 100% patient and graft survival, no rejection episodes, and excellent renal function. Cardiovascular and diabetes outcomes will be further evaluated.

STUDENT SUBMISSIONS

ADR/Drug Interactions

285. Retrospective observational study of drug interactions related to medication administration schedules in institutional patient care. Camilla B. Farrell, Pharm.D., Candidate, *Sol H. Park, B.S., Pharm.D., Candidate*, Michael J. Gonyeau, B.S., Pharm.D., BCPS; Northeastern University School of Pharmacy, Boston, MA
PURPOSE: To determine the occurrence of avoidable drug interactions among selected medications by oral administration schedule error and to evaluate the impact of such drug interactions on patient care in an institutional setting.
METHODS: Electronic medical records of all patients 18 years and older admitted to Brigham and Women's Hospital during a 6-month period were reviewed for one or more targeted drugs known to have clinically significant oral absorption interactions (quinolones, warfarin, levothyroxine, and bisphosphonates). Data collected included patient demographics, targeted and interacting drug dose, frequency, and administration date and time as well as any pertinent laboratory values when available.
RESULTS: One thousand two hundred nine potential drug interactions were identified in 924 patients. Specific interactions, their frequency, and any clinical sequelae are currently being assessed. Differences among medical services and hospital floors will be compared.
CONCLUSION: Medication administration is crucial to the clinical success of select agents. Inappropriate administration schedules resulting in drug interactions that decrease the oral absorption of a drug may have a negative effect on patient care. Educational efforts designed to increase health care professionals' awareness of such drug interactions should be initiated.

286. Risk of venous thromboembolism (VTE) in clozapine-treated patients. *Julie Lauffenburger, Pharm.D., Candidate*, Tanya J. Fabian, Pharm.D., Ph.D., Kim Coley, Pharm.D.; University of Pittsburgh School of Pharmacy, Pittsburgh, PA
PURPOSE: Antipsychotic agents have been associated with venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE). Although published cases suggest a link between clozapine and VTE and attempt to estimate risk, the incidence of VTE remains unknown because of the constraints of previous study designs. Therefore, we set out to identify the rate of VTE in patients newly initiated on clozapine.
METHODS: This was a retrospective cohort study of patients admitted to an academic psychiatric hospital over a 10-year time frame. Adult patients newly initiated on clozapine were identified

using the hospital's medical record data repository. Patient demographics, diagnoses, psychiatric history, VTE risk factors, and prescribed medications were collected for each patient for the index clozapine admission. Episodes of VTE were identified during the index psychiatric admission and for a 6-month period after hospital discharge by searching hospital records for ICD-9-CM codes for VTE as well as reviewing admission and discharge summaries. Radiology reports were reviewed to confirm a diagnosis of VTE. Descriptive statistics were used to analyze the study cohort.
RESULTS: There were 300 patients newly initiated on clozapine during the study time frame. The median age was 41 years; 168 (56%) were male, and 193 (64.3%) were white. We identified four cases of VTE, including two DVTs and two PEs. All VTEs occurred during the index psychiatric hospitalization after initiation of clozapine treatment, with a mean maximal dose of 294 mg. The incidence of VTE during clozapine use was 1.3%, indicating a much larger rate than estimated from previous studies. A detailed description of the VTE cases is pending.
CONCLUSION: The incidence of VTE in patients newly initiated on clozapine is 1.3%.

Ambulatory Care

287. Therapeutic lifestyle changes: are we really promoting them? A survey to examine behavioral counseling for high-risk patients. Magdi Awad, B.S., Pharm.D. Candidate, *Miki L. Finnin, Pharm.D., BCPS*; University of Minnesota College of Pharmacy, Duluth, MN
PURPOSE: To examine whether patients with hypertension, hyperlipidemia, or coronary heart disease (CHD) receive 1) information about the potential benefits, 2) counseling regarding desired goals, or 3) assistance to maintain or implement healthy lifestyle – some of the essential components of behavioral counseling – while being advised about weight management, diet, or exercise by their primary care providers (PCPs). Collected data were expected to present a preliminary assessment of the adequacy of counseling provided by PCPs to high-risk patients regarding therapeutic lifestyle changes (TLCs).
METHODS: Self-administered questionnaires were available to participants, at least 18 years old, who had at least one of the following: hypertension, hyperlipidemia, or CHD.
RESULTS: One hundred thirty-one questionnaires (response rate, 65.5%) were collected between March and August 2008. As a response to yes/no questions, 60.5%, 56.4%, and 80.7% of patients indicated that their PCPs talked with them about their weight, diet, and exercise, respectively. Unfortunately, less than one-third of those who indicated being counseled on weight management and exercise acknowledged receiving information about the potential benefits, counseling regarding desired goals, and assistance to maintain/implement healthy behaviors. Less than half received these same counseling components while being counseled on diet.
CONCLUSIONS: Although minimal data are available regarding the quality and content of TLC counseling given in the primary care setting, available indicators suggest that probably not all patients who indicate being counseled on TLCs have received the counseling necessary to initiate and sustain behavioral changes. As a result, these patients are missing an effective method of optimizing the management of their diseases. An emphasis on the adequacy of behavioral counseling needs to be taken together with efforts to eliminate identified TLC counseling barriers.

288. Pharmacist-performed medication reconciliation in an outpatient family medicine clinic. *Anna S. Milone, B.S.*,[1] Ila M. Harris, Pharm.D.,[2] Ann M. Philbrick, Pharm.D.[1]; (1) University of Minnesota College of Pharmacy, Minneapolis, MN; (2) Bethesda Family Medicine Clinic, Eden Prairie, MN
PURPOSE: Medication reconciliation is a useful tool to identify, classify, and resolve medication discrepancies in the electronic medical record (EMR); however, studies in the outpatient setting are limited. The goals of this study are to evaluate the incidence of medication discrepancies in EMR medication lists, classify and resolve the discrepancies, identify the most common medication classes involved, and assess the clinical importance of the discrepancies in an outpatient family medicine clinic. This is done by pharmacist-performed medication reconciliation.
METHODS: All patients with 10 or more medications listed in the EMR are eligible. The clinical pharmacist sees the patient before the physician, reviews the medication list with the patient, and makes corrections to the EMR medication list. When possible, a medication therapy management (MTM) visit is conducted. Data collected include patient demographics, the number of discrepancies by category, the number of clinically important discrepancies, and the medication classes most implicated.
RESULTS: Preliminary results include 122 patient visits with a total of 736 discrepancies identified and resolved, with an average of six discrepancies per patient. The highest number of discrepancies in one patient was 26. The most common discrepancy category was patient not taking medication on list. The most common medications involved were albuterol, calcium, acetaminophen, vitamin D, and aspirin. Of the 736 discrepancies, 47.6% were determined to be clinically important by the pharmacist. The pharmacist conducted MTM in around 30% of patients seen. Data collection is ongoing, and updated results will be presented.
CONCLUSION: Outpatient medication reconciliation by a pharmacist identified and resolved medication discrepancies and affected the accuracy of EMR medication lists. Because almost 50% of the discrepancies are important clinically, improving the accuracy of medication lists can have a positive impact on patient care. It also provides a convenient means of identifying appropriate patients for MTM.

Cardiovascular

289. Induction of matrix metalloproteinase-9 (MMP-9) in rats receiving muscle derived stem cell (MDSC). *Lena Yang, Pharm.D.*,[1] Nestor Gonzalez-Cadavid, Ph.D.,[2] Judy Wang, M.D.,[2] Arezoo Campbell, Ph.D.,[1] Dolores Vernet, Ph.D.,[2] Sheryl L. Chow, Pharm.D., BCPS[1]; (1) Western University of Health Sciences, Pomona, CA; (2) LA BioMed at Harbor/UCLA, Torrance, CA
Matrix metalloproteinases (MMPs) are responsible for the degradation of extracellular matrix components such as collagen, laminin, and proteoglycan. In particular, the gelatinases (MMP-2 and MMP-9) are believed to play a role in a wide range of biologic processes, including ventricular remodeling. Modulation of these biomarkers using novel therapies may provide insight into therapeutic mechanisms and responses.
PURPOSE: We hypothesized that in a rat model of myocardial infarction, the sildenafil or rat muscle derived stem cell (MDSC) treatment groups would demonstrate changes in either MMP-2 or MMP-9 expression compared with untreated control, thereby directly altering the natural progression in left ventricular remodeling.
METHODS: Thirty-six rats underwent permanent ligation of the LAD artery and were assigned to the following treatment groups for 4 weeks: control (ligation only), NaCl injection, low-dose sildenafil (LDS, 1.5 mg/kg/day), *N*-iminomethyl-l-lysine (L-NIL, an iNOS inhibitor) plus LDS, rat MDSC injection, and rat MDSC plus LDS. Serum samples were collected from each rat 4 weeks after ligation and were used for MMP analysis through gelatin zymography.
RESULTS: Gel zymography showed four bands exhibiting gelatin-degrading activity in all samples. All groups produced pro-MMP-9, pro-MMP-2, active MMP-2, and inactive MMP-2 by-products, whereas only groups treated with rat MDSC or rat MDSC plus LDS produced active MMP-9. Samples treated with rat MDSC or rat MDSC and LDS exhibited a fifth band identified as active MMP-9 that was less intense in samples from rats treated with rat MDSC plus LDS.
CONCLUSIONS: Stem cells appear to promote the generation and secretion of active MMP-9, and LDS attenuates these effects when used in combination. The implications of such a finding may be assessed after echocardiography and histochemical analysis of the cardiac tissue.

Community Pharmacy Practice

290. Comparison of efficiency between RX3000 and RX3000-2008 edition pharmacy management software: pharmacist perspective. Sandipan Bhattacharjee, B.S., *Hemalkumar B. Mehta, B.S.*, Swapna U. Karkare, B.S., Pei Kuo, Pharm.D., Sujit S. Sansgiry, Ph.D.; University of Houston, Houston, TX

PURPOSE: The aim of this study was to determine pharmacist's perception regarding the operational efficiencies of using RX3000-2008 pharmacy management software compared with RX3000.

METHODS: A survey was administered to 52 pharmacists employed at the Harris County Hospital District who have worked with both software systems. The pharmacists' perceptions regarding these systems were analyzed based on various parameters such as time spent on individual tasks, efficiency of drug-dispensing process, clinical interventions, patient profile recording, formulary or inventory management, and user friendliness. These parameters were measured using a 5-point Likert scale. Descriptive statistics and comparisons using a one-sample t-test (mu = 3) were conducted to analyze the differences between the two software systems at an a priori significance level of 0.05.

RESULTS: A response rate of 81% (42 of 52) was obtained. The pharmacists' overall opinions were slightly positive (3.53 ± 0.86) regarding the operational efficiency of the RX3000-2008 (Cronbach α = 0.74). The proportion of males and females was equal. All pharmacists were full-time employees with an average experience of 8 years 4 months. They agreed that the 2008 version performed significantly better ($p<0.05$) at checking medications (3.22 ± 0.87), different functions for clinical interventions (4.66 ± 0.77), online drug information access (4.68 ± 0.74), and updating patient information (4.73 ± 0.69). Pharmacists disagreed that time spent on order entry in RX3000-2008 was less (2.04 ± 0.84, $p<0.05$). No statistically significant differences were observed for features such as management of inventory or formulary (2.87 ± 1.69), time spent verifying prescriber's information (3.08 ± 0.97), and user friendliness (3.11 ± 0.98).

CONCLUSIONS: The use of pharmacy management software RX3000-2008 version may help reduce medication errors and improve patient safety by performing better clinical interventions. Proper training of the newer software could lead to better time management and help improve the overall productivity and operational efficiency of the pharmacy.

Critical Care

291. Comparison of heparin dosing based on actual body weight in obese and morbidly obese critically ill patients. *Jerilynn N. Folino, Pharmacy, Intern*, Anthony T. Gerlach, Pharm.D., BCPS; The Ohio State University, Columbus, OH

PURPOSE: Evaluation of heparin dosing based on actual body weight in obese (body mass index [BMI], 30–39.9) and morbidly obese (BMI greater than 40) critically ill patients.

METHODS: Retrospective review of obese patients admitted to the intensive care unit between July and December 2007 who received heparin for more than 24 hours. Prisoners, pregnant women, and those younger than 18 or older than 89 years were excluded. Patient charts were reviewed for demographics, heparin dosages, length of therapy, laboratory values, and bleeding. Steady-state (SS) heparin dosage was defined as three consecutive Ptt levels within target range. Major bleeding was defined as a documented cerebrovascular, gastrointestinal, or retroperitoneal bleed. Minor bleeding was defined as ecchymosis, epistaxis, hematoma, hematuria hemoptysis, petechiae, or oozing. Statistical analysis was performed by a Fisher exact test for nominal data and a Student t-test for continuous data.

RESULTS: Forty-two patients were included (22 obese and 20 morbidly obese). Only 55% reached SS including 50% of obese and 60% of morbidly obese patients, p=0.55. Five patients developed bleeding with no major bleeds reported. Mean weight-based heparin dosage was similar (10 vs. 11 U/kg/hour, p=0.44); the total heparin dosage was statistically higher in the morbidly obese (1000 vs. 1850 U/hour, p=0.001).

	BMI 30–39.9 (n=22)	BMI > 40 (n=20)	p-value
Mean age (years)	51.5 ± 13.2	52.9 ± 12.1	0.72
Mean weight (kg)	93.8 ± 15.1	160.33 ± 37.86	< 0.0001
Mean BMI	34.03 ± 30.3	55.25 ± 13.66	< 0.0001
Mean length of therapy (hours)	85.1 ± 54.5	65.5 ± 34.2	0.18
% reached SS	50	60	0.55
Mean weight-based heparin dosage at SS (U/kg/hour)	10.0 ± 4. 0	11.0 ± 1.4	0.44
Mean total heparin dosage at SS (U/hour)	1000 ± 420	1850 ± 620	0.001
% of patients with PTT > 120 seconds	45	40	0.76
% Bleed	9	15	0.66

CONCLUSION: Dosing of heparin based on actual body weight in morbidly obese ICU patients was associated with similar outcomes compared with obese patients, although about half reached SS. Targets for improvement have been identified.

Drug Information

292. The development of clinical trial results database of antineoplastic, cardiovascular and nonsteroidal anti-inflammatory agents. *Jin Yi Hong, B.S.*,[1] Bo Yoon Choi, B.S.,[1] Hye Jin Noh, B.S.,[1] Wan Gyoon Shin, Pharm.D., Ph.D.,[1] In Ja Son, Ph.D.,[2] Jung Mi 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: An accurate and reliable Web-based repository for clinical study results of marketed drugs in a reader-friendly and standardized format serves as timely communication and is a great way to stay up to date on the latest outcomes in clinical research. The aim of this study was to translate the results of clinical trials carried out worldwide into Korean and develop a central and standardized electronic database that could serve as a repository for published clinical studies for Korean scientists.

METHODS: The clinical trials of antineoplastic, cardiovascular, and nonsteroidal anti-inflammatory (NSAI) agents published within the past 10 years in SCI journals were identified from relevant electronic databases, registries, and clinical trial Web sites. Data were extracted from the included studies using a standard form, and all the information or data elements of the clinical trials were translated into Korean by clinical researchers who were fluent both in English and Korean. The database was validated and confirmed by independent clinical trial experts. The database was developed to be searchable by medical condition, drug name, or key words.

RESULTS: The clinical trial results database for antineoplastic, cardiovascular, and NSAI agents included details on study characteristics, participant characteristics, study designs, method of selecting subjects, intervention and control, specific trial efficacy, and safety end points, as well as adverse events reported.

CONCLUSION: A scientific and evidence-based standardized electronic database to serve as a repository for published clinical studies for Korean scientists was developed. The database will be expanded to include the clinical trial results of antibiotics, CNS, and respiratory system agents in coming years.

Education/Training

293. Evaluation of alcohol dependence in college students. Crystal D. Bishop, Pharm.D., Candidate,[1] *James T. Joseph, Pharm.D., Candidate*,[1] Brenda M. Paker, Pharm.D., MPH Candidate,[2] C. Renee Rust-Yarmuth, DMin,[3] James D. Nash, Pharm.D.[1]; (1) Sullivan University College of Pharmacy, Louisville, KY; (2) Rollins School of Public Health Emory University, Atlanta, GA; (3) The Sullivan University System, Inc., Louisville, KY

PURPOSE: The Alcohol Use Disorders Identification Test (AUDIT), developed by the World Health Organization (WHO), is a screening tool used to identify individuals with hazardous and harmful patterns of alcohol consumption. The primary objective of this

study was to determine whether Sullivan University Louisville (SUL) students were dependent or at risk of alcohol dependence using the AUDIT tool. Second, this study determined whether there was a difference in risk between Sullivan University College of Pharmacy (SUCOP) and non–College of Pharmacy (non-SUCOP) students.
METHODS: Non-SUCOP students were voluntarily screened for alcohol dependence using the AUDIT tool after an alcohol awareness event held on campus. In addition, in collaboration with SUCOP, professional year one (PY1) students were invited to be screened using the tool. Responses were recorded in a Microsoft Access database, and subsequent analyses were performed using SAS software.
RESULTS: The AUDIT tool was used to screen 254 students. Of those screened, 56% were female with a mean age of 25 years. The average cumulative score for all SUL students was 5, indicating that there is a low risk of alcohol dependence in the overall population. Within the overall population screened, 26% were SUCOP students. There was a statistically significant difference in mean cumulative scores (6.2 for non-SUCOP students vs. 1.6 for SUCOP students, $p<0.0001$). In addition, non-SUCOP students were more likely to be at risk of alcohol dependence than SUCOP students (RR = 3.64, 95% CI: 1.52, 8.73).
CONCLUSIONS: The AUDIT tool indicated that SUL students were at a low risk of alcohol dependence as an overall population. When comparing non-SUCOP with SUCOP students, there was a significant difference in alcohol-related dependence. Further statistical analysis is needed to identify potential confounders in the relationship, such as age and gender. All SUL students can be reassessed annually to determine whether alcohol dependence changes over time.

294. Self-assessment as a tool to evaluate value of instructional objectives. *Angela L. Bingham, Pharm.D., Candidate,*[1] Mary M. Hess, Pharm.D., FASHP, FCCM[2]; (1) South Carolina College of Pharmacy, Columbia, SC; (2) Jefferson School of Pharmacy, Philadelphia, PA
PURPOSE: This study evaluated pharmacy students' understanding of objectives in an applications course syllabus by self-assessment.
METHODS: The syllabus included select objectives from the Required & Elective Educational Outcomes, Goals, Objectives, and Instructional Objectives for Postgraduate Year One (PGY1) Pharmacy Residency Programs. Students independently performed a self-assessment against the identified objectives, which was then compared with the assessment made by the preceptor. Students were then provided the corresponding instructional objectives, and the process was repeated. Comparisons were made between student and preceptor evaluations of objectives (Mann-Whitney for Independent Samples), between student objective and instructional objective findings (independent sample t-test), and between student and preceptor evaluations of instructional objectives (Mann-Whitney for Independent Samples).
RESULTS: A total of 20 third-year professional students participated in this study. In comparing student objective assessment with that of the preceptor, no differences existed except for the objective "accurately assess the patient's progress toward the therapeutic goal" ($p<0.005$). Evaluation of student objective to instructional objectives was compared, differences were seen for "display initiative in preventing, identifying, and resolving pharmacy-related patient-care problems" and "accurately assess the patient's progress toward the therapeutic goals" ($p<0.005$). Results comparing instructional objectives indicated no difference between student and preceptor assessments.
CONCLUSION: Although students are introduced to professional terms and practice standards throughout their didactic career, their ability to absorb the full meaning is unclear until they are in a position of application. The results of this study indicate that the provision of instructional objectives may enable the self-directed learner to achieve the desired expectation by both learner and preceptor.

295. Impact of pharmacy students during an advanced pharmacy practice experience in internal medicine. *Christine K. Yocum, B.A., Pharm.D. Candidate*, Elias B. Chahine, Pharm.D., BCPS; Palm Beach Atlantic University Lloyd L. Gregory School of Pharmacy, West Palm Beach, FL
PURPOSE: Pharmacy students often spend their pharmacy practice experiences shadowing their preceptors and working on projects; however, it is very important to encourage students to participate in direct patient care by providing pharmacotherapy recommendations to the team during medical rounds. The objective of this study was to determine the clinical impact of pharmacy students during an advanced internal medicine rotation.
METHODS: As part of their rotation duties, two fourth-year pharmacy students were assigned to round with the medical team, interpret the microbiology culture and sensitivity reports, answer drug information questions, and document all of the information made during two consecutive internal medicine rotations at a tertiary care hospital. The interventions were categorized as drug initiation/selection/discontinuation, dose modification, intravenous to oral conversion, and drug information.
RESULTS: Pharmacy students were able to initiate 70 clinical interventions. Of these interventions, 35 (50%) were related to infectious disease pharmacotherapy, and 14 (20%) were related to cardiovascular pharmacotherapy. Interventions were classified under four categories: 42 (60%) drug initiation/selection/discontinuation, 8 (11%) dose modification, 7 (10%) intravenous to oral conversion, and 13 (19%) drug information. The vast majority of the interventions (97%) were accepted by the attending physician.
CONCLUSION: Under the direct supervision of their preceptor, pharmacy students were able to actively participate and contribute to the medical team. Despite the limited amount of time spent during an internal medicine rotation, their interventions had a positive impact on patient care. This study supports the role of clerkship students in optimizing drug therapy and improving therapeutic outcomes.

296. Value of first-year pharmacy students exploring clinical pharmacists' roles by attending ACCP-related regional, national, and international conferences. *Christine Guirgius, Pharm.D., Candidate,*[1] Maureen Shelley, Pharm.D., Candidate,[1] Katherine Yep, Pharm.D.,[2] Tina H. Denetclaw, Pharm.D., BCPS[3]; (1) California Northstate College of Pharmacy, Rancho Cordova, CA; (2) California Pacific Medical Center, San Francisco, CA; (3) University of California at San Francisco, San Francisco, CA
PURPOSE: To determine the value of first-year NCCCP student members attending American College of Clinical Pharmacy (ACCP) and Northern California College of Clinical Pharmacy (NCCCP) organizational events in terms of first-year pharmacy students better understanding clinical pharmacists' roles.
METHODS: NCCCP student members from the inaugural class of California North State (CNSP) attended the NCCCP student-driven program, "Clinical Pearls for Anticoagulation Monitoring: Meeting the New National Patient Safety Goals" in San Francisco, and the 2009 ACCP/ESCP International Congress on Clinical Pharmacy in Orlando. Student attendees reflected on their experiences and provided commentary on enhanced understanding of clinical pharmacy services based on these experiences. NCCCP student member campus activities are also described.
RESULTS: ACCP and NCCCP advocate advancement of clinical pharmacy through many patient care and research initiatives, including information on meeting national patient safety goals and other methods for supporting drug safety and the optimal use of medications. Two issues stood out for the overall experience of attending the ACCP/ESCP International Congress on Clinical Pharmacy: many different topics and challenges are related to clinical pharmacy practice, and there is an increasing need to cooperate across boundaries in the health care community. At NCCCP events, regional and national experts cover timely, cutting-edge information on significant patient care/drug-related topics, and students discuss these topics with students from other campuses and practicing clinical pharmacists in small-group roundtable sessions.
CONCLUSION: Attending ACCP and NCCCP events is useful for first-year pharmacy students gaining enhanced understanding of the clinical pharmacist's role. Students learn from these experiences that

clinical pharmacists have many areas of expertise and are a critical source of medical knowledge in promoting the safe use of medications and other significant issues.

297. Comparing on-campus recognition, support, and challenges for ACCP Regional Chapter student membership at the University of California, San Francisco and University of Pacific. *Steve Atallah, Pharm.D., Candidate,*[1] Jianna Tam, Pharm.D., Candidate,[1] Gloria Cheng, Pharm.D., Candidate,[1] Tam Thai, Pharm.D., Candidate,[2] Janjri A. Desai, Pharm.D., Candidate,[2] Katie Ahn, Pharm.D., Candidate,[2] Jessie Kim, Pharm.D., Candidate,[2] Katherine Yep, Pharm.D., FASHP,[3] Tina Denetclaw, Pharm.D., BCPS[1]; (1) University of California at San Francisco, San Francisco, CA; (2) University of Pacific, Stockton, CA; (3) California Pacific Medical Center, San Francisco, CA

PURPOSE: To compare organizational experiences for Northern California College of Pharmacy (NCCCP) student members on two different pharmacy school campuses and to provide examples of NCCCP student activities.
METHODS: Experiences of NCCCP student members at University of Pacific (UOP) and University of California, San Francisco (UCSF) are compared for administrative recognition, sources of campus-specific funding, benefits of administrative recognition, campus-specific challenges, and approaches to addressing challenges on each campus.
RESULTS: UCSF recognizes NCCCP student members as a Registered Campus Organization; UOP recognizes NCCCP student members as a co-chair committee under the Academy of Student Pharmacists (ASP). Associated Students School of Pharmacy funds NCCCP student activities at UCSF; ASP funds NCCCP student activities at UOP. Both campus groups experience similar benefits from administrative recognition, including conference room rental discounts, free use of classrooms, participation in school organization–based activities, display space, and participation in school calendars. Both groups are challenged by a lack of visibility and lack of NCCCP recognition by the student body. The UOP group sees a lack of final-year students participating in NCCCP all-campus programs designed to address residencies and clinical clerkship issues. Both groups participate in campus newsletters to increase awareness of NCCCP student activities, participate in health fairs and pharmacy organization fairs, and participate in other campus-based activities, in addition to continuing to advertise and participate in NCCCP all-campus events.
CONCLUSION: The forms of administrative recognition and sources of campus-specific funding differ between the two campuses; however, campus benefits, challenges, and approaches to addressing challenges are similar for both campus groups. Both groups have made significant progress in activities and visibility on each campus.

Endocrinology

298. Levothyroxine treatment and its effects on lipid levels. *Suhas S. Ghodiwala, Pharm.D., Candidate, 2010*, Amarita S. Randhawa, Pharm.D., Candidate, 2010, Michael J. Gonyeau, B.S., Pharm.D., BCPS; Northeastern University, Boston, MA
PURPOSE: To determine the effect(s) of levothyroxine therapy on lipid levels in hypothyroid patients and to assess the impact of adjunct statin therapy in patients on both therapies.
METHODS: Patients admitted to Brigham & Women's Hospital between January and June 2009 were retrospectively identified using electronic medical records. Eligible candidates were 18 years or older with an ICD-9 code for hypothyroidism or TSH level greater than 5.0 mU/L during hospitalization. Patients with documented kidney disease (CrCl less than 30 mL/minute) or hepatic disease were excluded. Data collected included patient demographics, levothyroxine and statin dose, route and frequency information, and pre- and post-TSH, free T4, T3 levels, and lipid panels (total cholesterol, triglycerides, HDL, and LDL) when available.
RESULTS: Eight hundred ninety-seven patients meeting inclusion criteria were identified. Lipid panels of patients receiving levothyroxine with and without statin therapy will be compared to determine any effect of adjunctive levothyroxine therapy on control of hyperlipidemia. Specific comparisons will evaluate dosing of agents and percentage of patients at ATP III lipid goals based on the presence or absence of statins, statin dose, and control of thyroid disease, as well as any differences among sex.
CONCLUSION: Thyroid substitution in patients with subclinical and clinical hypothyroidism may have beneficial effects on lipid parameters, which may confer a protective cardiovascular benefit.

Gastroenterology

299. Tpmt and the risk for hepatotoxicity after thiopurine therapy. *Jonathan Lee, Ph.D.*, Terreia Jones, Pharm.D., Anand Kulkarni, M.D., Cameila Johns, M.D., Joseph Barnes, M.S.; University of Tennessee Health Science Center, Memphis, TN
PURPOSE: Thiopurine drugs (i.e., mercaptopurine and thioguanine) are commonly used in the treatment of leukemia, inflammatory bowel diseases, and transplantation; however, thiopurine therapy has been associated with significant hepatotoxicity, including hepatitis, nodular regenerative hyperplasia, and veno-occlusive disease. The level of thiopurine methyltransferase (Tpmt) protein activity can predict the clinical efficacy and toxicity of thiopurine therapy. The *Tpmt-/-* phenotype confers a high-risk of severe myelosuppression; the wild-type *Tpmt* phenotype has been linked to an increased risk of hepatotoxicity. Whether Tpmt is indeed a risk factor for liver toxicity has not been definitively determined. In this study, we treated Tpmt mice of each genotype to thiopurines to determine whether Tpmt activity could predict the level of hepatoxicity.
METHODS: We treated *Tpmt+/+*, *Tpmt+/-*, and *Tpmt-/-* mice with thioguanine (0.25–0.75 mg/kg/day) for 15–40 weeks. At the time of sacrifice, mouse liver sections were obtained for RNA extraction or fixed in formalin and sectioned for histopathology analysis. Paraffin-embedded sections were analyzed by pathologists and judged using the Batts-Ludwig and Ishak grading systems. Gene expression studies will be performed on marker genes of thiopurine metabolism, inflammation, and hepatic oxidative stress using quantitative PCR (qPCR).
RESULTS: Preliminary data suggest that when Tpmt is high (*Tpmt+/+*), there is a higher incidence of liver toxicity. When the cumulative thiopurine dose and time of exposure were high, more severe pathology was observed. At the histologic level, we observed portal and acinar inflammation with mild perivenular necrosis. qPCR will be performed to compare the markers important to inflammation (five markers), thiopurine metabolism (four markers), and oxidative stress (three markers). This work is in progress and will be completed within 1–2 months.
CONCLUSIONS: Low Tpmt is associated with less hepatotoxicity after thiopurine treatment. Whether this can be explained by the expression of genes associated with liver inflammation or thiopurine metabolism will be determined.

Health Services Research

300. Workflow factors impacting the timeliness of first-dose antibiotic administration in a community hospital. *Monica Chan, Pharm.D., Candidate,*[1] Jennifer Chiok, Pharm.D., Candidate,[2] Homa Mirzazadeh, Pharm.D., Candidate,[2] Tina Denetclaw, Pharm.D., BCPS[1]; (1) University of California, San Francisco, CA; (2) Touro University College of Pharmacy (Mare Island), Vallejo, CA
PURPOSE: Baseline performance was assessed for timely administration of first-dose antibiotics, and causes for delay were noted to support specific changes in workflow, policy, and staff education in an effort to meet new first-dose antibiotic administration goals.
METHODS: For 5 days, 11 new antibiotic orders were randomly identified and monitored in a blinded manner through the process of handling the order, from the time of writing to the time of administration. Causes for avoidable delays were noted, as were unavoidable causes for delay.
RESULTS: Average time from writing to drug administration was

3.37 hours (range, 0.5–14.08 hours). Fifty-four percent of doses were given within 2 hours of order writing; 27% of doses were given 4 or more hours after order writing. These data correlate with similar time studies performed by others. The shortest time to administration (30 minutes) occurred for a patients with sepsis in the ICU, where Early Goal Directed Therapy has been the standard of care for about 3 years. The longest times to administration were associated with nursing change of shift as well as prolonged patient housing in the emergency department awaiting transfer to floor. The longest workflow delays occurred from time of writing to order scanning to pharmacy (range, 0.12–8.43 hours) and from time of order entry by pharmacy to drug retrieval by nursing from automated distribution system (range, 0.25–5.3 hours).
CONCLUSIONS: Opportunities for improvement were found at several points along workflow from order writing to drug administration, and all causes for delay in this data set were assessed to be amenable to specific changes in workflow, policy, and staff education. Based on the results of this study, educational efforts are designed, and specific workflow and policy changes are proposed.

301. Effectiveness of a pharmacist-run disease state management clinic on hypertension for the veteran population. *Jeannette H. Truong, B.S.*; UCSD School of Pharmacy, La Jolla, CA
PURPOSE: Hypertension is a critical disease that can often go undetected because many people who have it will experience no symptoms whatsoever. Worsening hypertension can increase the risk of heart attack, angina, stroke, kidney failure, and atherosclerosis. Hypertension is the most commonly treated chronic condition in Veterans Affairs (VA) hospitals. Because of the importance of controlling and treating hypertension, VA San Diego Healthcare System has established a pharmacist-run primary care clinic for managing hypertension to prevent the complications listed above. Thus, the primary objective of this study was to evaluate the effectiveness of the clinic in achieving blood pressure control for patients referred by primary care physicians based on *The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC 7).
METHODS: This is a retrospective chart review (January 2004–December 2007) with the intention to treat the population. The primary outcome of the experiment was to identify patients without diabetes and/or renal insufficiency who achieved a BP goal of less than 140/90 mm Hg and to identify patients with diabetes and/or renal insufficiency who achieved a BP goal of less than 130/80 mm Hg. The secondary outcome determined the time to BP goal, the change in BP from baseline, and any emergency depart-ment visits associated with hypo- and hypertension after referral.
RESULTS: The results are currently being statistically analyzed.
CONCLUSION: The conclusion will subsequently be completed once the analysis is completed.

Hematology/Anticoagulation

302. Prevalence of daily medication adherence among children with sickle cell disease: a one-year retrospective cohort analysis. *Niti G. Patel, Pharm.D., Candidate*,[1] Terianne Lindsey, MSN, RN, CPNP,[2] Robert C. Strunk, M.D.,[2] Michael R. DeBaun, M.D., MPH[2]; (1) St. Louis College of Pharmacy, St. Louis, MO; (2) Washington University School of Medicine, St. Louis, MO
PURPOSE: Patients with chronic disease often have poor adherence to medications that may result in increased morbidity. The primary objective of this study is to determine the prevalence of adherence to daily-prescribed medication among children with sickle cell disease (SCD).
METHODS: Daily medication adherence was measured in a retrospective cohort of children with SCD who were observed in the Sickle Cell Disease Medical Treatment and Education Center. Adherence was defined as a ratio between the number of days of supply for the medication and the difference in days between two refill periods. Prescription records from the past 12 months were obtained from a single health maintenance organization.
RESULTS: A total of 93 children were identified with SCD taking scheduled medication(s) with a single payer. The mean age was 7 years. Overall refill rate among patients taking daily medication was 58.4%. The refill rate for penicillin was 54.9% (n=62), daily asthma medications (e.g., Advair, Flovent, Pulmicort, Singulair) 59.3% (n=28), hydroxyurea 60.54% (n=4), and folic acid 61.29% (n=80). Patients adherent to one therapy were generally adherent to other therapies (correlation coefficient, 0.794).
CONCLUSION: Most patients with SCD refill their medications on time; however, a substantial number of refills are being missed. More formal strategies are required to identify barriers to prescription refills.

303. Management of elevated INR due to warfarin at a university teaching hospital. *Aleksandr Niyazov, Pharm.D., Candidate*,[1] Ruslana Kushnir, Pharm.D., Candidate,[1] Irfan Tejani, Pharm.D., Candidate,[1] Purvi Patel, Pharm.D., Candidate,[1] Roopali Sharma, B.S., Pharm.D., BCPS[2]; (1) Arnold & Marie Schwartz College of Pharmacy & Health Sciences, Brooklyn, NY; (2) State University of New York (SUNY) Health Sciences Center at Brooklyn's University Hospital of Brooklyn, Brooklyn, NY
PURPOSE: Warfarin has been the cornerstone of anticoagulation for more than 60 years, as established by clinical trials. Nevertheless, its use in clinical practice is still challenging because of its narrow therapeutic index, and it is subject to multiple drug-drug and drug-food interactions. Hence, warfarin use requires constant monitoring of the international normalized ratio (INR). Patients who develop an elevated INR are at risk of bleeding. Guidelines for the management of elevated INR have been published by the American College of Chest Physicians; however, those guidelines are not always adhered to. The purpose of this study was to assess whether patients on warfarin with an elevated INR were managed according to CHEST guidelines in a teaching hospital.
METHODS: This was a retrospective observational study and included patients with an INR greater than 3.5 from July to December 2008. Medical charts were reviewed, and data on patient demographics, warfarin indication, INR value, bleeding events, and their management was collected. Bleeding events were classified as major or minor bleeds. Major bleeds were defined as a gastrointestinal bleed, intracranial hemorrhage, or any bleed that leads to hemodynamic compromise or need for surgery. Minor bleeds were defined as uncomplicated bleeds that self-ceased. The data were analyzed by descriptive statistics.
RESULTS: A total of 74 charts were reviewed. The mean age was 65 years; 65% were female patients. Atrial fibrillation was the most common indication for which warfarin was used (n=26). The population consisted predominantly of African Americans. Eleven patients (15%) presented with bleeding events: one major, two not specified, and eight minor bleeds. Twenty-five (33.8%) patients were not treated according to CHEST guidelines.
CONCLUSION: CHEST guidelines were not followed in one-third of patients with respect to doses of vitamin K used, holding of warfarin, and timing of anticoagulation reversal.

Herbal/Complementary Medicine

304. Interactions between Korean red ginseng and warfarin in patients with cardiac valve replacement: a double-blind, randomized, crossover study. *Inkyung Yoon, B.S.*,[1] Yeonhong Lee, M.S.,[1] Byungkoo Lee, Ph.D.,[1] Byungchul Chang, M.D., Ph.D.,[2] Hyesun Gwak, Pharm.D., Ph.D.[1]; (1) Division of Life and Pharmaceutical Sciences, Ewha Womans University, Seoul, South Korea; (2) Division of Cardiovascular Surgery, Yonsei Cardiovascular Center and Research Institute, Yonsei University College of Medicine, Seoul, South Korea
PURPOSE: Safety of the use of Korean red ginseng (KRG) in patients during warfarin therapy is controversial. The objective of this study was to determine whether an interaction exists between warfarin and KRG that alters the international normalized ratio (INR) of prothrombin time and to assess the correlation of INR with weekly dose or blood concentration of warfarin.
METHODS: A prospective, double-blind, randomized, crossover study was conducted of 25 patients with cardiac valve replacement,

taking warfarin daily for anticoagulation therapy. One group initially received 1 g of KRG extract for 6 weeks and then received placebo for the same duration after a 3-week washout period. The alternative group received treatment in the opposite order. Warfarin concentration was determined by HPLC with a fluorescence detector.
RESULTS: Of the 25 patients, the median age was 56 years, and most patients (84%) were women. The mean warfarin dose per week was 40.60 mg, and the duration of therapy was 17.10 years. The mean INR at weeks 0 (baseline), 3, and 6 after receiving placebo and KRG were 2.47 ± 0.62, 2.42 ± 0.54, and 2.66 ± 0.74 and 2.53 ± 0.69, 2.35 ± 0.66, and 2.40 ± 0.53, respectively. Even though INR was lower in KRG group, compared with placebo group, there were no statistically significant differences in mean INR (p=0.78, 0.69, and 0.08, respectively). Moreover, there were no significant correlations between INR and weekly warfarin dose (r=0.13, 0.5<p<0.6), and INR and warfarin concentration at week 6 after receiving KRG and placebo (r=0.079, 0.7<p<0.8 and r=0.27, 0.1<p<0.2, respectively). No adverse event was reported during the study.
CONCLUSIONS: Based on the results, it was concluded that Korea red ginseng could be used with close monitoring and under appropriate education in patients on warfarin therapy.

HIV/AIDS

305. A pilot study to quantitate placental β-catenin using morphometric analysis of tissue microarray sections in women with gestational diabetes, HIV, and normal healthy pregnancies. *Andrew Tong, Pharm.D., Candidate,*[1] Albert Franco, M.D.,[2] Nilsa Ramirez, M.D.,[3] Thomas J. Barr, B.S., MBA,[3] William Beyer, BSEE, MSEE,[3] Daniel A. Brazeau, Ph.D.,[1] Patty Fan-Havard, Pharm.D.[1]; (1) University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (2) University of Charlotte, College of Medicine, Charlotte, NC; (3) The Research Institute at Nationwide Children's Hospital, Columbus, OH

PURPOSE: The human placenta is a highly vascularized organ with a primary function to permit maternal-fetal exchange of solutes and oxygen through endothelial paracellular passages. β-Catenin and vascular endothelial cadherin (VE-cadherin) are two adheren junctional proteins (AJPs) that regulate the adhesion and permeability of the vascular endothelium. Down-regulation of AJPs results in increased placental weight, permeability, and small-pore barrier dysfunction in placentas from women with gestational diabetic mellitus (GDM). Pregnant women with HIV-1 infection receive protease inhibitor (PI)-based antiretroviral chemoprophylaxis to reduce perinatal transmission. HIV-1 PIs are associated with metabolic adverse events including diabetes. The purpose of this pilot study was to examine whether antepartum PI-exposed antiretroviral chemoprophylaxis altered placental β-catenin expression.
METHODS: Placental tissues were formalin fixed and paraffin embedded after informed consent. In situ β-catenin protein expression in placental tissues was analyzed using immunohistochemistry staining of tissue microarray sections. Digital images of the placental specimens were acquired with ScanScope by Aperio. Chromogenic intensity of 3-3´-diaminobenzidine (DAB) was semiquantitated by visual inspection (0 = negative, 1 = weakly positive; 3 = strongly positive) by an independent placental pathologist and morphometrically quantitated using a positive pixel algorithm.
RESULTS: A total of 62 placental tissue cores (control, n=11; GDM, n=19; and HIV, n=32) were collected and examined. An increased trend in fetal and placental weight was observed in women with GDM. Of the 32 pregnant women with HIV infection, only one had an abnormal oral glucose screening. A decreased trend in β-catenin expression was noted in both the GDM and HIV-infected cohorts compared with control, mean scores 1.71 ± 0.46, 1.74 ± 0.52, and 1.9 ± 0.47, respectively. Morphometric analysis is under way.
CONCLUSION: Preliminarily, a decrease in β-catenin protein expression was observed in placentas from GDM and HIV-infected cohorts compared with control. Confirmation of this observation is under way using morphometric analysis.

Immunopharmacology

306. Immunomodulatory effects of doxycycline in cystic fibrosis airway epithelial cells. *Timothy J. Bensman, B.S.*, Paul M. Beringer, Pharm.D.; University of Southern California School of Pharmacy, Los Angeles, CA

PURPOSE: Cystic fibrosis (CF) is characterized by an intrinsic hyperimmune state. This primary inflammatory condition before bacterial infection is supported by clinical observations in neonates and young children with CF. Mounting evidence also suggests an exaggerated and prolonged inflammatory response to foreign invaders of the airways. The aim of this work was to evaluate the anti-inflammatory activity of doxycycline on the CF phenotypic bronchial airway epithelium.
METHODS: The CF compound heterozygote IB3-1 and rescued isogenic S9 cell lines were used to characterize doxycycline's effects on lung parenchyma inflammation and remodeling. Biologic markers IL-8 and MMP-9 were analyzed by ELISA and qRT-PCR after stimulation with IL-1β, TNF-α, or Pa-LPS at varying time points. Cytotoxicity was quantified by LDH assays.
RESULTS: Diminution of IL-8 release on doxycycline treatment in a dose-dependent manner was observed in both IB3 and S9 cell lines after immune activation with IL-1β. Pharmacodynamically, doxycycline exhibited a log EC_{50} = 0.89 ± 0.029 (CI: 0.83–0.95), 0.91 ± 0.079 (CI: 0.75–1.07), Hill Slope = –2.06 ± 0.27 (CI: –2.62 to –1.50), –1.32 ± 0.29 (–1.92 to 0.72), and r=0.81 and 0.71 for IB3 and S9, respectively. Immune activation and amelioration was observed as early as 4 hours. IL-8 release in IB3, but not S9, cells responded in a dose-response character on Pa-LPS challenge. TNF-α, but not IL-1β, at 24 and 48 hours induced MMP-9 protein production in both IB3 and S9 cell lines (effect of doxycycline on MMP-9 to be characterized). LDH assays showed minimal cytotoxicity, 20% and 25% in IB3 and S9, respectively, with doxycycline up to 100 µg/mL. TC_{50} could not be determined because of insolubility issues greater than 100 µg/mL.
CONCLUSION: Doxycycline exhibited immune-modulatory activity, without serious toxicity concerns, as measured by the inflammatory marker IL-8, airway remodeling marker MMP-9, and cytotoxic metabolite LDH in vitro.

Indigent Care

307. A description of an indigent pharmacy practice setting in Costa Rica. *Christine K. Yocum, B.A., Pharm.D. Candidate*, Elias B. Chahine, Pharm.D., BCPS; Palm Beach Atlantic University Lloyd L. Gregory School of Pharmacy, West Palm Beach, FL

PURPOSE: As part of the experiential curriculum, pharmacy students may choose to take an elective rotation in medical missions. The objective of this study was to describe a medical mission pharmacy practice setting.
METHODS: During an 8-day medical mission trip to Costa Rica, pharmacy students had the opportunity to interact with patients in remote settings where medical care was either scarce or nonexistent. Under the direct supervision of physicians and pharmacists, students performed various clinical duties including triaging of patients, physical examinations, medication management, and patient counseling. Total patients seen and number of prescriptions were recorded. All patients, regardless of their diagnosis, were given a 30-day supply of OTC vitamins.
RESULTS: Over an 8-day period, pharmacy students interacted with 445 patients who came to the indigent clinic seeking treatment of various disease states including, but not limited to, urinary tract infections, skin and skin structure infections, gynecologic infections, and respiratory tract infections. A total of 1227 medications were dispensed (both OTC and prescription), and one diabetic foot ulcer debridement was performed. Students assisted physicians and pharmacists in medication therapy management including drug selection, substitutions, compounding, and pediatric dosing. For each patient examined, a minimum of 3 hours was spent with the patient throughout the various stages of care.
CONCLUSION: Under the direct supervision of licensed medical professionals, pharmacy students were able to actively participate in the medication therapy management of indigent patients. They were

able to touch the lives of the patients they served beyond the scope of traditional patient care settings. Pharmacy students who elect medical mission rotations as part of their advanced pharmacy practice experience have a unique opportunity not only to develop their clinical skills, but also to build their characters and function as servant leaders.

Infectious Diseases

308. Seasonal variation in the incidence of community-associated MRSA (CA-MRSA) skin infections among pediatric patients admitted to United States hospitals. *Kelly R. Daniels, Pharm.D. Candidate*, Brittany R. Makos, Pharm.D., Christine U. Oramasionwu, Pharm.D., M.S., BCPS, Christopher R. Frei, Pharm.D., M.S., BCPS; University of Texas at Austin, Austin, TX

PURPOSE: Prior studies have demonstrated that U.S. children from the Southern region are at increased risk of CA-MRSA skin infections compared with children from other regions. This may be because of seasonal climate; therefore, we sought to quantify and compare the monthly incidence of CA-MRSA skin infections in four U.S. regions.

METHODS: Hospital discharge records of patients with a principal ICD-9 code for skin infection (680-684), collected from 2002 to 2006 by the U.S. National Center for Health Statistics, were analyzed. Noninstitutional, short-stay hospitals participated. The sample was limited to patients 19 years and younger. ICD-9 codes were used to define *S. aureus* (041.11) and CA-MRSA (V09.0). Patients who were transferred from another hospital or health care facility were excluded. Data weights were used to derive regional and national estimates. Population estimates were obtained from the U.S. Census Bureau, and incidence rates were reported per 100,000 individuals.

RESULTS: These weighted data represented 346,990 pediatric discharges for skin infections from U.S. hospitals from 2002 to 2006. *S. aureus* and CA-MRSA accounted for 27% and 16% of cases, respectively. CA-MRSA incidence was 13.6 cases per 100,000 U.S. children. This rate varied by region: South (22.6), West (10.8), Northeast (7.3), and Midwest (6.9). Peak CA-MRSA incidence occurred from May to December. The incidence in the Southern region was consistently higher, and the period of peak incidence was longer than in the other regions, lasting from March to December. The Northeast and West regions demonstrated peak incidence from July/August to December, whereas the incidence in the Midwest region was erratic, with three distinct peaks and no discernible pattern.

CONCLUSION: The higher incidence of CA-MRSA skin infections among pediatric patients in the Southern region of the United States may be partially attributable to seasonal climate, which may afford greater opportunity for CA-MRSA skin infection year-round.

309. Efficacy and safety of linezolid for the treatment of gram-positive bacteremia. *Melissa Chesson, Pharm.D., Candidate,*[1] Stacey Folse, Pharm.D., MPH, BCPS,[2] Greg Smallwood, Pharm.D.[2]; (1) Mercer University School of Pharmacy and Health Sciences, Atlanta, GA; (2) Emory University Hospital, Atlanta, GA

PURPOSE: Bloodstream infections (BSIs) are major causes of morbidity and mortality. The management of primary and complicated BSIs typically consists of the use of bactericidal antibiotics. Linezolid, a bacteriostatic agent, is increasingly considered an option for BSI management, although it is not FDA approved for this indication. Therefore, an investigation of the efficacy and safety of linezolid in the treatment of BSIs is warranted.

METHODS: A single-center retrospective cohort of patients admitted to Emory University Hospital from January 1, 2003, to December 31, 2007. Patients were included who were 18 years and older, received two or more consecutive doses of linezolid during hospitalization, and had positive blood cultures with a gram-positive organism. Exclusion criteria included use of vancomycin or daptomycin before starting linezolid. Baseline demographics, blood cultures, and adverse events were collected and analyzed.

RESULTS: Seventeen patients met inclusion criteria. Primary BSIs were more common than secondary BSIs (53% vs. 47%). Uncomplicated BSIs were more prevalent than complicated BSIs (59% vs. 41%). The most common causative pathogens were coagulase-negative *Staphylococcus* (41%) and vancomycin-resistant *Enterococcus* (VRE) (35%). Microbiologic efficacy was achieved in 90% of uncomplicated BSIs, defined as no growth from first set of follow-up blood cultures, whereas 57% of complicated BSIs required two or more sets of cultures to obtain no growth. Recurrence of causative pathogen after treatment was documented with uncomplicated BSIs caused by VRE (30%). Myelosuppression was the only documented adverse effect (17.7%).

CONCLUSIONS: The source of BSIs and causative pathogens is consistent with other studies' findings. The treatment of uncomplicated BSIs with linezolid resulted in microbiologic efficacy but higher incidence of VRE recurrence. In addition, use of linezolid for the treatment of complicated BSIs resulted in increased time to microbiologic efficacy. Further evaluation of the efficacy of linezolid for treatment of primary, complicated, and VRE BSIs is warranted.

310. Risk of invasive fungal infection and mortality with mannose-based glycopeptides: a meta-analysis. *Wesly A. Pierce, BSPharm,*[1] S. Travis King, BSPharm,[1] Daniel M. Riche, Pharm.D., BCPS, CDE,[2] John D. Cleary, Pharm.D., FCCP, BCPS[2]; (1) The University of Mississippi School of Pharmacy, Jackson, MS; (2) The University of Mississippi Schools of Pharmacy and Medicine, Jackson, MS

PURPOSE: Mannose-based glycopeptides (MBGs) are used widely in Europe for the treatment and prophylaxis of gram-positive infections, but they are used sparingly in the United States. Emergence of fatal fungal infections in mice models has recently been demonstrated, purportedly through systemic depletion of mannose-binding lectin by MBG mannose moieties. A meta-analysis was performed to evaluate the risk of fungal infection and mortality in patients treated with MBGs.

METHODS: A random-effects model meta-analysis was used to evaluate the incidence of fungal infection and mortality. A systematic literature search of PubMed citations through June 2009 was performed to identify published MBG trials. Included trials met the following criteria: 1) prospective, randomized trials that evaluated MBG versus other anti-infectives or placebo; 2) contained a descriptive protocol; and 3) provided data on fungal infection or mortality. Data are presented as relative risks (RRs) with 95% confidence intervals (CIs).

RESULTS: Thirteen active comparator trials (n=2769) reported mortality, whereas 10 active comparator trials (n=1421) reported fungal infections. Three placebo comparator trials (n=437) met the inclusion criteria. On meta-analysis, there was no difference in the incidence of any fungal infection (RR = 0.87 [95% CI: 0.47–1.61]) or mortality (1.03 [0.75–1.40]) in studies evaluating MBGs versus any antibiotic. There also was no difference in the incidence of any fungal infection or fungal superinfection in studies evaluating MBGs versus placebo. In the subgroup analysis, there was no difference in mortality (0.93 [0.56–1.54]) or fungal infection (0.87 [0.34–2.27]) between teicoplanin and vancomycin. No publication bias or statistical heterogeneity was identified in any group.

CONCLUSION: The results of this meta-analysis demonstrate that MBGs, particularly teicoplanin, do not appear to be associated with an increased risk of fungal infection or mortality when used in the treatment or prophylaxis of gram-positive infections. Future trials with MBGs that specifically assess fungal risk may confirm these findings.

Leadership

311. Enhancing Northern California College of Clinical Pharmacy (NCCCP) events by utilizing effective roundtable discussions. *Helen B. Kim, Pharm.D., Candidate,*[1] Stephanie A. Yoo, Pharm.D., Candidate,[1] Katherine Yep, Pharm.D.,[2] Tina H. Denetclaw, Pharm.D., BCPS[3]; (1) Touro University College of Pharmacy, Vallejo, CA; (2) California Pacific Medical Center, San Francisco, CA; (3) University of California at San Francisco, San Francisco, CA

PURPOSE: NCCCP strives to promote the growth of clinical

pharmacy in all practice settings. This organization uses roundtable discussions at educational events as a method to reinforce topics discussed by guest speakers. These discussions often include written case studies related to the presented material. Our objective was to develop successful leadership techniques to facilitate roundtable discussions.
METHODS: Discussion leaders for each table were asked to prepare in advance by reading case scenarios and studying articles (provided) related to each case. Discussion leaders were given an agenda and a set of instructions intended to optimize discussion and group participation. Instructions included asking the participants to introduce themselves to the group before reading case scenarios, allowing all opinions to be expressed while maintaining the focus of discussion, encouraging participation from all group members while managing time according to the agenda, and summarizing the main points before ending the roundtable discussion. Participants were asked to complete an opinion survey after the end of the program.
RESULTS: Using the techniques described promoted learning through active group participation. In addition, incorporating case studies into the discussion allowed the topics to be more clinically relevant. Participant survey results indicated that the discussions enhanced participant understanding of the lectures presented.
CONCLUSION: Including roundtable discussions at presentations improved audience participation and learning.

Managed Care

312. Antimicrobial prescribing patterns in Korean ambulatory pediatric population. *Jin Yi Hong, B.S.*,[1] Yoo Jin Moon, M.S.,[1] Eun Hee Ji, M.S.,[1] Wan Gyoon Shin, Pharm.D., Ph.D.,[1] In Ja Son, Ph.D.,[2] Jung Mi 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 antimicrobial prescribing rate is high in Korea, and a considerable proportion of its use is known to be inappropriate or unnecessary. Inappropriate use of antimicrobials is major cause of antibiotic resistance, and it has more significant consequences in pediatric patients. Because the appropriateness of antimicrobial use in pediatric patients has not been evaluated thoroughly, this study has aimed on determining the extent and rate of antimicrobial prescription in Korean ambulatory pediatric patients.
METHODS: The study performed a retrospective evaluation of pediatric outpatient prescriptions using the national insurance reimbursement database of the Health Insurance Review Agency of Korea from July 2005 to June 2006. The patterns of antimicrobial use among the four age groups and five medical institutions were estimated. Antimicrobials were divided into classes, and broad-spectrum antibiotics were evaluated separately as well as among diagnosis groups with respiratory tract infection. Prescribing patterns and antimicrobial use were analyzed by SAS version 8.2.
RESULTS: A total of 994,992 pediatric patients were prescribed with drugs during the study period. Among the patients who were prescribed with antibiotics, b-lactams (77.0%) were most widely used, followed by macrolides (13.5%). Amoxicillin-clavulanate (36.4%) and cefaclor (16.2%) were the most frequently used antibiotics in all age groups and institutions. More than 50% of patients were prescribed broad-spectrum antibiotics, and their use was more prevalent in tertiary hospitals than in clinics. Among patients who were given a diagnosis of upper respiratory tract infection, extended-spectrum penicillins (41.4%) were most frequently prescribed, followed by second-generation cephalosporins (19.1%).
CONCLUSION: This is the first study to thoroughly demonstrate the pattern of antimicrobial use in Korean pediatric outpatients. Our data have shown that broad-spectrum antibiotics are overused, whether appropriate or not. Health care professionals should make an effort to reduce antimicrobial prescribing among the Korean pediatric population.

Medication Safety

313. Second-generation antipsychotic monitoring in a correctional setting. *Kyle R. Mays, Pharm.D., Candidate*,[1] Philip J. Wenger, Pharm.D., BCPS[2]; (1) St. Louis College of Pharmacy, St. Louis, MO; (2) St. Louis College of Pharmacy, St. Louis, MO
PURPOSE: Second-generation antipsychotics (SGAs) are valuable tools in the treatment of psychiatric disorders. In addition to the benefit they provide, they carry risks for potentially serious adverse drug reactions (ADRs) including metabolic abnormalities, movement disorders, and hematologic complications. These potential ADRs make it vital to closely monitor patients who are taking SGAs to help prevent or reverse complications. The rapid turnover, large number of patients taking psychiatric medications, and provider-to-patient ratios in a jail setting can present challenges in ensuring optimal monitoring. The purpose of this study was to determine the current adherence rate at the Buzz Westfall Justice Center (BWJC) to recommended monitoring parameters of second-generation antipsychotics and, if necessary, propose improvements to the current system.
METHODS: A retrospective chart review will be conducted for BWJC patients receiving a second-generation antipsychotic for the 6-month period from December 1, 2008, to May 31, 2009. Information will be collected about the medication each patient was taking, monitoring parameters documented in the patient chart, and comparing the monitoring with current recommendations. The adherence rate will be calculated, and if necessary, recommendations will be made to the mental health and medical teams for improvements in monitoring adherence.
RESULTS: About 150 patients were identified who received a prescription for an SGA in the given period. Data collection is ongoing for monitoring data and adherence rates. All data collection and analysis will be completed before the presentation.
CONCLUSION: Pending.

Nutrition

314. Evaluation of antidiabetic activity of *Momordica cymbalaria* in streptozotocin induced diabetic rats. *Henis J. Patel, BPharm*, Kamal Modh, MPharm, I.S. Anand, BPharmacy, Ph.D.; Shree Sarvajanik Pharmacy College, Mehsana, Gujarat, India, Mehsana, India
PURPOSE: *Momordica cymbalaria* Fenzl., (*Cucurbitaceae*) widely distributed the in western parts of India and used ethnically by tribal people of India for controlling blood glucose. This prompted us to undertake a study to examine the possible antidiabetic activity of the aqueous extract of the roots by glucose tolerance test in normal and streptozotocin-induced diabetes in Wistar albino female rats.
METHODS: An oral glucose tolerance test was performed in normal rats after they had received glucose orally (10 g/kg). Diabetes mellitus was induced with streptozotocin (65 mg/kg, intraperitoneally), and graded doses of the aqueous root extracts were then administered orally to experimental diabetic rats for 30 days. Fasting serum glucose concentrations, serum lipid profiles, liver glycogen, peripheral glucose uptake, and changes in body weight and liver weight were evaluated.
RESULTS: The oral glucose tolerance test clearly indicated that aqueous extract (250 and 500 mg/kg orally) improves the glucose tolerance by 54.3% and 113.8% and glibenclamide doses by 224.39% at 30 minutes. In diabetic rats, treatments with aqueous extract (250 and 500 mg/kg orally) resulted in a significant reduction in serum glucose, serum cholesterol, and serum triglycerides and a significant elevation in serum HDL-cholesterol, liver glycogen, and body weight but no significant change in liver weight and in vitro glucose uptake comparable with that of glibenclamide (500 µg/kg orally).
CONCLUSIONS: The results of our study clearly show that the aqueous extract of roots of *Momordica cymbalaria*, Fenzl., exhibits a potent antidiabetic activity in streptozotocin-induced diabetic rats.

Oncology

315. Clinical diagnosis of K-*ras* codon12 mutations in lung adenocarcinomas by new high sensitive method PNA-clamp smart

amplification process version 2. *Takuya Araki, M.S.*,[1] Kimihiro Shimizu, M.D., Ph.D.,[2] Katsunori Nakamura, Ph.D.,[1] Tomonori Nakamura, Ph.D.,[1] Yasumasa Mitani, M.S.,[3] Kyoko Obayashi, Ph.D.,[4] Yukiyoshi Fujita, Ph.D.,[4] Seiichi Kakegawa, M.D.,[2] Yohei Miyamae, M.D.,[2] Kyoichi Kaira, Ph.D.,[5] Takefumi Ishidao, Ph.D.,[3] Alexander Lezhava, Ph.D.,[6] Izumi Takeyoshi, M.D., Ph.D.,[2] Yoshihide Hayashizaki, M.D., Ph.D.,[6] Koujirou Yamamoto, Ph.D.[1]; (1) Department of Clinical Pharmacology, Gunma University Graduate School of Medicine, Maebashi, Japan; (2) Department of Thoracic and Visceral Organ Surgery, Gunma University Graduate School of Medicine, Maebashi, Japan; (3) K.K. DNAFORM, Yokohama, Japan; (4) Department of Pharmacy, Gunma University Hospital, Maebashi, Japan; (5) Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi, Japan; (6) Omics Science Center, RIKEN Yokohama Institute, Yokohama, Japan

PURPOSE: Patients with non–small cell lung cancer who have K-*ras* mutations do not respond to tyrosine kinase inhibitors (TKIs); therefore, accurate detection of K-*ras* mutations is important for deciding therapeutic strategies. Although sequencing-related techniques have been frequently used, they are usually too complex, have low sensitivity, and are time-consuming for routine screening in clinical situations. In this study, we applied PNA-clamp smart amplification process version 2 (SmartAmp2) to clinical diagnosis of K-*ras* codon12 mutations and evaluated this method as a clinical diagnosis tool.

METHODS: K-*ras* codon12 mutations in 172 lung adenocarcinoma samples obtained from 172 consecutive patients who were surgically treated at the Gunma University Hospital (Gunma, Japan) between July 2002 and July 2008 were analyzed by PNA-clamp SmartAmp2, direct sequencing, enzyme-enriched sequencing, and PNA-enriched sequencing. Institutional approval and informed consent from all patients were obtained in writing.

RESULTS: Among 172 samples, direct sequencing, enzyme-enriched sequencing, and PNA-enriched sequencing showed that 16 (9.3%), 26 (15.1%), and 28 (16.3%) tumors contained K-*ras* mutations in codon12, respectively. Using PNA-clamp SmartAmp2, we could identify 31 (18.0%) tumors with K-*ras* mutations in codon12 within only 1 hour, three of which were undetected by PCR-related methods; however, we examined 30 nonmalignant lung tissue specimens and found no mutations in any of the samples.

CONCLUSION: Using the PNA-clamp SmartAmp2, we detected small amounts of mutant DNA that were not detected by traditional methods, and we identified patients about whom this assay provided clinical information that was unavailable from other tests. It is expected that this information will contribute to the therapeutic decisions. Furthermore, the sensitivity of this assay suggested a possibility of bringing the solution for clarifying the association between the effect of TKIs and the low levels of mutant K-*ras* alleles.

316. Prevalence of chronic kidney disease in anemic oncology patients. *Amber H. Diaz, B.S.*, Kyle Fox, B.S., Jeffrey A. Gilreath, Pharm.D., Robert E. Lewis, Pharm.D., George M. Rodgers, M.D.; Huntsman Cancer Hospital, Salt Lake City, UT

PURPOSE: Anemia is commonly seen in greater than 50% of oncology patients at some point during their disease course. Two options exist for treating anemia in patients with cancer are 1) blood transfusions or 2) erythropoiesis-stimulating agents (ESAs). Blood transfusions remain an option for most patients; however, only patients with cancer receiving myelosuppressive chemotherapy are eligible to receive an ESA. Patients who carry an alternative indication for treatment with an ESA, such as chronic kidney disease (CKD), may also be eligible to receive an ESA. The percentage of anemic patients with cancer having CKD is unknown. The primary goal of this retrospective review will be to characterize the prevalence of CKD in anemic oncology patients who are not receiving an ESA, but who are still eligible to receive an ESA because of their CKD. Patients may or may not be receiving chemotherapy.

METHODS: A retrospective chart review of 1000 patients will be performed to identify those with undiagnosed CKD (glomerular filtration rate of 60 mL/minute/1.73 m^2 or less for 3 months or more). Data to be collected will include cancer diagnosis, hematologic laboratory data, age, height, weight, serum creatinine, chemotherapy regimen, and ESA use. Patients will be stratified as receiving either chemotherapy or radiotherapy versus no treatment. Statistical analysis will be performed separately according to these two stratifications.

RESULTS: Results will be presented at the ACCP Annual Meeting.

CONCLUSIONS: Conclusions will be presented at the ACCP Annual Meeting.

317. Cytogenetical aberration and Ara-C treatment outcomes in normal karyotype (NK) AML patients. *Hye Jin Noh, B.S.*,[1] Tae Kyung Kim, B.S.,[1] Kyung Im Kim, M.S.,[1] Wan Gyoon Shin, Pharm.D., Ph.D.,[1] In Ja Son, Ph.D.,[2] Jung Mi 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: This study was carried out to 1) determine the frequency of LOH (loss of heterozygosity) and CNV (copy number variation) in normal karyotype (NK) Korean patients with acute myelogenous leukemia (AML); 2) identify the association between cytogenetic aberration and responses in patients with NK AML treated with Ara-C; and 3) identify the novel genes associated with the response of Ara-C.

METHODS: Patients with a diagnosis of NK AML in the tertiary hospital from 2003 to 2008 were included in the study, and their clinical and laboratory data were collected. We obtained DNA samples from bone marrow aspirates or peripheral blood samples at the time of diagnosis and then performed whole-genome SNP chip analysis. Genes in the LOH or CNV region were analyzed using the database from the NCBI and the HapMap database. In addition, Ara-C–resistant HEL cell lines in vitro (HEL-R) and ex vivo (HEL-BM1, HEL-BM2, and HEL-Lymph) were established to investigate the association between the gene and Ara-C resistance. The MTT assay and RT-PCR were performed to confirm the resistance and the variations in gene expressions, respectively. Paired *t*-test, χ^2 test, and analysis of variance were used according to their analytic aim.

RESULTS: A total of 50 patients were grouped according to the response of chemotherapy (remission, 33 of 50; persistence, 17 of 50). One hundred forty-seven LOHs were detected among 42 patients (remission, 26 of 33; persistence, 15 of 17). *SLC 17* family and *HIST1H* family genes were frequently found in LOH regions. CNV gain was identified in 36 individuals (remission, 24 of 33; persistence, 12 of 17) and CNV loss in 27 (18 of 33, 9 of 17). There were diverse genes in CNV regions in which the functions are not identified yet. Compared with the original HEL cell line, the expression level of *SLC29A1*, *dCK,* and *CDA* was altered in resistance cell lines.

CONCLUSION: This study found that *SLC17* family and *HIST1H* family genes were frequently located in the LOH region of patients with NK AML treated with Ara-C.

Pharmacogenomics/Pharmacogenetics

318. Aromatase genotype in the INternational VErapamil SR/trandolapril STudy (INVEST). *Megan L. Hames, B.S.*,[1] Gregory J. Welder, Pharm.D.,[1] Julia Wittmann, AA,[1] Rhonda M. Cooper-DeHoff, Pharm.D., M.S.,[1] Carl J. Pepine, M.D.,[2] Julie A. Johnson, Pharm.D.,[1] Amber L. Beitelshees, Pharm.D., MPH[3]; (1) University of Florida, College of Pharmacy, Department of Pharmacotherapy and Translational Research, Gainesville, FL; (2) University of Florida, College of Medicine, Department of Internal Medicine, Division of Cardiovascular Medicine, Gainesville, FL; (3) University of Maryland School of Medicine, Division of Endocrinology, Diabetes and Nutrition, Baltimore, MD

PURPOSE: Aromatase catalyzes the conversion of androgens to estrogens and is encoded by the *CYP19A1* gene. We previously found a sex-dependent association between *CYP19A1* and mortality after an acute coronary syndrome (ACS). We sought to replicate those findings in a population with hypertension (HTN) and stable coronary artery disease (CAD) in the INVEST.

METHODS: INVEST randomized stable HTNive patients with

documented CAD to an atenolol- or verapamil SR–based treatment strategy. We conducted a nested case-control study within INVEST with 273 patients who experienced a primary outcome event (all-cause death, nonfatal myocardial infarction [MI], or nonfatal stroke) and 781 age-, race-, and sex-matched event-free control subjects. We genotyped four SNPs in *CYP19A1,* namely -81371C>T, M201T, and R264C, and 32226G>T, by pyrosequencing. Logistic regression was performed including age, race, body mass index, smoking, diabetes, BP, heart failure, previous MI, stroke, BP treatments, and genotype. Models were conducted separately by sex, and genotype-sex interaction terms were evaluated.

RESULTS: The case-control group was composed of 51% female patients with a mean age of 70 ± 10 years. Minor allele frequencies were 0.22, 0.04, 0.05, and 0.31 for -81371C>T, M201T, R264C, and 32226G>T, respectively. We identified a significant interaction between the -81371C>T genotype and sex (p=0.0004). Increasing copies of the variant allele were associated with increased mortality in men, HR 1.55 (95% CI: 1.1–2.3) and decreased mortality in women, HR 0.52 (95% CI: 0.33–0.81). None of the other SNPs was associated with the primary outcome in either sex group or in the overall group.

CONCLUSION: Consistent with our previous findings in an ACS cohort, our results suggest that *CYP19A1* -81371C>T is associated with outcomes in a sex-specific manner in HTNive patients with stable CAD. These findings may contribute to our understanding of sex-based differences in cardiovascular disease.

319. Effect of transporter genetics on rosuvastatin pharmacokinetics and the magnitude of the drug-drug interaction between rosuvastatin and lopinavir/ritonavir in healthy volunteers. *Jessica A. Bannon, B.S.*, Christina L. Aquilante, Pharm.D., Dorie W. Hoody, Pharm.D., Julie A. Predhomme, RN, M.S., C-ANP, Charles J. Foster, B.S., Alyssa M. Walker, Pharm.D., Kyle P. Hammond, B.S., Jennifer J. Kiser, Pharm.D.; University of Colorado Denver, Aurora, CO

PURPOSE: We previously identified an interaction between rosuvastatin (ROS) and lopinavir-ritonavir (LPV/RTV). There was interindividual variability in the magnitude of this interaction, with LPV/RTV increasing ROS C_{max} and AUC[0,τ] 1.83–20 and 0.88- to 5.32-fold, respectively. The mechanism is unknown, but LPV and/or RTV may inhibit the drug transporters' organic anion transporting polypeptide 1B1 (OATP1B1) or breast cancer resistance protein (BCRP), causing an increase in ROS bioavailability. The purpose of this study was to determine whether *SLCO1B1* and *ABCG2* polymorphisms influence ROS pharmacokinetics (PK) and the magnitude of the interaction between ROS and LPV/RTV.

METHODS: We retrospectively genotyped 14 healthy subjects (11 whites, 3 Hispanics) with evaluable PK data from the parent ROS-LPV/RTV interaction study. *SLCO1B1* -11187G>A, -10499A>C, 388A>G, and 521T>C and *ABCG2* 34G>A and 421C>A genotypes were determined by pyrosequencing. *SLCO1B1* haplotypes and diplotypes were computationally assigned (*1A, *1B, *5, *15, *16, *17, and *21). ROS PK parameters and the magnitude of the interaction (using ROS AUC[0,τ] and C_{max}-fold change with and without LPV/RTV) were compared (paired *t*-test) between genotype groups.

RESULTS: Carriers of the variant *SLCO1B1* *5, *16, *21 haplotypes had 36% higher ROS AUC[0,τ] (p=0.003) and C_{max} (p=0.048) when ROS was given alone. On the addition of LPV/RTV, this difference was no longer significant (ROS AUC[0,τ] increased 21%, p=0.1545; C_{max} increased 16%, p=0.1997). The *SLCO1B1* diplotype did not significantly predict the magnitude of the ROS-LPV/RTV interaction. One *ABCG2* 34G>A and one *ABCG2* 421C>A heterozygote were identified in the study population; thus, no statistical analysis was performed.

CONCLUSION: ROS PK was influenced by the *SLCO1B1* haplotype, but we did not observe an effect of the *SLCO1B1* haplotype on the magnitude of the interaction between ROS and LPV/RTV, possibly because the study was small and retrospective. Future studies to determine the effect of *SLCO1B1* polymorphisms on ROS efficacy and toxicity are warranted.

320. Influence of pregnane X receptor gene polymorphisms on rosiglitazone pharmacokinetics in healthy volunteers. *Kyle P. Hammond, B.S.,*[1] Lane R. Bushman, B.S.,[1] Shannon D. Knutsen, B.A.,[1] Lisa A. Kosmiski, M.D.,[2] Christina L. Aquilante, Pharm.D.[1]; (1) University of Colorado Denver, Aurora, CO; (2) Division of Endocrinology, Diabetes, and Metabolism; University of Colorado Denver School of Medicine, Aurora, CO

PURPOSE: Rosiglitazone, an oral antidiabetic agent, is a *CYP2C8* substrate. Pregnane X receptor (PXR) is a nuclear receptor that transcriptionally regulates *CYP450* genes, including *CYP2C8*. Given the putative effect of PXR on *CYP2C8* expression, we sought to determine whether *PXR* gene polymorphisms contribute to interindividual variability in the pharmacokinetics of rosiglitazone.

METHODS: Healthy white subjects (n=25) were administered a single 4-mg oral dose of rosiglitazone, and blood samples were collected for 24 hours after dosing. Subjects were genotyped for the following *PXR* polymorphisms using pyrosequencing: 44477T>C (promoter), 63396C>T (intron 1), and 69789A>G (intron 1). Rosiglitazone plasma concentrations were determined by HPLC and analyzed using noncompartmental methods. Rosiglitazone pharmacokinetic parameters, $t_{1/2}$, C_{max}, T_{max}, $AUC_{0–24}$, oral clearance (CL), weight-adjusted oral clearance (CL/kg), and weight-adjusted volume of distribution (V/kg), were compared between genotype groups using ANCOVA, with the *CYP2C8*3* genotype as a covariate.

RESULTS: The study population consisted of 21 women and 4 men (mean age, 32 ± 10 years; mean weight, 66.8 ± 12 kg). Rosiglitazone $t_{1/2}$ was shorter in *PXR* 69789 variant allele carriers (3.6 ± 0.5 hours, n=12) compared with wild-type homozygotes (4.2 ± 0.9 hours, n=12; p=0.06). In *PXR* 69789 variant allele carriers compared with wild-type homozygotes, rosiglitazone CL/kg was 36.8 ± 9.8 mL/hour/kg versus 38.1 ± 9.1 mL/hour/kg (p=0.85), and V/kg was 0.19 ± 0.03 L/kg versus 0.22 ± 0.06 L/kg (p=0.08). Rosiglitazone pharmacokinetic parameters did not differ significantly between *PXR* 44477 genotype groups (n=3, T/T; n=12, T/C; n=8, C/C; n=2, unable to genotype) or *PXR* 63396 genotype groups (n=2, C/C; n=12, C/T; n=11, T/T).

CONCLUSION: These data suggest that *PXR* 44477T>C, 63396C>T, and 69789A>G polymorphisms do not substantially influence rosiglitazone pharmacokinetics in healthy volunteers. Given that *PXR* is a highly polymorphic gene, additional studies of the effects of *PXR* polymorphisms and haplotypes on the pharmacokinetics of *CYP2C8* substrates are warranted.

321. Effect of CYP2D6 polymorphism on the pharmacokinetics of metoprolol and á-hydroxymetoprolol in healthy Korean subjects. *Sung-Min Moon, B.S.*, Chang-Ik Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Metoprolol is a member of the β_1-selective antagonists used for the treatment of hypertension and is known to be metabolized predominantly by *CYP2D6*. Therefore, we investigated the effect of major polymorphisms of the *CYP2D6* on the pharmacokinetics of metoprolol and its major metabolite, α-hydroxymetoprolol, in Koreans.

METHODS: Thirty healthy Korean subjects were selected and grouped according to *CYP2D6* genotype. The number of subjects with the *CYP2D6*1/*1*, **10/*10,* and **5/*10* genotype was 15, 10, and 5, respectively. After an overnight fast, a 100-mg single oral dose of metoprolol was given to each subject. Blood samples were collected up to 24 hours after dosing, and the plasma concentrations of metoprolol and α-hydroxymetoprolol were measured by the HPLC-fluorescence method.

RESULTS: Maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve ($AUC_{0–\infty}$) of metoprolol in *CYP2D6*10/*10* and **5/*10* genotype groups were significantly higher than those in the *CYP2D6*1/*1* genotype group. Significantly longer half-lives ($t_{1/2}$) of metoprolol in *CYP2D6*10/*10* and **5/*10* genotype groups were shown than in the *CYP2D6*1/*1* genotype group. Each parameter of metoprolol in the *CYP2D6*5/*10* genotype group was also significantly greater than those in the *CYP2D6*10/*10* genotype group. The AUC ratio of metoprolol to its α-hydroxy metabolite ($AUC_{MT}/AUC_{α–OHMT}$) in *CYP2D6*10/*10* and **5/*10* individuals was significantly lower compared with that in *CYP2D6*1/*1* individuals.

CONCLUSION: The presence of *CYP2D6*5* and *CYP2D6*10* alleles can affect the pharmacokinetics of metoprolol and α-hydroxy-metoprolol in Koreans.

322. CYP2C19 genetic polymorphisms significantly affected the pharmacokinetics of gliclazide in healthy Korean subjects. *Do-Hoon Kim, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: It is reported that *CYP2C19* is mainly involved in the metabolism of gliclazide, a member of the sulfonylurea antidiabetic agents. In this study, the effect of *CYP2C19* genetic polymorphisms on the pharmacokinetics of gliclazide in Koreans was evaluated.

METHODS: Twenty-seven healthy Korean subjects were enrolled and classified into three groups – extensive metabolizer (EM, n=9), intermediate metabolizer (IM, n=11), and poor metabolizer (PM, n=7) – according to *CYP2C19* genotypes. After an overnight fast, each subject received an 80-mg single oral dose of gliclazide. Blood samples were collected up to 48 hours after dosing, and the plasma concentrations of gliclazide were measured by the HPLC-UV method.

RESULTS: Area under the plasma concentration-time curve ($AUC_{0-\infty}$) in *CYP2C19* PM and IM groups was 215% and 164% of *CYP2C19* EM groups, respectively, and these changes were statistically significant. Half-life ($t_{1/2}$) of gliclazide in both *CYP2C19* PM and IM groups was also significantly longer than that in the *CYP2C19* EM group (164% and 132% of EM, respectively). Oral clearance (CL/F) of gliclazide in the *CYP2C19* PM and IM groups was significantly reduced by 55% and 38% compared with the *CYP2C19* EM group.

CONCLUSION: *CYP2C19* genetic polymorphisms can affect the pharmacokinetics of gliclazide in Koreans.

323. Effect of OATP1B1 genetic polymorphisms on the pharmacokinetics of ezetimibe. *Do-Hoon Kim, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Ezetimibe is an antihyperlipidemic agent, used to lower cholesterol levels by inhibiting cholesterol absorption. Ezetimibe is a substrate of OATP1B1 (*SLCO1B1*), one of the hepatic drug uptake transporters. So we studied to determine whether *OATP1B1* genetic polymorphisms, particularly the *OATP1B1*15* allele, have an effect on ezetimibe pharmacokinetics in Koreans.

METHODS: Forty-six healthy Korean subjects participated in this study and were classified into three groups according to number of *OATP1B1*15* alleles (*OATP1B1*1/*1*, **1/*15,* and **15/*15*). After an overnight fast, each subject received a 10-mg single oral dose of ezetimibe. Blood samples were collected up to 48 hours after dosing, and the plasma concentrations of ezetimibe and its major metabolite, ezetimibe glucuronide, were measured by the LC/MC/MC method.

RESULTS: The number of subjects with the *OATP1B1*1/*1*, **1/*15,* and **15/*15* genotypes was 31, 11, and 4, respectively. Area under the plasma concentration-time curve ($AUC_{0-\infty}$) of ezetimibe for *OATP1B1*1/*1*, **1/*15,* and **15/*15* genotype groups was 103.4 ± 78.8, 90.7 ± 31.6, and 55.6 ± 30.3 ng/hour/mL, respectively; $AUC_{0-\infty}$ values of ezetimibe glucuronide for *OATP1B1*1/*1*, **1/*15,* and **15/*15* genotype groups were 359.3 ± 198.6, 332.9 ± 128.7, and 341.5 ± 78.0 ng/hour/mL, respectively. These changes, however, were not statistically significant. In addition, there were no significant differences in other pharmacokinetic parameters of ezetimibe and ezetimibe glucuronide between each group.

CONCLUSION: Although ezetimibe is known as a substrate of OATP1B1, our study results suggest that there are no significant changes in the pharmacokinetics of ezetimibe in relation to *OATP1B1* genetic polymorphisms.

324. Effect of genetic variation in CYP2C9 on the pharmacokinetics of flurbiprofen in healthy Korean subjects. *Sung-Min Moon, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Flurbiprofen is one of the nonsteroidal anti-inflammatory drugs (NSAIDs) used to treat pain and inflammation and is known as a substrate of *CYP2C9*. In this study, we evaluated the effect of *CYP2C9* genetic polymorphisms on the pharmacokinetics of flurbiprofen in Koreans.

METHODS: This study was performed with healthy Korean volunteers, with *CYP2C9*1/*1* and *CYP2C9*1/*3* genotypes. Each subject received a 40-mg single oral dose of flurbiprofen. Blood samples were collected up to 10 hours after dosing, and the plasma concentrations of flurbiprofen were determined by the HPLC-UV method.

RESULTS: Area under the plasma concentration-time curve ($AUC_{0-\infty}$) of flurbiprofen in the *CYP2C9*1/*3* genotype group (47.1 ± 12.2 μg/hour/mL) was significantly higher than in the *CYP2C9*1/*1* genotype group (29.3 ± 3.9 μg/hour/mL). Oral clearance (CL/F) of flurbiprofen in the *CYP2C9*1/*3* genotype group (0.9 ± 0.2 L/hour) was significantly lower than that in the *CYP2C9*1/*1* genotype group (1.4 ± 0.2 L/hour). The AUC ratio of flurbiprofen to 4′-hydroxyflurbiprofen was lower in *CYP2C9*1/*3* individuals than in *CYP2C9*1/*1* individuals.

CONCLUSION: The *CYP2C9*3* allele significantly affects the pharmacokinetics of flurbiprofen in Koreans.

325. Effect of MDR1 genotype on the pharmacokinetics of ezetimibe. *Sung-Min Moon, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Ezetimibe is used for the treatment of hypercholesterolemia through the inhibition of cholesterol absorption. *MDR1* (*ABCB1*), one of the drug efflux transporters, is highly distributed in the human body. We hypothesized that *MDR1* could contribute to the interindividual variability of ezetimibe pharmacokinetics.

METHODS: Forty-six healthy Korean subjects were recruited and classified into three groups according to *MDR1 C3435T* genotype (*MDR1* 3435CC, CT, and TT). The number of subjects in each genotype were 21, 20, and 5, respectively. After an overnight fast, a 10-mg single oral dose of ezetimibe was given to each subject. Blood samples were collected up to 48 hours after dosing, and the plasma concentrations of ezetimibe and its glucuronide metabolite (ezetimibe glucuronide) were determined by the LC/MS/MS method.

RESULTS: Maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve ($AUC_{0-\infty}$) of ezetimibe glucuronide were significantly lower in 3435T allele carriers (*MDR1* 3435CT and TT genotype groups) than in 3435T noncarriers (*MDR1* 3435CC genotype group). Changes in oral clearance (CL/F) of ezetimibe glucuronide between each group were in the opposite direction; however, the pharmacokinetic parameters of ezetimibe had no significance among the groups.

CONCLUSION: Although no significant changes are shown in the pharmacokinetics of ezetimibe, the major glucuronide metabolite, ezetimibe glucuronide, is shown to be a possible substrate of *MDR1,* and the *MDR1* genetic polymorphism has an effect of the pharmacokinetics of ezetimibe glucuronide.

326. Genetic polymorphisms of UGT1A8, UGT1A9, UGT2B7, and G.I. side effects of mycophenolic acid therapy in kidney transplant patients. *Taegun Kim, Pharm.D., candidate,*[1] Jae-Wook Yang, Ph.D., Pharm.D.,[2] Ian V. Hutchinson, Ph.D., DSc,[3] Tariq Shah, M.D.,[4] David I. Min, Pharm.D.[5]; (1) Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2) University of Kansas, Kansas City, KS; (3) USC School of Pharmacy, Los Angeles, CA; (4) National Institute of Transplantation and St. Vincent Medical Center, Los Angeles, CA; (5) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Pomona, CA

327. Genetic polymorphisms of UGT1A8, UGT1A9, UGT2B7, and GI side effects of mycophenolic acid therapy in kidney transplant patients. *Taegun Kim, Pharm.D., Candidate,*[1] Jae-Wook Yang, Ph.D.,

Pharm.D.,[2] Ian V. Hutchinson, Ph.D., DSc,[3] Tariq Shah, M.D.,[4] David I. Min, Pharm.D.[5]; (1) Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2) University of Kansas, Kansas City, KS; (3) USC School of Pharmacy, Los Angeles, CA; (4) St. Vincent Medical Center and National Institute of Transplantation, Los Angeles, CA; (5) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Los Angeles, CA

Mycophenolic acid (MPA) is one of most widely used immunosuppressants in organ transplantation.

PURPOSE: To determine the relationship between single nucleotide polymorphisms in *UGT1A8, UGT1A9,* and *UGT2B7* and the incidence and severity of the gastrointestinal (GI) symptoms in patients receiving MPA.

METHODS: Genotypes of *UGT1A8, UGT1A9,* and *UGT2B7* were determined, and the incidence and severity of GI symptoms were assessed using the validated Gastrointestinal Symptom Rating Scale (GSRS) at 1 week, 2 weeks, 3 months, and 6 months posttransplant. The mean overall GSRS score and five subscales for acute gastric pain, acid reflux, indigestion, diarrhea, and constipation were compared by the Kruskal-Wallis test at each time point.

RESULTS: The data from 77 patients were analyzed on the basis of our inclusion and exclusion criteria. Among three groups of *UGT1A8* (CC, CG, and GG), the total GSRS (21.6 ± 7.3, 19.3 ± 8.6, and 28.7 ± 7.5, p=0.008), diarrhea subscores (4.0 ± 2.2, 3.4 ± 1.7, and 5.1 ± 1.9, p=0.002), and constipation subscores (5.1 ± 3.0, 4.2 ± 2.8, and 8.3 ± 2.8, p=0.008) were significantly different at the 1-week point; however, at 2 weeks, only acid reflux subscores were significantly different (2.6 ± 1.3, 1.7 ± 0.7, and 1.8 ± 1.2, p=0.003). For *UGT1A9,* there were significant differences in diarrhea subscores at 1 week (3.6 ± 2.3, 3.8 ± 0.9, and 3.8 ± 2.2, p=0.043). For *UGT2B7,* diarrhea subscores at 2 weeks were significantly different among CC, CT, and TT groups (2.0 ± 1.3, 2.3 ± 1.2, and 3.0 ± 1.2, p=0.044). There were, however, no differences in the GSRS scores between patients receiving either MMF or enteric-coated MPA or between patients receiving the different calcineurin inhibitors.

CONCLUSION: This study demonstrates that among patients receiving MPA, there is evidence that genotypes of *UGT1A8, UGT1A9,* and *UGT2B7* may predict incidence and severity of its GI adverse effects at early posttransplant periods, but they are not useful in predicting GI adverse effects in later stages.

Pharmacokinetics/Pharmacodynamics/Drug

328. Effects of bile salts on the bioavailability of lovastatin in rats. *Kyunghee Kim, B.S.,*[1] Inkyung Yoon, B.S.,[1] Inkoo Chun, Ph.D.,[2] Taekrho Kim, Ph.D.,[3] Hyesun Gwak, Pharm.D., Ph.D.[1]; (1) Division of Life and Pharmaceutical Sciences, Ewha Womans University, Seoul, South Korea; (2) College of Pharmacy, Dongduk Women's University, Seoul, South Korea; (3) Pharmaceutical Research Institute, CJ Cheiljedang, Seoul, South Korea

PURPOSE: Lovastatin is a highly lipophilic drug with a low bioavailability. To improve its bioavailability, lovastatin solid dispersions containing bile salts were formulated. This study aimed to examine the effects of various bile salts on the absorption of lovastatin in rats using the formulated solid dispersions.

METHODS: Seven lovastatin solid dispersions were prepared at various ratios of lovastatin to carriers, such as sodium deoxycholate (SDC), sodium glycocholate (SGC), and 2-hydroxypropyl-b-cyclodextrin (HPCD). Prepared formulations were administered to rats at the dose of 2.5 mg/kg as lovastatin. Blood samples were collected at predetermined time intervals and analyzed by the LC-MS/MS system.

RESULTS: Compared with the marketed lovastatin tablet, all formulated solid dispersions increased peak plasma concentration (C_{max}). The order of effect magnitude was lovastatin-SDC (1:19) > lovastatin-SDC (1:69) > lovastatin-SGC (1:69) > lovastatin-SGC (1:19) > lovastatin-SGC (1:49) > lovastatin-SDC (1:49) > lovastatin-HPCD (1:49); lovastatin-SDC (1:19) increased C_{max} by 635%. Lovastatin-SDC (1:19), lovastatin-SDC (1:69), lovastatin-SGC (1:19), and lovastatin-SGC (1:69) increased area under the plasma concentration-time curve (AUC) by 443%, 514%, 183%, and 136%, whereas lovastatin-HPCD (1:49) and lovastatin-SGC (1:49) decreased AUC by 56% and 75%, respectively.

CONCLUSIONS: Results of this study indicate that the bioavailability of lovastatin solid dispersions with bile salts such as SDC or SGC is higher than the marketed lovastatin tablet or lovastatin solid dispersion with HPCD.

329. Lack of significant drug interactions between ursodeoxycholic acid (UDCA) and pitavastatin in healthy subjects. *Do-Hoon Kim, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Pitavastatin is a member of the HMG-CoA reductase inhibitors used for the treatment of hypercholesterolemia and is known as a substrate of OATP1B1. Ursodeoxycholic acid (UDCA) is known as an inhibitor of OATP1B1 activity; therefore, we studied whether UDCA affects on the pharmacokinetics of pitavastatin in Koreans.

METHODS: Thirteen healthy Korean subjects with the *OATP1B1*1a/*1b* genotype participated in this study. In phase I, each subject received a 2-mg single oral dose of pitavastatin. After 1 week of washout, in phase II, subjects were administered a 300-mg dose of UDCA twice daily for 14 days. On the 15th day, they took 2 mg of pitavastatin as described in phase I. Blood samples were collected up to 48 hours after dosing, and the plasma concentrations of pitavastatin were measured by the LC-MC/MC method.

RESULTS: After the pharmacokinetic analysis, maximum plasma concentration (C_{max}), area under the plasma concentration-time curve ($AUC_{0-\infty}$), half-life ($t_{1/2}$), oral clearance (CL/F), and volume of distribution (V_d) of pitavastatin between two phases were not significantly different.

CONCLUSION: This study showed that UDCA can safely be used together with pitavastatin because UDCA has no significant effect on the pharmacokinetics of pitavastatin.

330. The pharmacokinetic interactions of OATP1B1 inhibitor and pitavastatin. *Sung-Min Moon, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Pitavastatin is one of the HMG-CoA reductase inhibitors, and it is reported that OAPT1B1 is involved in the hepatic uptake of pitavastatin. Macrolide antibiotics are known as inhibitors of the OATP1B1 drug uptake transporter. In this study, the effect of clarithromycin, a member of the macrolide antibiotics, on the pharmacokinetics of pitavastatin was evaluated.

METHODS: Twelve healthy Korean subjects with the *OATP1B1*1a/*1b* genotype were selected to undergo an open-label, two clinical study phases separated by a 1-week washout period. In phase I, each subject received a 2-mg single oral dose of pitavastatin after an overnight fast. In phase II, 2 mg of pitavastatin was received, as in phase I, and 500 mg of clarithromycin was coadministered twice daily for 2 days. Blood samples were collected up to 48 hours after dosing, and the plasma concentrations of pitavastatin were measured by the LC-MS/MS method.

RESULTS: Maximum plasma concentrations (C_{max}) of pitavastatin in phases I and II were 46.9 ± 16.1 ng/mL and 86.5 ± 24.4 ng/mL, respectively. Area under the plasma concentration-time curve ($AUC_{0-\infty}$) of pitavastatin in each phase were 165.7 ± 57.7 ng/hour/mL and 213.0 ± 50.3 ng/hour/mL, respectively. These changes were all statistically significant; however, the pharmacokinetics of pitavastatin lactone had no significant differences between the two different phases.

CONCLUSION: Clarithromycin, an *OATP1B1* inhibitor, significantly affected the pharmacokinetics of pitavastatin. Coadministration of macrolide antibiotics with pitavastatin may increase the risk of the adverse events of pitavastatin.

331. Effect of ABCC2 (MRP2) genetic polymorphisms on the pharmacokinetics of ezetimibe. *Do-Hoon Kim, B.S.*, Chang-IK Choi, B.S., Jung-Woo Bae, M.S., Mi-Jeong Kim, Ph.D., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea

PURPOSE: Ezetimibe, an inhibitor of cholesterol absorption used

for the treatment of hypercholesterolemia, is known as a substrate of *MRP2* (*ABCC2*). We investigated the effect of genetic polymorphisms of *MRP2* on the pharmacokinetics of ezetimibe and its major glucuronide metabolite, ezetimibe glucuronide, in Koreans.
METHODS: Forty-three healthy Korean subjects were selected and classified into three groups according to *MRP2* C-24T genotype. After an overnight fast, each subject took a 10-mg single oral dose of ezetimibe. Blood samples were collected up to 48 hours after dosing, and the plasma concentrations of ezetimibe and ezetimibe glucuronide were measured by the LC-MC/MC method.
RESULTS: The number of each genotype group (CC, CT, and TT genotype) was 30, 7, and 6, respectively. Area under the plasma concentration-time curve ($AUC_{0-\infty}$) of ezetimibe for CC, CT, and TT genotype groups was 97.6 ± 81.3, 96.6 ± 37.3, and 105.4 ± 18.8 ng/hour/mL, respectively. $AUC_{0-\infty}$ values of ezetimibe glucuronide for CC, CT, and TT genotype groups were 357.3 ± 192.6, 295.3 ± 118.1, and 401.5 ± 178.7 ng/hour/mL, respectively; however, these changes were not statistically significant. Nor were there significant differences in other pharmacokinetic parameters of ezetimibe and ezetimibe glucuronide between each group.
CONCLUSION: Although ezetimibe is known as a substrate of *MRP2,* we suggest that the *MRP2* C-24T polymorphism has no significant effect on the pharmacokinetics of ezetimibe in Koreans.

Psychiatry

332. Drug attitude inventory: predictor of medication adherence behaviors among inpatients with bipolar disorder?
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PURPOSE: Predicting the problem of medication nonadherence among psychiatric patients is challenging, and few instruments exist for this purpose. The 10-item Drug Attitude Inventory (DAI-10) is valid and reliable at predicting medication adherence among outpatients with schizophrenia, but little is known about using the DAI-10 among other psychiatric populations. We conducted a naturalistic study to examine if the DAI-10 would predict medication adherence behaviors among hospitalized inpatients with bipolar disorder (BD).
METHODS: Face-to-face interviews were conducted with inpatients after admission and after formal diagnostic measures and standardized symptom rating scales had been administered. The DAI-10 (score range, –10 to +10) was included to measure patient attitudes toward their BD medication treatment plan. Medication adherence was calculated using a standardized dose ratio (medication taken/prescribed), and mean DAI-10 scores were then compared between adherent and nonadherent patients.
RESULTS: Fifty-four patients given a diagnosis of BD completed the study (n=30 medication adherent, n=24 medication nonadherent). The sample was predominantly white and 50% male, with a mean age of 37.74 years (range, 20–60). According to our primary outcome, medication-adherent patients demonstrated a statistically significantly higher mean DAI-10 score (M = 5.33, SD = 4.41) compared with nonadherent patients (M = –0.25, SD = 6.39) [$t(52) = 3.794$, $p<0.001$; effect size (standardized mean difference) = 1.0 (95% CI: 0.5–1.6)].
CONCLUSION: Given its ease of administration and straightforward scoring procedure, the DAI-10 can be used with additional patient information to help predict medication-taking behaviors among patients with BD upon hospitalization, allowing clinicians to focus on those at risk of nonadherence.

333. Evaluation of antipsychotic polypharmacy within a county-supported outpatient psychiatric clinic. *Cathy A. Chang, B.S.,*[1] Mindl Messinger, B.A.,[1] Jan D. Hirsch, Ph.D.,[2] Kelly C. Lee, Pharm.D., BCPP[1]; (1) University of California, San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, CA; (2) University of California, San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, San Diego, CA
PURPOSE: Antipsychotic monotherapy has been the mainstay treatment of psychotic disorders; however, with the introduction of second-generation antipsychotic medications, the use of polypharmacy is becoming prevalent. A recent study of antipsychotic polypharmacy among Medi-Cal beneficiaries in San Diego County reported an increase from 5% to 15% in a 6-year study period.
This study examined the rate of antipsychotic polypharmacy among county-contracted clients at the UCSD Outpatient Psychiatric Services (OPS) clinic. The primary aim was to determine the rate and type of polypharmacy among clients at the clinic. We hypothesized that the rate of polypharmacy would be greater than the 15% observed for San Diego Medi-Cal beneficiaries.
METHODS: This is a retrospective, cross-sectional study of clients who received an intake evaluation during 2008. Medical records will be reviewed for rate and type of antipsychotic (same- and multiclass polypharmacy). Demographic information, as well as psychiatric diagnoses and concomitant medications, will be recorded. The rate of antipsychotic polypharmacy will be compared with the 2004 Medi-Cal beneficiary rate (15%) using a χ^2 test. With a sample size of 259 clients, we should be able to detect a 15-point difference (15% vs. 30%) with greater than 90% power at a 0.05 significance level.
RESULTS: Data collection is currently ongoing and will be completed by September 1, 2009. So far, records for 17 subjects have been reviewed. Seven (41%) of 17 were female with an average age of 51 years (SD, ±9.4). Around 5 (29.4%) of 17 exhibited antipsychotic polypharmacy in their medication profile at the time of intake. Statistical analysis will be performed after complete data collection.
CONCLUSION: The rate of antipsychotic polypharmacy at the UCSD OPS clinic is about 30% based on partial data. Complete results will be presented at the ACCP Annual Meeting.

334. Evaluation of primary care integration within a county-supported outpatient psychiatric services clinic. *Mindl Messinger, B.A.*, Cathy A. Chang, B.S., Kelly C. Lee, Pharm.D., BCPP, Jan D. Hirsch, Ph.D.; University of California, San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, CA
PURPOSE: Patients with serious mental illness (SMI) also often have physical comorbidities such as cardiovascular disease, weight gain, and diabetes. The psychiatrist may be unaware of these coexisting physical illnesses; thus, it is important that these patients also be cared for by a primary care provider (PCP). This project examines the integration of primary care at a county-supported Outpatient Psychiatric Services Clinic (OPSC). The primary aim is to determine the proportion of patients at the OPSC who indicate they have a PCP. We hypothesize that greater than 50% of patients receiving care at OPSC will not have a PCP.
METHODS: This retrospective, cross-sectional study reviews medical records of patients who received an intake evaluation during 2008. Variables include PCP (yes/no), demographics, and diagnoses/medications (psychiatric and physical). A χ^2 test will be used to determine whether the percentage of patients without a PCP is significantly different from the estimated 50% for SMI patients overall. Using a sample size of 259 patients will allow detection of a 20% difference in the proportion of patients with a PCP with 90% power at a 0.05 significance level (SMI rate 50% vs. OPSC rate 60%).
RESULTS: The data collection portion of this summer research project has begun, but it is not expected to be complete until September 1, 2009. Results based on partial data collection (n=17) follow. Forty-one percent (n=7) of our sample were female with an average age of 51 (SD, ±9.4); 47.1% (n=8) of the patients indicated they had a PCP at intake. Complete results will be available for presentation at the October 2009 Annual Meeting.
CONCLUSIONS: Based on partial data, the proportion of patients at the OPSC who indicate they had a PCP appears to be similar to that estimated for the SMI patient population overall.

Public Health

335. An epidemiologic study of demographic and medical trends pre and post National Health Insurance in Sekyeri West district of Ghana. *Yussif Dokurugu, MPH, M.A.,* Perry Brown, MSPH, DrPH; Institute of Public Health, Tallahassee, FL

An epidemiologic study of demographic and medical trends pre– and post–National Health Insurance in Sekyeri West district of Ghana.
PURPOSE: The purpose of this study is to examine the demographic and medical changes in hospitalizations and outpatient visits in the Ashanti Region of Ghana before and after the institution of the National Health Insurance Scheme (NHIS).
METHODS: This project consists of two phases. Medical records of inpatient and outpatient records from 2001 to 2008 in the Sekyeri West District were reviewed. Phase 1 consists of pre- and post-NHIS data compilation and aggregation, variable construction, and univariate and bivariate descriptive statistics to provide an overview of the state of the health care system in Ghana. Phase 2 consists of a time-series analysis on 2001–2008 data. The SAS Proc ARIMA will be used to determine significant changes in the demographic characteristics of inpatients and outpatients occurring after the institution of the NHIS.
RESULTS: Ghana as a whole recorded 0.54 outpatient visits per capita in 2005 (before National Health Insurance). The hospital admission rate was 36.5 per 1000 in 2005. Skilled obstetric deliveries increased to 40.3% in 2005. It is against this background that trends in inpatient and outpatient medical visits will be analyzed. Trends by gender, age, and diagnostic group will be examined during an 8-year period.
CONCLUSIONS: Before 2006, the country instituted an NHIS plan. This plan provided free health coverage to all citizens. Before the NHIS, the predominant mode of payment for health care services was cash and carry. Rates of outpatient services provided and inpatient admissions have changed by age group, gender, and diagnosis after the institution of the NHIS in Ghana.

Transplant/Immunology

336. Clinical risk factors for posttransplant early and late anemia in kidney transplant patients. *Elham Lavy, Pharm.D.,*[1] Jae-Wook Yang, Ph.D., Pharm.D.,[2] Ian V. Hutchinson, Ph.D., DSc,[3] Tariq Shah, M.D.,[4] David I. Min, Pharm.D.[5]; (1) Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2) University of Kansas, Kansas City, KS; (3) USC School of Pharmacy, Los Angeles, CA; (4) National Institute of Transplantation and St. Vincent Medical Center, Los Angeles, CA; (5) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Los Angeles, CA

Posttransplant anemia occurs early and then later after transplantation and is strongly associated with significant cardiovascular morbidity and hospitalization.
PURPOSE: To identify clinical risk factors that may be associated with the early, late, and severe anemia after kidney transplantation.
METHODS: A total of 314 patients was reviewed retrospectively in this study for early and late anemia. Anemia was divided by mild anemia (10 g/dL less than or equal to hemoglobin less than 13 g/dL [male], 10 g/dL less than or equal to hemoglobin less than 12 g/dL [female]) and severe anemia (less than 10 g/dL [male and female]). Among the 314 patients, 48 were excluded because of lack of patient data availability. A total of 266 patients were analyzed for early anemia (within 6 months of posttransplant). A total of 146 patients were defined as having late anemia, which was defined as anemia at more than 6 months posttransplant. A total of 23 clinical risk factors for anemia were considered for this analysis. Categoric data were compared by χ^2 test, continuous data were compared by a Student *t*-test, and final data were analyzed by logistic regression. A $p<0.05$ was regarded as significant.
RESULTS: *Early anemia:* race, delayed graft function, EPO use, MPA use, ganciclovir, Bactrim use, Thymoglobulin use, hemoglobin, SCr, Alb, GFR, and patient survival were significantly associated with anemia ($p<0.05$). Logistic regression revealed that age (OR = 1.045, p=0.045), 6-month SCr (OR = 4.35, p=0.0001), MMF use (OR = 2.46, p=0.031), and Thymoglobulin use (OR = 4.00, p=0.0001) were associated with anemia. *Late anemia:* sirolimus use, female gender, and EPO use were the only risk factors significantly associated with anemia ($p<0.05$). Logistic regression revealed that female gender (OR = 2.2, p=0.0001) and sirolimus use (OR = 2.164, p=0.036) were significantly associated with late-onset anemia after kidney transplantation.
CONCLUSION: This study shows that there were different risk factors for anemia depending on the onset after kidney transplantation; this may help us develop a different therapeutic approach for anemia in kidney transplant patients.

337. Vascular endothelial growth factor gene polymorphisms may predict early renal function after kidney transplantation. *Hayeon Noh, Pharm.D., Candidate,*[1] Hyesun Gwak, Pharm.D., Ph.D.,[2] Jae-Wook Yang, Pharm.D., Ph.D.,[3] Ian V. Hutchinson, Ph.D., DSc,[4] Tariq Shah, M.D.,[5] David I. Min, Pharm.D.[6]; (1) Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2) Division of Life and Pharmaceutical Sciences, Ewha Womans University, Seoul, South Korea; (3) University of Kansas, Kansas City, KS; (4) USC School of Pharmacy, Los Angeles, CA; (5) National Institute of Transplantation and St. Vincent Medical Center, Los Angeles, CA; (6) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Pomona, CA

Microvessel injury and ischemia are associated with the development of renal dysfunction after renal transplantation, whereas vascular endothelial growth factor (VEGF) promotes angiogenesis and may have an impact on early renal function.
PURPOSE: The current study aimed to determine the impact of kidney recipient and donor VEGF-A gene polymorphisms on the early renal function measured by creatinine concentration after kidney transplantation.
METHODS: Recipient and donor polymorphisms for four alleles of VEGF-A (-1154 G/A, -2578A/C, -460C/T, and -936 C/T) were determined by TaqMan allelic discrimination real-time polymerase chain reaction from 81 kidney transplant patients, and creatinine concentrations and creatinine clearances were collected and compared on days 3, 7, and 14.
RESULTS: This study is in progress and will be presented at the meeting.
CONCLUSION: Will be presented at the meeting.

RESEARCH INSTITUTE

Hematology/Anticoagulation

338. Evaluation of bivalirudin versus heparin for maintaining hemofilter patency in continuous renal replacement therapy. *Tyree H. Kiser, Pharm.D.,*[1] Robert MacLaren, Pharm.D.,[1] Douglas N. Fish, Pharm.D.,[1] Kathryn L. Hassell, M.D.,[2] Isaac Teitelbaum, M.D.[2]; (1) University of Colorado School of Pharmacy, Aurora, CO; (2) University of Colorado School of Medicine, Aurora, CO

PURPOSE: The aim of this study was to evaluate the safety and efficacy of bivalirudin compared with heparin for preventing hemofilter occlusion in patients undergoing continuous venovenous hemofiltration (CVVH).
METHODS: This prospective, randomized, double-blind study included critically ill patients older than 18 years receiving CVVH by a Gambro Prisma continuous renal replacement therapy (CRRT) machine; these were patients who, without anticoagulation, experienced hemofilter failure within 24 hours. Patients with a contraindication to study medications and those who required anticoagulation for a systemic thrombosis, had a coagulopathy, or active bleeding in the past 48 hours were excluded. Bivalirudin (2 mg/hour) or heparin (400 U/hour) was administered into the circuit prefilter by a syringe pump. Anticoagulation was titrated to achieve circuit aPTTs 1.5–2.5 times baseline and systemic aPTTs 1–1.4 times baseline. CVVH hemofilters, blood flow rates, and replacement fluid rates were standardized.
RESULTS: Ten patients (median age, 58 years; 70% male) were enrolled; five received bivalirudin and five received heparin. Patients had a median APACHE II score of 24, a SOFA score of 11, and reduced antithrombin III activity (75.5 U/dL). Baseline characteristics were not different between groups. Forty hemofilters were evaluated (18 bivalirudin and 22 heparin). Compared with no anticoagulation, the addition of bivalirudin or heparin improved mean hemofilter survival time (10 ± 5 hours vs. 22 ± 18 hours, p=0.0005). Mean hemofilter survival time was significantly increased in patients receiving bivalirudin compared with heparin

(29.6 ± 20.7 hours vs. 16.5 ± 13.6 hours, respectively; p=0.045). One patient developed alveolar hemorrhage, and one patient developed a new lower extremity DVT during heparin therapy compared with none receiving bivalirudin.
CONCLUSIONS: Bivalirudin was superior to no anticoagulation and heparin for prolonging hemofilter survival time and was well tolerated. Additional studies of bivalirudin for prevention of hemofilter clotting in patients on CRRT are warranted.

Pediatrics

339. Drug safety in pediatric patients. *Rusudan G. Jashi,* Scientific Research Institute of Pediatrics, Tbilisi, Georgia
PURPOSE: In Georgia, the greater part of infant mortality falls to neomortality in the structure of neomortality. The purpose of this study was to conduct a detailed analysis of causes and elaborate on them. Among the potential risk factors identified was attention to medication risk.
METHODS: Retrospective study, clinical pharmacologic analysis of diseased newborns and maternal medical histories (n=126). Evaluated mothers: age, disease, medications used during pregnancy and delivery; newborns: gestational age at delivery, birth weight, diagnosis, and medications used. Analyzed the relevance of prescription medications in newborns and medications used in mothers during pregnancy and delivery.
RESULTS: The study revealed that RDS in newborns had been caused by maternal oxytocin use during delivery (58%), and magnesia sulfas in newborns (18%) caused symptoms of magnesia sulfa intoxication – disturbance of CNS reduction of suction. In newborns with convulsion syndrome, rurosemidum (placental transfer T1/2, 33.8 and more), together with oxytocin, was used. In these cases, newborns need transfusion of liquid. Use of aminoglicosides (18%) was irrelevant because their adverse effects intensify. Newborn asphyxiation was related to maternal diazepam use during delivery (22%). Apnea, hypotony, depression, and hypothermia identified in these newborns could have been caused by these medications. In one case, a maternal medication history revealed that, during pregnancy, the woman had systematically used naphthyzinum because of difficulty breathing. Four hours after the birth, neuroreflectory excitation, periodic breath, apnea, and convulsions developed in the newborn. Neonatal abstinence syndrome was not considered.
CONCLUSIONS: Data regarding maternal medication use must be included in patient care system software (PCS, IBM) for immediate detection of possible drug interactions in newborns. This software could be a useful tool for the systematic detection of ADR and improvement of drug safety in neonatal patients. Using computerized methods could allow a significant gain in time and cost-effectiveness.

LATE BREAKERS

Adult Medicine

340. Hyperglycemia and insulin practices among medical patients in a community teaching hospital. *Pamela M. Moye, Pharm.D., BCPS,*[1] Lisa M. Lundquist, Pharm.D., BCPS,[1] Janene Marshall, Pharm.D.,[2] Candace Sampson, Pharm.D.[3]; (1) Mercer University College of Pharmacy and Health Sciences, Atlanta, GA; (2) Chicago State University School of Pharmacy, Chicago, IL; (3) Hampton University School of Pharmacy, Hampton, VA
PURPOSE: To determine the relationship between insulin ordering practices and glycemic control on an internal medicine service.
METHODS: A prospective chart review was performed from February to April 2009. Patients were eligible for inclusion if they were admitted to an internal medicine service (IMS) and had a known diagnosis of diabetes mellitus or a random glucose measurement of more than 200 mg/dL at admission; exclusion criteria included diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemia. Patients were identified through the pharmacy database by insulin orders. Data from the medication administration record (MAR) were collected for each patient for 5 days. Study outcomes included the percentage of glucose readings defined as hypoglycemia (60 mg/dL or less) and hyperglycemia (180 mg/dL or greater). All process and outcome measures were analyzed using descriptive statistics.
RESULTS: Ninety patients were prospectively identified for inclusion in the study. Fourteen patients were excluded: 10 who did not have diabetes or inpatient hyperglycemia, 2 who were not managed by an IMS, and 2 who had DKA. Seventy patients met inclusion criteria: 61% female and mean age (SD), 64.8 (12.8) years. Three patients had no previous diagnosis of diabetes; 50% were taking insulin before admission, and 30% had severe diabetic complications. The mean percentage of hyperglycemia readings per patient was 49%. Basal insulin was ordered for 59% of patients; scheduled rapid acting was ordered for 28%. No change was made to the insulin orders of 55% of patients who had at least one episode of hypo- or hyperglycemia. Based on the MAR, 94% of patients had at least one error in insulin dosing and/or inaccurate documentation.
CONCLUSIONS: Management of hyperglycemia on an IMS revealed several deficiencies in process and outcome. Possible targets for improvement include educating physicians, nurses, and pharmacists on the importance of rapid-acting insulin with meals, daily insulin adjustments in response to hyperglycemia, and appropriate administration of sliding scale insulin.

Ambulatory Care

341. Interventions by clinical pharmacists leading to improved diabetes care in a safety net population. *Rory E. O'Callaghan, Pharm.D.*, Steven Chen, Pharm.D., FASHP, Kathleen Johnson, Pharm.D., MPH, Ph.D.; University of Southern California School of Pharmacy, Los Angeles, CA
PURPOSE: Diabetes is an epidemic in the United States, accounting for almost 20% of national health care costs. As the economy struggles, the demand for safety net clinic services rises. These clinics serve a predominance of ethnic minorities who have an increased prevalence of diabetes. Studies have demonstrated an association between clinical pharmacy services and improved diabetes control; however, most studies provide limited details on the specific types of treatment interventions made by clinical pharmacists. The primary objective of this study was to identify the types of problems addressed and interventions made by clinical pharmacists for patients with diabetes receiving care in safety net clinics. The secondary objective was to describe commonly occurring medication safety problems and the interventions implemented to resolve them.
METHODS: This was a retrospective analysis of 77 adults with diabetes receiving clinical pharmacy services in safety net clinics from January 1, 2004, to December 31, 2006. Data regarding specific problems, interventions, and outcomes were collected from an electronic medical record and grouped into predefined discrete categories.
RESULTS: Eight hundred thirteen problems with corresponding interventions were identified in the 77 patients reviewed. Problems were categorized into four groups including quality of care (65%), medication safety (29%), cost (5%), and legal/dispensing (less than 1%). Pharmacists most commonly changed doses or drug intervals (31%), added medications (27%), or substituted medications (20%). Medication safety problems most commonly involved underuse of medication or the risk of an adverse drug reaction. Ninety-four percent of medication safety problems were resolved or improved by clinical pharmacist interventions.
CONCLUSION: Clinical pharmacists improve patient outcomes by identifying quality-of-care issues. They frequently optimize medication therapy by increasing the number and dosage of medications. Pharmacists play an important role in identifying and resolving medication safety issues. Pharmacist interventions almost always result in resolution or improvement of the identified problem.

Critical Care

342. Evaluation of electrolyte serum control after the institution of an electrolyte repletion protocol in a surgical intensive care unit.

Jodianne Couture, MS(Pharm),[1] Anne Letourneau, MS(Pharm),[1] Annie Dubuc, MS(Pharm),[1] Hughes Blain, MS(Pharm),[1] Julie Perron, MS(Pharm),[1] Benoit Cossette, M.S.,[1] David R. Williamson, MS(Pharm), BCPS[2]; (1) Centre Hospitalier Universitaire de Sherbrooke, Fleurimont, Quebec, Canada; (2) Faculté de pharmacie, Université de Montréal, Montreal, Quebec, Canada

PURPOSE: Electrolyte imbalances are frequently encountered in the intensive care unit (ICU). Implementation of electrolyte repletion protocols (ERPs) to ensure and facilitate proper electrolyte control is common practice; however, few protocols have been evaluated and validated. This study aimed at evaluating the effectiveness and safety of an ERP in a surgical ICU at the Centre Hospitalier Universitaire Sherbrooke (CHUS).

METHODS: This retrospective study compared patients receiving the ERP with historical controls receiving traditional electrolyte replacement. The primary objective was to compare the mean proportion of patients who achieved potassium normal serum concentrations on daily morning controls. The magnesium, phosphate, and ionized calcium normal serum concentrations were also evaluated. The safety of the protocol was estimated by comparing the proportions of morning control that were below or above the normal values for each electrolyte and the proportion of ionized calcium-phosphate product more than 2.2 $mmol^2/L^2$. The incidence of cardiac arrhythmias, adhesion to the protocol, and nurses' satisfaction were also evaluated.

RESULTS: A total of 627 cardiac surgery patients were included, 312 in the control group and 315 in the ERP group. The mean proportion of normal morning potassium controls was significantly higher in the ERP group (84.3%) than in the control group (80.3%) (p=0.039). No differences in the normal serum concentrations were found with other electrolytes. The mean proportion of serum concentrations below and above the normal for the different electrolytes was similar between the groups. The incidence of cardiac arrhythmias was also similar between both groups. Adhesion to the protocol was 87%, 86%, 78%, and 78% for potassium, magnesium, phosphate, and calcium, respectively. Nurses were satisfied with the protocol and felt its use should be maintained.

CONCLUSION: Using an ERP in an ICU is efficacious, safe, and well accepted by the multidisciplinary team.

ACCP Chapter Posters

343. Highlighting the Dallas Fort Worth Chapter of the American College of Clinical Pharmacy (DFW-ACCP). *Marissa E. Quinones, Pharm.D.,*[1] Lisa M. Chastain, Pharm.D.,[2] Susan M. Duquaine, Pharm.D., BCPS,[3] Michelle L. Horan, Pharm.D.,[4] April Allen, Pharm.D.[5]; (1) Parkland, Dallas, TX; (2) Texas Tech University Health Sciences Center School of Pharmacy Dallas/Ft. Worth Regional Campus, Dallas, TX; (3) VA North Texas Health Care System, Dallas, TX; (4) North Texas Veterans Affairs, Dallas, TX; (5) Texas Tech HSC School of Pharmacy Dallas Ft. Worth Regional Campus, Dallas, TX

PURPOSE: To highlight the Dallas Fort Worth Chapter of the American College of Clinical Pharmacy (DFW-ACCP).

BACKGROUND: The chapter was established in 1998 by clinical pharmacists in the area. Chapter membership consists of pharmacists, residents, and students who practice in a wide range of settings. The current officers are in charge of finding nonpromotional educational programs for the membership, and each officer plays a major role in ensuring the chapter is reaching goals and growing each year. The officers plan about three or four educational sessions/meetings per year, including a resident clinical controversial competition and cosponsored educational session at the Texas Health System Pharmacists annual meeting. This year, we are offering an opportunity for community service.

METHODS: A survey was conducted in 2006 and 2009 through an Internet Web site (*SurveyMonkey.com*) and sent to the membership by e-mail. The survey asked a variety of questions regarding degrees, practice sites, participation in organizations, and information regarding topics for future meetings, as well as if the chapter would consider an increase in dues.

RESULTS: DFW-ACCP membership has increased during the past 3 years. From 2006 to 2009, there has been an increase in the number of our members with doctor of pharmacy degrees (84.9%–92.3%) and BCPS certification (67.7%–80%). Most of our members continue to practice in hospital-clinical settings or academia and specialize in internal medicine or ambulatory care. Most of our members continue to participate in national organizations, such as ACCP and ASHP. We found that the primary motivation for participating in the chapter was networking (71%). Ninety-seven percent of our members would consider an increase in dues by $5–$10 for 2009.

CONCLUSIONS: DFW-ACCP continues to grow each year and has provided networking and educational opportunities for our members.

Drug Information

344. Effect of alvimopan on clinical outcomes after bowel resection (BR) with intravenous patient-controlled analgesia (IV-PCA) or thoracic epidural analgesia: a 6-month drug use evaluation (DUE) at a community health care system. *Abbey Pitzenberger, Pharm.D.*; Mercy Medical Center – North Iowa, Mason City, IA

PURPOSE: This 6-month DUE assessed alvimopan, an oral peripherally acting mu-opioid receptor antagonist approved by the FDA in May 2008 to accelerate time to upper and lower GI recovery after partial large or small BR. Alvimopan is available for short-term in-hospital use for hospitals enrolled in the Entereg Access Support and Education (E.A.S.E.) program.

METHODS: From September 2008 to March 2009, 30 patients with open or laparoscopic BR who received alvimopan 12 mg (once preoperatively and then twice daily postoperatively for 7 days or less or until hospital discharge; max = 15 doses) were randomly selected and compared with 30 patients who did not receive alvimopan. Return to bowel function (first bowel movement) and length of stay (LOS) were collected.

RESULTS: The mean age was 68.5 years, and 73% and 40% of patients were male in alvimopan and control groups, respectively (data from four surgeons). Ninety-three percent and 80% of patients in the alvimopan and control groups underwent an open BR, respectively. Opioid-based thoracic epidurals were used in 53% of the alvimopan group patients and in 67% of the control group patients; all other patients received opioid-based IV-PCA. Patients in the alvimopan group received a mean of 8.5 doses and recovered bowel function 2.0 days earlier than patients in the control group (alvimopan 12 mg, 2.7 days; control, 4.7 days). Patients in the alvimopan group remained in the hospital 1.8 days less than patients in the control group (alvimopan 12 mg, 5.6 days; control, 7.4 days). Differences between alvimopan and control groups were similar regardless of route of opioid administration.

CONCLUSION: Because of this DUE, continued use of alvimopan is recommended. Although the cost of alvimopan is almost $60/dose, potential cost savings could be realized because of substantial reductions in LOS. Moreover, quicker recovery of bowel function may enable a patient to switch to oral rather than intravenous medications (a more cost-effective option).

Education/Training

345. Comparative efficacy of conventional teaching methods with and without an active learning exercise in teaching doctor of pharmacy students medication adherence counseling skills. *Kari J. Furtek, Pharm.D.*, Mark Best, M.D., MBA, MPH, Teresa Schweiger, Pharm.D., BCPS, Heather Petrelli, M.S., Julie Wilkinson, Pharm.D., BCPS; Lake Erie College of Osteopathic Medicine School of Pharmacy, Bradenton, FL

PURPOSE: The World Health Organization recommends that medical and allied health care institutions develop a medication adherence curriculum. We sought to compare students' abilities to identify, assess, and develop a medication adherence treatment plan between those who did and did not participate in a unique active learning exercise as part of a newly developed medication adherence course.

METHODS: Students who consented and enrolled in the study were

randomized 1:1 to complete the exercise or serve as controls. Active group participants took a candy placebo regimen twice daily for 3 months and received monthly adherence counseling from the course instructor. Adherence was quantified using MEMS caps, refill history, pill counts, and subjective reporting. Groups were compared using descriptive statistics. A t-test was used to compare final examination scores between the groups. Adherence rates (prescribed number of doses taken) were correlated with examination scores using the Pearson correlation coefficient.
RESULTS: Thirty-five students were enrolled (17 control; 18 active group). Mean age, race, sex, and cumulative grade point average were similar between the groups at baseline (p=NS). Final examination scores were higher in the active group (82.8% ± 8.7) compared with control (79.8% ± 7.4%); however, this difference was not statistically significant (p=0.284). There was no statistically significant correlation between adherence rate and final examination score; however, mean adherence scores improved over time with adherence rates of 74.9%, 77.1%, and 79.6% at months 1, 2, and 3, respectively. Students in the active group used empathetic responses better than controls and scored higher in five of seven adherence counseling techniques.
CONCLUSION: Students participating in the active learning experience achieved higher mean final examination scores and used empathetic responses better than controls. Adherence rates to the placebo regimen increased over time with pharmacist intervention. Future studies using this technique may improve doctor of pharmacy students' medication adherence counseling skills.

346E. Clinical interventions by doctor of pharmacy students on advance pharmacy practice experience at a community teaching hospital: acceptance rates and therapeutic areas. *Pamela M. Moye, Pharm.D., BCPS*, Lisa M. Lundquist, Pharm.D., BCPS, Phillip S. Owen, Pharm.D., BCPS; Mercer University College of Pharmacy and Health Sciences, Atlanta, GA
PURPOSE: To determine acceptance rates and therapeutic areas of pharmacy students' clinical interventions at a community teaching hospital. In addition, to determine the types of clinical interventions that give students opportunities to interact with other health care professionals.
METHODS: Clinical interventions of fourth-year pharmacy students completing faculty-precepted advanced pharmacy practice experiences (APPEs) were documented and compiled. The students' recommendations were made to resident and/or attending physicians in ambulatory care clinic, during critical care daily rounds, and during internal medicine daily rounds. Interventions, both accepted and declined, from May 2008 to October 2008 were included in the study. All intervention data were recorded on a data collection form and separated into respective therapeutic areas: cardiology, endocrinology, hematology, infectious diseases, musculoskeletal/pain, neurology, pulmonology, and other (gastroenterology, women's health, and genito-urology). Descriptive statistics were used to analyze study outcomes.
RESULTS: A total of 455 clinical interventions were attempted (246 ambulatory care, 134 internal medicine, 75 critical care). The overall acceptance rate was 80%. Therapeutic areas of intervention included cardiology (n=169, 82% accepted), infectious disease (n=61, 71% accepted), other (n=59, 81% accepted), endocrinology (n=57, 90% accepted), hematology (n=34, 71% accepted), neurology (n=32, 75% accepted), musculoskeletal/pain (n=28, 79% accepted), and pulmonology (n=15, 93% accepted).
CONCLUSIONS: In accordance with ACPE's APPE standards and guidelines, pharmacy students on faculty-precepted APPE have the potential for more than 400 opportunities to interact and collaborate with other health care professionals and affect patient care in various therapeutic areas. With 167 interventions attempted, cardiology may provide students with the most opportunities to make clinical interventions, but with acceptance rates of 90% and 93%, endocrinology and pulmonology provide the highest acceptance of student interventions. The types of interventions seen most often were recommendations for medication initiation/ discontinuation, medication dose/frequency changes, and laboratory monitoring.
Presented at American Association of Colleges of Pharmacy, Boston, MA, July 18–22, 2009.

Gastroenterology

347. Assessing the effect of proximal Roux-en-Y gastric bypass on upper gastrointestinal transit time: a pilot study. *Lingtak-Neander Chan, Pharm.D., BCNSP*,[1] Yvonne S. Lin, Ph.D.,[2] John R. Horn, Pharm.D.,[1] David R. Flum, M.D., MPH,[3] Brant K. Oelschlager, M.D.,[3] Rodney J.Y. Ho, Ph.D.,[2] Danny D. Shen, Ph.D.[1]; (1) University of Washington, Department of Pharmacy, Seattle, WA; (2) University of Washington, Department of Pharmaceutics, Seattle, WA; (3) University of Washington, Department of Surgery, Seattle, WA
PURPOSE: This pilot study aimed to determine the effect of Roux-en-Y gastric bypass operations (RYGBs) on upper gastrointestinal transit time.
METHODS: Twelve morbidly obese patients undergoing RYGBs were enrolled in this study. Upper gastrointestinal transit time was determined by comparing the pharmacokinetics of oral acetaminophen absorption. Each patient received 1500 mg of acetaminophen oral liquid after an overnight fast on three separate study visits: pre-RYGB and 3 and 12 months after RYGB. Plasma samples were collected at 0, 10, 20, 30, 40, 50, 60, 75, 90, 120, 180, 240, 360, 720, and 1440 minutes after dose administration. Plasma acetaminophen concentrations were determined using HPLC. Pharmacokinetic parameters were estimated using WinNonlin. Absorption kinetics from the two postoperative visits were compared with pre-RYGB using the area under the concentration-time curve (AUC) from time zero to the time when peak plasma concentration was observed using the trapezoidal rule.
RESULTS: All patients received proximal RYGBs, with the average length of the Roux limb at 127.5 cm. The average body mass indices were 51.1, 40.7, and 38.3 kg/m^2 at pre-RYGB, 3 months, and 12 months postoperatively, respectively. The mean peak concentration was almost doubled after RYGB, and the mean time to peak concentration was significantly shortened. The mean estimated volume of distribution was significantly lower, and the mean clearance was significantly higher after RYGB (35 ± 15, 23 ± 11, and 23 ± 11 L/hour at pre-RYGB, 3 months, and 12 months, respectively). The terminal half-life was unchanged. The mean fraction of the AUC from time zero to peak represented 10% of the AUC_{inf} at baseline and 5% of the AUC_{inf} postoperatively.
CONCLUSION: Upper gastrointestinal transit time, as determined by the oral absorption rate of acetaminophen liquid, is significantly shortened after proximal RYGB; the change may also have led to incomplete oral bioavailability. Concomitant changes in glucuronidation and/or sulfation of acetaminophen are also possible.

Geriatrics

348E. Are the effects of oxybutynin on cognition dependent upon the route of administration – topical or oral? A double-blind placebo controlled study employing sensitive cognitive and psychomotor testing. Gary G. Kay, Ph.D.,[1] David R. Staskin, M.D.,[2] Scott MacDiarmid, M.D.,[3] Marilyn McIlwain, B.S.,[4] *Naomi V. Dahl, Pharm.D.*[4]; (1) Cognitive Research Corporation, St. Petersburg, FL; (2) Tufts University School of Medicine, Boston, MA; (3) Alliance Urology Specialists, Greensboro, NC; (4) Watson Laboratories, Morristown, NJ
PURPOSE: Oral oxybutynin has been demonstrated to impair cognitive function in older adults. This study compares the effects of topically administered oxybutynin chloride gel (OTG) and of immediate-release oral oxybutynin (OXY-IR) with placebo on older adults' performance during a battery of cognitive and psychomotor tests (CPTs).
METHODS: In this double-blind study, healthy subjects, 60–79 years, were randomized 1:1:1 to 1 g of OTG 10% once daily plus placebo capsules, OXY-IR 5 mg 3 times/day plus placebo gel, or placebo gel plus placebo capsules for 1 week. Subjects returned to the clinic to take study medication under observation and to undergo CPTs. Differences in scores among treatment groups were compared by ANCOVA. Pairwise comparisons were made between each active group and placebo.
RESULTS: One hundred fifty-two subjects were enrolled (mean age, 68.2 ± 5.76 years; 99 female; 140 white). Performance on the

primary end point, name-face association delayed recall, showed no significant treatment effect (p=0.273). Pairwise comparisons also revealed nonsignificant differences (OTG vs. placebo, p=0.155; OXY-IR vs. placebo, p=0.177). The Misplaced Objects Test showed a significant treatment effect (p=0.023), with placebo and OTG scores both improving and OXY-IR decreasing (OTG vs. placebo, p=0.368; OXY-IR vs. placebo, p=0.069).
Remaining tests of delayed and immediate recall showed no significant treatment group–related differences. Analysis of reliable change scores in the Hopkins Verbal Learning Test-Total Free Recall indicated that 10 subjects showed a significant decline on OXY-IR, compared with 6 placebo and 5 OTG subjects.
Dry mouth was the most common adverse event (OXY-IR 75%, OTG 6%, placebo 8%).
CONCLUSION: In healthy elderly adults, OTG is comparable to placebo in its lack of effects on sensitive tests of recent memory and other cognitive functions. It is unknown whether the central nervous system effects seen with oral oxybutynin are dependent on peak plasma concentrations of the parent compound and/or the metabolite *N*-desethyloxybutynin.
Presented at the 39th Annual Meeting of the International Continence Society, San Francisco, CA, September 29–October 3, 2009.

HIV/AIDS

349. Pharmacy experiences of HIV-positive women. *Jennifer M. Cocohoba, Pharm.D.,*[1] Mardge Cohen, M.D.,[2] Haihong Hu, MPH,[3] Anjali Sharma, M.D., M.S.,[4] Stephen J. Gange, Ph.D.,[5] Ruth M. Greenblatt, M.D.[1]; (1) University of California, San Francisco, San Francisco, CA; (2) Stroger Hospital and Rush Medical College, Chicago, IL; (3) Georgetown University Medical Center, Washington, DC; (4) SUNY Downstate Medical Center, Brooklyn, NY; (5) Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
PURPOSE: Optimal use of pharmacy services is essential for maintaining health. Because of stigma, privacy, and complex therapies, patients who are HIV positive may use pharmacies suboptimally, such as going to multiple pharmacies, going to distant pharmacies, or avoiding pharmacist consultation. Patients with HIV may also be at increased risk of adverse pharmacy experiences such as medication errors or privacy violations. The objective of this study was to determine the association between HIV status and suboptimal pharmacy use or adverse pharmacy experiences.
METHODS: Cross-sectional study nested within the Women's Interagency HIV Study, October 2007–April 2008. Logistic regression assessed associations between HIV and suboptimal pharmacy use or adverse pharmacy experiences and between suboptimal pharmacy use, adherence, and virologic suppression.
RESULTS: Participants (n=807) were HIV positive (82%), African American (65%) women with a median age of 45 years (IQR = 39–51). Women who were HIV positive were as likely as women who were HIV negative to use multiple pharmacies (24%, p=0.9) or pharmacies distant from their homes (6% vs. 3%, p=0.2). Women who were HIV positive were more likely to avoid talking to the pharmacist (14% vs. 5%, p=0.003). In multivariate analyses, HIV (OR = 1.58; 95% CI: 1.06–2.37) and depression (OR = 1.87; 95% CI: 1.37–2.56) were associated with using pharmacies suboptimally, whereas having a high school education was protective (OR = 0.68; p=0.03). Similar proportions of women who were HIV positive and HIV negative reported experiencing pharmacy medication errors (10% vs. 7%, p=0.4) or privacy violations (9% vs. 5%, p=0.2). Having a high school education (OR = 0.51; 95% CI: 0.32–0.81) and depression (OR = 1.75; 95% CI: 1.17–2.62), but not HIV status, were associated with reporting an adverse pharmacy experience in multivariate analyses.
CONCLUSION: Women who are HIV positive appear to be at risk of medication errors or privacy violations similar to women who are HIV negative, although they are more likely to avoid talking to the pharmacist. Pharmacists should increase efforts to consult with women who are HIV positive to avoid missing opportunities to provide pharmaceutical care.

Infectious Diseases

350. Clinical experience with daptomycin for the treatment of methicillin-susceptible *Staphylococcus aureus* (MSSA). *Marianne Billeter, Pharm.D., BCPS,*[1] Joseph J. Kishel, Pharm.D.,[2] Ellie Hershberger, Pharm.D.,[2] Katherine P. Holloway, Pharm.D.[2]; (1) Ochsner Clinic Foundation, New Orleans, LA; (2) Cubist, Lexington, MA
PURPOSE: β-Lactams are first-line therapy for MSSA. Vancomycin is used in patients intolerant of β-lactams; however, it has been associated with higher relapse rates and delayed responses compared with nafcillin. In controlled trials, daptomycin was noninferior to anti-staphylococcal β-lactams. This study evaluated outcomes with daptomycin in patients with MSSA infections.
METHODS: All patients with confirmed MSSA infection in CORE 2005–2008, a retrospective, multicenter, observational registry, were studied. The primary outcome (cure, improved, failure, or nonevaluable) was the investigator's clinical assessment at the end of daptomycin therapy; a secondary outcome was the sponsor assessment, which additionally assessed daptomycin discontinuations because an adverse event, death attributable to any cause, and any indicator of lack of response as failures. Success was defined as cure or improved. The patient characteristics and efficacy analysis were based on the investigator-evaluable population; all patients were included in the safety analysis.
RESULTS: Four hundred seventeen patients with MSSA infection were identified; 341 (82%) had an evaluable outcome: 26% were older than 65 years; 11% had CrCl less than 30 mL/minute. Infection types were cSSSI 83 (24%) of 341, bacteremia 79 (23%) of 341, osteomyelitis 64 (19%) of 341, foreign body 40 (12%) of 341, and endocarditis 11 (3%) of 341. Twenty-one percent and 9% reported β-lactam and vancomycin allergy, respectively. Daptomycin median (min, max) initial dose was 6 mg/kg (3, 9), and length of therapy was 14 days (1, 166). Two hundred sixty-seven (78%) of 341 patients received prior antibiotics, and 26% experienced failure in prior therapy. The primary outcome of success was reported in 91% (310 of 341), including 16 (84%) of 19 whose prior vancomycin therapy had failed. The secondary outcome of success was 84% (292 of 349). Twenty-nine patients (7%) experienced 29 adverse events possibly related to daptomycin; 7 were serious, and 16 (4%) of 417 discontinued therapy because of treatment-related adverse events.
CONCLUSION: Daptomycin is an effective treatment in patients with MSSA infections; therefore, it may be an appropriate empiric therapy for *S. aureus* infections.

351E. Clinical experience with daptomycin for the treatment of vancomycin resistant enterococcal bacteremia (VRE-B). Monica M. Gaffney, Pharm.D.,[1] Peggy S. McKinnon, Pharm.D.,[1] *John F. Mohr, Pharm.D.,*[1] Marcus J. Zervos, M.D.[2]; (1) Cubist, Lexington, MA; (2) Henry Ford Health System and Wayne State University School of Medicine, Detroit, MI
PURPOSE: Enterococci are the second most common cause of nosocomial bacteremia, with mortality rates of 17%–36%. Viable treatment options for VRE-B are lacking. This study describes daptomycin outcomes for patients with VRE-B.
METHODS: All patients with VRE-B in CORE 2007–2008, a retrospective, multicenter, observational registry, were studied. The primary outcome was the investigator assessment (success/failure) at the end of daptomycin therapy; a secondary sponsor outcome classified patients' therapy as a failure if daptomycin was discontinued because of an adverse event (AE) or the patient died of any cause. Patient characteristics were based on the investigator-evaluable population; all patients were included in the safety analysis.
RESULTS: One hundred thirty-nine patients with VRE-B were identified; 113 (81%) had an evaluable outcome. Thirty-six percent were older than 65 years; 39% ANC less than 1000 cells/mm^3; 44% received daptomycin in an ICU; 22% had CrCl less than 30 mL/minute, and 20% were on dialysis. Forty-five percent had catheter-related bacteremia, 11% had complicated skin infection, and 7% had endocarditis. Pathogens were 82% VR *E. faecium*, 11% VR *E. faecalis,* and 8% VR *Enterococcus* sp. Median daptomycin

(min, max) initial dose was 6 mg/kg (4, 8.3), and median daptomycin length of therapy (IQR) was 14 days (7–16). Eighty-one percent received 6 mg/kg/dose or more; 27% of patients received prior VRE therapy (90% linezolid). Success was observed in 89 (79%) of 113: 92% in catheter-related bacteremia and 68% for all others. No statistical differences in outcomes were found when assessed by initial dose, first-line use, or renal dysfunction. Sponsor success rate was 74 (58%) of 128 because of 30 patients whose therapy was reassessed as a failure (26 deaths, 4 discontinued because of an AE). Seventeen patients (12%) experienced 31 AEs that were possibly related to daptomycin; three were serious. Discontinuation rates attributable to any AE were 7 (5%) of 139, and the overall mortality rate was 39 (28%) of 139.
CONCLUSION: In this population, daptomycin appears to be a useful agent for VRE-B. Further studies are warranted.
Presented at Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology, San Francisco, CA, September 12–15, 2009.

352E. Outcomes with daptomycin in the treatment of *Staphylococcus aureus* infections with varying vancomycin minimum inhibitory concentrations. Jason A. Crompton, Pharm.D., Donald S. North, Pharm.D., MinJung Yoon, MPH, Judith N. Steenbergen, Ph.D., *Kenneth C. Lamp, Pharm.D.*; Cubist Pharmaceuticals, Lexington, MA
PURPOSE: Recent recommendations for *S. aureus* (SA) treatment suggest alternative agents when vancomycin MICs are 2 µg/mL or greater. This study examined the outcome of patients treated with daptomycin for SA infections with recorded vancomycin MICs.
METHODS: All patients with SA infections with vancomycin MICs in CORE 2005–2008, a retrospective, multicenter, observational registry, were studied. The outcome (cure, improved, failure, or nonevaluable) was the investigator's assessment at the end of daptomycin therapy. Success was defined as cure or improved.
RESULTS: A total of 1158 patients with SA infections with vancomycin MICs were identified; of these, 729 (63%) had an evaluable outcome together with discrete vancomycin MICs (MIC less than 2: 606 [83%]; MIC of 2 or more: 123 [17%]). The MIC of 2 or more group included three VISAs (MIC of 4) and one VRSA (MIC more than 256). Fifty-two percent were male, and 59% were older than 50. No differences were found between vancomycin MIC groups for daptomycin (initial dose, duration, monotherapy, first-line use [19%]), prior vancomycin (47%), or failure (11%). The vancomycin MIC group of 2 or more had more patients with hematologic malignancy (7% vs. 3%; p=0.02). The success rates for vancomycin MICs less than 2 and for 2 µg/mL or more, respectively, were as follows: all patients (n=729), 571 of 606 (94), 113 of 123 (92); cSSSI (n=263), 214 of 222 (96), 39 of 41 (95); uSSSI (n=124), 102 of 103 (99), 21 of 21 (100); bacteremia (n=135), 99 of 107 (93), 24 of 28 (86); endocarditis (n=25), 15 of 19 (79), 4 of 6 (67); osteomyelitis (n=99), 82 of 86 (95), 12 of 13 (92); all others (n=83), 59 of 69 (86), 13 of 14 (93); none was statistically different. A multivariate logistic regression also failed to identify vancomycin MIC as a predictor of daptomycin failure. Adverse event rates were similar: vancomycin MICs less than 2 (7%) and 2 or greater (9%).
CONCLUSION: In this diverse population, daptomycin was associated with similar outcomes for patients whether the vancomycin MIC was less than 2 or 2 µg/mL or greater. Further studies are warranted.
Presented at Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology, San Francisco, CA, September 12–15, 2009.

353. Potential impact of medications on *Clostridium difficile* toxin screening and cultures. *Jean A. Patel, Pharm.D., BCPS,*[1] Marc H. Scheetz, Pharm.D., M.S., BCPS,[2] Michael J. Postelnick, RPh, BCPS[1]; (1) Northwestern Memorial Hospital, Department of Pharmacy, Chicago, IL; (2) Midwestern University, Department of Pharmacy Practice, Chicago, IL
PURPOSE: This study evaluated inpatients being screened for *Clostridium difficile* infection (CDI) to identify pharmacologic causes of diarrhea that are often overlooked.
METHODS: A retrospective cohort study evaluated inpatients with CDI screens between June 1, 2008, and June 30, 2008. Data collected included number of CDI toxin/culture screens, test outcome, receipt of target drugs known to cause diarrhea, and receipt and duration of treatment directed at CDI.
RESULTS: Eighty-eight patients (191 individual screens) were identified and reviewed. Seven patients (8.0%) tested positive for CDI. Nineteen patients (21.6%) with negative screens received target medications at the time of initial screening, and 18 (95%) of these continued to receive target medications for at least one additional dose after initiation of CDI screening. Target medications most frequently encountered included senna/docusate (n=10), metoclopramide (n=5), lactulose (n=3), docusate (n=2), and polyethylene glycol (n=2). Of the 81 patients with negative screens, 18 (22.2%) were treated empirically with metronidazole for an average of 5.1 days (range, 1–19). No patients who were negative for CDI were treated with oral vancomycin during this time.
CONCLUSIONS: Few patients (8%) tested positive for CDI. Reasons for diarrhea were more likely attributable to pharmacologic concurrence of medications associated with diarrhea, and most patients never had these nonessential therapies discontinued. Assessment of concomitant medications in the patient being examined for CDI is prudent, and preemptive discontinuation of the nonessential medications likely to cause diarrhea could improve screening paradigms.

Managed Care

354. Impact of a prior authorization process on exenatide utilization. *Anthony G. Staresinic, Pharm.D.*, William Reay, Pharm.D.; Physicians Plus Insurance Corporation, Madison, WI
PURPOSE: To evaluate exenatide's use in a small managed care plan and the impact of a drug prior authorization process on persistence to therapy.
METHODS: The study period was January 1, 2006, to May 31, 2009. To be included, members had to have at least one paid claim for exenatide, at least 12 months of continuous enrollment, at least 3 months of pharmacy claim history before the index claim for exenatide, and at least 6 months of pharmacy claim history after the exenatide index claim.
RESULTS: During the study period, 189 members received at least one prescription for exenatide. Exenatide use remained flat during the study period. After 12 months, 67% of the members remained on exenatide. For a subset of members, removal of the prior authorization resulted in a lower 12-month persistence rate compared with the group undergoing the prior authorization. The largest decrease in persistence occurred within the first 3 months after starting therapy. In a subset of members, starting exenatide therapy during the prior authorization process had a 17% decline in total medical costs, whereas removal of the prior authorization process demonstrated a median increase of 85%.
CONCLUSION: This study is one of the first to illustrate the potential clinical impact of a drug prior authorization program. The largest drop in the persistence rate within the first 3 months of therapy likely reflects tolerability to the medication, whereas decreases in persistence later on reflect efficacy and adherence issues. Exenatide drug prior authorization may be an effective way of assisting providers in proper patient selection.

Medication Safety

355. Evaluation of the efficacy of pharmacists performing medication reconciliation in a nursing home in Taiwan. *Chun Nan Kuo, M.S.*; Wanfang Hospital, Taipei, Taiwan
PURPOSE: According to the published data, 20%–72% of the adverse events of hospitalization were adverse drug events and medication errors, and 7%–12% of them may cause permanent disabilities and death. Medication errors that might cause severe harm occur easily when patients are transferred between wards. Medication reconciliation is a process of verifying medication use, identifying variances, and rectifying medication errors during transitions. In Taiwan, there are an average of 2.36 chronic diseases in the elderly aged 65–74 years and 2.75 chronic diseases in the

elderly older than 75 years. In addition, residents in nursing homes use, on average, 5.74 medications. Under this condition, medication reconciliation plays an important role in nursing homes.
OBJECTIVE: To evaluate the efficacy of pharmacists performing medication reconciliation in the nursing home of Wanfang Hospital in Taiwan.
METHOD: We compared the number and types of discrepancies before and after 3 months of performing medication reconciliation on admission and discharge for nursing home residents. The primary end point was the difference in the number of medication discrepancies before and after pharmacists performed medication reconciliation.
RESULTS: Before performing medication reconciliation, there were 209 discrepancies, 9% of which were undocumented discrepancies, not explained in progress notes. After performing medication reconciliation, there were originally 266 discrepancies, 17% of which were undocumented discrepancies. Pharmacists consulted physicians about the undocumented discrepancies, and 19 discrepancies were corrected. Comparing the intentional changes and corrected discrepancies of undocumented discrepancies in two groups, pharmacists performing medication reconciliation was related to the decrease in discrepancies ($p<0.01$). Most discrepancies were new drugs and omission in two groups.
CONCLUSION: Pharmacists performing medication reconciliation for nursing home residents is significantly related to reducing medication discrepancies.

Oncology

356. Cost-efficacy analysis of cetuximab in first-line treatment of kras wild-type metastatic colorectal cancer patients. *Armando Alcobia, Pharm.D.*, Ana Leandro, Pharm.D.; Hospital Garcia de Orta, Almada, Portugal
PURPOSE: In recent years, the therapy for metastatic colorectal cancer (mCRC) has evolved from single-agent chemotherapy (fluorouracil with leucovorin modulation) to combination regimens that include irinotecan or oxaliplatin (FOLFIRI and FOLFOX, respectively).The introduction of target therapeutics such as cetuximab greatly increased the associated costs. This drug was recently approved for first-line setting use, based on results published in the first half of 2009. The aim of this study was to evaluate the cost-efficacy of cetuximab in the first-line treatment of KRAS wild-type patients with mCRC.
METHODS: Based on the CRYSTAL and OPUS studies, the efficacy of FOLFIRI or FOLFOX, respectively, was evaluated, with or without cetuximab. The treatment costs were calculated on the basis of the direct cost of the drugs in 2009.
RESULTS: Adding cetuximab to FOLFIRI resulted in a marginal efficacy of 0.10 years (36 days) compared with FOLFIRI alone. The marginal costs associated were 33.127€ (U.S.$46.379). The incremental cost-efficacy ratio calculated for FOLFIRI plus cetuximab was 331.275€ (U.S.$463.786). The association of cetuximab with FOLFOX had an even smaller marginal efficacy (0.04 years = 14 days) compared with FOLFOX itself. The marginal costs were 25.588€ (U.S.$35.824). The incremental cost-efficacy ratio calculated for FOLFOX plus cetuximab was 639.706€ (U.S.$895.589).
CONCLUSION: Based on this analysis, the incremental cost-efficacy ratios calculated for the cetuximab regimens are too high to be considered cost-effective options. With limited budgets, cost-efficacy analyses are useful tools for the Pharmacy & Therapeutics Committee decisions on drug selection and for clinics in their therapeutic decision.

Pediatrics

357E. Nephrotoxicity associated with vancomycin in children. *Maximillian W. Jahng, Pharm.D.,*[1] Jennifer Le, Pharm.D., BCPS-ID,[2] Susan McKamy, Pharm.D., BCPS[3]; (1) Long Beach Memorial Medical Center, Long Beach, CA; (2) University of California San Diego, Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, CA; (3) Miller Children's Hospital, Long Beach, CA
PURPOSE: Extrapolated from studies in adults, the practice of attaining high vancomycin troughs is being applied to the pediatric population. This study aimed to estimate the incidence of nephrotoxicity associated with high troughs in children.
METHODS: Medical records of 171 patients 19 years and younger who received 48 hours or more of vancomycin from December 2007 to April 2009 were retrospectively reviewed. Nephrotoxicity was defined as increase in serum creatinine (SCr) of 0.5 mg/dL or greater or by 50% on at least 2 consecutive days.
RESULTS: Mean ages of patients with (n=24) and without (n=147) nephrotoxic reactions were similar (7.0 ± 6.4 and 6.8 ± 5.5 years, p=0.86). Race, gender, and underlying illnesses (e.g., renal disease) did not differ between groups. More patients with nephrotoxic reactions, compared with those without, stayed in the intensive care unit (92% vs. 53%, p=0.003; median duration, 18 [range, 3–140] vs. 5 [1–55] days, p<0.001), received other nephrotoxic agents (58% vs. 29%, p=0.004), and experienced shock (50% vs. 19%, p<0.001). Overall, 24 (14%) children experienced nephrotoxic effects, including 4 with SCr of 1.4 or more and 14 occurring before increase in vancomycin troughs. Median time to nephrotoxicity was 4 (2–13) days. Mean duration of vancomycin was longer (14 ± 8 vs. 9 ± 6 days, p=0.007), and clearances were lower (1.3 ± 1.2 vs. 2.4 ± 2.0 L/hour, p=0.021) in patients with nephrotoxic reactions. Patients with nephrotoxic reactions achieved higher mean trough levels (average, 18 ± 6 vs. 12 ± 5 mg/L; maximum, 32 ± 16 vs. 14 ± 7 mg/L; both p<0.001) but received lower vancomycin daily doses (mean, 36 ± 10 vs. 44 ± 11 mg/kg, p<0.001). Patients with average trough attainment of 15 mg/L or greater were more likely to experience nephrotoxic reactions (odds ratio, 5.9; 95% confidence interval: 2.3–15.2; p<0.001).
CONCLUSION: The incidence of nephrotoxic reactions associated with vancomycin was 14% in children. Vancomycin troughs of 15 mg/L or greater, together with other factors, increased the risk of nephrotoxicity. Renal function and trough levels should be closely monitored during therapy.
Presented at Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 12–15, 2009.

358. Our experience with enteral methadone to prevent opioid withdrawal due to sedation and analgesia in critically ill children. *Sean P. O'Neill, Pharm.D.*, Daniel Pung, Pharm.D., Vijay Srinivasan, M.D.; The Children's Hospital of Philadelphia, Philadelphia, PA
PURPOSE: To describe our experience with enteral methadone (EM) to prevent opioid withdrawal because of sedation and analgesia in critically ill children.
METHODS: An IRB-approved retrospective review of mechanically ventilated children admitted to the PICU from November 2004 to February 2008, 0–18 years, on fentanyl infusion more than 5 days. Data on demographics, severity of illness, withdrawal and pain scores, fentanyl and EM dosing, time to weaning, and rescue opioids were obtained. Patients were grouped as early wean group (EWG) if weaned in less than 48 hours or as late wean group (LWG) if weaned in more than 48 hours. Primary outcome was withdrawal scores. Other outcomes were pain scores, ventilator-free days (VFDs), length of stay (LOS), and rescue opioids. Analysis was by *t*-test, χ^2, and regression.
RESULTS: Forty-two children were included; 21 (50%) were EWG (25 hours, IQR 19–34 hours), and 21 (50%) were LWG (109 hours, IQR 77–240 hours). Both groups were similar in age, weight, gender, diagnosis, severity of illness, duration of fentanyl (9 vs. 10 days, p=0.48), and dose of fentanyl (6 vs. 6.8 µg/kg/hour, p=0.41) before wean. The EWG had lower withdrawal scores at 7 days (5 vs. 6, p=0.03), lower pain scores at 7 days (3 vs. 6, p=0.007), more VFDs (18 vs. 8 days, p=0.006), shorter LOS (17 vs. 39, p=0.05), and less rescue opioids (3 vs. 12, p=0.003). The starting daily median methadone dose was 2.3 times the daily median fentanyl dose in the EWG, compared with 1.1 times in the LWG (p=0.049). Both groups had similar starting EM (64 vs. 60 µg/kg, p=0.62); by 7 days, EWG had a significantly lower EM dose compared with LWG (30 vs. 189 µg/kg, p=0.02).
CONCLUSIONS: Weaning from opioid infusions to enteral methadone to prevent opioid withdrawal from dependence in critically ill children is feasible within 48 hours.

Pharmacoepidemiology

359. Estimating the risk of hepatotoxicity associated with fluoroquinolone use: a case-control study using the National Veterans Affairs Database. *Thamir M. Alshammari, M.S., BPharm,*[1] Kerry L. Laplante, Pharm.D.,[1] Brian J. Quilliam, Ph.D.,[2] Robert G. Laforge, ScD,[2] E. Paul Larrat, Ph.D.[2]; (1) University Of Rhode Island and Veterans Affairs Medical Center, Providence, RI; (2) University of Rhode Island, Kingston, RI

PURPOSE: The aim of the study was to assess the risk of hepatotoxicity with fluoroquinolone use (ciprofloxacin, levofloxacin, and moxifloxacin) among patients admitted to Veterans Affairs facilities nationally.

METHODS: Matched case-control design (time of admission) was used among a national cohort of patients admitted to all Veterans Affair facilities between January 1, 2002, and December 31, 2008. Conditional logistic regression was used to compute odds ratios and their 95% confidence interval (CI). Multivariate models were built to adjust and control for the potential clinical conditions or covariates that might influence hepatotoxicity risk. A stepwise backward elimination method (noncomputer generated) was used to build the final model.

RESULTS: A total of 7842 patients in the case group and 45,512 patients in the control group were entered in the final analysis. The mean age of the cases was 58 years, and most patients were males (96%) and white (59%), followed by the black race (18%) and Hispanic (4%). After adjusting for potential confounders, fluoroquinolone use was significantly (OR = 1.20; 95% CI: 1.04–1.40; p=0.012) associated with increased risk of developing hepatotoxicity.

CONCLUSION: The use of fluoroquinolones was associated with an increased risk of hepatotoxicity in a national cohort of veterans.

Pharmacogenomics/Pharmacogenetics

360. Association between severe anemia and genotypes of transmembrane serine protease 6 or transferrin in kidney transplant patients. *Jae-Wook Yang, Ph.D., Pharm.D.,*[1] Jisun Choi, Pharm.D.,[2] Ian V. Hutchinson, Ph.D., DSc,[3] Tariq Shah, M.D.,[4] David I. Min, Pharm.D.[5]; (1) University of Kansas, Kansas City, KS; (2) Western University of Health Sciences, College of Pharmacy, Pomona, CA; (3) USC School of Pharmacy, Los Angeles, CA; (4) National Institute of Transplantation and St. Vincent Medical Center, Los Angeles, CA; (5) Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Pomona, CA

Various factors affect posttransplant anemia in kidney transplant patients.

PURPOSE: This study aimed to determine the association between severe anemia, which requires erythropoietin therapy, and gene polymorphisms of transmembrane serine protease 6 (TMPRSS6) and transferrin (Tf).

METHODS: A total of 308 patients receiving kidney allografts between 2004 and 2007 were included in this study. Among these, 220 patients were determined to have anemia according to World Health Organization criteria (hemoglobin less than 13 g/dL [male] and less than 12 g/dL [female]). Severe anemia is defined as anemia with hemoglobin less than 10 g/dL and requiring EPO therapy after kidney transplant. Among anemic patients, 112 (50.9%) had severe cases. DNAs were genotyped for transferrin (rs3811647) and transmembrane serine protease 6 (rs4820268). Genotyping distribution was analyzed by contingency table 2x3, and allelic frequency was analyzed by 2x2; $p<0.05$ was regarded as statistically significant. The χ^2 test was used to confirm Hardy-Weinberg equilibrium of the observed allele frequencies.

RESULTS: Overall incidences of anemia were not significantly different among genotypes of TMPRSS6 (p=0.26) or Tf (p=0.59) in the study population; however, for severe anemia, the AG group (50.4%) or GG group (47.0%) was significantly more common compared with the AA group (29.1%) (p=0.013). The odds ratio for the patients with the G allele versus the A allele for severe anemia was 1.49 (1.05–2.12). There were no significant differences in the incidence of severe anemia among Tf genotypes (p=0.96).

CONCLUSION: This study demonstrated that genetic polymorphisms of TMPRSS6 might be associated with incidence of severe anemia in posttransplant anemia among kidney transplant recipients. Patients with the G allele in TMPRSS6 had a higher risk of severe anemia after kidney transplant; however, genotypes of Tf were not significantly associated with posttransplant anemia in our study.

Pharmacokinetics/Pharmacodynamics/Drug

361. Assessing the effect of Roux-en-Y gastric bypass on CYP3A activity. *Lingtak-Neander Chan, Pharm.D., BCNSP,*[1] Yvonne S. Lin, Ph.D.,[2] Brant K. Oelschlager, M.D.,[3] David R. Flum, M.D., MPH,[3] Danny D. Shen, Ph.D.,[1] John R. Horn, Pharm.D.,[1] Edward J. Kelly, Ph.D.,[2] Rodney J.Y. Ho, Ph.D.[2]; (1) University of Washington, Department of Pharmacy, Seattle, WA; (2) University of Washington, Department of Pharmaceutics, Seattle, WA; (3) University of Washington, Department of Surgery, Seattle, WA

PURPOSE: This pilot study aimed to determine how Roux-en-Y gastric bypass operations (RYGBs) affect *CYP3A* activity using midazolam as a probe drug.

METHODS: Twelve morbidly obese patients undergoing RYGB as medically indicated were enrolled in this longitudinal study. Each patient received 2 mg of midazolam as oral liquid after an overnight fast on three separate study visits: before RYGB (baseline) and 3 and 12 months after RYGB. Serial plasma samples were collected for 24 hours after dosing. Plasma midazolam and 1´-hydroxymidazolam concentrations were determined using LC/MS. Pharmacokinetic parameters were calculated by WinNonlin. Data from the two postoperative visits were compared with baseline using the Student paired t-test.

RESULTS: The age of the 12 patients was 44.2 ± 6.8 years, with average body mass indices of 51.1, 40.7, and 38.3 kg/m^2 at baseline, 3 months, and 12 months postoperatively, respectively. The average amount of weight loss at 3 and 6 months was 34.8 and 38.0 kg, respectively. Nine patients completed all three phases of the midazolam study. After RYGB, the peak concentrations of both midazolam and 1´-hydroxymidazolam were higher, and the time to peak concentration occurred earlier. The mean midazolam area under the plasma concentration-time curve (AUC) and absolute apparent volume of distribution were not significantly different among the three phases. In contrast, the terminal half-life of midazolam was significantly decreased after RYGB (8.7 ± 2.5, 7.3 ± 2.9, and 6.4 ± 2.5 hours at baseline, 3 months, and 6 months postoperatively, respectively), whereas the terminal half-life of 1´-hydroxymidazolam remained unchanged postoperatively. The metabolite-to-parent ratio was increased at the 3-month time points, and the differences were attenuated 12 months postoperatively.

CONCLUSION: *CYP3A* activity is altered after RYGB. The increased peak plasma midazolam concentration may be associated with decreased intestinal first-pass metabolism through the upper intestinal bypass component of RYGB. Conversely, RYGB could have increased hepatic *CYP3A* activity, as suggested by the decrease in midazolam terminal half-life.

362. Effect of proximal Roux-en-Y gastric bypass on oral bioavailability of P-glycoprotein substrates. *Lingtak-Neander Chan, Pharm.D., BCNSP,*[1] Yvonne S. Lin, Ph.D.,[2] Brant K. Oelschlager, M.D.,[3] David R. Flum, M.D., MPH,[3] Kristen K. Patton, M.D.,[4] Danny D. Shen, Ph.D.,[1] John R. Horn, Pharm.D.,[1] Rodney J.Y. Ho, Ph.D.,[2] Edward J. Kelly, Ph.D.[1]; (1) University of Washington, Department of Pharmacy, Seattle, WA; (2) University of Washington, Department of Pharmaceutics, Seattle, WA; (3) University of Washington, Department of Surgery, Seattle, WA; (4) University of Washington, Department of Medicine, Seattle, WA

PURPOSE: This pilot study aimed to determine how Roux-en-Y gastric bypass operations (RYGBs) affect oral bioavailability of P-glycoprotein substrates using digoxin as the probe.

METHODS: Twelve obese patients with no known cardiac diseases undergoing RYGB were enrolled in this pilot study. Each patient received 500 µg of oral digoxin after an overnight fast on three separate study visits: before RYGB (baseline) and 3 and 12 months after RYGB. Twelve-lead electrocardiogram (EKG) was monitored every 30 minutes for the first 2 hours. Plasma samples were

collected 0, 10, 20, 30, 40, 50, 60, 75, 90, 120, 180, 240, 360, 720, and 1440 minutes after dose administration. Plasma digoxin concentrations were determined using LC/MS. Pharmacokinetic parameters were estimated by WinNonlin. Because of the limited duration of plasma collection compared with the half-life of digoxin, extrapolation of the data to infinite time was not performed. Trapezoidal rule was used to calculate the areas under the plasma concentration-time curve (AUCs) from 0 to 4 and 48 hours. Pharmacokinetic parameters from the two postoperative visits were compared with baseline values using a Student t-test.
RESULTS: The average body mass indices of the 12 patients were 51, 41, and 38 kg/m^2 at baseline, 3 months, and 12 months postoperatively, respectively. The average length of the Roux limb was 128 ± 25 cm. After RYGB, the mean peak digoxin concentration was unchanged; however, the mean time to peak concentration was significantly earlier than at baseline. The AUCs of digoxin from 0 to 4 hours and from 0 to 48 hours were unchanged at 3 and 12 months postoperatively compared with baseline. Heart rate and EKG pattern at the postoperative visits were also similar compared with baseline.
CONCLUSION: Although the rate of absorption appears to be increased, the overall oral bioavailability of digoxin appears not to be affected by proximal RYGB.

363. Daptomycin plasma concentrations during cardiopulmonary bypass: a prospective, open-label pharmacokinetic investigation. *Megan H. Nguyen, Pharm.D.,*[1] Samantha J. Eells, MPH,[2] Jennifer Tan, MHS,[2] Bassam O. Omari, M.D.,[3] Tina Sheth, M.D.,[3] Loren G. Miller, M.D., MPH[3]; (1) Western University of Health Sciences, Pomona, CA; (2) Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA; (3) Harbor-UCLA Medical Center, Torrance, CA
BACKGROUND: Vancomycin will soon become the standard of care for surgical site infection prophylaxis in cardiothoracic surgery; however, not all patients can tolerate vancomycin, and no alternative antibiotics are recommended for patients undergoing surgery who cannot receive vancomycin and are at high risk of methicillin-resistant *Staphylococcus aureus* (MRSA). Daptomycin, which has activity against MRSA strains, is possibly an agent that can be considered as an alternative to vancomycin for surgical prophylaxis in patients undergoing cardiopulmonary bypass.
PURPOSE: To study the pharmacokinetics of daptomycin in subjects undergoing coronary artery bypass graft (CABG) surgery and its clinical outcomes.
METHODS: Subjects undergoing CABG surgery were screened for enrollment if they met the inclusion and exclusion criteria. A single dose of daptomycin 8 mg/kg was administered as the surgical prophylaxis antibiotic. We collected pharmacokinetic and clinical outcomes data.
RESULTS: We enrolled eight hospitalized patients undergoing CABG surgery. Daptomycin plasma concentrations were well above the MIC_{90} for *S. aureus* and *S. epidermidis* for at least 24 hours and were consistently maintained during cardiopulmonary bypass procedures in the study subjects. There were no cases of muscle weakness or myalgia in patients receiving daptomycin. There were no signs or symptoms of a surgical site infection in any subjects.
CONCLUSION: We found that daptomycin achieves adequate plasma concentrations against common pathogens that cause infections in patients undergoing cardiopulmonary bypass surgery. The drug was well tolerated as a single dose. Daptomycin may be an effective alternative to vancomycin for prophylaxis of surgical site infections for patients undergoing cardiothoracic bypass surgery who are unable to tolerate vancomycin.

PRN Posters

364. Highlighting the Ambulatory Care PRN. *Sheila L. Stadler, Pharm.D., BCPS,*[1] Agnes Chou, Pharm.D., BPCS,[2] Jennifer N. Clements, Pharm.D., BCPS,[3] Lea E. dela Pena, Pharm.D., BCPS,[4] Chris Terpening, Ph.D., Pharm.D.[5]; (1) Kaiser Permanente of Colorado, Lafayette, CO; (2) The Brooklyn Hospital Center, Brooklyn, NY; (3) Bernard J. Dunn School of Pharmacy, Shenandoah University, Winchester, VA; (4) Midwestern University Chicago College of Pharmacy, Downers Grove, IL; (5) West Virginia University, Charleston, WV
PURPOSE: 1) Increase visibility and membership of the Ambulatory Care PRN within ACCP and 2) increase awareness of professional development and networking opportunities available to members of the Ambulatory Care PRN.
METHODS: A brief update of each of the Ambulatory Care PRN committees will be presented. The Research and Scholarship committee conducted a survey of the PRN regarding the petition to the Board of Pharmaceutical Specialties requesting recognition of Ambulatory Care Pharmacy Practice as a specialty. A summary of these findings will be highlighted, together with comments from selected survey participants. To promote research and scholarly activity, a summary of the grant recipients and their projects will be provided. Information regarding the Survival Guide and benefits of the PRN will be provided.
RESULTS: None to be presented.
CONCLUSIONS: Overall, the poster will provide a summary of the various professional activities within the Ambulatory Care PRN.

PRN History Posters

365. 17 years of promoting ambulatory care: the history of the Ambulatory Care PRN. *Sunny A. Linnebur, Pharm.D.,*[1] Eric J. MacLaughlin, Pharm.D.,[2] Timothy J. Ives, Pharm.D., MPH,[3] Terry Seaton, Pharm.D.[4]; (1) University of Colorado Denver School of Pharmacy, Aurora, CO; (2) Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX; (3) University of North Carolina at Chapel Hill, Chapel Hill, NC; (4) St. Louis College of Pharmacy, St. Louis, MO
PURPOSE: To describe the activities of the Ambulatory Care PRN.
HISTORY: The Ambulatory Care PRN was established as the second PRN in 1992. There were 63 members the first year, with the membership increasing to about 1100 members in 2008. The Ambulatory Care PRN is one of the largest PRNs, with members from many different practice settings. To increase knowledge of PRN activities, the PRN began regularly producing a newsletter in March 1998. The PRN also hosts a very active e-mail list that serves as a communication route for PRN officers to disseminate PRN updates and allows members to pose clinical questions to other members. A highlight of the PRN is the "ACCP Ambulatory Care New Practitioner Survival Guide/Resource Manual," which is a published tool for ACCP and PRN members in ambulatory care clinical practice. The PRN also highly values scholarship and research endeavors and has donated $21,475 to ACCP campaigns to further pharmacy research. In addition, in 2006, the PRN initiated the Ambulatory Care PRN Pilot Grant Program to fund small research projects related to ambulatory care. The PRN has published joint opinion papers in collaboration with other PRNs, and our members have been integral in developing multiple ACCP Position Statements and White Papers. To highlight individuals who have been outstanding PRN members, an Ambulatory Care PRN Achievement Award was initiated in 2005.
CONCLUSION: Although the PRN does not have a published mission, our interest lies in supporting clinical pharmacists practicing in ambulatory care settings. We strive to provide high-quality educational, research, and service opportunities to our members and to facilitate communication and idea sharing. We support ACCP on research and legislative initiatives, especially if they apply to pharmacists practicing in ambulatory settings. In addition, our PRN values collaboration with other PRNs to achieve our goals.

366. The history and growth of the Endocrine and Metabolism PRN. *Marissa E. Quinones, Pharm.D.,*[1] Patricia R. Wigle, Pharm.D., BCPS,[2] Rosalyn S. Padiyara, Pharm.D., CDE,[3] Dawn E. Havrda, Pharm.D., BCPS,[4] Natasha Harrigan, Pharm.D.,[5] Molly E. Graham, Pharm.D.[6]; (1) Parkland, Dallas, TX; (2) University of Cincinnati, Cincinnati, OH; (3) Midwestern University–Chicago College of Pharmacy, Downers Grove, IL; (4) Bernard J. Dunn School of Pharmacy, Shenandoah University, Winchester, VA; (5) Hampton University School of Pharmacy, Hampton, VA; (6) Texas Tech HSC School of Pharmacy–Abilene Campus, Abilene, TX

PURPOSE: To describe the history and growth of the Endocrine and Metabolism PRN (Endo-PRN). History: The Endo-PRN was established in 2004 at the ACCP meeting in Dallas, Texas. Led by Kent Porter, Pharm.D., M.S., BCPS, a total of 21 founding members established the goals and objectives of the PRN. In 2005, the Board of Regents unanimously approved the PRN for acceptance and ratification. The first official meeting of the PRN was held at Myrtle Beach, South Carolina, and the first educational session was held in San Francisco, California, in 2005. The PRN has 182 active members as of October 2007. The membership includes students, residents, and pharmacists who practice in a variety of settings.
METHODS: In 2008, the Endo-PRN's Communications Committee was charged with creating, implementing, and compiling the results of a membership survey. A 14-item survey was created and was administered online by the PRN e-mail list. The results of the survey were compiled and disseminated to members present at the 2008 PRN business meeting in Louisville, Kentucky.
RESULTS: Eighty members of the ACCP Endo-PRN responded to the survey. Forty-five percent have been members for 1–3 years, and 33.8% have been members for less than 1 year. Founding members of the Endo-PRN consisted of 21.2%. The most common pharmacy practice settings of the members of the Endo-PRN are ambulatory care clinics (43.8%) and academia (43.8%). Fifty-three percent of our members are Board-Certified Pharmacotherapy Specialists (BCPS), and 27.5% are Certified Diabetes Educators (CDE).
CONCLUSIONS: The Endo-PRN has grown rapidly, and as it continues to grow, it will continue to give back to ACCP and the clinical pharmacy profession through innovative focus sessions, advocacy involvement, publishing within the therapeutic area of endocrine and metabolism, and increasing overall leadership within ACCP.

367. Pharmaceutical Industry PRN: a history of its accomplishments. *Clara K. Song, Pharm.D.,*[1] Andrea J. Anderson, Pharm.D.,[2] Julie O. Maurey, Pharm.D., BCPS, FCCP,[3] Leigh M. Vaughan, Pharm.D., MBA, RAC,[4] Vandana Slatter, Pharm.D., MPA[5]; (1) ISTA Pharmaceuticals, Inc., Irvine, CA; (2) Genentech, Inc., South San Francisco, CA; (3) Pfizer, Inc., Mentor, OH; (4) Talecris Biotherapeutics, Inc., Rtp, NC; (5) Roche Laboratories, Nutley, NJ
BACKGROUND: In January 1998, the Pharmaceutical Industry PRN became official, with 77 charter members. The first chair was Vandana Slatter from Pharmacia, and the PRN was launched at the November Annual Meeting.
MISSION STATEMENT: To support ACCP members practicing in the pharmaceutical industry and to provide awareness and education to members practicing in other settings.
Objectives:
To provide networking opportunities for clinical pharmacists practicing in all aspects of industry
To provide educational and developmental programs for clinical pharmacists practicing in industry
To provide information, to the general membership of ACCP, about pharmacy practice in industry
To development and facilitate research-based, educational, and pharmaceutical care collaboration between clinical pharmacists in the pharmaceutical industry and clinical practice pharmacists in academia or other clinical settings
Successes:
Eight focus sessions between 1999 and 2009
These broad-based sessions reflected the diversity of roles within our membership at the interfaces of the clinical, regulatory, safety, and commercial environments.
Outreach to pharmacy students to alert them of the varied industry-based career options
Growing recognition by ACCP of the role of pharmacists in industry and the involvement of industrial pharmacists in ACCP leadership positions
Several publications and poster presentations
Several Industry PRN members served as authors/contributors on the "Pharmacists and Industry: Guidelines for Ethical Interactions" white paper.
High visibility and commitment to ACCP committees
Challenges:
To continue to demonstrate to our industry colleagues, the public, and others the value of the unique background, training, and thinking that we bring to any role
To have a positive impact on the pharmacy profession as well as the health care environment, in a time of rapid change within and outside the pharmaceutical industry
CONCLUSIONS: The PRN will continue to grow and be a value-added service to ACCP. This PRN provides a safe haven for clinical pharmacists in industry to connect with one another and to share roles, challenges, and opportunities.

368. Critical Care Practice and Research Network: an evaluation of historical significance. *Tyree H. Kiser, Pharm.D., BCPS,*[1] Erica L. Horinek, Pharm.D.,[2] Sarah Fichuk, Pharm.D.,[3] Lance J. Oyen, Pharm.D., BCPS, FCCM[4]; (1) University of Colorado School of Pharmacy, Aurora, CO; (2) Sky Ridge Medical Center, Lonetree, CO; (3) Detroit Medical Center, Detroit, MI; (4) Hospital Pharmacy Services, Mayo Clinic, Rochester, MN
PURPOSE: The aim of this project was to highlight the history, accomplishments, and contributions of the Critical Care Practice and Research Network (PRN) to the American College of Clinical Pharmacy (ACCP).
METHODS: Retrospective review of data collected from the Critical Care PRN newsletters, document warehouse, financial statements, and ACCP from 1992 to 2008. The Critical Care PRN membership was surveyed to obtain data unavailable from historical documents and also to validate and approve information collected.
RESULTS: The Board of Regents approved the creation of the Critical Care PRN in August 1992 with 109 members, and the membership has since increased to 1034 members in 2008. Critical Care PRN members have served as ACCP President, Board of Regents, *Pharmacotherapy* editorial board, PSAP editorial board, and the Research Institute board. Forty Critical Care PRN members have obtained fellowship status with ACCP. The PRN has awarded nine travel grants to critical care residents for presentation at ACCP meetings. The Critical Care PRN has held focus sessions at every major ACCP meeting since 1997. The Critical Care PRN has worked collaboratively with other PRNs to develop premeeting symposia for discussing pharmacology issues that span common networking forums. Working groups of Critical Care PRN members have published position papers regarding critical care pharmacy services and guidelines relative to intensive care unit pharmacology. From January 2003 to December 2008, the Critical Care PRN contributed a total of $25,003.00 to the Frontiers Fund.
CONCLUSIONS: The Critical Care PRN has experienced continued success during the past 16 years, and its membership has grown extensively during that time. Dedication to achieving the original mission of the PRN has helped foster excellence and innovation in clinical pharmacy practice, research, and education. Critical Care PRN members have enthusiastically supported the overall mission of ACCP by actively contributing to educational initiatives, scholarly activity, and the Research Institute.

369. Central Nervous System (PRN) history. *Kimberly Tallian, Pharm.D., BCPP,*[1] Lawrence J. Cohen, Pharm.D., BCPP, FCCP[2]; (1) University of California, San Diego Medical Center, San Diego, CA; (2) Washington State University–Spokane, Spokane, WA
PURPOSE: To characterize the history of the Central Nervous System (CNS) PRN and highlight the key roles that the PRN has played in the success of the College.
BACKGROUND: The CNS PRN was established by four ACCP members – Larry Cohen, Larry Ereshefsky, Barbara Wells, and Nina Graves – in November 1993. The PRN has provided a forum to encourage networking among more than 200 pharmacists specializing in disorders of the CNS. The PRN offers high-quality programming on CNS diseases often in collaboration with other PRNs, and it mentors young professionals interested in developing leadership, research, and presentation skills. The CNS PRN was the first PRN to establish a mini-sabbatical, which has served as an exemplary model for subsequent mini-sabbaticals offered through the College. In addition, several members have held leadership roles ranging from president of the Board of Regents to chair of the Research Institute Board of Trustees to PRN chairs. Its members

have received numerous awards including Young Investigator, Investigator Development Research, and Best Poster; also, it has been recognized with one of the College's highest honors, Fellow of ACCP.

370. History of the Education and Training Practice and Research Network. *Nancy L. Shapiro, Pharm.D., BCPS,*[1] Anna Wodlinger Jackson, Pharm.D., BCPS,[2] Tina Denetclaw, Pharm.D., BCPS,[3] Patricia Orlando, Pharm.D., FCCP[4]; (1) University of Illinois at Chicago College of Pharmacy, Chicago, IL; (2) Temple University School of Pharmacy, Philadelphia, PA; (3) University of California, San Francisco, San Francisco, CA; (4) University of Utah College of Pharmacy, Salt Lake City, UT

PURPOSE: The purpose of the Education and Training Practice and Research Network (E&T PRN) is to provide an opportunity to network with others who share similar interests and to work collaboratively to develop programs and projects to advance pharmacy education and training.

METHODS: The E&T PRN was officially recognized as a PRN on January 15, 2002, and the first business meeting was held on April 8, 2002, in Savannah, Georgia, at the 2002 Spring Forum. The mission of the E&T PRN is to promote dialog and interaction among members and to develop programs that enhance the knowledge and skills of members involved in education and training within clinical pharmacy. Our PRN's focus on education and training occurs in an environment respectful of its members, with support for diversity in teaching methods and postgraduate training while considering assessments and outcomes.

RESULTS: Membership in the PRN has increased from the original 52 interested individuals to 285 current members. Through the years, the PRN has developed many successful programming sessions of interest to preceptors, faculty, residents, and students. At each spring and fall meeting, the PRN holds a business meeting and networking forum, which is open to all current and prospective members. Recently, it was decided that the networking forums at the Annual Meeting would focus on student/resident training and recruitment concerns and that the spring meetings would focus on other education and training topics the membership wishes to discuss.

CONCLUSION: The PRN continues to promote dialog and interaction among members by the e-mail list and interactive networking at our twice-yearly business meetings. We also continue to develop programs that enhance the knowledge and skills of members involved in education and training within clinical pharmacy.

371. The history of the Immunology/Transplantation PRN. Immunology Transplantation PRN members,[1] *Tiffany E. Kaiser, Pharm.D.*[2]; [1]American College of Clinical Pharmacy, Lenexa, KS; [2]University of Cincinnati, Cincinnati, OH

PURPOSE: The Immunology/Transplantation PRN was founded to establish communication, collaboration, and education between immunology/transplant practitioners across the country. The PRN has grown considerably since its inception in 1993 from about 80 members to a current peak of about 255 members. Members include pharmacy students, residents, fellows, and active pharmacy practitioners from multiple practice settings. The goal of the PRN is to promote quality research, clinical practice, innovation, and education in the areas of immunology and solid organ transplantation.

METHODS: The PRN is dedicated to achieving this goal by an active e-mail list, enabling a collaborative environment for information exchange such that members are able to share and tally their experiences. In addition, the PRN provides networking opportunities during ACCP Annual Meetings and the PRN-hosted networking sessions.

RESULTS: To encourage participation in clinical and outcomes research, the group recently established a resident/fellow travel grant to encourage transplant residents and fellows to get involved in research and attend the ACCP Annual Meeting. Members of the Immunology/Transplantation PRN have worked to establish specialty groups within other societies such as the American Society of Health-System Pharmacists (ASHP) and the American Society of Transplantation (AST). Working in concert with other groups has allowed our members to be instrumental in the development of PGY2 transplant residency standards with ASHP as well as collaborate with the AST group in writing a white paper on the role of the transplant pharmacist.

CONCLUSION: Although we have accomplished a lot in just a few years, additional efforts are needed to establish standardized training and credentialing for immunology/transplantation pharmacists to be recognized as providers and receive payment for clinical services. Training of young clinicians and motivation of the current membership will enable the PRN to serve as the epicenter for communication and collaboration in the future.

372. History of the ACCP GI/Liver/Nutrition PRN. *David R. Foster, Pharm.D.,*[1] Maria Ballod, Pharm.D.,[2] Michael D. Kraft, Pharm.D.[3]; (1) Purdue University, Department of Pharmacy Practice, Indianapolis, IN; (2) Mayo Clinic, Jacksonville, FL; (3) University of Michigan Health System, Ann Arbor, MI

PURPOSE: To characterize the history of the ACCP GI/Liver/Nutrition PRN as part of the 30-year anniversary celebration of the College, including the founding of the PRN, highlights of the PRN's mission and values, and contributions of the PRN to the College and the profession.

METHODS: Input and historical information was solicited from PRN members at the PRN Business Meeting and Networking Forum at ACCP Annual Meetings and from current and former PRN officers. A draft PRN history document was created, circulated to PRN members through the PRN e-mail list, and modified based on member feedback.

RESULTS: The GI/Liver/Nutrition PRN was established to create a network of clinical pharmacists who are interested in gastrointestinal/liver diseases and nutrition to promote practice, research, and education in these areas. The first exploratory meeting of this PRN was held at the 1999 ACCP Annual Meeting. The founding PRN officers were Drs. Rosemary R. Berardi (Chair) and William R. Garnett (Secretary/Treasurer). On January 17, 2000, the GI/Liver/Nutrition PRN was officially recognized as a Practice and Research Network of the American College of Clinical Pharmacy. Membership has grown from 56 members to 162 members. The GI/Liver/Nutrition PRN has consistently presented focus sessions at ACCP Annual and Spring Meetings, traditionally alternating between gastroenterology and nutrition-focused presentations. Special initiatives of the PRN include establishment of a travel award to support the travel of members to present an abstract at an ACCP meeting (with an emphasis on supporting members in training) and contributions to the Research Institute of the College.

CONCLUSION: The GI/Liver/Nutrition PRN will continue to serve its members by offering high-quality educational and networking opportunities, fostering and promoting advanced training in practice and research related to gastroenterology and nutrition, and promoting collaborations both within and outside ACCP.

373. Pediatrics Practice and Research Network History. *Katherine P. Smith, Pharm.D., BCPS*; University of Southern Nevada College of Pharmacy – South Jordan Campus, South Jordan, UT

PURPOSE: The purpose of this poster is to present the history of the Pediatrics Practice and Research Network.

METHODS: With the help of ACCP staff and the pioneers of the Pediatrics PRN, the history of the founding of the PRN was researched. An e-mail solicitation for old newsletters and meeting minutes went out so that important milestones and major events involving the PRN or PRN members could be included. As a final step in the project, a survey went out to current and previous PRN members. The survey inquired about where each member received pediatric training (from whom) and collected information about pediatric resident training (if applicable). These data were used to construct a family tree of pediatric pharmacy training.

RESULTS: The poster will present the pediatric training family tree and will highlight some of the major contributions of Pediatrics PRN members. Copies of old newsletters, e-mail list strings, and publications generated by the PRN will also be shared.

CONCLUSION: The Pediatrics PRN has had an interesting past and

certainly has a bright future. One of the strongest features of the history has been in the area of collaboration, with PPAG and with other ACCP PRNs. The continuing inclusion of the international pediatrics community in future meetings and projects will also expand resources for those wishing to contribute to pediatrics research and improve pediatric patient care.

374. A brief history. A long future. The Emergency Medicine Practice Research Network. *Michael C. Thomas, Pharm.D.*,[1] Nicole M. Acquisto, Pharm.D.,[2] Kyle A. Weant, Pharm.D.,[3] Mary Beth Shirk, Pharm.D.,[4] Victor Cohen, Pharm.D.,[5] Pamela Lada Walker, Pharm.D.,[6] Asad E. Patanwala, Pharm.D.[7]; (1) South University, Savannah, GA; (2) University of Rochester Medical Center, Rochester, NY; (3) University of Kentucky HealthCare, Lexington, KY; (4) The Ohio State University Medical Center, Columbus, OH; (5) Maimonides Medical Center, Brooklyn, NY; (6) University of Michigan Hospital, Ann Arbor, MI; (7) University of Arizona, Tucson, AZ

PURPOSE: The emergency department (ED) setting is susceptible to medication errors and adverse events because of high patient volumes, large diversity, high frequency of verbal orders, and use of high-risk medications, all historically with the lack of prospective pharmacist medication order review. The role of clinical pharmacists practicing in the ED was described in 1977. Recently, Joint Commission Standard 4.10 addressed pharmacists' review of medication orders for ED patients. Consequently, a rapid growth in emergency medicine (EM) pharmacists transpired, which created a nucleus of practitioners with common interests.

METHODS: A formal application with at least 50 ACCP members must be filed with the ACCP Board of Regents. On April 14, 2008, an e-mail questionnaire was sent to members of another PRN to demonstrate interest. The minimum number was met, and the application was filed on May 14, 2008.

RESULTS: The EM Practice Research Network (EMED PRN) was founded August 6, 2008. The first business meeting was October 20, 2008, in Louisville, Kentucky. This was well attended and included nationally known practitioners and stakeholders in EM. The EMED PRN membership has almost tripled to more than 150 members since it was founded. In its first year, the PRN established a planning committee to organize a focus session at the 2009 ACCP Annual Meeting and a media committee that distributed its first newsletter.

CONCLUSION: Emergency medicine provides a unique practice environment for clinical pharmacists who can significantly affect patient care and financial outcomes in the ED. The development of the EMED PRN provides this distinctive group with educational and research opportunities, mentoring and leadership training, and collaboration and practice-site experience sharing. Future directions include continued support for EM as a specialty, advocacy for EM residency programs, a formalized mentor program, development of educational programs, and expansion of EM into pharmacy student education.

375. History of the Nephrology PRN. *Ruth Ann Subach, Pharm.D., BCPS*; Chair, Nephrology PRN (2008–2009), West Conshohocken, PA

PURPOSE: To document the history of the Nephrology PRN.

METHODS: E-mails and telephone calls to current and former members of the Nephrology PRN (NephPRN) were sent beginning in February 2008, soliciting historical information about the formation and activities of the NephPRN. A draft outline was presented at the April 2008 meeting. Several drafts of the paper were circulated by e-mail for review, contributions, and comments. More than 20 current and former NephPRN members and ACCP staff contributed information for the paper. The final draft was presented at the April 2009 meeting, together with the first poster draft.

RESULTS: The NephPRN was formed in 1993 with 73 initial members. Gary Matzke was the first elected chair. Current membership is around 180. Formal and ad hoc committees have actively pursued their charges; several publications have resulted from committee projects. Preceptors have trained more than 75 health care professionals in programs including residencies, fellowships, degree programs, and mini-sabbaticals. The NephPRN has hosted or collaborated with other PRNs on 19 educational programs at ACCP. NephPRN members have planned and/or presented at other nephrology meetings, including NKF, and are actively involved in federal programs serving patients with kidney disease. NephPRN members have been awarded NIH grants and distinguished awards within ACCP and other organizations. At last count, 20 NephPRN members are Fellows of ACCP.

CONCLUSION: The NephPRN has been, and will continue to be, a welcoming group within ACCP, focused on serving health care professionals and patients through research, training, patient advocacy, and direct patient care initiatives.

376. Clinical Administration PRN history. *Bob Lobo, Pharm.D.*,[1] Andrea Balog, Pharm.D.,[2] Herbert Mathews III, Pharm.D.,[3] Emilie Karpiuk, Pharm.D., BCOP,[4] Suzanne B. Wortman, Pharm.D., BCPS,[5] John Noviasky, Pharm.D.[6]; (1) Vanderbilt University, Nashville, TN; (2) Loma Linda University Medical Center and School of Pharmacy, Loma Linda, CA; (3) Carroll Hospital Center, Westminster, MD; (4) Froedtert Hospital, Milwaukee, WI; (5) DuBois Regional Medical Center, DuBois, PA; (6) SUNY Upstate Medical University, Syracuse, NY

The Clinical Administration PRN was founded in 2002 to serve the networking and professional needs of ACCP members who identify themselves as clinical pharmacy leaders in health systems. Membership, which has increased to more than 250 people, continues to grow.

A membership survey was conducted in 2005 to describe the interests and activities of members. Sixty of the 134 members responded. Fifty percent each were women, had practiced for more than 15 years, and were clinical coordinators. A wide variety of hospital types and sizes were represented, but most practiced in a nongovernmental, nonprofit teaching hospital. Most respondents were involved in teaching pharmacy students or residents. About one-half had at least one pharmacy resident and at least five clinical pharmacists on staff. A majority of members were involved in adverse drug reaction, medication error and clinical intervention reporting, clinical program development, competency testing, drug information, Pharmacy and Therapeutics (P&T) Committee preparation, nonformulary drug control, order set and protocol development and review, Joint Commission preparations, personnel management, and the pharmacy budget. Most were members of key hospital committees including Medication Safety, Infection Control, Joint Commission Readiness, and P&T.

The PRN has numerous accomplishments, most notably the provision of 11 outstanding educational programs, focus sessions, and interactive workshops at ACCP Spring and Annual Meetings. These programs have been well attended, and several were developed and presented in collaboration with other PRNs.

The Clinical Administration PRN has grown rapidly and has made important contributions to ACCP, especially in the area of educational programming, since its inception in 2002. Many members are in clinical pharmacy leadership or management roles and are involved in improving medication use in health systems around the country.

377. Hematology/Oncology Practice and Research Network: fifteen years of growth. *Karen R. Smethers, Pharm.D., BCOP*,[1] Stacy S. Shord, Pharm.D., BCOP,[2] Jodi L. Grabinski, Pharm.D., M.S., BCOP[3]; (1) Beth Israel Deaconess Medical Center, Boston, MA; (2) FDA, Silver Spring, MD; (3) South Texas Accelerated Research Therapeutics, San Antonio, TX

PURPOSE: The Hematology/Oncology Practice and Research Network (PRN) was established in 1994 as a forum for hematology/oncology pharmacists to network and collaborate on scientific, educational, and political issues affecting clinical practice, teaching, and research.

METHODS: Membership information, advancements, and PRN accomplishments were compiled from PRN members and ACCP records. Responses were collected by current PRN officers, and the information was used to document the history of the PRN.

RESULTS: The Hematology/Oncology Practice and Research Network group was established in May 1994 with 50 active members. The membership has grown each year to the current total of more than 500 members. Members are employed in several practice settings including university, community, and government hospitals (51%), colleges of medicine and pharmacy (29%), ambulatory clinics (7%), pharmaceutical industry (6%), managed care (1%), and community pharmacy practices (1%). The PRN supported the diverse practice needs of its membership by bringing together pharmacists in this unique area of clinical practice to help foster its growth. Because of PRN member efforts, a majority of the sessions at the American Society of Clinical Oncology Annual Meeting are accredited by the ACPE, a specialty course is offered yearly in conjunction with ASHP to prepare for the BCOP examination, and members can take advantage of the BCOP recertification program at the ACCP Annual Meeting. Members also have found opportunities to improve patient care by supporting hematology/oncology research, collaborating with colleagues at ACCP meetings, and communicating through the PRN e-mail list.
CONCLUSION: The Hematology/Oncology Practice and Research Network has grown significantly during the past 15 years to more than 500 pharmacists. Members work to advance the care of the hematology/oncology patient by supporting practitioner education, certification, and interdisciplinary collaboration and research.

378. ACCP Geriatrics PRN history poster. Jeannie K. Lee, Pharm.D., BCPS,[1] *Heather Bieber, Pharm.D., CGP, BCPS,*[2] Carlos Rojas-Fernandez, Pharm.D., BCPP[3]; (1) University of Arizona, College of Pharmacy Practice and Science, Tucson, AZ; (2) North Florida/South Georgia Veterans Health System (NF/SG VHS), Lake City, FL; (3) Bristol-Myers Squibb, Gaithersburg, MD
PURPOSE: To give a brief history of the Geriatrics PRN.
METHODS: Review of ACCP records for growth of the PRN, special awards, and monetary contributions. Review of PRN members' CVs for accomplishments (e.g., publications, offices held within ACCP, research and geriatric contributions outside ACCP).
CONCLUSION: The Geriatrics PRN continues to contribute to the practice of pharmacy with a focus on the special population of geriatrics.

379. History of the American College of Clinical Pharmacy's Infectious Diseases Practice and Research Network (ID-PRN). *Elizabeth B. Hirsch, Pharm.D.,*[1] Melinda M. Neuhauser, Pharm.D., MPH,[2] Elizabeth Dodds Ashley, Pharm.D., MHS, BCPS,[3] Jason C. Gallagher, Pharm.D., BCPS,[4] Elizabeth D. Hermsen, Pharm.D., MBA, BCPS (AQ-ID),[5] Daryl D. DePestel, Pharm.D., BCPS (AQ-ID),[6] Erika J. Ernst, Pharm.D., FCCP, BCPS (AQ-ID)[7]; (1) St. Luke's Episcopal Hospital, Houston, TX; (2) U.S. Department of Veterans Affairs, Chicago, IL; (3) University of Rochester Medical Center, Rochester, NY; (4) Temple University School of Pharmacy, Philadelphia, PA; (5) The Nebraska Medical Center, Omaha, NE; (6) University of Michigan Health System, Ann Arbor, MI; (7) College of Pharmacy, The University of Iowa, Iowa City, IA
PURPOSE: In February 2008, Gary Matzke, ACCP president, asked all PRN chairs to characterize the history of their PRN. A paper and poster highlighting the founding, mission, values, and contributions to the College and profession will be used as part of the 30th anniversary celebration of the College in 2009.
METHODS: Membership records and historical data were collected from ACCP headquarters. Past ID-PRN chair members were contacted and asked to provide specific information and insight into their leadership of the PRN. A draft of each document was approved by the PRN membership and the ID-PRN Board Liaison.
CONCLUSION: This poster highlights the ID-PRN's founding, mission, values, and contributions to the College and the pharmacy profession.

380. American College of Clinical Pharmacy, Women's Health Practice and Research Network: a history. *Shareen Y. El-Ibiary, Pharm.D., BCPS,*[1] Annie Kai I. Cheang, Pharm.D., M.S., BCPS,[2] Alicia B. Forinash, Pharm.D., BCPS, CCD,[3] Patricia R. Wigle, Pharm.D., BCPS,[4] Jennifer McIntosh, Pharm.D.,[5] David L. Lourwood, Pharm.D., BCPS, FCCP[6]; (1) Midwestern University, College of Pharmacy–Glendale, Glendale, AZ; (2) VCU Medical College of Virginia, Richmond, VA; (3) St. Louis College of Pharmacy, St. Louis, MO; (4) University of Cincinnati, Cincinnati, OH; (5) Northeastern University-Bouve College of Health Sc, Boston, MA; (6) Poplar Bluff Regional Medical Center, Poplar Bluff, MO
PURPOSE: To provide a history and description of the founding, growth and accomplishments of the Women's Health PRN.
METHODS: A review of ACCP historical documents and a discussion with founding and current members was conducted to collect and synthesize information describing the history and future of the Women's Health PRN.
RESULTS: The Women's Health PRN consists of almost 140 members whose interests range from contraception and prenatal care to the aging issues of osteoporosis and heart disease to gender-related pharmacokinetics. Its purpose is to provide ACCP members a community for exchange of practice ideas and an opportunity for collaborative research in the area of women's health. Accomplishments include the development of women's health modules for pharmacy schools in partnership with AACP; an ACCP white paper on Research in Women and Special Populations; and the development of two textbooks covering women's health issues and drug therapy during pregnancy. The roles of the various PRN officers will be outlined, in addition to the activities of the various PRN committees. Future goals of the PRN will also be discussed. Among these are participation with outside organizations such as Pharmacy Access Partnership and the Adult Women's Health Alliance, as well as developing an opinion paper regarding over-the-counter use of hormonal contraceptives.
CONCLUSIONS: The Women's Health PRN seeks to address multiple aspects of women's health. For the past 10 years, members of the Women's Health PRN have participated and furthered the education and practice of gender-based issues in pharmacy care in several initiatives inside and outside ACCP. The significance of the PRN will continue to be stronger as the PRN grows to foster and shape policies, education, practice, and research in women's health. It is a dynamic, accomplished group of diverse members who enjoy collaborating with one another as well as specialists from other disciplines.

381. The history of the Pharmacokinetics/Pharmacodynamics (PK/PD) PRN. *Philip E. Empey, Pharm.D., Ph.D., BCPS,*[1] Brian R. Overholser, Pharm.D.,[2] Daniel A. Lewis, Pharm.D., BCPS,[3] Julie H. Oestreich, Pharm.D., Ph.D.[4]; (1) School of Pharmacy, University of Pittsburgh, Pittsburgh, PA; (2) School of Pharmacy & Pharmaceutical Sciences, Purdue University and School of Medicine, Indiana University, Indianapolis, IN; (3) University of Kentucky HealthCare, Lexington, KY; (4) University of Kentucky, Lexington, KY
PURPOSE: To detail the origin, accomplishments, and future direction of the PK/PD PRN as well as the achievements of its membership in a history document.
RESULTS: The PRN was established in 1997 with 63 founding members to focus on PK/PD-related issues in clinical practice, research, and drug development. Membership includes a unique blend of about 150 clinical practitioners, research intensive faculty, and industrial representatives. Since its inception, the PRN has consistently contributed to ACCP through educational and networking initiatives (focus sessions, premeeting symposia, and bookstore offerings) and has fostered student and trainee development. In 2002, the PRN established a specific fellow/graduate student travel award in honor of M. Kelli Jordan to allow recipients to present their PK/PD research to colleagues at the PRN business meeting each year at the ACCP Annual Meeting. Member achievements over this relatively short time frame, which have also been significant, are detailed within the history document. Several members have held leadership positions within ACCP such as president (most recently Dr. John Murphy) and regent and have received ACCP awards including the Russell R. Miller Award and the New Educator Award as well as numerous association-sponsored research grants. In addition, 38 members have been named a Fellow of the College. Looking toward the future, the PRN

has recently expanded its stated focus to include the maturing field of pharmacogenomics.
CONCLUSION: The completed history document provides a retrospective analysis of the accomplishments of the PK/PD PRN and its esteemed members. It is truly an exciting time for our PRN as it builds on the solid foundation of its first decade of member involvement.

382. Getting to the heart of the Cardiology Practice and Research Network: a historical evaluation and reflection. Toby Trujillo, Pharm.D., BCPS,[1] *Robert Lee Page II, Pharm.D., MSPH, FCCP, FAHA, BCPS,*[1] Orly Vardeny, Pharm.D., BCPS,[2] Barbara Wiggins, Pharm.D., FAHA, FNLA, BCPS, CLS[3]; (1) University of Colorado Denver School of Pharmacy, Aurora, CO; (2) Pharmacy Practice Division, University of Wisconsin School of Pharmacy, Madison, WI; (3) University of Virginia Health System, Charlottesville, VA
PURPOSE: This descriptive evaluation documented the inception, professional goals, mission, accomplishments, and future directions of the American College of Clinical Pharmacy (ACCP) Cardiology Practice and Research Network (PRN).
METHODS: A retrospective analysis of PRN newsletters, e-mails, letters, and financial records from 1993 to 2009 obtained from ACCP world headquarters was performed to form a historical framework of the PRN. Interviews of PRN members and PRN leadership were obtained to provide past and future perspectives.
RESULTS: The PRN was established May 5, 1993, and has grown to 796 members. Members have included 7 ACCP presidents, 11 Board of Regents, and 60 Fellows. Members have also been elected Fellows of medical organizations, have served on editorial boards of peer-reviewed journals, and have been nominated to national therapeutic guideline committees. The PRN, which established a mini-sabbatical and heart failure traineeship, was instrumental in developing Added Qualifications in Cardiology through the Board of Pharmaceutical Specialties. The PRN has published eight bibliographies, one position paper in conjunction with the American Heart Association, and one opinion paper as well as donated $15,000 to the Frontiers Fund.
CONCLUSION: The Cardiology PRN has a distinguished history within the College and a national reputation because of the dedication and contribution of its membership. The PRN has made great strides in advancing the practice and research of cardiovascular pharmacotherapy through its involvement at local, state, and national levels of both pharmacy and medical organizations.

383. What's HOt in ACCP? A history of the American College of Clinical Pharmacy's Health Outcomes Practice and Research Network. *Brenda M. Parker, Pharm.D., BCPS,*[1] Doug Steinke, Ph.D.,[2] Joseph A. Paladino, Pharm.D.,[3] Glen T. Schumock, Pharm.D., MBA,[4] Kathy Bungay, Pharm.D.,[5] Marianne McCollum, Ph.D., RPh,[6] Daniel R. Touchette, Pharm.D., M.A.[7]; (1) Humana Inc., Louisville, KY; (2) University of Kentucky HealthCare, Lexington, KY; (3) CPL Associates LLC, Buffalo, NY; (4) Center for Pharmacoeconomic Research, University of Illinois at Chicago, Chicago, IL; (5) Tufts-New England Medical Center, Boston, MA; (6) University of Colorado School of Pharmacy, Denver, CO; (7) University of Illinois at Chicago, Chicago, IL
PURPOSE: In 2007, ACCP President Gary Matzke charged each PRN with the task of developing a document that characterized the PRN to commemorate the 30-year anniversary of the College in 2009. In response, the Health Outcomes PRN created an account of where the PRN has been, where it is now, and where it hopes to go in the future.
METHODS: Past PRN leadership was contacted to gather information related to the founding of the PRN and to create a documentary of the journey from then until now. Current PRN officers, under the informed direction of recent leadership, developed a road map of sorts to tell the story of where the PRN is headed. The compilation was submitted to the entire PRN for review and approval, and the final product was submitted to the College.
RESULTS: An account of the PRN through time was created, which is being presented in paper and poster format.
CONCLUSION: The history is a précis for PRN and College members of the Health Outcomes PRN's creation, mission and values, and contributions to the College as well as to the profession.

384. History of the Adult Medicine Practice and Research Network. Darcie L. Keller, Pharm.D., BCPS,[1] *Joel C. Marrs, Pharm.D., BCPS,*[2] Beth H. Resman-Targoff, Pharm.D., FCCP,[3] Suzanne B. Wortman, Pharm.D., BCPS[4]; (1) Kansas City Veterans Affairs Medical Center, Kansas City, MO; (2) Oregon State University College of Pharmacy, Portland, OR; (3) University of Oklahoma College of Pharmacy, Oklahoma City, OK; (4) DuBois Regional Medical Center, DuBois, PA
PURPOSE: Describe the membership, activities, and achievements of the Adult Medicine Practice and Research Network (PRN).
BACKGROUND: For the past 10 years, the Adult Medicine PRN has grown into a thriving group of more than 750 clinical pharmacists practicing in a variety of inpatient and outpatient settings. A 2008 survey (20% response rate) demonstrated that 61% of respondents had completed a PGY1 residency, 70% were board certified in pharmacotherapy, and 10% held other certifications. Forty percent had academic appointments, and 47% served as preceptors. In addition, 96% devoted time to research. Communication, collaboration, and leadership are the PRN's primary objectives. These goals are achieved through PRN focus sessions and other educational presentations at ACCP meetings, PRN business meetings, and the PRN e-mail list, which provides opportunities for networking, sharing clinical experience, and providing support for all levels of clinical pharmacy practice. In addition, a document repository was designed to archive information shared among members to allow efficient retrieval. Eight committees have been established to provide members an opportunity to become actively involved in PRN endeavors. In addition, our members have participated in many facets of ACCP leadership, such as conducting board certification review courses and serving on editorial boards, committees, and task forces. Members have also demonstrated leadership through authorship on five white papers and one position paper. Member accomplishments have been recognized with ACCP Fellowship status and awards.
CONCLUSION: Throughout the years, our PRN has maintained a commitment to the practice of evidence-based medicine and fostered leadership within the PRN and ACCP by promoting active involvement in scholarly activities, development and presentation of research and innovative pharmacy practice, and education. As the PRN and its members look to the future, initiatives have been developed aimed at advancing the practice of clinical pharmacy and encompassing the core focuses of ACCP: education, service, and research.

385. History of the Pain and Palliative Care Practice and Research Network. *Lee A. Kral, Pharm.D.,*[1] David Craig, Pharm.D.[2]; (1) Pain and Palliative Care PRN, Iowa City, IA; (2) H. Lee Moffitt Cancer Center, Tampa, FL
PURPOSE: To give the history of the Pain and Palliative Care Practice and Research Network (PPC PRN).
RESULTS: The PPC PRN is an organization of pharmacy practitioners, clinical scientists, pharmacy educators, and others. Its objectives are to provide a supportive network for practitioners, provide quality education, and build leadership skills in young practitioners. The PRN was established in 2000 as the Pain Management PRN but was renamed the Pain and Palliative Care PRN in 2004 to more accurately reflect its membership. The PRN membership, which is extremely diverse, has been growing steadily since it was established. The PPC PRN has provided financial support for the Frontiers Fund since 2003 and has sponsored a mini-sabbatical program since 1999.
The Clinical Pharmacy Pain & Palliative Care Forum, the PRN's newsletter, was first published in 2003 in both hard copy and electronically. The newsletter has included news, debate columns, conference highlights, practitioner profiles, clinical pearls, resident's corner, and pain management resources sections. The PRN also published a Joint Opinion Statement on the "Management of Chronic Nonmalignant Pain with Nonsteroidal Antiinflammatory Drugs" with the Ambulatory Care and the Cardiology PRNs in *Pharmacotherapy* in 2008.

The PRN has hosted educational programs at the Annual Meetings and Spring Practice and Research Forums including focus sessions on the treatment of pain in chemically dependent patients, pain management and the law, The American Pain Society Cancer Pain Guidelines, opioid use and risk management, the convergent paths of pharmaceutical care and palliative care, treatment of fibromyalgia, health disparities in managing pain, and clinical dilemmas in pain management. Continuing education credits have also been offered for presentations at the PRN business and networking meetings.
CONCLUSION: The PPC PRN reflects a strong foundation that continues to strive to meet member needs.

Urology

386E. Silodosin, an α-blocker for the treatment of the signs and symptoms of benign prostatic hyperplasia, can be sprinkled on applesauce without effect on bioavailability. *Naomi V. Dahl, Pharm.D.*, Weining Volinn, M.S., Scott Olsen, MPH; Watson Laboratories, Morristown, NJ

PURPOSE: Urinary symptoms related to benign prostatic hyperplasia (BPH) are common in older men and are usually treated with α-blockers. Patients who have difficulty swallowing a capsule (or pill) might prefer to sprinkle its contents on a soft food. This study evaluated the bioavailability of the new α-blocker silodosin administered orally as an intact capsule and with the capsule contents sprinkled on applesauce.
METHODS: In this single-center, open-label, randomized, two-period crossover study, single-administration pharmacokinetics of silodosin was evaluated in healthy men. Silodosin 8 mg was administered orally after breakfast as an intact capsule or with the contents of the capsule sprinkled on 1 tablespoon of applesauce. Plasma samples before and up to 24 hours after dosing were analyzed for maximum concentration (C_{max}) and total exposure (AUC[24h]) of silodosin and its main metabolites. Modes of administration were compared by analysis of variance using log-transformed values.
RESULTS: Twenty participants (mean age, 35 years) completed the study. Silodosin mean exposure was 383.3 ng/hour/mL for intact capsule and 365.2 ng/hour/mL for sprinkled contents; mean ratio of exposure was 0.95 (90% CI: 0.88–1.03). Silodosin mean C_{max} was 70.6 ng/mL for intact capsule and 64.3 ng/mL for sprinkled contents; mean ratio of C_{max} was 0.94 (90% CI: 0.86–1.03). The 90% CIs of the ratios for AUC and C_{max} were within boundaries of 0.80–1.25, meeting the criteria for bioequivalence of the two administration modes.
CONCLUSION: Unlike other α-blockers, silodosin 8-mg capsules may be opened and the contents sprinkled on applesauce without an effect on bioavailability.
Presented at 22nd Annual National Conference of the National Association Directors of Nursing Administration/Long Term Care, Phoenix, AZ, July 11–15, 2009.

Women's Health

387E. Side effects of oral nifedipine as a tocolytic. *Ema Ferreira, Pharm.D., M.S., BPharm,* Laurence Spiesser-Robelet, DPharm, Brigitte-Zoé Martin, M.S., BPharm, François Audibert, M.D., Jean-François Bussières, M.S., MBA, BPharm; CHU Ste-Justine – Université de Montréal, Montreal, Quebec, Canada

PURPOSE: Describe the adverse effects reported after oral nifedipine for tocolysis.
METHODS: Retrospective cohort study held at CHU Ste-Justine. Women to whom the standard nifedipine protocol was prescribed were identified through the pharmacy computer program. Data were retrieved (demographics, vital signs before and after each dose, and adverse effects) from medical charts using a standardized form.
RESULTS: We reviewed 216 charts of women who received nifedipine for tocolysis between January 1, 2004, and March 1, 2007. The protocol consisted of nifedipine 20–40 mg (capsules) initially, followed by 20 mg orally every 8 hours for 24 hours with close monitoring. Patients demographics were as follows: mean age, 28.8 years (16–43); and mean gestational age when nifedipine was started, 30 weeks (233/7–345/7). One hundred forty (69%) women had at least a 10% increase in heart rate after the bolus dose (n=204). A 10-mm Hg or more decrease in systolic and diastolic blood pressure was noted in 93 (44%) and 3 (1%) women after the bolus dose (n=210). One hundred thirty-three (62%) women had at least one adverse effect. The adverse effects involved the following systems: central nervous (65%), cardiovascular (58%), gastrointestinal (30%), respiratory (14%), neuromuscular (2%), and other (6%). More serious adverse effects noted in the charts were pulmonary edema (n=6), hypotension (n=40), tachypnea/dyspnea (n=18), chest tightness (n=7), and desaturation (n=6).
CONCLUSION: Adverse effects were frequently noted after oral nifedipine for tocolysis. Diastolic blood pressure was not affected in most women. Our nifedipine protocol includes close monitoring, which seems justified according to these results.
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