Scientific Abstracts

ORIGINAL RESEARCH

ADR/Drug In teractions

1. **Evaluating the usefulness of triggers to detect adverse drug reactions (ADRs) in the medical intensive care unit (ICU).** *Cassandra J. Bellamy, Pharm.D.*, Sandra L. Kane-Gill, Pharm.D., M.Sc., Margaret M. Verrico, R.Ph., Melissa I. Saul, M.S., Steven M. Handler, M.D., M.S., Robert J. Weber, M.S., FASHP; University of Pittsburgh, Pittsburgh, Pa.

PURPOSE: Triggers are signals that alert clinicians to the possible occurrence of ADRs, such as medication antidotes including protamine, phytonadione, and methylprednisolone. Usefulness of triggers to detect ADRs has not been studied in the ICU. The primary objective was to evaluate positive predictive values (PPVs) of triggers for detection of ADRs in the ICU. The secondary objective was to compare the number of ADRs detected using triggers to those voluntarily reported.
METHODS: Adult patients admitted to the medical ICU from July 1, 2005, to June 30, 2006, who received protamine, phytonadione, and methylprednisolone were eligible for the study. A random sample of 50 patients from phytonadione and methylprednisolone groups was evaluated for related ADRs through retrospective chart review. Only 11 patients received protamine during the study period; all were evaluated. ADR occurrence was determined by a clinical pharmacist using an objective assessment instrument. ADRs were defined as undesirable clinical manifestations consequent to and caused by the administration of a drugs. PPVs were calculated as the proportion of triggers that occurred, divided by the number of times that triggers occurred and ADRs were confirmed. Demographics and data to calculate severity of illness scores (SAPSII, SOFA) were obtained from an electronic data repository.
RESULTS: For the 111 patients (51.4% male), the mean ± SD age was 58 ± 16 years. The mean SAPSII score on admission date was 49.2 ± 15.7, and the SOFA score on date of trigger occurrence was 8.3 ± 4.7. PPVs were 0.36, 0.18 and 0.0 for protamine, phytonadione and methylprednisolone, respectively. None of the ADRs detected using these triggers were reported via the institution's voluntary reporting system.
CONCLUSIONS: When developing methods to detect ADRs as part of ICU patient safety surveillance systems, protamine and phytonadione are useful triggers because they result in more frequent ADR detection than voluntary reporting.

2. **Imipenem, meropenem and ertapenem differentially lower serum valproic acid levels in humans.** *Min Jung Kim, M.S.*[1], Young Mi Kim, B.S.[2], Kyoung Ho Park, Ph.D.[1], In Ja Son, Ph.D.[1], Sang Geon Kim, Ph.D.[2]; (1)Department of Pharmacy, Seoul National University Hospital, Seoul, South Korea; (2)College of Pharmacy, Seoul National University, Seoul, South Korea.

PURPOSE: Case reports suggest that concomitant administration of carbapenem decreases serum concentrations of valproic acid in humans. The present study retrospectively evaluates valproic acid levels during carbapenem therapy in Korean patients and compares the possible differential effects of representative carbapenems on valproic acid pharmacokinetics.
METHODS: Consulted therapeutic pharmacokinetic monitoring data for valproic acid were retrospectively reviewed in the patients concomitantly taking imipenem, meropenem or ertapenem (N=36; October 15, 2004– May 31, 2007; female/male, 16/20; Age: 53.8 ± 20.6 years). The clearance of valproic acid was estimated by ABBOTTBASE Pharmacokinetic System software (Abbott Lab) and subjected to Mann-Whitney test and Kruskal-Vallis test (95% CI).
RESULTS: A total of 135 valproic acid serum levels were collected from the SNU database. In the patient records examined, serum concentrations of valproic acid were all decreased after administration of each carbapenem. Estimated clearance of valproic acid in the patients taking valproic acid alone, or valproic acid in combination with imipenem, meropenem or ertapenem was 0.0121 ± 0.0034 L/hr/kg, 0.0163 ± 0.0052 L/hr/kg, 0.0348 ± 0.0130 L/hr/kg, and 0320 ± 0.0098L/hr/kg, respectively. Although imipenem significantly decreased the serum level of valproic acid, this drug interaction was not distinct in a certain group of patients. However, either meropenem or ertapenem consistently lowered serum valproic acid levels in all patients. Moreover, the decreases in valproic acid serum levels by meropenem or ertapenem were more distinguished than that by imipenem. No correlation was noted in the parameters of age and gender.
CONCLUSION: Although combination treatment of valproic acid with carbapenems is not recommended due to their drug interactions, carbapenems are sometimes inevitably used in combination with valproic acid. Our present

findings showing the differential effects of carbapenems on valproic acid pharmacokinetics provide information that may be used for the selection of drugs in clinical practice.
Ambulatory Care

3. **Comparison of efficacy outcomes in three models of anticoagulation management.** *Kelly M. Rudd, Pharm.D., BCPS*; Bassett Healthcare, Cooperstown, NY.

PURPOSE: Both the pharmacy and medical literature suggest that specialized anticoagulation clinics improve the efficacy of therapy management. However, no direct comparisons exist to determine whether pharmacist-managed clinics improve quality of care over existing models. This study was designed to produce a head-to-head comparison of three models in anticoagulation management: 1) usual-care by physicians and/or mid-level providers, 2) a specialty clinic staffed by nurses operating a simple protocol with physician support, and 3) a specialty clinic staffed by a pharmacist and a nurse, operating on the clinical judgement of a pharmacist in a collaborative-practice arrangement.
METHODS: The three models were compared using the efficacy markers of Percent International Normalized Ratios (INRs) in the therapeutic range and Percent Time in Range, as calculated by the Rosenthal method. One year of INRs from chronically anticoagulated General Internal Medicine patients was queried. Anticoagulation indication and INR goals were extracted from the medical record. If the INR goal was not documented, a range was assigned as appropriate from the CHEST anticoagulation guidelines. INRs were considered "in range" if they were within +/- 0.2 from the goal range.
RESULTS: Baseline characteristics were similar between the study groups. The pharmacist- and nurse-operated anticoagulation clinic yielded the highest rates of both Percent Time in Range and Percent INRs in range. The Pharmacist and Nurse (n=6243), Nurse and Protocol (n=3618), and Physician-Midlevel/Usual Care (n=842) models yielded Percent Time in Range values of 83.6%, 71.8%, and 57.4%, respectively (p<0.002.) Percent INRs in range were 74.9%, 67.3%, and 49.4%, respectively (p<0.002.)
CONCLUSIONS: Each study group yielded efficacy outcomes consistent with the literature. Based on the results of this study, it is recommended that all anticoagulated patients within our system be managed by a specialized Anticoagulation Clinic, operating under the clinical judgement of a pharmacist, with nursing and physician support.

4. **Characterization and attainment of LDL-cholesterol goals in high risk family medicine patients.** *Joseph P. Vande Griend, Pharm.D.*, Joseph J. Saseen, Pharm.D., University of Colorado Health Sciences Center, Denver, Colo.

PURPOSE: The National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines recommend a low density lipoprotein-cholesterol (LDL-C) goal of < 100 mg/dL for patients with coronary heart disease (CHD) or risk equivalence (non-coronary atherosclerotic vascular disease [AVD], diabetes). An optional LDL-C goal of < 70 mg/dL is recommended for patients at "very high risk," but this category is vague and not well defined. The primary objectives of this study were to characterize patients with CHD or risk equivalence that were eligible for an LDL-C goal of < 70 mg/dL, and to assess goal attainment rates according to varying definitions of "very high risk."
METHODS: This retrospective study evaluated patients within the University of Colorado Family Medicine system over 2 years with CHD or risk equivalence, identified using ICD-9 codes (n = 445). Five definitions of "very high risk" were determined using ATP III risk parameters. Data were extracted from medical records to categorize patients according to the definitions of "very high risk."
RESULTS: Twenty seven patients did not have LDL-C measurements, and were excluded. Using the 5 definitions, categorization as "very high risk" was 10.8% (AVD plus smoking), 21.5% (AVD plus metabolic syndrome plus uncontrolled hypertension or smoking), 47.1% (AVD plus metabolic syndrome), 52.2% (AVD plus diabetes) and 67.2% (AVD only). LDL-C < 70 mg/dL was attained in 26.7%, 31.1%, 39.0%, 35.8%, and 35.2%, respectively (p=0.4). Overall, 67.2% of patients achieved an LDL-C < 100 mg/dL, 32.5% achieved < 70 mg/dL, and 72% were prescribed a regimen capable of providing at least 30%–40% LDL-C reduction.
CONCLUSION: Classifying patients as "very high risk" is highly variable depending on individual definitions, but this does not appear to predict differences in rates of LDL-C goal attainment of < 70 mg/dL. For simplicity, clinicians should target LDL-C < 70 mg/dL in all patients with AVD, regardless of other risk factors.

Analgesia

5E. **Local analgesia within 1–3 minutes for pediatric venipuncture and peripheral venous cannulation procedures using needle-free powder lidocaine delivery system.** *William T. Zempsky, M.D.*[1], Jolene Bean-Lijewski, M.D., Ph.D.[2], Ralph E. Kauffman, M.D.[3], Jeffrey Koh, M.D.[4], Shobha Malviya, M.D.[5], John

B. Rose, M.D.[6], Michael S. Leong, M.D.[7]; (1)Connecticut Children's Medical Center, Hartford, Conn; (2) Scott and White Memorial Hospital, Temple, Tex; (3)Children's Mercy Hospitals and Clinics, Kansas City, Mo; (4)Oregon Health & Science University, Portland, Ore; (5)University of Michigan Health System, Ann Arbor, Mich; (6)Children's Hospital of Philadelphia, Philadelphia, Pa; (7)Anesiva, Inc., South San Francisco, Calif.

PURPOSE: Despite recent trends showing improvements in pain management among children, peripheral needle-stick procedures remain a common source of pain and anxiety in this population. This study examined whether needle-free powder lidocaine delivery system, a sterile, prefilled, disposable system that delivers lidocaine powder into the epidermis, produces effective local analgesia within 1–3 minutes for venipuncture and peripheral venous cannulation procedures in children.
METHODS: This was a prospective, single-dose, multicenter, double-blind, placebo-controlled study. Pediatric patients (age 3–18 years) were randomly assigned to receive needle-free powder lidocaine delivery system (0.5 mg lidocaine/20 bar pressure; n=289) or placebo (n=285) from an identically configured system at the antecubital fossa or back of the hand. Comfort of administration was reported by the patient immediately after actuation of active system or sham placebo using the Wong-Baker FACES pain-rating scale (0–5). One to 3 minutes later, the resulting pain of venipuncture or peripheral venous cannulation procedures was self-reported using the Wong-Baker FACES scale. Safety was assessed by monitoring adverse events (AEs) and by screening the administration site for erythema, edema, pruritus, and petechiae.
RESULTS: Demographic characteristics, proportion of venipuncture and cannulation procedures, and delivery sites were similarly distributed in both treatment groups. Immediately following actuation, the mean FACES scores were 0.54 and 0.24 in the active system and sham placebo groups, respectively. After venipuncture and cannulation, adjusted mean FACES scores were 1.73 and 2.08 in the active system and sham placebo groups, respectively (p=0.007). All treatment-related AEs were mild and resolved without sequelae. These included mild erythema and edema. Petechiae were more frequent in the active system group and were generally mild.
CONCLUSIONS: The needle-free powder lidocaine delivery system was well tolerated and produced significant analgesia within 1–3 minutes in children undergoing venipuncture and peripheral venous cannulation procedures.

6. **Oral transmucosal fentanyl citrate (OTFC) for dyspnea in terminally ill patients: a pilot study.**
Sheila Kang, Pharm.D.[1], Erica Swatko, Pharm.D., candidate[1], Alberto Gauna, M.D.[2], Mary Triano, CRNP-C[2], Vincent J. Vanston, M.D.[2]; (1)Wilkes University Nesbitt College of Pharmacy and Nursing, Wilkes Barre, Pa; (2)Scranton Temple Residency Program, Scranton, Pa.

OBJECTIVE: To evaluate the efficacy and safety of oral transmucosal fentanyl citrate (OTFC) in terminally ill patients who are experiencing dyspnea.
METHODS: A prospective, open-label, non-controlled pilot study conducted from May 2006 to May 2007. Eligible patients were 18 years or older with a satisfactory baseline cognitive status and a terminal illness (cancer, end-stage COPD, or end-stage CHF) who were admitted to the hospice unit complaining of dyspnea on exertion or at rest. Patients with moderate to severe mucositis, contraindications or allergies to the study drug, a psychiatric disease, or a history or suspicion of substance abuse were excluded from the study. At the onset of dyspnea, enrolled patients received a 200 mcg OTFC lozenge. Higher doses were available for more opioid-experienced patients. Patients were asked to verbally rate their dyspnea using a 10-point visual analog scale (10 = severe shortness of breath). Severity of dyspnea, RR, and SaO$_2$ were recorded at baseline and every 15-minutes for 60 minutes by a study nurse. Failure to alleviate dyspnea by at least 50% at 30 minutes resulted in either a second dose of OTFC (same strength) or the administration of an alternative opioid for dyspnea at the discretion of the principal investigator. Patients receiving OTFC for dyspnea were evaluated for about 48 hours.
RESULTS: Four patients were enrolled. All patients experienced relief as soon as 5 minutes and achieved at least a 50% reduction in dyspnea within 15 minutes. No significant adverse events were reported.
CONCLUSION: This pilot study suggests OTFC may serve as a safe alternative agent to standard opioid therapy for dyspnea relief in patients who are terminally ill. Given its rapid onset of action and accessible delivery system, OTFC may provide a convenient self-management approach for dyspnea for outpatient and inpatient hospice programs. The initial findings in our pilot study are promising and warrant further research.

Cardiovascular

7E. **Attainment of blood pressure goals in patients with Stage 2 hypertension treated with olmesartan medoxomil/hydrochlorothiazide or benazepril/amlodipine besylate.** *Joel Neutel, M.D.*[1], Dean Kereiakes, M.D.[2], Henry Punzi, M.D.[3], Findlay Walker, M.D.[4], Robert Dubiel, Pharm.D.[4], Jianbo Xu,

M.S.[4]; (1)Orange County Research Center, Tustin, Calif; (2)The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, Ohio; (3)Punzi Medical Center and Hypertension Research Institute, Carrollton, Tex; (4)Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: Most patients with Stage 2 hypertension require two or more blood pressure (BP)-lowering agents to achieve BP goals. BP-lowering efficacy of olmesartan medoxomil (OM) plus hydrochlorothiazide (HCTZ) versus benazepril (BEN) plus amlodipine besylate (AML) was assessed in a randomized, double-blind, multicenter titration study.
METHODS: After a 3–4-week placebo run-in, 190 patients with Stage 2 hypertension were randomized to increasing doses of OM (20 mg week 0–2 and 40 mg week 2–4) and BEN (10 mg week 0–2 and 20 mg week 2–4). In weeks 4–8, patients received either OM 40 mg/HCTZ 12.5 mg or BEN 20 mg/AML 5 mg. In weeks 8–12, HCTZ and AML doses increased to 25 mg and 10 mg respectively. Secondary end points were cumulative percentage of patients achieving the following BP goals at weeks 2 and 4 (monotherapy) and weeks 8 and 12 (combination therapy): combined goals < 140/90 mm Hg, < 130/85 mm Hg, or < 130/80 mm Hg. Patients (non-cumulative %) achieving BP goals at each dose level were also assessed.
RESULTS: Significantly more patients achieved BP goals with OM 40 mg/HCTZ 12.5 mg than with BEN 20 mg/AML 5 mg 43.6% vs 20.8%, $p=0.003$ [< 140/90 mm Hg]; 24.5% vs 6.3%, $p=0.001$ [< 130/85 mm Hg]; 14.9% vs 4.2%, $p=0.022$ [< 130/80 mm Hg] and by significantly more patients in the OM 40 mg/HCTZ 25 mg group than in the BEN 20 mg/AML 10 mg group 60.6% vs 38.5%, $p=0.011$ [< 140/90 mm Hg]; 41.5% vs 18.8%, $p=0.002$ [< 130/85 mm Hg]; 29.8% vs 12.5%, $p=0.009$ [< 130/80 mm Hg]. At the end of combination therapy, significantly more patients given OM plus HCTZ (40/12.5 mg and 40/25 mg) achieved BP goal of < 140/90 mm Hg versus BEN plus AML (20/5 mg and 20/10 mg), 66% vs 45% respectively, ($p=0.006$), as well as the BP goals of < 130/85 mm Hg (45% vs 21%, respectively, $p=0.001$) and < 130/80 mm Hg (33% vs 14%, respectively, $p=0.006$).
CONCLUSIONS: The combination of OM+HCTZ is effective at lowering BP in patients with Stage 2 hypertension. A greater percentage of patients achieved target BP goals than those treated with the combination of BEN+AML.
Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, Chicago, Ill, May 19-22, 2007.

8E. **Correlation of Shortened Ambulatory Blood Pressure Monitoring Sessions with Full 24-hour Sessions**. Cindy Weber, Pharm.D.[1], *Michael Ernst, Pharm.D.*[2], Jeffrey Dawson, Sc.D.[3], George Bergus, M.D.[4], Barry Carter, Pharm.D.[5]; (1)College of Pharmacy, University of Iowa, Iowa City, Iowa; (2)College of Pharmacy; and, Dept of Family Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa; (3)College of Public Health, University of Iowa, Iowa City, Iowa; (4)Dept of Family Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa; (5)College of Pharmacy, and Dept of Family Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa.

PURPOSE: Ambulatory blood pressure monitoring (ABPM) is highly useful in evaluating cardiovascular risk. The purpose of the study was to ascertain whether shorter ABPM sessions can predict overall blood pressure (BP) average determined from a full 24-hour session.
METHODS: 338 previously performed ABPM sessions were used for this study. Hourly averages were used. The first hour of each session was excluded from analysis as preliminary analyses showed the first hour to be an average of 5.4 mm Hg higher compared with the subsequent 23 hours ($p<0.001$). Shortened sessions of 4, 6, and 8 hours were considered. Pearson correlations were calculated. In addition to determining correlations between the shortened time periods and the whole time period (e.g., 2nd–4th hour vs. 2nd–24th hour), we also calculated correlations between the shortened time periods and the remainder of the time period (e.g., 2nd–4th hour vs. 5th–24th hour).
RESULTS: The Table shows the time periods analyzed and their correlation. All p-values were < 0.001. Incremental benefit of correlation is greatest when increasing the monitoring session from 4 to 6 hours. When adjusted for time-of-day, correlations were nearly identical to those reported in the Table.

Shortened Time Period vs. Entire Time Period

Time Period (Correlation)
2nd–4th hour vs. 2nd–24th hour (0.726); 2nd–6th hour vs. 2nd–24th hour (0.824); 2nd–8th hour vs. 2nd–24th hour (0.865)

Shortened Time Period vs. Remainder of Time Period

Time Period (Correlation)
2nd–4th hour vs. 5th–24th hour (0.633); 2nd–6th hour vs. 7th–24th hour (0.702); 2nd–8th hour vs. 9th–24th hour (0.700)

CONCLUSIONS: Shortened ABPM sessions of 6 hours duration may be reasonable for evaluating a patient's overall BP. However, they will not characterize diurnal variation, and a full 24-hour session may remain preferred for research purposes and to evaluate overall cardiovascular risk.

Presented at American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, Chicago, Ill, May 19-22, 2007.

9. **Factors predicting a successful ambulatory blood pressure monitoring session.** *Michelle A. O'Connor, Pharm.D.*[1], Michael Ernst, Pharm.D., BCPS[2], Cindy Weber, Pharm.D.[3], Jeffrey Dawson, Sc.D.[4], Barry L. Carter, Pharm.D., FCCP, FAHA, BCPS [5], George Bergus, M.D.[6]; (1)University of Iowa Hospitals and Clinics, Iowa City, Iowa; (2)College of Pharmacy; and, Dept of Family Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa; (3)College of Pharmacy, University of Iowa, Iowa City, Iowa; (4)College of Public Health, University of Iowa, Iowa City, Iowa; (5)Center for Research in the Implementation of Innovative Strategies in Practice (CRIISP), Iowa City VA Medical Center, University of Iowa College of Pharmacy, Iowa City, Iowa; (6)Dept of Family Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa.

PURPOSE: During a typical ambulatory blood pressure monitoring (ABPM) session, blood pressure (BP) measurements are obtained every 20–30 minutes over 24 hours, resulting in a total of 50–70 readings. Although ABPM has specific advantages over office BP monitoring, it is costly and recommended only for certain indications. Standards for ABPM maintain that the number of valid BP readings obtained during a session should equal at least 80% of the total readings attempted to be considered successful. Anecdotal experience suggests that certain patients obtain incomplete ABPM results. The purpose of this study is to identify patient characteristics predictive of unsuccessful ABPM sessions.

METHODS: Logistic regression was performed on a random sample of previously completed ABPM sessions. The percentage of successful readings obtained out of the total number attempted during the session was the dependent variable. Age, gender, weight, height, BMI, occupation, clinic BP, travel distance to clinic, presence of diabetes mellitus (DM) or renal disease, and number of antihypertensive medications were examined as independent predictors.

RESULTS: The analysis included 297 subjects. ABPM session completion was analyzed as a continuous variable (0%–100% successful readings) and dichotomous variable (0%–79% or 80%–100% successful readings). Negative association with ABPM session completion was found with DM (continuous variable analysis: p=0.002; dichotomous variable analysis: OR = 0.29; 95% CI = 0.12–0.69; p=0.005) and renal disease (continuous variable analysis: p=0.009; dichotomous variable analysis: OR = 0.31; 95% CI = 0.11–0.87; p=0.026). The significance of the association seen with renal disease was lost after controlling for DM.

CONCLUSIONS: ABPM is successful for most subjects; however, a diagnosis of DM is associated with less complete ABPM results. Additional research is needed to clarify this association. Adaptation and individualization of the ABPM process may be necessary to improve results for certain patients, such as those with DM.

10. **Accuracy of Automated Community Pharmacy-Based Blood Pressure Devices.** *Alan J. Zillich, Pharm.D.*, Jasmine D. Gonzalvo, Pharm.D.; Purdue University School of Pharmacy, Indianapolis, Ind.

PURPOSE: The purpose of this study is to estimate the accuracy and reproducibility of fixed-location automated blood pressure devices.

METHODS: A stratified, random sample of 100 community pharmacy-based (chain, independent, grocery, mass merchandise) fixed-location automated blood pressure devices (ABPDs) was compared to a scientifically validated self-home blood pressure device (HBPD). Upon agreement to participate, the pharmacy was visited by 1 of 5 nonhypertensive subjects. On site, a questionnaire was presented to the pharmacy manager to collect information about the ABPD. The questionnaire elicited information on make, model, production year, maintenance history, and date of installation of the ABPD as well as pharmacy name, geographic location, and prescription volume. In accordance with printed instructions provided with the store-based machines, subjects obtained blood pressure readings and compared these to blood pressure measures collected according to standard techniques for HBPDs. A random order of three readings for each device was recorded and averaged during the pharmacy visit. Each measurement was separated by 1 minute of rest. The average readings for each device were compared using paired-samples t-test.

RESULTS: The average age of the ABPDs was 5.2 years, and most were calibrated once every 6 months. The mean systolic blood pressure for participants using the HBPD and the ABPD was 116 (+/- 11.3) mm Hg and 119 (+/- 12.5) mm Hg, respectively (p<0.01). The mean diastolic blood pressures were 71 (+/- 8.6) mm Hg with the HBPD and 70 (+/- 8.9) mm Hg with the ABPD (p=0.27).

CONCLUSIONS: Blood pressure monitoring in the community setting using ABPDs was 3 mm Hg higher than HBPDs among nonhypertensive subjects. Larger-scale studies are necessary to examine the clinical significance

of the variability among different blood pressure measurement devices in the community setting among patients with hypertension.

11. **The prevalence and overlap of select cardiovascular co-morbidities among US adults with dyslipidemia, by lipid-lowering medication use status.** *Sean D. Candrilli, M.S.*[1], Andreas Kuznik, Ph.D.[2], Amy E. Rudolph, Ph.D.[2]; (1)RTI Health Solutions, Research Triangle Park, NC; (2)Pfizer, Inc., New York, NY.

PURPOSE: Using the combined 1999-2000, 2001-2002, and 2003-2004 (99-04) National Health and Nutrition Examination Surveys (NHANES), we generated current estimates of the prevalence and overlap of select cardiovascular comorbidities among US adults ≥ age 20 years with dyslipidemia (DYS), stratified by lipid-lowering medication use.
METHODS: We analyzed 5,403 NHANES respondents ≥ age 20 years who had complete data for a number of clinical and self-reported parameters necessary for analysis. Sampling weights scaled to the US Census' 2007 projected US adult population were used to generate nationally representative estimates. Respondent-specific self-reported and laboratory data were used to assess the prevalence and overlap of DYS, congestive heart failure (CHF), coronary heart disease (CHD), history of stroke, and diabetes, stratified by lipid-lowering medication use.
RESULTS: Using the 99-04 NHANES, we estimated that among US adults ≥ age 20 years (218 million [M]), 74.9M (36.4%) have DYS. Of these, 3.5M (4.4%) have CHF, 11.1M (13.9%) have CHD, 4.3M (5.4%) have a history of stroke, 13.6M (17.1%) have diabetes, and 25.1M (31.5%) have ≥ 1 of these comorbidities. Among the 22.4M (28.2%) with DYS who are taking a lipid-lowering medication, these figures are 1.3M (5.8%), 5.4M (24.3%), 1.9M (8.6%), 5.4M (24.1%), and 10.2M (45.5%), respectively. Finally, among the 57.2M (71.8%) with DYS who are not on a lipid-lowering medication, these figures are 2.2M (3.9%), 5.6M (9.9%), 2.4M (4.2%), 8.2M (14.4%), and 14.9M (26.1%), respectively.
CONCLUSIONS: Nearly 33% of US adults with DYS have one or more of the cardiovascular conditions studied. Among adults with DYS who are receiving lipid-lowering medication, 45.5% report having comorbidities that put them at high risk for new or recurring cardiovascular events. However, a significant proportion (26.1%) of adults with DYS who are not taking a lipid-lowering medication also have significant comorbidities, posing a potentially considerable public health concern.

12. **Cost effectiveness of glycoprotein receptor inhibitors in diabetics with non-STEMI ACS.** *Mark Malesker, Pharm.D., FCCP*, Daniel Hilleman, Pharm.D., FCCP; Creighton University Medical Center, Omaha, Neb.

PURPOSE: Patients with diabetes presenting with non-STEMI ACS have higher morbidity/mortality than patients without diabetes. The purpose of the present analysis was to evaluate the cost-effectiveness of the three commercially available glycoprotein IIb/IIIa inhibitors (GPI) in patients with diabetes enrolled in non-STEMI ACS mortality trials.
METHODS: Trials of GPI in non-STEMI ACS were identified via literature search of PubMed, Embase, Medline, and the Cochrane Library. Citations reporting mortality outcomes in diabetic subgroups of patients were identified. Absolute risk reductions were calculated for diabetic patients in each identified trial and included in a meta-analysis. A traditional cost-effectiveness ratio was calculated using 2007 costs for GPI and study-specific data concerning drug dosing and efficacy [CE ratio equals (cost difference of treatment divided by absolute risk reduction) x 100].
RESULTS: Four trials (PRISM, PRISM-Plus, PURSUIT, GUSTO-IV) using three GPI (abciximab, epitifibatide, tirofiban) were identified. A total of 4889 diabetic patients were included in these trials. Pooled 30-day mortality was 6.46% for placebo and 4.49% for GPI (RRR = -30.5%; 95% CI = -8.5% to -45.8%; p=0.004). The calculated absolute risk reduction for each trial was 1.0% for PURSUIT, 2.4% for PRISM, 3.1% for PRISM-Plus, 2.7% GUSTO-IV, and 2.0% for the pooled data. The cost-effectiveness ratio was $182,500 for PURSUIT, $35,417 for PRISM, $27,419 for PRISM-Plus and $101,889 for GUSTO-IV. Only tirofiban (PRISM, PRISM-Plus) was determined to be cost-effective in patients with diabetes.
CONCLUSIONS: GPI therapy reduces mortality in patients with diabetes admitted with non-STEMI ACS, but the cost-effectiveness of these agents is not consistent across the class of drugs. Tirofiban was the only cost-effective GPA in diabetic patients with non-STEMI ACS.

13. **The effect of selective adenosine diphosphate (ADP) platelet receptor inhibition on coated-platelet production.** *Nicholas B. Norgard, Pharm.D.*[1], George L. Dale, Ph.D.[2]; (1)University of Oklahoma Health Sciences Center, College of Pharmacy, Oklahoma City, Okla; (2)University of Oklahoma Health Sciences Center, Department of Medicine, Oklahoma City, Okla.

PURPOSE: Coated platelets are a subpopulation of activated platelets generated upon dual-agonist stimulation with collagen plus thrombin. These cells have an enhanced ability to generate thrombin and are thought to play a major role in the initiation and maintenance of thrombotic occlusions. Adenosine diphosphate (ADP) is a relatively weak platelet agonist that can amplify the platelet response to stronger agonists. When ADP is added to thrombin and collagen, *in vitro*, the percentage of platelets that are converted to coated platelets is significantly increased. ADP has two receptors on the platelet surface, $P2Y_1$ and $P2Y_{12}$, and inhibition of either ADP receptor reduces ADP-induced platelet aggregation. This study was designed to determine whether the amplifying effect of ADP on coated-platelet production could be neutralized by selectively inhibiting either $P2Y_1$ or $P2Y_{12}$.

METHODS: Blood samples were drawn from consenting healthy volunteers. Platelet samples were stimulated with 500 ng/mL convulxin and 0.5 U/mL thrombin, with or without 6 μM ADP, in the presence of the $P2Y_1$ inhibitor, MRS2179 (100 μM), or the $P2Y_{12}$ inhibitor, MRS2395 (100 μM). Flow cytometry was used to analyze coated-platelet levels, expressed as % of total platelets.

RESULTS:

$P2Y_1$ Inhibition

Convulxin plus thrombin (C/T) ±6 mM ADP ± 100 mM MRS2179

C/T (n=3)	C/T+ MRS2179	C/T+ ADP	C/T + ADP+ MRS2179
34.0 ± 14.3	32.3 ± 14.2	47.4 ± 4.6	49.6 ± 1.5

$P2Y_{12}$ Inhibition

Convulxin plus thrombin (C/T) ± 6mM ADP ± 100 mM MRS2395

C/T (n=4)	C/T+ MRS2395	C/T+ ADP	C/T+ ADP+ MRS2395
37.7 ± 6.1	8.3 ± 0.5	54.5 ± 7.7	16.2 ± 2.3

CONCLUSION: $P2Y_1$ receptor inhibition had no effect on either coated platelet formation or ADP-mediated stimulation of coated-platelet generation. Surprisingly, $P2Y_{12}$ receptor inhibition significantly reduced overall coated-platelet production but still allowed some ADP-mediated stimulation. Although the mechanism of this observation remains unknown, it could represent a new anti-thrombotic mechanism of the selective $P2Y_{12}$ receptor inhibitors and justifies further study of possible effects of clopidogrel administration on coated-platelet production.

14. **The prevalence and overlap of select cardiovascular co-morbidities among the US elderly with dyslipidemia, by lipid-lowering medication use status.** *Sean D. Candrilli, M.S.*[1], Andreas Kuznik, Ph.D.[2], Amy E. Rudolph, Ph.D.[2]; (1)RTI Health Solutions, Research Triangle Park, NC; (2)Pfizer, Inc., New York, NY.

PURPOSE: Using the combined 1999-2000, 2001-2002, and 2003-2004 (99-04) National Health and Nutrition Examination Surveys (NHANES), we generated current estimates of the prevalence and overlap of cardiovascular co-morbidities among US adults ≥ age 65 years (elderly) with dyslipidemia (DYS), stratified by lipid-lowering medication use.

METHODS: We analyzed 1331 elderly 99-04 NHANES respondents who had complete data for a number of clinical and self-reported parameters. Respondent-specific self-reported and laboratory data were used to assess the prevalence and overlap of DYS, congestive heart failure (CHF), coronary heart disease (CHD), history of stroke, and diabetes, stratified by lipid-lowering medication use. NHANES sampling weights scaled to the US Census 2007 projected US elderly population were used to generate nationally representative estimates.

RESULTS: Using the 99-04 NHANES, we estimated that among the US elderly (32.6 million [M]) with DYS (22.7M, 69.4%), 1.9M (8.6%) have CHF, 5.8M (25.8%) have CHD, 2.2M (9.6%) have a history of stroke, 4.7M (20.9%) have diabetes, and 10.6M (47.0%) have one or more of these co-morbidities. Among the 8.5M with DYS on lipid-lowering medication, these figures are 0.6M (7.0%), 2.7M (31.8%), 1.0M (12.1%), 2.1M (24.9%), and 4.4M (52.2%), respectively. Finally, among the elderly with DYS but who are not on a lipid-lowering medication (14.1M), these figures are 1.4M (9.6%), 3.1M (22.2%), 1.1M (8.0%), 2.6M (18.5%), and 6.2M (43.8%) respectively.

CONCLUSIONS: Nearly half (47.0%) of elderly US citizens with DYS have ≥ 1 of the cardiovascular conditions studied. Among those who are on a lipid-lowering medication, 52.2% report having comorbidities that put them at high risk for new or recurring cardiovascular events. Even more noteworthy is that a high proportion (43.8%) of untreated elderly patients with DYS also have significant comorbidities, which highlights a critical unmet medical need for this growing population.

15. **Benefit of clopidogrel therapy beyond 12 months in patients receiving drug-eluting stents.** *Paul P. Dobesh, Pharm.D.*, Donald G Klepser, Ph.D.; University of Nebraska Medical Center, Omaha, Neb.

PURPOSE: Patients with intracoronary stent deployment should receive dual antiplatelet therapy (DAT) with aspirin and clopidogrel to prevent platelet aggregation and stent thrombosis. Initial recommendations for the duration of DAT after receiving a drug-eluting stent (DES) were 3–6 months. A recent science advisory has now recommended up to 12 months of DAT for patients receiving a DES. This new recommendation is based on a number of retrospective cohort studies demonstrating an increase in stent thrombosis out to 1 year after discontinuation of DAT at 6 months. The outcomes associated with continuing DAT for beyond a year are unknown and may significantly affect patients receiving DES.

METHODS: This retrospective cohort study used claims data from a private insurer (04/2003-01/2007). Patients with a DES deployment and 24 months of continuous follow-up were identified using Diagnosis Related Group and Current Procedure Terminology codes. The duration of clopidogrel therapy after the stent deployment was calculated from prescription claims. Duration of therapy was categorized as $\leq$ 12 months or > 12 months. The number of cardiac events was compared between the groups using the Kruskal-Wallis test.

RESULTS: We identified 422 patients who received a DES and had 24 months of continuous follow up. Mean age was 65 years and 68% were male. Patients receiving > 12 months of clopidogrel (n=118) demonstrated a 16% reduction in cardiac events compared with patients receiving clopidogrel for $\leq$ 12 months (n=304) (65% vs. 77%; p=0.018). Patients taking clopidogrel for $\leq$ 12 months and > 12 months had an average of 3.50 and 2.37 cardiac events, respectively, over the 24 month period (p=0.011).

CONCLUSIONS: Patients with > 12 months of clopidogrel use had fewer cardiac events in the 24 months following the deployment of a DES. Therefore, continuing clopidogrel for longer than the current recommended time may need to be considered for DES patients.

16E. **Use of perioperative nesiritide improves clinical outcomes and decreases resource utilization in heart failure patients undergoing cardiac surgery.** *Jennifer R. Smith, Pharm.D.*; Barnes-Jewish Hospital, Saint Louis, Mo.

PURPOSE: To evaluate the impact of nesiritide (NES) on resource utilization, survival, and postoperative complications in patients with heart failure (HF) undergoing cardiac surgery.

METHODS: The Nesiritide Administered Peri-Anesthesia in Patients Undergoing Cardiac Surgery (NAPA) trial was a prospective, multicenter, randomized, double-blind trial. Patients (n=279) at 52 US centers undergoing CABG surgery utilizing CPB, ± MVR, and LVEF $\leq$ 40% were randomized to NES (0.01 mcg/kg/min, no bolus) or placebo (PLB) plus usual care for 24–96 hrs after induction of anesthesia. GFR, adverse events, LOS, and 180-day mortality were prespecified end points. Multivariable regression was performed to adjust for demographics and comorbidities.

RESULTS: Patients were randomized and treated with NES (n=141) or PLB (n=138). Mean age was 64 ± 11 yrs. Hospital LOS (days) was significantly shorter (p<0.016) in NES (9.1 ± 0.7) than PLB (11.5 ± 0.7 days). This relationship persisted after adjusting for risk factors in all patients and high-risk subgroups based on acute renal failure and valve procedures in addition to CABG. 30-day readmission rates were similar (p=0.387) for NES (16%) and PLB (12%). NES patients had significantly decreased mortality at 180 days (HR = 0.44; 95% CI = 0.19–1.01, p=0.046). Postoperative atrial fibrillation and GFR decrease > 25% were also less with NES.

CONCLUSIONS: Perioperative use of nesiritide in HF patients undergoing cardiac surgery significantly improved survival, reduced LOS, and decreased postoperative complications, including AF and reduced GFR. Published in JACC 2007;49(9, suppl 1):301A–302A. Abstract 1009-15.

17E. **Atorvastatin inhibits interleukin 1-beta-induced production of epithelial neutrophil-activating peptide from human endothelial cells in a dose-dependent fashion.** *Gregory J. Welder, A.A.*[1], Nasser Chegini, Ph.D.[2], Issam Zineh, Pharm.D.[1]; (1)Department of Pharmacy Practice and Center for Pharmacogenomics, University of Florida College of Pharmacy, Gainesville, Fla; (2)Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, Fla.

PURPOSE: Endothelial inflammation has been implicated in cardiovascular disease (CVD). A prototypical inflammatory cytokine interleukin-1beta (IL-1β) stimulates endothelial expression of epithelial neutrophil-activating peptide (ENA-78), which may be important in early inflammatory processes in CVD. HMG-CoA reductase inhibitors (statins) reduce CVD morbidity and mortality in part due to anti-inflammatory actions. We therefore investigated whether atorvastatin inhibits IL-1β-induced ENA-78 production in human umbilical endothelial cells (HUVEC).

METHODS: We cultured HUVEC (Cambrex BioScience Inc., Walkersville, MD) to 80% confluence in growth media at physiological temperature and 5% CO2. Treatment groups included unstimulated control, 2 ng/ml IL-1β alone, and IL-1β plus atorvastatin calcium ranging from 1–50 μM. Experiments were performed in duplicate. ENA-78 levels were measured using cytometric fluorescence detection (R&D Systems, Minneapolis, Minn;

Luminex 100IS, Luminex Corp., Austin, Tex). ENA-78 concentrations were normalized to total protein. One-way ANOVA with post-hoc Tukey was performed; p<0.05 was considered significant.
RESULTS: Constitutive and IL-1β-stimulated ENA-78 concentrations were 69 ± 11 and 4075 ± 360 pg/mg, respectively (p<0.0001). Atorvastatin inhibited ENA-78 production in a dose dependent-fashion, ranging from 38% to 99% inhibition (p<0.0001) with atorvastatin 1μ M–50 μM. In stimulated HUVEC treated with atorvastatin ≥ 25 μM, ENA-78 concentrations were no different from control (p≥0.99).
CONCLUSION: Atorvastatin dose dependently inhibits IL-1β-stimulated release of ENA-78 from HUVEC. Our finding offers novel insight into the potential anti-inflammatory role of statins. The mechanism of our finding and clinical implications should be further investigated.
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18. **Efficacy of intensive insulin protocols in the hospitalized cardiac patient.** *John P. Lindsley, Pharm.D.*[1], Michelle M. Gearhart, Pharm.D.[1], Emily J. Young, Pharm.D., BCPS[1], Ryan Steadman, Pharm.D.[2], Mercedes Falciglia, M.D.[3]; (1)University Hospital, Cincinnati, Ohio; (2)University of Cincinnati College of Pharmacy, Cincinnati, Ohio; (3)University of Cincinnati College of Medicine, Cincinnati, Ohio.

PURPOSE: To evaluate the efficacy of newly initiated intensive insulin protocols in the hospitalized cardiac patient.
METHODS: A retrospective evaluation of the impact of intensive insulin protocols was conducted. On July 1, 2006, new intravenous and subcutaneous intensive insulin protocols were instituted in the Coronary Care Unit, Cardiac Stepdown, and Telemetry units of a large, tertiary medical center. Data was collected from computerized medical records. The primary outcome, mean blood glucose was compared retrospectively in patients admitted pre and post initiation of the intensive insulin protocol. Secondary outcomes included median blood glucose, hypoglycemic episodes, intensive care unit length of stay, hospital length of stay, ventilator days, mortality, number of discharge regimens, and differences in discharge regimens compared to admission.
RESULTS: One hundred and ninety patients were evaluated in the pre-protocol group and 176 patients were evaluated in the post-protocol group. Mean blood glucose in the pre-protocol group was 168.1 mg/dL versus 154.1 mg/dL in the post-protocol group (p=0.021). Median blood glucoses in the pre-protocol group were 154.5 mg/dL versus 139.0 mg/dL in the post-protocol group (p=0.046). Hypoglycemic episodes in the pre-protocol group were 0.0713 per patient day versus 0.0668 per patient day in the post-protocol group (p=0.83).
CONCLUSIONS: Initiation of intensive insulin protocols in the hospitalized cardiac patient was effective in decreasing mean blood glucose and resulted in no change in the number of hypoglycemic episodes.

19. **Impact of screening protocol in improving aspirin utilization for primary prevention of coronary heart disease.** *Eunice P. Chung, Pharm.D.*, Bryan A. Katuin, Pharm.D., Jeany K. Jun, Pharm.D., Ryan Quist, Ph.D., Alan D. Cundari, D.O.; Western University of Health Sciences, College of Pharmacy, Pomona, Calif.

PURPOSE: The primary objective was to evaluate the impact of screening protocol in increasing aspirin use for primary prevention of coronary heart disease (CHD). Secondary objective was to identify factors associated with underutilization of aspirin for primary prevention of CHD prior to the protocol implementation.
METHODS: A protocol to determine the need for aspirin therapy for primary prevention of CHD was developed based on guidelines from American Heart Association and American Diabetes Association. Using the protocol, all patients > age 40 years with no prior history of myocardial infarction, receiving care at a family medicine clinic were screened and initiated on aspirin. A retrospective chart review was conducted for all patients screened during the 8 weeks (2/26/07–4/20/07) to evaluate the rate of ASA usage before and after the protocol and to identify potential factors associated with aspirin underutilization prior to the protocol implementation. The primary outcome was evaluated based on superiority test of proportions. Spearman correlation test with Bonferroni adjustment was used for evaluation of the secondary objective.
RESULTS: Of the 176 patients screened, 74 met the criteria for aspirin therapy for primary prevention of CHD according to the protocol. Aspirin use increased significantly from 34 (45.9%) patients at baseline to 66 (89.2%) patients (p<0.001) after the protocol implementation. Although lower usage of aspirin was identified among male patients, Hispanic patients, and patients with local government funded health coverage, the results did not reach statistical significance. No identifiable factors were associated with underutilization of aspirin at baseline.
CONCLUSION: Aspirin is underutilized for primary prevention of CHD despite ample evidence substantiating the benefits. The results of the study suggest that implementing a screening protocol is an effective method of improving aspirin use for primary prevention of CHD in a primary care setting.

20. **Negative and positive predictors of adherence in patients with heart failure.** *Kaysey R. Cloud, Pharm.D.*, Toni L. Ripley, Pharm.D., BCPS, Donald L. Harrison, Ph.D.; University of Oklahoma College of Pharmacy, Oklahoma City, Okla.

PURPOSE: A recent post-hoc analysis of the CHARM study showed that good medication adherence in the heart failure (HF) population was independently associated with decreased morbidity and mortality, regardless of treatment assignment. The specific aim of this study was to identify both negative and positive influences on medication adherence in patients with HF. The primary hypothesis is that an inverse relationship exists between the complexity of medication regimens and patient adherence.
METHODS: A survey was verbally administered to patients with a current diagnosis of HF at a faculty-based HF clinic, which was designed to collect data regarding adherence behaviors, as well as existing beliefs about medications. The survey was adopted from a validated questionnaire and showed good reliability (reliability, per Cronbach's test ranged from 0.767 to 0.779). Additional information was collected to assess patient medication regimens, medical history, and social history. The complexity of each medication regimen was quantified using the validated Medication Regimen Complexity Index (MRCI), which assigned numerical values to regimens based upon a combination of dosage form, frequency, and any additional directions.
RESULTS: A total of 50 patients were surveyed, with a median number of medications and a MRCI score of 12 and 19.5, respectively. The analysis revealed that complexity was directly, not inversely, related to adherence ($p<0.01$). Significant predictors of poor adherence included confusion with medication administration, presence of adverse effects or generally feeling worse, interference with daily plans, and taking fewer medications ($p<0.05$).
CONCLUSION: These findings challenge the concept that more complex medication regimens are associated with worse adherence. These results indicate that the patients with less complex regimens tend to be less adherent than those with more complex regimens. The results also provide data that could help identify patients at higher risk of non-adherence.

21. **Carvedilol increases blood pressure response to phenylephrine infusion in class C heart failure subjects: Evidence of improved vascular α_1-receptor signal transduction.** *Benjamin W. Van Tassell, Pharm.D., BCPS*[1], Matthew Rondina, M.D.[2], Franklin Huggins, Pharm.D.[1], Edward M. Gilbert, M.D.[2], Mark A. Munger, Pharm.D., FCCP[1]; (1)University of Utah, College of Pharmacy, SLC, Utah; (2)University of Utah, School of Medicine, SLC, Utah.

PURPOSE: Myocardial α_1-receptor (α_1R) stimulation produces myocyte hypertrophy and in animal models. Increased myocardial α_1R signal transduction occurs in human heart failure (HF) due to increased sympathetic tone and a relative increase in myocardial α_1R density. These findings suggest a possible role for α_1R antagonists to reverse pathologic myocardial remodeling in HF. To date, signal transduction at the vascular α_1R has been poorly characterized in HF subjects and may be regulated independently of myocardial α_1Rs. Preliminary reports suggest that vascular α_1Rs are desensitized in HF. We examined α_1R signal transduction in HF subjects by measuring BP response to phenylephrine (PE) infusions during carvedilol up-titration and chronic carvedilol therapy.
METHODS: 12 HF subjects (NYHA class II-III, LVEF < 0.40) were up-titrated to maximum tolerable carvedilol doses (12.5–50 mg BID). Subjects underwent α_1R stimulation testing (PE infusion) at baseline, 2 weeks after each carvedilol dose titration, and after 6 months maintenance with maximum tolerated carvedilol dose. PE infusions were titrated from 0.5 to 5.0 mcg/kg/min with BP recorded every 5 minutes. PE dose response was evaluated by the PE rate required to elicit a 20 mm Hg increase in systolic BP, designated PS_{20}.
RESULTS: All doses of carvedilol produced significant reductions in pre-infusion measures of heart rate, systolic BP, and mean arterial pressure (MAP). However, carvedilol produced a paradoxical trend toward reduction in PS_{20} (indicating increased PE response) that attained significance with carvedilol 25 mg (PS_{20} ratio vs baseline = 0.67, $p<0.001$). All effects were maintained over a 6-month treatment period with no evidence of tolerance.
CONCLUSIONS: Increasing BP response to PE infusion suggests a biological improvement in vascular α_1R signal transduction with chronic carvedilol therapy. This effect is evident despite no detectable tolerance to pre-infusion BP reductions. The different affinities of carvedilol and PE for α_1R subtypes may contribute to these findings.

22E. **COMBOS: The combination of prescription omega-3s with simvastatin: a randomized, double-blind, placebo-controlled study to assess the efficacy and safety of prescription omega-3 (Lovaza™) added to stable statin therapy in hypertriglyceridemic patients.** *James J. McKenney, Pharm.D.*[1], Michael H. Davidson, M.D., FACC, FACP[2], Harold Bays, M.D., FACP[3], Evan A. Stein, M.D., Ph.D., FCAP, FRCP(C)[4], Kevin C. Maki, Ph.D.[5], Ralph Doyle, B.A.[6], Robert Shalwitz, M.D.[6]; (1)School of Pharmacy, National Clinical Research, Inc, Richmond, Va; (2)Radiant Research, Chicago, Ill; (3)Louisville Metabolic and Atherosclerosis Research Center, Louisville, Ky; (4)Metabolic and Atherosclerosis Research Center, Cincinnati, Ohio; (5)Provident Clinical Research, Bloomington, Ind; (6)Reliant Pharmaceuticals, Inc., Liberty Corner, NJ.

PURPOSE: Elevated serum triglycerides (TGs) are often associated with elevated non–high-density lipoprotein cholesterol (non–HDL-C). The National Cholesterol Education Program Third Adult Treatment Panel (NCEP ATP III) identifies non–HDL-C as a secondary therapeutic target in patients with high triglycerides, but treatment goals may not be reached with statin monotherapy. This study assessed whether the addition of prescription omega-3-acid ethyl esters (P-OM3) to stable statin therapy can further improve non–HDL-C and other lipid variables in subjects with persistent hypertriglyceridemia.

METHODS: The study was multicenter, randomized, double-blind, placebo-controlled. During the 8-week lead-in phase, subjects followed the Therapeutic Lifestyle Changes diet and received simvastatin 40 mg/day. Following lead-in, eligible subjects (TGs 200–499 mg/dL and LDL-C ≤ 10% of NCEP ATP III goal) continued open-label simvastatin 40 mg/day and were randomly assigned to also receive either 4 g P-OM3 (Lovaza™, 3.4 g EPA+DHA) or placebo for 8 weeks.

RESULTS: After 8 weeks of treatment, the P-OM3+simvastatin group showed significant reductions vs the placebo+simvastatin group in non–HDL-C (-9.0% vs -2.2%; p<0.0001), TG (-29.5% vs -6.3%; p=0.0001), VLDL-C (-27.5% vs -7.2%; p<0.0001), and total-C (-4.8% vs -1.7%; p=0.001), total-C to HDL-C ratio (-9.6% vs -0.7%; p<0.0001), and apo B (-4.2% vs -1.9%; p=0.02). HDL-C was increased (+3.4% vs -1.2%; p<0.0001). The LDL-C response (+0.7% vs -2.8%; p<0.0522) did not differ significantly between groups. Study medications were well tolerated, and adverse events were comparable in the two groups.

CONCLUSIONS: The addition of P-OM3 to simvastatin substantially improved the lipid and lipoprotein profile of statin-treated subjects with persistent hypertriglyceridemia.

Study funded by Reliant Pharmaceuticals Inc.

Presented at Poster at the 3rd Annual Scientific Forum of the Midwest Lipid Association, Kansas City, Mo, October 20-22, 2006.

23. **Differences between traditional and guideline-driven blood pressure measurements in hypertensive patients.** *Gretchen M. Ray, Pharm.D.*[1], Joe R. Anderson, Pharm.D.[2], James J. Nawarskas, Pharm.D.[2]; (1)University of New Mexico Hospitals, Albuquerque, NM; (2)University of New Mexico College of Pharmacy, Albuquerque, NM.

PURPOSE: This study investigated whether current methods of blood pressure assessment in ambulatory clinics result in significantly different blood pressure measurements from those obtained by following the American Heart Association (AHA) recommendations.

METHODS: This was a randomized, crossover study in 40 patients with hypertension presenting to the UNMH Adult Internal Medicine Clinic. Blood pressure was measured in all patients in random order by the clinic staff, using the traditional triage method, and by the principal investigator, using the AHA-recommended method. Trained observers documented the techniques used by both methods.

RESULTS: There was no significant difference in mean systolic blood pressure (SBP) between the two methods, although the difference in mean diastolic blood pressure (DBP) was significantly lower with the triage method (77.6 mm Hg ± 11.9) compared with the AHA method (80.4 mm Hg ± 10.5; p=0.02). Individual results varied greatly with readings differing by ≥ 5 mm Hg in either direction for 68% of patients with respect to SBP and for 50% of patients with respect to DBP measurements. Overall, 65% of patients were not at their goal blood pressure when measured with the AHA method compared with 53% with the triage method (p<0.001). Multiple technical errors seen during the triage method likely accounted for the variation in blood pressure measurements.

CONCLUSION: When comparing the two methods of blood pressure measurement, clinically significant differences were observed in at least half of the patients studied. Differences in SBP went in both directions, resulting in a neutral mean effect. Differences in DBP also went in both directions, but on average tended to be lower when assessed with the triage method.

24E. **Distribution of blood pressure response in patients receiving an olmesartan medoxomil-based titration regimen.** *Steven Chrysant, M.D.*[1], Joel Neutel, M.D.[2], Jianbo Xu, M.S.[3], Kathleen Chavanu, Pharm.D.[3]; (1)Oklahoma Cardiovascular & Hypertension Center, Oklahoma City, Okla; (2)Orange County Research Center, Tustin, Calif; (3)Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: Angiotensin receptor blockers effectively reduce blood pressure (BP) and, in combination with hydrochlorothiazide (HCTZ), provide greater BP reductions in patients with hypertension. This study evaluated the distribution of BP-lowering responses resulting from a titration regimen using olmesartan medoxomil (OM) alone and combined with HCTZ.

METHODS: A 12-week open-label study of an OM-based treatment regimen was conducted in 169 patients with Stage 2 systolic hypertension (SBP ≥ 160 mm Hg). After a 3–4 week placebo run-in, patients followed an algorithm in 3-week steps: OM 20mg/d, OM 40 mg/day, OM 40/HCTZ 12.5 mg/day, OM 40/HCTZ 25 mg/day. Patients exited the study if BP was normalized (< 120/80 mm Hg).

RESULTS: The percentage of patients with a decrease in seated systolic BP (SeSBP) of ≤ 15 mm Hg (48% [OM 20 mg], 43% [OM 40 mg], 13% [OM 40/HCTZ 12.5 mg], and 8% [OM 40/HCTZ 25 mg]) or 16–30 mm Hg (34, 34, 35, and 26%, respectively) generally decreased with each titration step and the percentage of patients with SeSBP decrease of 31–45 mm Hg (16, 21, 33 and 45%, respectively) or > 45 mm Hg (2, 2, 18 and 21%, respectively) increased with each step. Similarly, the percentage of patients with a reduction in seated diastolic BP (SeDBP) of ≤ 15 mm Hg generally decreased with each titration step (89% [OM 20 mg], 86% [OM 40 mg], 67% [OM 40/HCTZ 12.5 mg], and 61% [OM 40/HCTZ 24 mg]) whereas the percentage of patients with a reduction in SeDBP of 16-30 mm Hg (11, 14, 31, and 36%, respectively) or > 31-45 mm Hg (0, 0, 2, and 4%, respectively) generally increased. CONCLUSIONS: An OM-based titration regimen enabled 66% of Stage 2 patients to achieve a > 30 mm Hg SBP decrease with 21% achieving a > 45 mm Hg decrease at the highest dose. OM/HCTZ combination therapy resulted in large BP reductions in a majority of Stage 2 hypertension patients including those patients most resistant to antihypertensive therapy (i.e., those patients uptitrated to the highest dose of OM/HCTZ).
Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, May 19-22, 2007, Chicago, Ill.

25. **Switching from metoprolol to carvedilol results in improved blood pressure control in patients with heart failure.** *Vicki L. Groo, Pharm.D.*[1], Clare Mohrman, Pharm.D.[2], Deidra Fontana, R.N., B.A.[2], Thomas Stamos, M.D.[3]; (1)University of Illinois at Chicago, College of Pharmacy and Medicine, Chicago, Ill; (2)University of Illinois at Chicago, Chicago, Ill; (3)University of Illinois at Chicago, College of Medicine, Chicago, Ill.

PURPOSE: Blood pressure (BP) remains elevated in many heart failure patients despite treatment with standard heart failure therapy. Compared with metoprolol (M), carvedilol (C) may have greater BP lowering effects due to its a_1-receptor blocking properties. We sought to determine whether switching heart failure patients from M to C results in improved BP control.
METHODS: Patients with hypertension despite maximum doses of vasodilator therapy and therapeutic doses of M, were switched to C. Average BPs 3 months prior to switching to carvedilol were compared with average BPs 3 months after by the Student's paired t test.
RESULTS: Forty-four patients were enrolled. Mean ± SD age was 56 ± 14 years, and 75% were African-American. All but four patients were on the metoprolol succinate formulation at baseline. In addition to vasodilator therapy and M, concomitant antihypertensive therapy at baseline consisted of thiazide diuretics (n=6), calcium channel blockers (n=14), loop diuretics (n=29), and other antihypertensive (n=4). Median M dose prior to switch to C was 200 (range 50–400) mg. C was titrated to a median dose of 50 (range 6.25–100) mg . The intensity of concomitant antihypertensives was increased in 39% of patients after switching to M. Thus, a subgroup analysis was done on the 61% of patients whose only intervention was switching from M to C. Results of BP changes are summarized in the table.

	SBP All (n=44)	DBP All (n=44)	SBP Subgroup (n=27)	DBP Subgroup (n=27)
Metoprolol	147 ± 12	80 ± 11	147 ± 12	79 ± 11
Carvedilol	130 ± 16	72 ± 10	125 ± 16	70 ± 9
P value	< 0.001	< 0.001	< 0.001	< 0.001

CONCLUSION: Switching from metoprolol to carvedilol in patients with heart failure who remain hypertensive resulted in a significant reduction in blood pressure.

26E. **Comparative blood pressure-lowering efficacy of olmesartan/hydrochlorothiazide and benazepril/amlodipine in patients with stage 2 hypertension.** *Dean Kereiakes, M.D.*[1], Joel Neutel, M.D.[2], Henry Punzi, M.D.[3], Findlay Walker, M.D.[4], Robert Dubiel, Pharm.D.[4], Jianbo Xu, M.S.[4]; (1)The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, Ohio; (2)Orange County Research Center, Tustin, Calif; (3)Punzi Medical Center and Hypertension Research Institute, Carrollton, Tex; (4)Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: The present study assessed the efficacy of olmesartan medoxomil (OM) combined with hydrochlorothiazide (HCTZ) vs benazepril (BEN) combined with amlodipine besylate (AML) in patients with Stage 2 hypertension.
METHODS: Following a 3–4 week placebo run-in, patients (n=190) with either a) mean seated diastolic BP (SeDBP) ≥ 90 mm Hg but < 115 mm Hg and mean seated systolic blood pressure (SeSBP) ≥ 160 mm Hg but < 200 mm Hg or b) mean SeDBP ≥ 100 mm Hg but < 115 mm Hg were randomized to increasing doses of OM (20 mg weeks 0–2 and 40 mg weeks 2–4) or BEN (10 mg weeks 0–2 and 20 mg weeks 2–4). In weeks 4–8, patients received either OM 40 mg/HCTZ 12.5 mg or BEN 20 mg/AML 5 mg. In weeks 8–12, HCTZ and AML increased

to 25 mg and 10 mg. Patients were titrated to the next treatment period if BP ≥ 120/80 mm Hg. Patients exited the study if BP < 120/80 mm Hg was achieved. The primary end point was the change from study baseline in mean SeSBP after 12 weeks active therapy.

RESULTS: After 12 weeks, SeBP was 133/84 mm Hg (baseline 167/102 mm Hg) in the OM/HCTZ group and 140/86 mm Hg (baseline 170/101 mm Hg) in the BEN/AML group. Mean change in SeSBP was significantly greater in the OM 40 mg/HCTZ 12.5 mg group (n=89) than in the BEN 20 mg/AML 5 mg group (n=85) [-27 vs -22 mm Hg; p = 0.034] and in the OM 40 mg/HCTZ 25 mg group (n=94) compared with the BEN 20 mg/AML 10 mg group (n=96) [-34 vs -29 mm Hg; p=.021]. In addition, with OM + HCTZ (40/12.5 mg and 40/25 mg) more patients achieved BP goal of < 140/90 mm Hg compared with BEN + AML (20/5 mg and 20/10 mg) [66 vs 45%; p=.006].

CONCLUSIONS: In patients with Stage 2 hypertension, the combination of OM + HCTZ (40/12.5 mg and 40/25 mg) was more effective than BEN + AML (20/5 mg and 20/10 mg) at reducing SeSBP and enabled more patients to achieve BP goal.

Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, May 19-22, 2007, Chicago, Ill.

27. **Pharmacokinetic interaction study between prescription omega-3-acid ethyl esters (P-OM3) and atorvastatin in healthy subjects.** Gaetano Morelli, M.D.[1], Mike Di Spirito, M.Sc.[1], Ralph Doyle, B.A.[2], Judith Johnson[2], *James J. McKenney, Pharm.D.*[3]; (1)MDS Pharma Services, Montreal, Quebec, Canada; (2)Reliant Pharmaceuticals, Inc., Liberty Corner, NJ; (3)School of Pharmacy, National Clinical Research, Inc, Richmond, Va.

PURPOSE: Combination pharmacotherapy is often indicated for treatment of dyslipidemia to achieve NCEP ATP III goals, and co-administration of prescription omega-3-acid ethyl esters (P-OM3) with a statin may present an option for patients with mixed hyperlipidemia.

HYPOTHESIS: That co-administration of prescription omega-3-acid ethyl esters (P-OM3) with a statin would not interfere with the statin pharmacokinetics.

METHODS: This open-label, randomized, 2-way crossover, drug interaction study evaluated the effect of P-OM3 capsules on plasma atorvastatin and 2-hydroxyatorvastatin pharmacokinetics in 50 healthy volunteers. Under fasted conditions, a single oral dose 80 mg atorvastatin was administered once daily in the morning with or without 4 g of P-OM3 for 14 days, followed by another 14-day period in which subjects received the alternate treatment.

RESULTS: After 14-days of once-daily dosing, the ratio of the least-squares means of the natural log–transformed area under the plasma concentration vs. time curve (AUC_t) over the final dosing interval (0–24 hours) for the concomitant administration of P-OM3 plus atorvastatin vs. atorvastatin alone was 102.7 (90% CI = 97.0–108.6) for atorvastatin, and 101.0 (90% CI = 95.7–106.6) for the 2-hydroxyatorvastatin active metabolite. The ratio of the least-squares means of the day 14 maximum measured plasma concentration (Cmax, ss) over the final dosing interval (0–24 hours) for P-OM3 plus atorvastatin vs. atorvastatin alone was 102.9 (90% CI = 93.1–113.7) for atorvastatin and 94.8 (90% CI = 85.1–105.6) for 2-hydroxyatorvastatin. No serious adverse events (AE) were reported, and of 50 subjects, only 1 in the P-OM3 arm was withdrawn for an AE, which was coded as "not serious" and "possibly related to study drug."

CONCLUSIONS: Concomitant treatment with recommended clinical doses of P-OM3 plus atorvastatin did not significantly affect the steady-state pharmacokinetics of atorvastatin or its major metabolite. The combination of P-OM3 capsules and atorvastatin appeared to be well tolerated.

Study Funded by Reliant Pharmaceuticals Inc.

28E. **A randomized, double-blind, placebo-controlled factorial study evaluating the efficacy and safety of amlodipine besylate plus olmesartan medoxomil combination therapy compared with monotherapy in patients with mild-to-severe hypertension.** *Steven Chrysant, M.D.*[1], Michael Melino, Ph.D.[2], Sulekha Karki, BAMS[2], James Lee, Ph.D.[2], Reinilde Heyrman, M.D.[2]; (1)Oklahoma Cardiovascular & Hypertension Center, Oklahoma City, Okla; (2)Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: Most patients will need 2 or more antihypertensive agents to attain a blood pressure (BP) goal of < 140/90 mm Hg. Combining the calcium channel blocker amlodipine besylate (AML) and the angiotensin receptor blocker olmesartan medoxomil (OM) may potentially improve BP-lowering efficacy without additional safety concerns.

METHODS: We conducted a randomized, double-blind, placebo-controlled factorial study in 1940 patients with mild-to-severe hypertension (seated diastolic BP [SeDBP] ≥ 95 mm Hg and ≤ 120 mm Hg) to determine whether combining AML 5–10 mg/day and OM 10–40 mg/day for 8 weeks has a significant benefit versus respective

monotherapy components. Primary and secondary end points included mean change from baseline in SeDBP and seated systolic BP (SeSBP), respectively, at week 8.

RESULTS: Each combination had significantly greater reductions in SeDBP and SeSBP compared with its monotherapy components (p<0.001 for all comparisons). The greatest mean reductions in SeSBP and SeDBP occurred with AML 10 mg + OM 40 mg (-30.1/-19.0 mm Hg vs -19.7/-12.7 mm Hg with AML 10 mg, and vs -16.1/-10.2 mmHg with OM 40 mg). OM 10 mg and 20 mg reduced BP by 11.5/8.3 and 13.8/9.2 mm Hg, respectively; AML 5 mg reduced BP by 14.9/9.4 mm Hg; AML/OM 5/10, 5/20, and 5/40 mg reduced BP by 24.2/13.8, 23.6/14.0, and 25.4/15.5 mm Hg; AML/OM 10/10 and 10/20 mg reduced BP by 25.3/16.0 and 29.2/17.0 mm Hg. Adverse event (AE) incidence for the AML + OM combination treatment groups was 52.7% (511/970 patients); the AE incidence in the placebo group was 56.2% (91/162 patients). Most AEs were mild in intensity. The AE profile for each of the combinations was similar in nature to the monotherapy components.

CONCLUSIONS: The combination of AML + OM produced greater reductions in BP compared with respective monotherapies. BP reductions were dose-related, and all regimens were well-tolerated.

Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, May 19-22, 2007, Chicago, Ill.

29. **Contrasting early versus delayed effects of catecholamines on cardiac repolarization.** *Brian R. Overholser, Pharm.D.*, Xiaomei Zheng, M.S., James E. Tisdale, Pharm.D.; Department of Pharmacy Practice, Purdue University School of Pharmacy and Pharmaceutical Sciences, Indianapolis, Ind.

PURPOSE: Catecholamines prompt biological alterations that influence cardiac repolarization and may induce arrhythmias. The purpose of this study is to characterize changes in ventricular repolarization following catecholamine administration in the presence of mild I_{Kr} inhibition.

METHODS: Male Dunkin-Hartley guinea pig hearts were excised and perfused in a retrograde manner with oxygenated Krebs-Henseleit buffer at constant aortic pressure (60 mm Hg) at 37° C. Hearts were paced (240 bpm), and left ventricular monophasic action potentials and ECGs were recorded. Hearts were assigned to: 1) Control 1 (no sparfloxacin; SPAR), 2) Control 2 (no epinephrine/norepinephrine; EPI/NE) or 3) Experimental Group (SPAR and EPI/NE). Following equilibration, SPAR (20 µ/mL) or vehicle (Control 1) was administered (10 min) through a tube adjoining the aorta. Bolus EPI/NE or vehicle (Control 2) was administered 10 and 20 minutes following SPAR. Action potential duration was determined at 90% repolarization (APD_{90}). Comparisons were made using Friedman's test for repeated measures and Dunn's test, if necessary.

RESULTS: Eighteen hearts were included in the analysis. APD_{90} increased in all hearts (n=13) exposed to SPAR (p<0.01). The median (Interquartile Range [IQR]) %APD_{90} increase at 20 min was 4.4% (2.5, 4.9) relative to control. EPI/NE altered the time-course of APD_{90} at 5.0/3.0 nM EPI/NE, p<0.05, and 10.0/6.0 nM EPI/NE, p<0.01. There was an initial median (IQR) decrease in APD_{90} immediately following EPI/NE administration of -1.8% (-1.7, -2.3) for the high concentration (p<0.05 versus control). Subsequently following the initial decrease, APD_{90} increased from baseline 2 minutes following NE/EPI administration by median (IQR) of 3.7% (3.1, 3.8), p<0.05, before returning to baseline. Similar patterns were observed in the lower EPI/NE concentrations studied.

CONCLUSIONS: Catecholamines alter repolarization in a time-dependent manner during I_{Kr} inhibition. Investigations are warranted into potential mechanisms of the observed early and delayed effects of adrenergic stimulation on cardiac repolarization.

30. **HMG-CoA Reductase Inhibitors reduce all-cause mortality in patients with established heart failure: a meta-analysis.** *Erin J. Myers, Pharm.D.*[1], Paul E. Nolan, Jr., Pharm.D.[1], Marion K. Slack, Ph.D.[1], Barry E. Bleske, Pharm.D.[2]; (1)(1) University of Arizona College of Pharmacy, Department of Pharmacy Practice and Science, Tucson, Ariz; (2)University of Michigan, Ann Arbor, Mich.

PURPOSE: The purpose of this study was to use meta-analysis to evaluate the effect of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) on all-cause mortality in patients with established heart failure (HF).

METHODS: Studies for inclusion were found electronically via MEDLINE, Cochrane Central Register of Controlled Trials, International Pharmaceutical Abstracts, and Evidence-Based Medicine Review databases from the year 1950 to April 2007. These results were supplemented by manual review of electronically selected references. The following Medical Subject Headings and keywords were used: hydroxymethylglutaryl coenzyme A reductase inhibitors, HMG-CoA reductase inhibitors, statins, heart failure, congestive heart failure, cardiomyopathy, and ventricular dysfunction. To be included, studies must have evaluated statin use in patients with established HF, and be published in the English language. Studies included could be prospective or retrospective in design. Pooled odds ratios and 95% confidence intervals were calculated and forest and funnel plots constructed.

RESULTS: 15 studies (n=134,485 patients) were found to be eligible for inclusion and were subsequently grouped by design as follows: Group 1: prospective cohort studies (n=2); Group 2: retrospective analyses of randomized controlled trials (n=5); Group 3: retrospective chart reviews (n=2); and Group 4: retrospective database analyses (n=6). When studies within each group and across groups were analyzed, it was found that the use of statins significantly decreased all-cause mortality (OR = 0.50; [95% CI = 0.49–0.52] Z test; p<0.001). Results for individual groups were found to be: Group 1 (OR = 0.45; CI =- 0.34–0.61; p<0.001); Group 2 (OR = 0.73; CI = 0.65–0.82; p<0.001); Group 3 (OR = 0.48; CI = 0.36–0.64; p<0.001); and Group 4 (OR = 0.49; CI = 0.47–0.51; p<0.001).
CONCLUSIONS: Statins were found to consistently reduce mortality in patients with established heart failure despite differences in study design. These results support the rationale for two large ongoing prospective, randomized, controlled trials evaluating the use of statins in patients with HF.

31. **Long-term efficacy and safety of the novel β-blocker, nebivolol, in mild-to-moderate hypertension: focus on obese patients.** *John Martin, M.D.*; Forest Research Institute, Jersey City, NJ.

PURPOSE: To compare the long-term antihypertensive efficacy and safety of nebivolol, a nitric-oxide-mediated vasodilatory and highly cardioselective β1-receptor-blocker, in obese (body mass index ≥ 30kg/m²) versus non-obese patients.
METHODS: Mild-to-moderate hypertensive patients (sitting diastolic blood pressure [SiDBP] ≥ 95 and ≤ 109 mm Hg) completed 3-month nebivolol studies and entered a long-term extension study receiving once-daily nebivolol 5 mg, 10 mg, or 20 mg for 9 months. Mean change from original baseline to study end in trough BP (measured 24 ± 2 hours post-dose) was analyzed.
RESULTS: In total, 607 patients were treated; of these, 42.0% were obese. Overall, sitting trough systolic BP (SiSBP) was significantly reduced from baseline to study end (-14.8 mm Hg [95% Confidence Interval = -16.6– -13.1]), as was SiDBP (-15.0 mm Hg [95% CI = -15.9– -14.1]). Mean reductions in SiDBP were similar in obese versus non-obese patients (-15.1 mm Hg [95% CI = -16.3– -13.9] vs -14.9 mm Hg [95% CI = -16.1– -13.7], respectively). At study end, 78.2% of patients overall responded to nebivolol treatment (DBP < 90 mm Hg or decreased by ≥ 10 mm Hg from baseline). Nebivolol was well tolerated with a low incidence of adverse events (AEs) and a comparable incidence of AEs between obese and non-obese patients, decreasing over time in both groups (incidence of AEs was 45.4% vs 34.9%, respectively, after 77 days decreasing to 18.3% vs 14.9% over the last 3 months of the study). Furthermore, nebivolol was associated with a low incidence of typical β-blocker-related adverse effects (e.g., fatigue and erectile dysfunction) and, importantly, neutral effects on metabolic parameters (e.g., serum glucose and lipids).
CONCLUSIONS: Significant BP reductions were achieved with once-daily nebivolol treatment in both obese and non-obese patients with mild-to-moderate hypertension. Long-term nebivolol treatment was safe and well tolerated in both groups. These data suggest that nebivolol may be an effective option for treatment of obese patients with hypertension.

32. **The efficacy and safety of monotherapy with nebivolol, a novel, highly cardioselective, β1-blocker with vasodilating properties, in patients with mild-to-moderate hypertension.** Mark Greathouse, M.D.[1], *John Martin, M.D.*[2], Robert Weiss, M.D.[3]; (1)South Hills Cardiology Associates of Pittsburgh, Pittsburgh, Pa; (2)Forest Research Institute, Jersey City, NJ; (3)Androscoggin Cardiology Associates, Auburn, Maine.

PURPOSE: To determine the antihypertensive efficacy and safety of nebivolol, a cardioselective β1-adrenoceptor blocker with nitric-oxide-mediated vasodilatory properties, in patients with mild-to-moderate hypertension.
METHODS: Data were pooled and analyzed from two similarly designed, 3-month, multicenter, double-blind, randomized, placebo-controlled, parallel-group, dose-ranging studies in a general hypertensive population with sitting diastolic blood pressure (SiDBP) ≥ 95 mm Hg and ≤ 109 mm Hg, who received once-daily nebivolol monotherapy (1.25, 2.5, 5, 10, 20 and 40 mg) or placebo.
RESULTS: All doses of nebivolol significantly decreased trough SiDBP (measured 24 ± 2 hours post-dose) compared with placebo (p≤0.005). Similar findings were observed for trough sitting systolic BP (p<0.005 for nebivolol 2.5 mg; p<0.001 for nebivolol 5–40 mg). The proportion of patients who were considered treatment responders (average trough SiDBP < 90 mm Hg, or decrease of ≥ 10 mm Hg from baseline by study end) ranged from 45.8% to 64.5% with nebivolol 1.25 mg–40 mg. This was statistically significant for nebivolol doses of 2.5 mg-40 mg (p≤0.026) compared with placebo (36.5%). Discontinuation rates were similar between the combined nebivolol dose groups and placebo group. The incidence of adverse events (AEs) was low and similar between the total combined nebivolol dose groups and placebo group. In addition, the overall incidence of -blocker–associated AEs, such as fatigue, erectile dysfunction and dizziness, was also low and comparable between treatment groups. Furthermore, nebivolol had neutral effects on metabolic parameters (e.g., serum glucose and lipids).

CONCLUSION: Nebivolol was an effective and safe treatment for mild-to-moderate hypertensive patients. These data suggest that once-daily nebivolol may provide a valuable addition to the therapeutic armamentarium for treating hypertension.

33. **Evaluating aspirin response among patients with cardiovascular disease.** *Kari L. Olson, Pharm.D.*[1], Tom Delate, Ph.D.[1], Deanna Kurz, B.A., CCRP[1], Dorothy M. Adcock, M.D.[2], John A. Merenich, M.D.[1]; (1) Kaiser Permanente Colorado Region, Aurora, Colo; (2)Esoterix, Inc, Aurora, Colo.

PURPOSE: Resistance to aspirin may be a potential reason that patients experience recurrent coronary events while taking the medication. Urinary-11–dehydrothromboxane B2 (DHTB2) levels can reliably identify patients who do/do not respond to aspirin. This study determined whether aspirin response differed between patients who did and did not have recurrent coronary events and assessed whether a dose-response relationship to aspirin response was present.
METHODS: This cross-sectional study identified patients with an incident and no recurrent coronary event (NRE) (acute myocardial infarction (AMI) or percutaneous coronary intervention (PCI)) between 06/01/98 and 12/31/04 and patients with a recurrent cardiac event (RE) (AMI or PCI) within the same time period. Patients were invited to attend a one-time clinic visit at which demographics, medical history, and a urine sample were collected. Urine samples were analyzed by Esoterix Coagulation, according to standard procedures and reported as platelet urinary response ratio (PURR). Patients with < 400 PURR were classified as aspirin responders. Descriptive statistics were used for baseline characteristics. Student's t-tests were used to assess differences in mean values between groups; $\beta2$ tests were used for between group comparisons on dichotomous outcomes.
RESULTS: A total of 98 patients (n=47 RE, n=51 NRE) were evaluated. The mean age was 62 ± 20 years; 72.4% were male. There were no differences in demographic characteristics between groups (p>0.05). The median DHTB2 levels were 347 and 318 in the NRE and RE groups, respectively (p>0.05). There were no differences between groups in the proportion of patients who were aspirin responders (57% vs.66%, p>0.05). There was no difference in aspirin response based on dose (81 mg vs. 325 mg, p>0.05).
CONCLUSION: Aspirin response did not differ between patients who did and did not have a recurrent coronary event. Larger studies evaluating aspirin response in this population are warranted.

34. **Fenofibrate effects on endothelial colony-stimulating factor production under inflammatory conditions.** *Elvin T. Price, Pharm.D.*, Gregory Welder, A.A., Issam Zineh, Pharm.D.; University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, Fla.

PURPOSE: Early atherosclerosis is characterized by a cycle of endothelial dysfunction and inflammation. Colony-stimulating factors (e.g., GCSF, GMCSF) stimulate production of cells (e.g., neutrophils and monoxytes) known to contribute to endothelial dysfunction and atherosclerotic plaque formation. Fibrates are lipid-lowering drugs with anti-inflammatory effects. It has been hypothesized that cardioprotection by fibrates is partially due to these anti-inflammatory effects. Their ability to modulate endothelial GCSF and GMCSF production under inflammatory conditions is unknown. We examined the effects of fenofibrate on the production of these cytokines.
METHODS: Human umbilical vein endothelial cells (HUVECs) were cultured and treated with IL-1 (2 ng/mL) to induce inflammation and fenofibrate 1–50 uM. GCSF and GMCSF were measured in cell culture supernates by cytometric immunofluorescence. ANOVA with Tukey correction was performed to test drug effect across doses, with significance set at P<0.05.
RESULTS: IL-1α stimulated the production of GCSF more than 260 times higher than control (mean ± SEM: 13.06 ± 2.97 pg/mg vs 3468 ± 1551 pg/mg, p<0.005) and GMCSF more than 3000 times higher than control (2.08 ± 0.11 pg/mg vs 7202 ± 616 pg/mg, p<0.001). Fenofibrate significantly reduced GMCSF by 55%–70% at concentrations ranging from 10 uM to 50 uM (mean ± SEM after 10, 25, 50 uM treatments: 3255 ± 311, 3249 ± 371, 2137 ± 345 pg/mg total protein respectively). There was no effect on GCSF (not shown).
CONCLUSIONS: Fenofibrate blunts IL-1α-mediated GMCSF production with no effect on GCSF. This represents a novel mechanism of fenofibrate anti-inflammatory effect, which may be important in cardiovascular and other diseases.

35. **A simplified logistic regression model to predict atrial fibrillation after cardiac surgery.** *Brian J. Barnes, Pharm.D.*, Sue-Min Lai, Ph.D., M.S., M.B.A., Patricia A. Howard, Pharm.D., FCCP, Michael E. Gorton, M.D., Jeffrey B. Kramer, M.D., Gregory F. Muehlebach, M.D., William A. Reed, M.D.; University of Kansas Medical Center, Kansas City, Kan.

PURPOSE: Postoperative atrial fibrillation (POAF) is prevalent after cardiac surgery. Amiodarone is frequently used to prevent POAF, which is associated with significant morbidity. Our prior research concluded that the

benefit of amiodarone is dependent upon baseline risk for the arrhythmia. In patients at elevated risk, amiodarone is clearly beneficial. However, in patients who are at low baseline risk for POAF, its benefit remains questionable. Prediction of the probability of developing POAF, at the time amiodarone is prescribed, is of interest when balancing the risks versus benefits of amiodarone. A previous model is available, but its practicality is limited by the inclusion of 11 variables, of which 7 are determinable only after surgery. The objective of this research was to derive a simplified model that accurately predicts the probability of developing POAF.

METHODS: Retrospective, observational data from 509 adult patients who underwent cardiac surgery in 2003 were used for analyses. Data sources included The Society of Thoracic Surgeons national database, medical, and medication administration records. Univariate analyses and unconditional, stepwise, logistic regression were used to update and simplify this previously published model (JAMA 2004;291:1720–9). Patients with chronic atrial fibrillation or missing data were excluded from analyses.

RESULTS: The mean patient age was 63 years, 27% were female, 80% underwent coronary artery bypass grafting, and 29% underwent valve surgery. Age, past history of atrial fibrillation or lung disease, valve surgery, and the use of amiodarone prophylaxis were independent predictors of POAF. The simplified model accurately predicts the development of POAF in this cohort (area under ROC curve = 0.72).

CONCLUSIONS: The derived model is simple and discriminantly predicts which patients will develop POAF. This model can be used by providers to aid in selectively prescribing amiodarone to those patients at elevated risk for POAF and avoid unnecessary toxicity in patients at minimal risk for the arrhythmia.

36. **Comparison of two laboratory methods for measuring aspirin inhibition of platelet aggregation.**
Kathryn M. Momary, Pharm.D., BCPS, Nancy L. Shapiro, Pharm.D., Larry Brace, Ph.D., Stacy S. Shord, Pharm.D., Marlos A.G. Viana, Ph.D., Cathy M. Helgason, M.D., Edith A. Nutescu, Pharm.D., Larisa H. Cavallari, Pharm.D.; University of Illinois at Chicago, Chicago, Ill.

PURPOSE: Incomplete platelet inhibition with aspirin has been associated with an increased risk of serious vascular events. The gold standard assay for measuring aspirin response is *ex-vivo* platelet aggregation; however, this test is costly and time consuming. Measurement of urinary 11-dehydrothromboxane B2 (dTxB2) levels, which is an inactive metabolite of thromboxane A2, may be a less expensive and more efficient alternative to *ex-vivo* platelet aggregation. We sought to assess the correlation between *ex-vivo* platelet aggregation and urine thromboxane B2 levels in determining aspirin response.

METHODS: Sixty subjects on aspirin for primary or secondary prevention were enrolled, and clinical and demographic information were collected. Blood was obtained for determination of *ex-vivo* platelet aggregation (by the method of Born). Subjects were classified as complete or partial responders to aspirin based on the level of inhibition of platelet aggregation on exposure to arachidonic acid, collagen, adenosine diphosphate, and epinephrine. Urine was obtained for assessment of dTxB2 levels using a commercially available quantitative ELISA kit, with increased dTxB2 levels associated with impaired aspirin response. Subject characteristics and dTxB2 levels were compared between patients classified as complete and partial responders to aspirin based on *ex-vivo* platelet aggregation testing.

RESULTS: Fifty-one percent of subjects were classified as partial responders. Patient characteristics did not differ between complete and partial responders. Mean ± SD dTxB2 levels also did not differ between complete and partial responders (1034 ± 531 vs. 990 ± 729 pg/mg creatinine).

CONCLUSIONS: Our data suggest that dTxB2 levels do not correlate with results of *ex-vivo* platelet aggregation in patients taking aspirin. This lack of correlation possibly highlights the importance of non-COX-1 mediators of platelet aggregation. Further studies to assess the correlation between *ex-vivo* platelet aggregation and other less expensive and less time consuming methods of measuring aspirin response may be necessary.

37E. **Trends in amiodarone laboratory monitoring in a VA hospital following the implementation of computerized clinical reminders.** *Aisha Hussain, Pharm.D.*, Wafa Y. Dahdal, Pharm.D., Todd Lee, Pharm.D., Ph.D., Robert Silverman, Pharm.D.; Edward Hines, Jr. VA Hospital, Hines, Ill.

PURPOSE: In January 2003, results of an internal quality improvement report to the Pharmacy and Therapeutics committee at the Hines VA hospital and its affiliated community outpatient clinics indicated that only 6% of sampled patients fulfilled all amiodarone laboratory monitoring criteria based on the North American Society of Pacing and Electrophysiology guidelines. In response to the findings, a computerized clinical reminder system was established to assist the provider in ordering amiodarone laboratory testing. The primary objective of this study was to determine whether there was a significant difference in the proportion of patients who received all defined safety monitoring [liver function tests (LFT), thyroid function test (TFT), electrocardiogram (EKG), pulmonary function test (PFT), and Chest X-ray] before and after implementation of amiodarone clinical reminders. Secondary objectives include subgroup analyses on the basis of amiodarone dosage.

METHODS: This retrospective cohort study consisted of laboratory data extraction for all patients newly started on amiodarone during 2 date ranges: October 4, 2002, through October 4, 2003 (pre-intervention), and October 5, 2004, through October 5, 2005 (post-intervention). The electronic medical record for each patient was queried to extract dates of above listed tests spanning from 1 month before the index date through 13 months after. The date of the first prescription fill for each patient was the index date. The percentage of patients receiving appropriate monitoring was compared before and after introduction of the clinical reminders. Outcome measures were compared between groups using chi-square analysis. Logistical regression was performed adjusting for intergroup variation.
RESULTS: No patients fulfilled the primary end point criteria. Minor significant differences were noted in subgroup analyses.
CONCLUSIONS: Clinical reminders did not result in improved amiodarone laboratory/ diagnostic safety monitoring within a local VA hospital. Presented at the Great Lakes Pharmacy Resident Conference, West Lafayette, Ind., April 25-27, 2007.

Critical Care

38. **Mortality rates of patients treated with drotrecogin alfa for severe sepsis based on PROWESS eligibility.** *Megan L. Goodwin, Pharm.D., BCPS*[1], Richard H. Drew, Pharm.D., M.S., BCPS[1], Elizabeth S. Dodds Ashley, Pharm.D., M.H.S., BCPS[2], Ann C. Scates, Pharm.D.[2], D. Byron May, Pharm.D., BCPS[1]; (1)Duke University Medical Center and Campbell University School of Pharmacy, Durham, NC; (2)Duke University Medical Center, Durham, NC.

PURPOSE: This study examined mortality rates of patients receiving drotrecogin alfa (rAPC) in a large, academic, medical center to 1) compare 28-day mortality in patients meeting PROWESS inclusion criteria to those excluded, 2) explore possible risk factors for mortality with rAPC therapy, and 3) describe demographic characteristics and treatment outcomes.
METHODS: All courses of rAPC in patients ≥ 18 years of age at Duke University Hospital between November 21, 2001, and February 28, 2006, were reviewed. Medical history, in-hospital course, rAPC treatment criteria, and treatment outcomes were recorded.
RESULTS: rAPC utilization increased from 25 courses in 2002 to 60 in 2005. 188 courses were identified, of which 17 were excluded for various reasons: no rAPC given (n=9), incomplete chart (n=7), or enrolled in ADDRESS study (n=1). For the 171 evaluable rAPC courses, the 28–day mortality was 39.18% (67/171) and the overall in-hospital mortality was 43.86% (75/171). For patients with at least one PROWESS exclusion criteria, the OR for 28-day mortality was 1.95 (95% CI = 1.04–3.64). The most commonly identified PROWESS exclusion criteria were history of a transplant (n=21), use of specific anticoagulants (n=16), and baseline platelets less than 30,000 (n=15). Univariate analyses revealed an association between in-hospital mortality and treatment in the MICU (OR = 2.01; 95% CI = 1.09–3.72), ≥ 3 dysfunctional organ systems (OR = 3.50; 95% CI = 1.54–7.92), and ANC < 1000 at rAPC initiation (OR = 8.26; 95% CI = 0.97–70.18). Treatment in the SICU appeared protective (OR = 0.40; 95% CI = 0.21–0.75) and those with no pathogen isolated also appeared to do better (OR = 0.51; 95% CI =0.26–1.01).
CONCLUSIONS: Mortality rates associated with rAPC therapy appear higher in those who did not meet PROWESS inclusion criteria. Several variables are associated with rAPC therapy and increased in-hospital mortality. The population most likely to benefit from rAPC therapy is still unclear.

39. **Evaluation of dexmedetomidine versus propofol therapy in mechanically ventilated cardiac surgery patients at a tertiary academic medical center.** *Kevin E. Anger, Pharm.D, BCPS*, Paul M. Szumita, Pharm.D, BCPS, Steven A. Baroletti, Pharm.D, M.B.A., BCPS, Matthew Labreche, Candidate for Pharm.D., Fanikos John, R.Ph., M.B.A.; Brigham and Women's Hospital, Boston, Mass.

PURPOSE: To determine differences in sedation and analgesia requirements, duration of mechanical ventilation, hemodynamic and ventilatory parameters, and length of stay between postoperative mechanically ventilated cardiac surgery patients receiving dexmedetomidine versus propofol therapy upon arrival to the intensive care unit.
METHODS: We conducted a single center, descriptive study of clinical practice at a 20-bed cardiac surgery intensive care unit in a tertiary academic medical center. Consecutive patients undergoing cardiac surgery receiving dexmedetomidine as their primary sedation agent were prospectively matched 1:1 by procedure with a patient receiving propofol as their primary agent between October 20, 2006, and December 15, 2006. Data collected included duration of mechanical ventilation; hemodynamic and ventilatory parameters; length of stay in hospital and ICU; levels of sedation and analgesia; and sedative/analgesic consumption.

RESULTS: 58 mechanically ventilated post cardiac surgery patients were evaluated and included in the analysis. Baseline demographics were similar in both groups with the exception of more males in the dexmedetomidine group (17 (58.6%) vs. 24 (82.7%); p=0.0434). Use of propofol or dexmedetomidine was associated with similar postoperative length of stay (7.24 ± 2.5 vs 6.93 ± 3.06 days; p=0.67), ICU length of stay (58.41 ± 31.66 vs. 60.41 ± 32.08 days; p=0.81), duration of mechanical ventilation (15.81 ± 5.86 vs. 13.98 ± 4.46 hours; p=0.186), respectively. More hypotension (19 [65.5%] vs. 9 [31%]; p=0.009), and morphine use (11 [37.9%] vs. 1 [3.45%]; p=0.001) was associated with dexmedetomidine therapy versus propofol, respectively.

CONCLUSIONS: Use of dexmedetomidine or propofol yielded similar results in relation to clinical efficacy and safety end points. Further multicenter trials are needed to assess the clinical, safety, and economic impact of propofol and dexmedetomidine based sedation on mechanically ventilated post-cardiac surgery patients.

40. **Evaluation of an evidence-based protocol for the diagnosis and management of ventilator-associated pneumonia in the surgical intensive care unit.** *Neil E. Ernst, Pharm.D.*[1], Laura Lim, Pharm.D.[2], Eric W Mueller, Pharm.D.[1], Karyn Butler, M.D.[1]; (1)The University Hospital, Cincinnati, Ohio; (2)University of Cincinnati, College of Pharmacy, Cincinnati, Ohio.

PURPOSE: Ventilator-associated pneumonia (VAP) is a serious complication of mechanical ventilation. Accurate diagnosis, adequate empiric antibiotic therapy, and antibiotic de-escalation are imperative. We evaluated the effectiveness of an updated evidence-based protocol for diagnosis and management of VAP in surgical intensive care unit (SICU) patients. The protocol sought to to: 1) encourage a bronchoalveolar lavage (BAL) diagnostic threshold > 100,000 cfu/mL; 2) differentiate early and late VAP; and 3) limit antibiotic therapy duration.

METHODS: All patients treated for VAP during the 1-year post-protocol period (study) were retrospectively compared to consecutive pre-protocol (control) VAP patients treated during the immediate preceding 6 months. Primary end points included nature and adequacy of empiric antibiotic therapy; antibiotic therapy duration; and patient outcome.

RESULTS: Sixty-three study and 45 control patients were included. There were no differences in demographic or baseline characteristics. Study patients more often had BAL growth > 100,000 cfu/mL (65% vs 34%; p=0.004). Adequacy of empiric therapy was not different (78% vs 73%; p=0.76) despite trends toward decreased number of empiric antibiotics (1.8 ± 0.7 vs 2.1 ± 0.7; p=0.06), as well as decreased early VAP anti-Pseudomonal antibiotics (50% vs 72%; p=0.46) and vancomycin (14% vs 45%; p=0.20) in study patients. VAP antibiotic duration was shorter in study patients (8[5–17] vs 10[4–18] days; p=0.033). There were no differences in ICU or hospital lengths of stay, pulmonary infection recurrence, or in-hospital mortality.

CONCLUSIONS: The updated VAP protocol was associated with a stricter diagnostic threshold and decreased duration of antibiotic therapy. The protocol may limit the number and spectrum of empiric antibiotic drugs without compromising the adequacy of empiric therapy.

41. **Comparison of argatroban dosing in critically ill and non-critically ill patients with presumed or confirmed heparin-induced thrombocytopenia.** *Shaun P. Keegan, Pharm.D.*, Erika M. Rolik, Pharm.D., Neil E. Ernst, Pharm.D., Eric W. Mueller, Pharm.D.; The University Hospital, Cincinnati, Ohio.

PURPOSE: Argatroban is a common treatment for heparin-induced thrombocytopenia (HIT). Appropriate dosing of argatroban in critically ill patients is unknown. We hypothesized that critically ill patients require lower therapeutic argatroban dosages (AD) compared to non-critically ill patients.

METHODS: Adult patients who received argatroban for > 24 hours between May 2003 and December 2006 were retrospectively reviewed. Patients with severe hepatic dysfunction (Child-Pugh class C) were excluded. Patients managed by a board-certified critical care physician service were considered critically ill. Therapeutic AD was that required to achieve two consecutive (at least 4 hours apart) activated partial thromboplastin times (aPTTs) 1.5–3 times baseline.

RESULTS: Fifty-three patients were included (critically ill, n=34; non-critically ill, n=19). Critically ill patients had higher median (range) APACHE II scores (17 [7–40] vs. 10 [0–29]; p=0.007) and number of organs failed. Critically ill patients required lower mean ± SD therapeutic AD (0.6 ± 0.5 vs. 1.4 ± 0.9 mcg/kg/min; p<0.001). There was no difference in time to therapeutic aPTT (22 ± 23 vs. 23.4 ± 16 hours;p=0.171) or proportion of aPTTs within therapeutic range (73% vs. 67%; p=0.05). AD was inversely related to number of organs failed (0 organs, 1.36 ± 0.93 mcg/kg/min; 1 organ, 0.98 ± 0.48; 2 organs, 0.62 ± 0.44; 3 organs, 0.54 ± 0.55; 4 organs, 0.32 ± 0.05; p=0.002). Critical illness was independently associated with AD < 0.75 mcg/kg/min (OR 15.1; 95%CI = 2.7–84.2). Adverse events were not different between groups.

CONCLUSIONS: Critically ill patients require lower therapeutic AD than non-critically ill patients. Starting AD < 0.75 mcg/kg/min should be considered for all critically ill patients with particular consideration for lower dosages in patients with multi-organ dysfunction.

42. **Low-dose recombinant factor VIIa for INR reversal in warfarin-associated intracranial hemorrhage.** *Ryan D. Tabis, Pharm.D.*, A. Shaun Rowe, Pharm.D., BCPS; The University of Tennesee Medical Center, Knoxville, Tenn.

PURPOSE: Recombinant Factor VIIa (rFVIIa) is a recombinant coagulation factor that is approved for the treatment of hemophilia A or B with inhibitors to Factor VIII or Factor IX. Currently, there is some evidence that low, fixed-dose rFVIIa (1.2 mg) may safely and effectively decrease PT/INR in patients with warfarin-associated intracranial hemorrhage. The purpose of this study was to evaluate low, fixed-dose rFVIIa compared to higher doses of rFVIIa for effect on coagulation factors and length of stay in the surgical intensive care unit (SICU).
METHODS: In this single-center, retrospective cohort analysis, patients who received rFVIIa for warfarin-associated intracranial hemorrhage were divided into two groups based on total dose received. Group 1 (n=16) received a single 1.2 mg dose, while Group 2 (n=9) received any dose greater than 1.2 mg (range 2.4 mg–10.6 mg). The groups were compared based on achievement of INR less than 1.5 for at least 3 hours, peak INR after rFVIIa administration, and SICU length of stay.
RESULTS: In Group 1, 87.5% of patients achieved an INR of less than 1.5 for at least 3 hours, compared with 100% of patients in Group 2 (p=0.520). There was also no detectable difference in regards to time to reach an INR of less than 1.5, highest INR within 24 hours of dosing, and length of stay in the SICU. When adjusted for only patients who did not expire, patients in Group 2 had a significantly longer SICU length of stay (13.14 days) than Group 1 (2.89 days, p<0.001).
CONCLUSIONS: A low, fixed-dose (1.2 mg) of rFVIIa appears to be as fast and effective as higher doses for decreasing INR to less than 1.5. Future studies are needed to confirm these findings.

43E. **An observational study of bleeding events (BE) associated with low-dose unfractionated heparin (LDUFH) in a neurologic intensive care unit (NSICU).** *Denise Rhoney, Pharm.D.*, Xi Liu, Pharm.D., Dennis Parker, Pharm.D.; Wayne State University, Detroit, Mich.

PURPOSE: Although DVT and pulmonary embolism (PE) remain a significant cause of morbidity and mortality in critically ill patients, clinicians are often reluctant to initiate early LDUFH prophylaxis due to the fear of BE. We sought to describe the BE incidence and associated risk factors related to the use of prophylactic LDUFH in NSICU patients.
METHODS: Patients admitted to the NSICU over a 9-month period were included. A major BE was defined as clinically overt blood with a decrease in Hgb by >2 gm/dL and/or a transfusion of 2U PRBC; minor BE were all other BE.
RESULTS: A total of 181 patients were included, the majority admitted with hemorrhagic stroke (41%) or traumatic brain injury (27%). BE occurred in 14.9% (n=25) patients (41% major) 3 (1–25) days after initiation of LDUFH with the majority gastrointestinal. Demographics were similar except for APACHE II: BE 15 (2–24), NBE 10 (0–36)(p=0.03). The only difference in baseline labs was glucose, which was increased in patients with BE (p=0.02). LDUFH prophylaxis was administered in 93% of patients with BE and 84% with NBE, primarily at a dose of 5000 U every 12 hours (82%)(p=0.38). LDUFH was initiated within 24 hours of hospital admission in 84% of patients in both groups. The overall incidence of DVT and PE was 2%. Significant risk factors for BE in patients who received LDUFH are below. Logistic regression revealed two independent predictors of BE; NSAID use and mechanical ventilation 39 80 < 0.01 Presence of ICP monitor 20 44 0.02 Use of NSAIDs 26 52 0.02 Surgical intervention 37 63 0.03 Mechanical ventilation 39 80 < 0.01 Presence of ICP monitor 20 44 0.02 Use of NSAIDs 26 52 0.02
CONCLUSION: Early use of LDUFH prophylaxis was not associated with increased BE risk in this NSICU cohort even in patients with intracranial bleeding. Identified risk factors for bleeding may indicate that patients are at risk from other factors besides LDUFH prophylaxis.
Presented at the Annual Congress of the Society of Critical Medicine, Orlando, Fla February 17-21, 2007.

44E. **A Comparison of Medication Errors Reported in Intensive Care Unit (ICU) and non-ICU Patients.** *Sandra L. Kane-Gill, Pharm.D., M.Sc.*[1], Joanne G. Kowiatek, R.Ph., M.P.M.[2], Robert J. Weber, M.S., FASHP[2]; (1)University of Pittsburgh, Pittsburgh, Pa; (2)University of Pittsburhg Medical Center, Pittsburgh, Pa.

PURPOSE: To compare type, process node, cause, drug class and outcome for medication errors (ME) reported in ICU and non-ICU patients.
METHOD: Staff record ME using MEDMARX, an internet capable voluntary anonymous medication error reporting system, with a standard form and ME definition. ME are reviewed by an expert panel to validate reported information. Following IRB approval, ME from July 2001 to December 2005 were obtained from MEDMARX. ME data were compared for all ICUs (coronary, medical, neurosurgical, surgical, trauma) to non-ICUs. Most frequent types, process node, causes, drug classes and resulting level of care were determined. Chi-square was used for statistical analysis.

RESULTS: 541 and 2,711 ME were reported in the ICUs and non-ICUs, respectively. Primary types of MEs were prescribing (39%) in the ICU and omission (38%) in the non-ICU. The prescribing and administration nodes were the most common stages for MEs in the ICU and non-ICU. Leading causes of ME were procedure/protocol not followed (21%) and knowledge deficit (17%) for the ICU and workflow disruption (21%) and human deficit (21%) for the non-ICU. Top three drugs associated with ME in the ICU were narcotic analgesics (13%), beta-lactam antimicrobials (8%), and blood coagulation modifiers (6%). In the non-ICU they were antiasthma/bronchodilators (16%), narcotic analgesics (13%), and vaccines (10%). Level of care after the error was observation increased/initiated (15%) in the ICU and none (44%) in non-ICU. Prolonged hospitalization was a result of ME in 1% of the ICU cases and 0.4% of the non-ICU (p=0.056). MEs were associated with harm in 12% and 6% of the cases in the ICU and non-ICU, respectively (p<0.001).

CONCLUSION: Type, cause, and drug classes involved in ME differ in the ICU and non-ICU so it is important to develop surveillance systems that analyze ICU specific data allowing systematic changes for this patient population.

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45E. **Titration protocol reduces hypotension during dexmedetomidine infusion in critically ill surgical patients.** *Anthony Gerlach, Pharm.D., BCPS*, Joseph F Dasta, M.S., Scott Armen, M.D., Jason Smith, M.D., Steven Steinberg, M.D., Larry Martin, M.D., Charles Cool, M.D.; The Ohio State University Medical Center, Columbus, Ohio.

PURPOSE: We have previously demonstrated by retrospective review a significant incidence of adverse effects when dexmedetomidine (DEX) infusions are titrated quickly in critically ill surgical patients. This study evaluates the effect of a titration protocol upon these adverse effects.

METHODS: A dosing and titration protocol for DEX was developed, allowing titrations no sooner than every 30 minutes. Prospectively collected data was compared to historic data before protocol initiation. Data collected included demographics, indication, dosing, length of therapy, time between dosage adjustment, and adverse effects. Hypotension was defined as mean arterial blood pressure (MAP) < 60 mm Hg, and bradycardia was defined as heart rate < 50 bpm. Statistical analysis was performed by Fisher's exact test for nominal data and student's t-test for continuous data. A sample size of 18 patients per group was calculated to demonstrate 40% difference in hypotension with alpha = 0.05 and power = 0.8.

RESULTS: Forty-six patients were evaluated, 27 on protocol and 19 historic controls. Both groups had comparable demographics, initial and maximum infusion rates. Patients treated with DEX on protocol had fewer dosing changes (mean 4.8 vs 7.8, p=0.01), less hypotension (14.8% vs 69.2% p=0.0004), and no difference in bradycardia (18.5% vs 15.5%, p=1) when compared to historic controls.

	Protocol N=27	Historic Controls N=19	P value
Age (Years)	47.3 Years	55.5 Years	0.15
Female (%)	22.2	15.4	0.72
Bolus dose given (%)	7.4	7.7	1
Initial infusion rate (mcg/kg/hr)	0.26	0.22	0.21
Maximum dose rate (mcg/kg/hr)	0.45	0.54	0.11
Length of infusion (Hours)	33	19.2	0.17
Mean number of dosing changes	4.8	7.8	0.01
Total ADR (%)	25.9	76.9	0.0008
Hypotension	14.8	69.2	0.0004
Bradycardia	18.5	15.4	1
Mean nadir MAP (mmHg)	51.8	51.1	0.87

CONCLUSION: A dosing/titration protocol significantly decreased the incidence of hypotension associated with DEX in critically ill surgical patients.

Presented at the Society of Critical Care Medicine 32nd Annual Critical Care Congress, Orlando Fla, February 2007.

46. **National survey of acute hypertension management.** Jessica Bollinger, Pharm.D., Anthony Gerlach, Pharm.D., *Joseph Dasta, M.Sc.*; College of Pharmacy, The Ohio State University, Columbus, Ohio.

PURPOSE: National practice guidelines do not exist for the general treatment of acute hypertension (AH) in the critically ill adult. One of the first steps toward guideline development is to document the current prescribing

patterns of intravenous (IV) antihypertensives in the pharmacotherapy of AH, which serves as the purpose of this survey.

METHODS: An e-mail to participate in this 32-question, Web-based survey was sent to 1370 critical care pharmacist members of the American College of Clinical Pharmacy or the Society of Critical Care Medicine. The survey, which requested responses concerning the most common practice in the respondents' intensive care unit (ICU), opened February 6, 2007, and closed May 11, 2007. A survey was excluded if it was less than 75% complete, from a pediatric ICU, or from respondents not in practice.

RESULTS: One hundred fifty (10.9%) responses were returned; 16 were excluded. The most common practice site (38.1%) was a mixed-population ICU. Forty-two (32.3%) respondents reported that a guideline exists in their institution for the treatment of hypertensive emergency in acute hemorrhagic stroke (AHS), whereas only 6 (4.5%) had guidelines for the non-stroke (NS) patient. Systolic blood pressures (mean ± SD) used to initiate IV antihypertensives were 177.6 ± 22.9 and 167.0 ± 23.3 in NS and AHS patients, respectively. The most common duration of IV therapy was 24–48 hours in both populations. Intermittent IV labetalol (26.5%), sodium nitroprusside (26.5%), and nicardipine (16.7%) were the top three drugs of choice in NS patients, with nicardipine (36.2%), intermittent IV labetalol (29.3%), and sodium nitroprusside (16.4%) in AHS patients. Fifty-seven respondents (43.8%) have seen a symptomatic patient with cyanide/thiocyanate toxicity receiving sodium nitroprusside.

CONCLUSIONS: Because most institutions do not have guidelines in place, the variability described herein regarding the pharmacotherapy of AH provides the rationale for developing a national guideline.

47E. **Diagnostic criteria and intensity of surveillance affect reportable ventilator-associated pneumonia rates.** *Lee E. Morrow, M.D., FCCP*, Mark Malesker, Pharm.D., FCCP, Kristi Farrington, RRT; Creighton University Medical Center, Omaha, Neb.

PURPOSE: Public disclosure of institutional nosocomial infection rates is proposed as a means of improving the quality of medical care. However, institutions use differing diagnostic criteria and do not mandate uniform levels of surveillance. This study assessed the effects of varying diagnostic criteria and intensity of surveillance on ventilator-associated pneumonia (VAP) rates.

METHODS: We prospectively studied all patients receiving mechanical ventilation at our hospital. Each patient was evaluated for VAP using four different criteria: clinical diagnosis by the treating physician; American College of Chest Physicians (ACCP) criteria; Clinical Pulmonary Infection Score (CPIS ≥ 6); and National Nosocomial Infection Survey (NNIS) criteria. The effect of active VAP screening was assessed by comparing the VAP rate using NNIS criteria prospectively for all patients to the VAP rate reported by the institutional infection control office using the NNIS criteria retrospectively for patients with positive culture data.

RESULTS: 134 patients received mechanical ventilation for > 48 hours during the 90-day study period (mean 6.4 ± 8.0 days). VAP rates were 22% using treating physicians clinical diagnosis, 29% using ACCP criteria, 25% using the CPIS and 31% using NNIS criteria. The correlation among diagnostic strategies was high only for the ACCP and NNIS criteria (Pearson correlation coefficient 0.95). Correlation coefficients for the remaining strategies ranged from 55% to 67%. Active application of the NNIS criteria to all patients resulted in a significantly higher VAP incidence rate (31%) than if the NNIS criteria were passively used according to institutional infection control policies (2%).

CONCLUSIONS: These data highlight how dramatically VAP rates are affected by the choice of diagnostic criteria and intensity of VAP surveillance

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48E. **Epidemiology of renal insufficiency in patients with ventilator-associated pneumonia.** *Lee E. Morrow, M.D., FCCP*, Mark Malesker, Pharm.D., FCCP; Creighton University Medical Center, Omaha, Neb.

PURPOSE: Although renal insufficiency (RI) is common in the ICU and is associated with worse outcomes, little is known about its epidemiology in patients with ventilator-associated pneumonia (VAP). Given the implications for dosing many commonly used ICU medications, this study was undertaken to describe changes in renal function after the onset of VAP.

METHODS: We prospectively collected data from 117 consecutive patients with VAP diagnosed between 1/1/02 and 12/31/03 at a single academic hospital's adult ICU. Patients with pre-existing renal failure were not studied. Data abstraction included demographics, comorbid illness, daily laboratory values, antibiotic prescription, and length of stay measures. Creatinine clearance (CrCl) was calculated daily using the Cockroft-Gault equation. Patients were classified as having no RI (CrCl > 90 mL/minute), mild RI (CrCl 51–90 mL/minute), moderate RI (CrCl 10–50 mL/minute), or severe RI (CrCl < 10 mL/minute). Renal dosing was deemed necessary if patients had moderate or severe RI. Subset analysis were repeated for geriatric (age > 65 years) and non-geriatric patients.

RESULTS: The cohort was 71% male with an average age of 53 years. Overall, 16% of patients with VAP had RI severe enough to merit consideration of renal dosage adjustment (CrCl ≤ 50 mL/minute) at enrollment. This

increased to 25% over the next 14 days. Significantly more geriatric patients had RI severe enough to merit consideration of renal dosage adjustment (32% vs. 8%, p<0.001). Similarly, more geriatric patients developed RI severe enough to merit consideration of renal dosage adjustment over the ensuing 14 days (46% vs. 14%, p<0.001).
CONCLUSIONS: RI is common in patients with VAP and is more likely to occur in geriatric patients. This study highlights the need for daily assessment of renal function in patients with VAP in order to optimize pharmacotherapy.
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49. **A nursing survey comparing attributes of the Richmond Agitation Sedation Scale and the Ramsay scale.** *Lama H. Nazer, Pharm.D., BCPS*, Eun An, Pharm.D.; Western University of Health Sciences, Pomona, Calif.

PURPOSE: To compare critical care nurse opinions regarding the following five attributes of the Richmond Agitation Sedation Scale (RASS) and the Ramsay Scale: ease of use, accuracy, reliability, generalizability, and clinical utility.
METHODS: A self-administered survey was distributed to all critical care nurses (n=56) at Glendale Memorial Hospital, a 324-bed community hospital, after 6 months of switching from the Ramsay Scale to the RASS. The attributes of the sedation scales were compared using a 10-point Likert scale, with higher numbers indicating more agreement. The responses between the scales were examined for percentage differences using Fisher's Exact Chi-Square test.
RESULTS: Forty-four nurses (79%) completed the survey. The results were analyzed by combining choices 8–10 on the Likert scale and considering them as "near complete agreement or complete agreement." For all five attributes, a higher percentage of nurses felt that the RASS displayed better attributes, compared to the Ramsay Scale. A statistically significantly larger percentage of nurses rated the RASS higher than the Ramsay Scale in reliability (51.2% vs 25.6%, p=0.02), generalizability (62.8% vs 32.6%, p=0.01), and accuracy (55.8% vs 20.9%, p=0.001). Although not statistically significant, a higher percentage of nurses rated a "10" (complete agreement) in judging the RASS, compared to the Ramsay Scale in all five attributes: ease to use (41.9% vs 30.2%), clinical utility (16.3% vs 7%), generalizability (16.3% vs 11.6%), accuracy (11.6% vs 9.3%), and reliability (9.3% vs 7%).
CONCLUSION: Nurses rated the RASS significantly superior to the Ramsay Scale in reliability, generalizability, and accuracy. The findings support the ongoing use of RASS at Glendale Memorial Hospital.

50E. **Does initiation of stress ulcer prophylaxis in the intensive care unit lead to therapy continuation?** *Jill A. Rebuck, Pharm.D, FCCM, BCPS*[1], Catherine Murphy, Pharm.D., BCPS[2], Alison Stevens, Pharm.D.[3], Nicholas Ferrentino, M.D.[4], Bruce Crookes, M.D., FACS[4], James Hebert, M.D., FACS[4], Carter Freiburg, M.D.[4]; (1)Lancaster General Hospital, Inpatient Pharmacy, Lancaster, Pa; (2)Duke University Medical Center, Raleigh, NC; (3)St. Louis College of Pharmacy, St. Louis, Mo; (4)Fletcher Allen Health Care, Burlington, Vt.

PURPOSE: Although the initiation of gastric acid-suppressive (AS) medications for stress ulcer prophylaxis (SUP) in the intensive care unit (ICU) is often justified, therapy is frequently continued after risk factors subside and patients are no longer critically ill.
METHODS: Prospective, observational study at an academic tertiary care hospital. All consecutive adults admitted to a surgical ICU during a 6-month period initiated on AS therapy with a proton pump inhibitor (PPI) or histamine2-receptor antagonist (H2RA) were evaluated. Exclusion criteria: AS therapy prior to admission or H2RA or PPI for indications other than SUP.
RESULTS: A total of 248 ICU patients met inclusion criteria and were initiated on SUP. The majority (95.6%) of AS initiation were associated with at least one gastrointestinal bleed (GIB) risk factor. Continuation of AS therapy for the remainder of post-ICU hospitalization was common. Sixty patients (24.2%) were discharged on AS therapy, predominantly to skilled nursing/rehabilitation centers; 8 patients (3.2%) were discharged home. Patients continued on AS post-hospital required prolonged mechanical ventilation (71 vs. 18 hours, P=0.001), possessed more GIB risk factors (P<0.001), were frequently discharged on anticoagulant therapy (50 vs. 18%, p<0.001), exhibited longer hospital and ICU stays (15 vs. 7 days and 5 vs. 2 days, respectively, p<0.001), demonstrated GCS < 8 ± head injury (65 vs. 35%, p<0.001), hepatic failure (15 vs. 4%, p=0.004), and suffered major trauma (p=0.049) more frequently than when AS therapy was discontinued.
CONCLUSIONS: The majority of patients were continued on AS therapy during post-ICU hospitalization. Few patients were discharged home on AS therapy. The presence of early risk factors for stress ulcer-related GIB appears to influence post-hospital AS therapy continuation.
Presented at the Society of Critical Care Medicine 36th Critical Care Congress, Orlando, Fla, February 18-21, 2007.

51E. **Lansoprazole attenuates neutrophil-mediated tissue damage of liver following visceral ischemia-reperfusion injury.** *Jill A. Rebuck, Pharm.D., BCPS, FCCM*[1], William Eward, M.D.[2], Marissa Slusarczyk[2], Benjamin Suratt, M.D.[2], Joe Petty[2], James Hebert, M.D., FACS[2]; (1)Lancaster General Hospital, Inpatient Pharmacy, Lancaster, Pa; (2)Fletcher Allen Health Care, Burlington, Vt.

PURPOSE: Visceral ischemia-reperfusion (I/R) injury is an important pathophysiological mechanism in critically ill patients that leads to neutrophil-mediated local and remote tissue injury. The anti-inflammatory effects of proton pump inhibitors, such as lansoprazole, and histamine-2 receptor antagonists, such as ranitidine, may be related to their effects on neutrophil margination.
METHODS: Visceral I/R injury was induced by clamping both the cranial mesenteric artery and the celiac trunk for 20 min followed by 1 hour of reperfusion. Sixty adult female C57B6 mice underwent either I/R injury or sham-operated laparotomy only. Lansoprazole, ranitidine, or saline were administered to mice intraperitoneally 1 hour before vascular clamping or 1 hour prior to laparotomy in the sham-operated control group. Leukocyte count and tissue accumulation of neutrophils via myeloperoxidase activity were measured.
RESULTS: Visceral I/R injury was associated with a significant decrease in absolute neutrophil count (p=0.022) and a significant increase in liver myeloperoxidase accumulation (p=0.013) in animals pretreated with saline only. Both of these effects were ameliorated in I/R injured animals pretreated with lansoprazole (p<0.001).
CONCLUSIONS: Lansoprazole decreases neutrophil accumulation in liver and margination from peripheral blood in the setting of visceral I/R injury in mice, suggesting that lansoprazole may have prophylactic or therapeutic value in visceral I/R injury.
Presented at the Society of Critical Care Medicine 36th Critical Care Congress, Orlando, Fla, February 18-21, 2007.

52E. **Influence of Variable Cyclosporin-A Concentrations on Brain Neurochemistry in Severe Traumatic Brain Injury Patients.** *Gretchen M. Brophy, Pharm.D.*[1], James R. Robles, Ph.D.[1], Satjit S. Brar, Ph.D.[1], Anna T. Mazzeo, M.D.[2], Thomas Karnes, Ph.D.[1], Ross Bullock, M.D.[1]; (1)VCU Medical College of Virginia, Richmond, Va; (2)University of Messina, Messina, Italy.

PURPOSE: Cyclosporin-A (CsA) has potential to be neuroprotective by attenuating mitochondrial dysfunction in traumatic brain injury (TBI). Our group previously reported the results of a randomized, placebo-controlled trial using CsA for neuroprotection in TBI patients. To evaluate these data further, we conducted a subgroup analysis to determine the correlation between variable CsA blood exposure and brain neurochemistry from start of the CsA infusion to 24 hours post infusion.
METHODS: Patients were divided into 3 groups: 1) CsA patients with a larger CsA area under the curve (AUC) as compared to the mean CsA AUC for the entire group (n=14); 2) CsA patients with a smaller CsA AUC (n=17); and 3) those receiving placebo (n=12). The average rate of change per hour and the AUC of the brain extracellular fluid (ECF) glutamate, lactate and pyruvate in each CsA group and between the larger CsA AUC group and placebo was then compared. Statistical analysis was performed using the Welch Two sample t-test of differences of the means. The groups were trimmed to eliminate global outliers.
RESULTS: Patients achieving a larger CsA AUC had a greater average decrease per hour in lactate concentrations as compared to those with a smaller AUC (p=0.002) and the placebo group (p=0.049). There was also a positive trend in the average change per hour for glutamate (p=0.23) and lactate/pyruvate ratio (p=0.76) in the larger CsA AUC group, but a negative trend was seen for pyruvate (p=0.2). AUC for lactate was also significantly greater for the larger CsA AUC group (p=0.047).
CONCLUSIONS: These results show that greater CsA exposure does positively affect average hourly changes in ECF lactate concentrations. However, these effects may not be obvious when evaluating AUC. Larger studies are needed to confirm if greater CsA exposure positively influence brain neurochemistry in severe TBI patients.
Presented at the 25th Annual National Neurotrauma Society Symposium, Kansas City, Mo, July 33, 2007. J Neurotrauma 2007(in press).

53. **Enteral Nutrition in Neurocritical Illness.** *Sommer D. Zarbock, Pharm.D.*, Jimmi Hatton, Pharm.D., Doug Steinke, Ph.D., Barbara Magnuson, Pharm.D., Kelly M. Smith, Pharm.D., Aaron M. Cook, Pharm.D.; University of Kentucky HealthCare, Lexington, Ky.

PURPOSE: Adequate calorie intake is associated with improved outcome in neurocritical illness, but factors influencing the provision of enteral nutrition (EN) have not been systematically evaluated. The primary goal of the study was to determine the EN intake of neurosurgical ICU patients within the first week of illness and the contributing factors to achieving caloric goals.

METHODS: A retrospective cohort of adult patients admitted to the neurosurgery service (NS) during August 2005 to August 2006 were randomly selected and stratified into 3 groups based on their ICU-admission Glasgow Coma Scale Score (GCS) (GCS > 11, GCS 8–11, GCS 4–7). Daily EN intake, GCS, and other clinical data were collected. Baseline characteristics of groups and the impact of the clinical factors were statistically analyzed using ANOVA and multiple linear regression.

RESULTS: Seventy-one patients were included (GCS > 11 = 23, GCS 8–11 = 23, GCS 4–7 = 25). Admitting diagnoses included traumatic brain injury (32%), subarachnoid hemorrhage (32%), and intracerebral hemorrhage (17%). The overall in-hospital mortality was 23.9%. Overall, the maximum daily mean calories provided was 1100 kcal (mean of 55% of caloric goal on hospital day 6). The mean time to feeding was about 3 days in each group. GCS did not appear to significantly affect mean % of caloric goal provided in patients with a minimum daily GCS ≤ 11 (GCS 8–11 = 43%, GCS 4–7 = 34%, GCS 3 = 30%; p=0.053). Multivariate analysis revealed that clinical care factors, such as time to EN orders and enteral access confirmation, were significant factors impeding EN provision. (p=0.001).

CONCLUSION: System-based clinical care factors appear to be a major contributing factor to the successful provision of EN in the first week of neurocritical illness.

Drug Information

54. **Factors associated with database searching among pharmacy faculty and students: PubMed vs. Google Scholar.** *Maisha Kelly Freeman, Pharm.D., BCPS*, Stacy A. Lauderdale, Pharm.D., BCPS, Michael G. Kendrach, Pharm.D., Robert H. Schrimsher, MLIS, Ed.D.; Samford University, Birmingham, Ala.

PURPOSE: Google Scholar use among medical professionals has increased since its introduction in November 2004. In 2005, Google Scholar linked more visitors to biomedical journal Web sites than PubMed. The purpose of this study was to determine the factors associated with database searching among pharmacy faculty and students, including the following: primary reasons for searching; frequency and satisfaction of database access; and the number of Web pages participants are willing to review to answer a question.

METHODS: A 26-item survey was developed and delivered to Samford University, McWhorter School of Pharmacy faculty (n=35) and fourth-year students (n=113). Survey results were entered into SPSS, Version 15.0 and analyzed via descriptive statistics. The research was IRB approved.

RESULTS: Approximately 77% (n=27) of the faculty and 64% (n=72) of the students responded to the survey. Approximately 52% and 15% of responders denied use of Google Scholar and PubMed, respectively. The top 3 reasons for searching Google Scholar were ease of use, speed, and availability of free, full-text articles; whereas the top 3 reasons for PubMed searching were efficiency and accuracy of searches and availability of free, full-text articles. About 37% and 68% of responders used Google Scholar and PubMed 1–5 times weekly, respectively. More responders were satisfied with search features of PubMed (86%) compared with Google Scholar (32%). The most frequent response for pages to search was 1–5 for Google Scholar (50%) versus 6–10 for PubMed (36%). Only 5% of responders were willing to search over 10 pages of Google Scholar compared with 20% for PubMed.

CONCLUSIONS: The availability of free, full-text articles was a top reason for using both PubMed and Google Scholar. Responders felt that the search features of PubMed were superior compared with Google Scholar and were more willing to search additional PubMed pages compared with Google Scholar.

Education/Training

55. **Student opinions about the use of a "peripheral brain" during a professional pharmacy curriculum.** *Julie A. Murphy, Pharm.D.*, Patrick M. Finnegan, Pharm.D., Suzanne G. Bollmeier, Pharm.D., Alicia B. Forinash, Pharm.D.; St. Louis College of Pharmacy, Saint Louis, Mo.

PURPOSE: Students assembled a pocket reference book, the "peripheral brain" (PB) to 1) increase opportunities to practice higher-order thinking skills on exams in the therapeutics sequence, and 2) provide a reference tool for students on their advanced practice experiences. For one group of students, use of the PB was allowed in the second professional year, but not during the third professional year. This study evaluated how this group's opinions of the PB developed during their second through fourth professional years.

METHODS: Similar surveys were administered to the same group of students after one semester when the PB was allowed, after one semester when the PB was not allowed, and during their fourth professional year. Students could answer yes, no, or not sure to the following: do you view the PB as a valuable learning tool, does the PB enhance your learning of therapeutics, and do you understand the purpose of the PB? Differences were evaluated using a two-way 2 x 3 contingency table.

RESULTS: One-hundred fifty students were eligible to respond to the survey. During the second, third, and fourth professional years, 84%, 69%, and 67% of the students responded, respectively. The results of the survey

demonstrate that students' opinions about the PB were altered from the second, third, and fourth professional years, respectively, as follows: they view the PB as a valuable learning tool (88% to 68% to 52%, p=0.0001); they feel the PB enhances their learning of therapeutics (79% to 56% to 37%, p<0.0001); and they understand the purpose of the PB (98% to 90% to 72%, p=0.0354).

CONCLUSIONS: As students progressed through the professional curriculum, it appears that fewer students viewed the PB as a valuable learning tool, as they did not feel it enhanced their learning. Their perceived understanding of the purpose of the PB changed.

56. **Evaluation of the readiness of New York City pharmacists to serve as public health providers.** *Judy W. Cheng, B.S., Pharm.D., M.P.H.*[1], Gary Rosenberg, Ph.D.[2], Stanley Feifer, M.S.[1], Harold L. Kirschenbaum, M.S., Pharm.D.[1], Emily Senay, M.D., M.P.H.[2]; (1)Long Island University, New York, NY; (2)Mount Sinai School of Medicine, New York, NY.

PURPOSE: One of the objectives of Healthy People 2010 is to increase the number of health professional schools whose curriculum includes a core competency of public health. Core competency includes four components: 1) epidemiology/ outcome assessment, 2) disease preventions/health promotion, 3) health systems/ policy, and 4) community/cultural aspects of practice. Traditional pharmacy education has not included a major emphasis on public health. To understand how to revise pharmacy curriculum to best achieve this objective, we evaluated the understanding of public health of community pharmacists practicing in New York City (NYC) and their readiness to serve as public health providers. Recommendations on curriculum revision were made based on the study results.

METHODS: Pharmacists practicing in community pharmacies that serve as clerkship sites for a college of pharmacy in NYC were invited to complete a survey asking them to 1) define public health, 2) select among a list of pharmacy practice activities, those that were public health related, 3) describe any public health services provided by their pharmacies, and 4) describe areas of public health services that they believed pharmacists were qualify to perform.

RESULTS: Sixty-eight (24%) pharmacists completed the survey. They are most aware of public health relating to disease prevention and health promotion (62 [91.2%]). The public health services provided most by them are education on safe medication use (64[94.1%]) and disease prevention (53 [77.9%]). Pharmacists have little understanding of other components of public health (e.g., epidemiology, public health system/health policy development, and cultural aspects of practice). Pharmacists also expressed concern regarding lack of time and incentive to perform other activities beyond prescription dispensing.

CONCLUSIONS: Future pharmacy curriculum should incorporate courses that address the other three components of public health. Pharmacy organizations should advocate, through health policy development, to increase incentives for pharmacists to expand their scope of practice.

57. **Using personal digital assistants as tools to enhance learning of infectious diseases in pharmacy students.** *Amy L. Pakyz, Pharm.D., M.S.*; Virginia Commonwealth University School of Pharmacy, Richmond, Va.

PURPOSE: Antimicrobials are commonly used drugs that are often implicated in the occurrence of medical errors. Pharmacists are trained in the area of therapeutics to provide comprehensive drug management. Training in this area is a priority in the education of pharmacy students. The use of portable information technology in areas of infectious diseases may allow access to relevant resources at the point-of-care. This study assessed the student use of a Personal Digital Assistant (PDA) reference specific to antimicrobial management, the Sanford Guide to Antimicrobial Therapy, in a pharmacy infectious diseases pharmacotherapy course as a real time educational tool in the classroom.

METHODS: All students were provided with a PDA Application of the Sanford Guide to Antimicrobial Therapy to install on their PDAs as a resource for in-class infectious diseases case-based discussions. The utility of the guide as a learning tool and of case-based discussions as a teaching method was assessed by student feedback in a six-question survey. Students were also tested on their ability to effectively use the guide during in-class exams.

RESULTS: A total of 60 out of 61 students (98%) completed the survey. There was high agreement by students that information on antimicrobials and infectious diseases management was easy to retrieve on the PDA application (90% and 86%, respectively). The students found that being tested on using the application was helpful (95% agreement). There was also agreement that a case-based approach to learning infectious diseases enhances learning (92%) and prepares for professional practice (85%).

CONCLUSIONS: Use of the PDA-based reference and case-based teaching methodology was viewed positively by students and enhanced their learning of infectious diseases.

58E. **Identification of required core activities for advanced community pharmacy clerkship training.** *Peggy G. Kuehl, Pharm.D.*, Patricia A. Marken, Pharm.D.; University of Missouri - Kansas City School of Pharmacy, Kansas City, Mo.

PURPOSE: The UMKC School of Pharmacy developed a process to assess quality and consistency in and among our community advanced pharmacy practice experiences (APPEs). Factors necessitating such a process included: new ACPE standards, increased class size, suspected lack of consistency among current sites, need to provide direction for APPE preceptors during site development, ability to assess change in sites over time, and need for an objective method to assess site readiness to begin training students.
METHODS: Five community preceptors known to practice patient-focused care served as the expert panel. Panel members rated the importance of various practice activities and site characteristics as part of an APPE experience. Activities and site characteristics were extracted from the Community Practice Metrics portion of the AACP Academic-Practice Partnership Initiative's Site Specific Criteria for Excellence. Ratings ranged from 4 (core competency) to 1(not important). Mean ratings > 3.5 indicated an activity or characteristic that is a core competency.
RESULTS: Seven activities/characteristics were identified as core competencies for APPEs in community settings. They are provision of 1) MTM/DSM services, 2) OTC consultations, 3) polypharmacy consultations, 4) documentation using SOAP notes, 5) provision of recommendations to patients' physicians, and requirements that students 6) provide drug information and 7) complete a project.
CONCLUSIONS: Faculty and community pharmacy preceptors will use the core competencies to assess the readiness and ongoing ability of community sites to offer APPEs. This list should also stimulate discussion of new services among affiliated community sites and spur their development.
Presented at the 2007 Annual Meeting of the American Association of Colleges of Pharmacy, Lake Buena Vista, Fla, July 15, 2007.

59E. **Students' perceptions of preparedness for oral examinations.** *Lisa M. Lundquist, Pharm.D., BCPS*, Justine S. Gortney, Pharm.D., BCPS; Mercer University, Atlanta, Ga.

PURPOSE: To determine students' perceptions of preparedness for oral examinations.
METHODS: A case-based oral examination was administered to all second professional year students enrolled in Cardiovascular/Renal III therapeutics course. Prior to the oral examination, survey completion was requested to assess perception of preparedness based on therapeutic topics and previous introductory pharmacy practice experiences (IPPE). Students were asked to rate the adequacy of their preparedness on a 4-point Likert scale with 1 being extremely unprepared, 2 unprepared, 3 prepared, and 4 extremely prepared. Students' perceptions of preparedness were compared to performance on the oral examination.
RESULTS: One hundred forty-one students (96%) completed the survey. Mean overall perception of preparedness for the oral examinaed was 3.30. Students that achieved 90–100 on their oral examination perceived preparedness as 3.44, those with 80–89 perceived preparedness as 3.34, and those with 70–79 perceived preparedness as 3.17. Students who scored less than 70 had the lowest perception of preparedness at 3.15. Students felt most prepared in their ability to calculate cholesterol values (3.81), identify goals and stages of hypertension (3.57), and identify objective evidence to support diagnosis (3.45). Students' perception of preparedness in the ability to identify disease-drug interactions (3.20) was the lowest. Most students thought that IPPE helped in their preparation for the oral examination.
CONCLUSION: The case-based oral examination represents an additional tool that may contribute to the development of a student's connection between knowledge, effective communication, and pharmacy practice.
Presented at the American Association of Colleges of Pharmacy, Orlando, Fla July 16, 2007.

60. **Evaluation of opinions and performance on an objective structural clinical examination to assess problem-based learning.** *Francine D. Salinitri, Pharm.D.*, Candice L. Garwood, Pharm.D., Victoria Tutag-Lehr, Pharm.D., Karina Abdallah, Pharm.D., Mary Beth O'Connell, Pharm.D.; Wayne State University, Detroit, Mich.

PURPOSE: 1. Assess opinions of faculty and 3rd year pharmacy students on the use of objective structural clinical examinations (OSCE) to test knowledge, skills, and abilities gained from a Problem-Based Learning (PBL) curriculum. 2. Compare results of 3rd year pharmacy student's performance on OSCE vs a multiple choice (MC) examination.
METHODS: Fifty-four 3rd year pharmacy students responded to a survey regarding the OSCE they took. A similar survey was distributed to 8 faculty, who evaluated the student's performance on the OSCE. These surveys assess perceived use of OSCEs to appropriately test PBL. The percent of agreeable, neutral, and disagreeable responses were calculated for each item. Correlation testing was used to compare student's scores on MC test versus OSCE.

RESULTS: Surveys returned yielded a response-rate of 90% (55/60) from students and 100% (8/8) from faculty regarding their opinions of the OSCE. Of students surveyed ≥ 75% agreed in the following areas: OSCE reflected material learned in PBL and important aspects of PBL; and OSCE was a good measure of knowledge, communication, and clinical skills. Only 51% felt OSCE best tested clinical skills, while 44% felt OSCE was an accurate reflection of their clinical skills. More than 75% of faculty agreed with the following: drug related problems are presented appropriately in the OSCE; OSCEs do evaluate knowledge communication, clinical, and problem solving skills, and OSCE should be part of the standard PBL testing. Correlation between performance on MC and OSCE was poor because r = 0.16. Similarly, there was poor correlation between scores on MC and OSCE when evaluating quartiles from examination results.
CONCLUSIONS: Our findings suggest a high degree of agreement with the use of OSCE as a testing tool for PBL. Overall, there does not appear to be a strong association between students' performance on OSCE and their performance on MC examinations.

61. **Evaluation of an Audience Response System on pharmacy student test performance.** *Lynette R. Moser, Pharm.D.*[1], Christine M. Brubaker, Pharm.D.Candidate[2], James S. Kalus, Pharm.D.[2]; (1)Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Mich; (2)Wayne State University College of Pharmacy and Health Sciences, Detroit, Mich.

PURPOSE: The audience response system (ARS) is a collection of electronic handheld response devices that anonymously records students' answers to multiple choice questions posed during lecture. It has been suggested that this technology promotes learning and retention by offering the opportunity to actively participate in the lesson. To date, no study has analyzed the educational outcomes of the audience response system in pharmacy curriculum.
METHODS: Second-year pharmacy students enrolled in the cardiovascular therapeutics module were included (n=86, mean grade point average [GPA] = 3.0 ± 0.42, mean grade in cardiology module = 81.6% ± 5.9%). Students were randomized to attend a 2-hour lecture on rhythm control in atrial fibrillation using the ARS or an identical control lecture, which posed the same questions, but in which students did not use ARS devices. The same instructor provided both lectures and time spent on discussion during each lecture was recorded by an observer. One week after the lectures, the students were required to answer 10 questions on rhythm control as part of their final examination. Performance on these questions was compared between groups.
RESULTS: Each study group contained 43 students. The percentage correct on the 10 questions was 65.8 ± 15.3 in ARS group and 57.9 ± 15.7 in control group (p=0.020). There was a qualitative increase in the amount of time spent in interactive discussion during the ARS lecture (24:25 min) as compared to the control lecture (16:15 min). Overall professional GPA was similar between groups (3.0 ± 0.42 vs. 3.0 ± 0.43; p=0.409).
CONCLUSION: Use of the ARS resulted in better examination scores and increased in-class interaction between students and instructor. These results suggest that the audience response system is an effective tool in promoting learning and should be used throughout the pharmacy curriculum.

62. **Evaluation of a human patient simulator on pharmacy student test performance.** *Christine M. Brubaker, Pharm.D.Candidate*, Lynette R. Moser, Pharm.D., James S. Kalus, Pharm.D.; Wayne State University College of Pharmacy and Health Sciences, Detroit, Mich.

PURPOSE: The human patient simulator (HPS) is a lifelike mannequin commonly used to teach and assess clinical skills and knowledge to medical and nursing students. It is currently unknown whether implementation of this technology in pharmacy curriculum could enhance understanding and retention of course material.
METHODS: Second-year pharmacy students enrolled in a cardiovascular therapeutics module were included (n=86, mean grade point average [GPA] = 3.0 ± 0.42, mean grade in cardiology module = 81.6% ± 5.9%). Students were randomized either to attend a 1-hour traditional lecture on rate control in atrial fibrillation or to participate in an HPS scenario. The HPS scenario simulated a patient requiring rate control in the emergency department setting. Prior to the activity, students in the HPS group received a written handout that would be used during the traditional lecture. The HPS activity was completed in groups of 5 or 6. A survey of students participating in the HPS activity was done to determine student perception of the exercise. One week later, students were required to answer five questions on rate control as part of their final examination. Performance on these questions was compared between groups.
RESULTS: The traditional lecture was attended by 44 students, and 42 students participated in the HPS Exercise. The percentage correct of examination questions was 69.5 ± 24.3 in the HPS group and 72.7 ± 18.3 in the lecture group (p=0.491). There was no significant difference in overall GPA between groups (2.9 ± 0.42 vs. 3.1 ± 0.42; p=0.123). Twenty students completed the survey. Results indicated a favorable perception of the exercise.

CONCLUSION: Student performance on rate control examination questions was similar, regardless of teaching method used. Given the favorable perception with the HPS exercise, this may be an improved method of teaching in pharmacy courses.

63E. Completion of pre-pharmacy requirements at community colleges: what is the association with Pharm.D. GPA? *Philip Hall, B.S., Pharm.D.*, Roger White, B.S., Pharm.D.; South Carolina College of Pharmacy, Medical University of South Carolina, Charleston, SC.

BACKGROUND: Barron's Profiles ranks the competitiveness of undergraduate (UG) institutions; however, community colleges (CC) are not included. Previously, we found that UG-grade point average (GPA) and pharmacy college admission test (PCAT) were associated with Pharm.D. GPA (COP-GPA) in each didactic year (P1–P3); however, only UG-GPA and UG ranking were associated for P4. Because some applicants complete prepharmacy requirements at CC, we evaluated UG ranking and CC attendance as a predictor of performance in a Pharm.D. program.
METHODS: We evaluated relationships between UG ranking and GPAs of 2003-06 Pharm.D. graduates. UG institutions at which these graduates completed prepharmacy courses were categorized and ranked as follows: most competitive (MC=5), highly competitive (HC=4), very competitive (VC=3), competitive (C=2), less competitive (LC=1) and community college (CC=0). Relationships between UG-GPA, PCAT, UG ranking, and Pharm.D. GPA were assessed by univariate and multivariate regression.
RESULTS: Records were available for 191 students (MC=2, HC=79, VC=33, C=43, LC=10, CC=24) from 67 institutions. Mean P4 GPAs were: MC=3.6, HC=3.4, VC=3.2, C=3.3, LC=2.7, CC=3.1). By univariate analysis, UG-GPA($p<0.0001$), PCAT ($p<0.0001$), and UG ranking ($p=0.0003-0.0069$) were associated with GPA in each year (P1–P4). R-squared values for P1-P3 were consistent for UG-GPA (0.328–0.355), PCAT (0.248–0.285) and UG ranking (0.038–0.047), but lower for UG-GPA (0.016) and PCAT (0.126) and higher for UG ranking (0.069) for P4. Multivariate analysis found only UG-GPA and PCAT significant for P1-P3 GPA. In P4, UG ranking and CC attendance were also significant.
CONCLUSIONS: When UG-GPA and PCAT are used, UG ranking and CC attendance were associated with Pharm.D. GPA only in the P4 year.
Presented at the American Association of Colleges of Pharmacy, Orlando, Fla, July 14-18, 2007.

64. Impact of an introductory Advanced Pharmacy Practice Experience course on clinical skills in the fourth year. *Jane R. Mort, Pharm.D.*, Dennis D. Hedge, Pharm.D., Thomas J. Johnson, Pharm.D., Heather R. Kruse, Pharm.D.; South Dakota State University, Sioux Falls, SD.

PURPOSE: The study sought to determine the impact of the First Steps Course (FSC), an introductory Advanced Pharmacy Practice Experience (APPE) course, on subsequent clinical skills of fourth year students.
METHODS: The FSC (implemented in 2006) introduces students to clinical activities in a 4-week course prior to APPEs. The course includes community and hospital experiences, a journal club project, case presentations, drug information assignment, medication history write-up, and student seminar on an over-the-counter product. To measure the impact of the course, full-time University faculty members completed a clinical skills evaluation tool for each student they precepted on the first APPE of the fourth year (not all students had their first APPE with a University faculty member). The tool was completed in the third week of the first APPE. The tool examined nine clinical skills on a five point Likert scale (1 being always and 5 being never). The evaluation was performed in 2005 as a baseline measurement and 2006 after the FSC. Institutional Review Board approval was obtained for this project.
RESULTS: The sample involved 38.6% (n=22) of the class in the baseline group and 41.1% (n=23) of the students having taken the FSC. Students who took the FSC scored better (i.e., lower mean) on all nine skills and had a better average clinical skills value (2.3) compared to the baseline group (2.6, $p<0.01$).
CONCLUSION: The FSC improved students' clinical skills, which will allow students to achieve higher levels of learning in their initial APPEs.

65. Volunteer, optional exam discussion as a way of active learning in course coordination strategies. *Tracy Danielle Baher, Pharm.D.*[1], Rocsanna Namdar, Pharm.D.[2]; (1)University Of Wyoming, School of Pharmacy, Laramie, Wyo; (2)University of New Mexico Health Sciences Center, Albuquerque, NM.

INTRODUCTION: The incorporation of integrative active learning improves learning strategies and retention in didactic settings. Introduction to Therapeutics is a team-taught course consisting of a series of didactic lectures. At our institution, this class does not have a discussion session. Our aim was to incorporate a unique active learning strategy and to assess student satisfaction and exam performance.

METHODS: Examinations were composed of case-based and multiple choice questions. After examinations were administered, open forum discussion was used as a method to critically evaluate the material. During debriefing, every question and key was reviewed. Students were then encouraged to volunteer their time and provide written feedback comments related to the quality of the questions that were missed and detailed analysis of the material. Students were asked to write detailed justification for the answers they provided. References, including notes, were permitted. Outcome measures included evaluation of overall student satisfaction and reasons and number of questions that were discarded after student rebuttals. Feedback was incorporated for future exams.

RESULTS: n=49 students, 3 exams, 45 questions each. Forty six, 48, and 49 students volunteered to stay an average 1.5 hrs after the first, second, and third examination, respectively. After review, students wrote rebuttal comments on 20, 15, and 12 questions for the first, second and third examination, respectively. The collective discussion sessions resulted in a total of eight questions being discarded. All students received a passing grade.

CONCLUSION: Student feedback was positive in finding the review session useful as a means for active learning. The volunteer discussion sessions resulted in students becoming more engaged and active in learning the material more comprehensively. The process of preparing rebuttals for questions missed on the examination resulted in more in depth learning strategy. The student comments assisted professors in examination writing skills.

Emergency Medicine

66. **The impact of pharmacist-initiated interventions for acute ischemic stroke in the emergency department.** *Patricia Schuler, Pharm.D.*[1], Terri Howard, Pharm.D.[2], Michael Brown, M.P.H.[2]; (1)The Ohio State University Medical Center, Columbus, Ohio; (2)Pitt County Memorial Hospital, Greenville, NC.

PURPOSE: The purpose of this study was to 1) increase the number of acute ischemic stroke (AIS) patients who are considered for intravenous recombinant tissue plasminogen activator (t-PA) administration in the emergency department (ED), 2) improve clinician documentation, and 3) enhance clinician knowledge of AIS care.

METHODS: A retrospective chart review was conducted from October 1, 2005, through March 31, 2006. An acute stroke care protocol was initiated in January 2006 along with a pharmacist-initiated educational session regarding best practices for acute stroke care. Data collected from October 1, 2005, through December 31, 2005, were compared to data collected from January 1, 2006, through March 31, 2006, to evaluate the impact of the protocol implementation and educational sessions. The outcomes studied included: documented consideration rates for t-PA, administration rates of t-PA, and documented reasons for avoidance of t-PA utilization.

RESULTS: A total of 143 patients were included in the study. Sixty-four patients were included in the pre-intervention phase; 5 patients (7.81%) had documented consideration for t-PA. Seventy-nine patients were included in the post-intervention phase; 46 patients (58.22%) had documented consideration for t-PA. A Chi-Square Analysis was performed indicating statistical significance (Pearson Chi-Value 39.166, p<0.001). There was no change in the t-PA administration rates between the pre-and-post intervention periods.

CONCLUSION: The integrated model of clinician education and protocol initiation was successful in increasing clinician documentation of t-PA consideration for the treatment of AIS; however, increased consideration of t-PA did not lead to an increase in the administration of t-PA. This study demonstrated that pharmacist-initiated efforts have the potential to enhance clinician knowledge and improve the quality of patient care for AIS in the emergency department.

67E. **Impact of a severe sepsis guideline on compliance with bundle elements in patients admitted to the emergency department.** *Angela T. Gilchrist, Pharm.D.*, BeeBee Y. Hu, Pharm.D., Brian S. Smith, Pharm.D.; UMass Memorial Medical Center, Worcester, Mass.

PURPOSE: Severe sepsis affects more than 750,000 patients in the United States yearly with an overall mortality rate of 29%. Several institutions have implemented evidence-based practices, such as sepsis guidelines, to improve morbidity and mortality in septic patients. UMass Memorial Medical Center recently implemented a Severe Sepsis/Septic Shock Therapeutic Guideline with bundle elements. The objective of this study was to evaluate the impact of the guideline on compliance with bundle elements post implementation.

METHODS: Two retrospective chart reviews were performed on a random sampling of adult patients admitted to the emergency department with severe sepsis or septic shock pre and post guideline implementation. Patients were included if they met sepsis criteria and were excluded if they were not septic in the emergency department or were transferred from another institution. A total of 18 patients were included in each review. Data collected included demographic information, specific data for bundle elements, and selected morbidity and mortality data.

RESULTS: Each resuscitation goal improved post guideline implementation. The results were as follows: lactic acid measurement increased from 22% to 100%(p<0.001) of patients, central venous catheter placement: 39% to 78%(p=0.04), central venous pressure monitoring: 0% to 56%(p<0.001), mixed venous oxygenation monitoring: 0% to 17%(p=0.22), blood cultures drawn prior to antibiotic administration: 57% to 100%(p=0.02), appropriate and timely antibiotic administration: 29% to 50%(p=0.44), central venous pressure, mixed venous oxygenation,

and mean arterial pressure goals: 0% to 67%(p<0.001), 0% to 11%(p=0.49), 78% to 89%(p=0.66) respectively. Morbidity and mortality outcomes were similar between groups.

CONCLUSION: Post-implementation data shows an increase in compliance with bundle elements and demonstrates several opportunities for continued improvement. Resources should be allocated to continue education of medical staff to further increase compliance. Also, a study with a larger sample size is needed to achieve adequate power to detect statistical differences in morbidity and mortality. Presented at the 26th Annual Eastern States Conference, Baltimore, Md, May 11, 2007.

Endocrinology

68E. **Patient satisfaction and cost-savings observed with insulin pens in a hospital setting.** *Estella M. Davis, Pharm.D.*, Carla M Christensen, Pharm.D., Kelly K Nystrom, Pharm.D., Pamela A Foral, Pharm.D., Chris Destache, Pharm.D.; Creighton University Medical Center - School of Pharmacy and Health Professions, Hixon-Lied Sceince Building, Omaha, Neb.

PURPOSE: The purpose of this study was to evaluate the outcomes and cost-savings associated with prefilled, disposable insulin pens compared to conventional vial and syringes in hospitalized patients.
METHODS: A prospective, randomized, controlled, pilot study was conducted to evaluate insulin pens compared to the conventional vial and syringe method in patients with diabetes reliant upon subcutaneous insulin injections during hospitalization on two general medical-surgical units. All subjects were followed to determine the extent of glucose control while hospitalized. Patients completed a survey before discharge regarding their satisfaction with their method of insulin delivery. Patients were given a telephone survey about 4 weeks after discharge to determine home insulin use. Cost-savings were determined based on the average wholesale price of insulin vials/syringes or pens.
RESULTS: A total of 75 patients were enrolled in the two groups (40 control, conventional vial/syringe; 35 insulin pen). There were no significant differences between admit and discharge blood glucose levels or hypoglycemic and hyperglycemic events between the two groups. Significantly more patients prepared or "dialed" up their own dose (p<0.05) of insulin, as well as self-injected their dose using insulin pens during hospitalization (p<0.05). Patients in the insulin pen group were significantly more satisfied with multiple aspects of their insulin experience during their hospitalization (p<0.001). A significant savings of US $40 per patient was determined if insulin pens were used during the entire hospital stay compared with the conventional method (p<0.05). A significantly higher percentage of patients in the insulin pen group continued to use pens at home compared with the conventional method (41% vs. 10% respectively, p<0.05).
CONCLUSIONS: Patient satisfaction, significant cost-savings and continuation of insulin pen use at home were observed in patients receiving insulin pens compared to the conventional vials/syringes. The hospital has adopted the use of insulin pens for all non-critical care patients.
Will be published in Diabetes 2007, 67th Scientific Sessions Abstract Book, June Supplement. Anticipated citation: Published in Diabetes 2007;56(6)Suppl:A2104-PO.

69. **Tight glycemic control in non-intensive care unit patients.** Gita W. Patel, Pharm.D., *Randy L. Shulkin, R.Ph.*, Nicki Roderman, R.N., M.S.N., CCRN, Jeffrey Glass, Pharm.D.; Medical Center of Plano, Plano, Tex.

PURPOSE: This study examined the effect of sliding scale insulin (SS) versus a subcutaneous tight glycemic control (TC) protocol on the blood sugars (BS) of patients that were not in the intensive care unit (ICU). The target BS range was 80–150 mg/dL.
METHODS: IRB-approved, retrospective analysis was done on subcutaneous SS patients from March through May of 2006 and subcutaneous TC patients from October through December of 2006, all of whom were on the respective regimens for a minimum of 3 days. SS patients who received oral hypoglycemics, insulin aspart mix, insulin detemir, insulin glargine, insulin glulisine, insulin NPH, or insulin 70/30 were excluded. TC patients who received oral hypoglycemics, insulin aspart mix, insulin detemir, insulin glulisine, insulin NPH, or insulin 70/30 were excluded. Demographics, co-morbidities, and BS were examined.
RESULTS: Sixty-nine SS patients and 70 TC patients met criteria. Demographics, percentage of diabetic patients, co-morbidities, and length of therapy were not statistically different between the two groups. The mean BS was 168.6 mg/dL in SS patients and 162.1 mg/dL for TC patients (p=0.004). For SS patients, 0.6% of the BS were 0–60 versus 1.7% for TCI. A BS in the 61–79 mg/dL range was achieved by 1.6% of SS and 5.4% of TCI BS. In the SS patient group, 41.6% of the BS were in the target range of 80–150 mg/dL versus 45.4% of the BS in the TCI group. Hyperglycemia (BS > 150 mg/dL) was found in 56.3% of the SS BS versus 47.5% of the TCI BS.

CONCLUSION: The TC protocol yielded a higher percentage of patients in the target BS range and a lower incidence of hyperglycemia. Hypoglycemia rates were similar between the two groups. The TC protocol for non-ICU patients was more effective and did not significantly increase hypoglycemia rates compared to SS.

70. **Evaluation of diabetes outcomes and management in a multi-disciplinary diabetes management clinic compared to usual care.** *Mikayla L. Spangler, Pharm.D.*, Beth B. Phillips, Pharm.D., Deanna L. McDanel, Pharm.D., Erin N. Newkirk, Pharm.D.; University of Iowa Hospitals and Clinics, Iowa City, Iowa.

PURPOSE: The American Diabetes Association supports medical care from a multidisciplinary team. Studies including a pharmacist as part of the team are lacking. The purpose of this study was to evaluate patient outcomes in a multidisciplinary diabetes management clinic (MDMC) compared to usual care, defined as primary care provided to patients with type 2 diabetes mellitus (T2DM) in the Internal Medicine or Family Medicine clinics at the University of Iowa Hospitals and Clinics.
METHODS: Adult patients with T2DM (n=140) were included in a 2:1:1 ratio from the MDMC, Internal Medicine and Family Medicine clinics, respectively. Patients with a 2–6 month follow-up and baseline and follow-up A1c values were included.
RESULTS: At baseline, usual care patients had lower A1c levels (7.6% vs. 8.7%, p<0.001), lower diastolic blood pressures (DBP) (72 mm Hg vs. 79mm Hg, p<0.01) and more patients were at A1c goal versus the MDMC group (40% vs. 21%, p<0.05). The MDMC patients had a significant decrease in A1c during the study period (8.7% to 7.4%, p<0.001), as did the usual care group (7.6% to 7.0%, p<0.001). Other significant findings from baseline to follow-up in the MDMC included a decrease in DBP (79 mm Hg to 74 mm Hg, p<0.01) and weight (108 kg to 106 kg, p<0.01). When comparing change in the different parameters from baseline to follow-up, MDMC patients had larger decreases in A1c (p<0.05) and DBP (p<0.01). More patients in the MDMC than usual care were prescribed aspirin at follow-up (89% vs. 61%, p<0.001). More patients were screened for microalbuminuria appropriately in the MDMC by follow-up (81% vs. 60%, p<0.01) compared to usual care.
CONCLUSIONS: Patients referred to the MDMC had more severe disease, but achieved greater improvements in diabetes-related care. A MDMC that includes a pharmacist improves patient outcomes.

71. **Accuracy and precision of four value-added blood glucose meters: the Abbott Optium, the DDI Prodigy, the HDI True Track, and the Hypoguard Assure Pro.** *Catherine A. Sheffield, Pharm.D.*[1], Michael P. Kane, Pharm.D.[1], Gary Bakst, M.D.[2], Robert S. Busch, M.D.[2], Jill M. Abelseth, M.D.[2], Robert A. Hamilton, Pharm.D.[1]; (1)Albany College of Pharmacy, Albany, NY; (2)The Endocrine Group, LLP, Albany, NY.

PURPOSE: To compare the accuracy and precision of four value-added (generic) blood glucose (BG) meters to each other and to a laboratory reference glucose measurement.
METHODS: In an ACP IRB approved study, finger-stick glucose measurements in consenting adults with diabetes undergoing venipuncture for glucose testing were performed using the Abbott Optium, DDI Prodigy, HDI True Track, and the HypoGuard Assure Pro. Within 5 minutes following venipuncture, finger BG measurements from four ipsilateral fingers were taken in duplicate. Meter sequence was randomly assigned. Finger glucose measurements were compared with laboratory reference results. Accuracy was assessed by a Clarke error grid analysis (EGA), a Parke EGA, and within 10%, 15%, and 20% of the laboratory value criteria (chi-square). Meter precision was determined by calculating absolute mean differences in glucose values between duplicate samples (paired t-test).
RESULTS: Finger sticks were obtained from 125 diabetes patients during 4 days of testing; 90.4% of patients were Caucasian, 51.2% were female, 83.2% had type 2 diabetes, and average age was 59 years (S.D. + 14). Mean venipuncture BG was 151 mg/dL (+ 65; range 58–474). Clinical accuracy (Zone A) by Clarke EGA was demonstrated in 94% of Optium, 82% of Prodigy, 61% of True Track, and 77% of the Assure Pro samples (p<0.05). By Parke EGA, the TrueTrack was significantly less accurate than the other three meters. Accuracy rates based on meter values falling within 10% of the laboratory reference values were 59%, 54%%, 30%, and 43%, respectively (p<0.05 for Optium, Prodigy, and Assure Pro compared to True Track). Significantly more Optium results demonstrated within 15% and 20% accuracy compared with the other meters. There were no differences in meter precision (6%–10.0%; 9–15 mg/dL).
CONCLUSIONS: The Abbott Optium was significantly more accurate than the other studied meters. All meters demonstrated similar precision.

72. **Does sitagliptin improve β-cell function?** *Daniel M. Riche, Pharm.D., BCPS*[1], Krista M. Dale, Pharm.D., BCPS[2]; (1)The University of Mississippi School of Pharmacy, Jackson, Miss; (2)The University of Mississippi Medical Center, Jackson, Miss.

PURPOSE: Progressive β-cell dysfunction and β-cell failure are fundamental pathogenic consequences of type 2 diabetes. Dipeptidylpeptidase-IV (DPP-IV) inhibitors are a novel approach to the treatment of type 2 diabetes that may exhibit improvement on preclinical measures of both β-cell function, homeostasis model assessment of β-cell (HOMA-β) index, and β-cell dysfunction, proinsulin/insulin ratio (P/I ratio). Improvements in these pre-clinical measures may correlate to β-cell survival and neogensis.
METHODS: A systematic literature search of MEDLINE, EMBASE, CINAHL, and Web of Science from January 1966 through June 2007 was conducted to extract a consensus of clinical trial data of randomized controlled trials of sitagliptin therapy on measures of β-cell function. A random effects model meta-analysis evaluated outcome measures, which included effects on HOMA-β and P/I ratio versus placebo. Subgroup analysis comparing sitagliptin to sulfonylureas (glipizide) was also conducted. Studies were included if they met the following criteria: 1) randomized, controlled clinical trials, 2) well-described protocol, and 3) data reported with effect on HOMA-β or P/I ratio.
RESULTS: A total of 6 trials (n=2,151) reported effects on HOMA-β and 5 trials (n=1,716) on P/I ratio versus placebo. Two trials (n=975) were included in the glipizide subgroup analysis. Sitagliptin significantly improved HOMA-β index by 10.84% (95% CI = 6.91–14.76) versus placebo. Sitagliptin also significantly decreased P/I ratio -0.07 (95% CI = -0.09– -0.05). Upon subgroup analysis, there was a significant difference favoring glipizide 9.25% (95% CI = 1.65–16.85) in HOMA-β index improvement. P/I ratio was not sufficiently reported for subgroup evaluation. Statistical heterogeneity was not seen in the primary or subgroup analysis (p>0.1 for all).
CONCLUSIONS: Despite significant improvement in HOMA-β index and P/I ratio from placebo, there does not appear to be a benefit of DPP-IV inhibitors over sulfonylureas with respect to β-cell function.

73. **Impact of dipeptidylpeptidase-IV inhibitors on hemoglobin A1C and body weight in diabetes: a meta-analysis.** *Daniel M. Riche, Pharm.D., BCPS*[1], Krista M. Dale, Pharm.D., BCPS[2]; (1)The University of Mississippi School of Pharmacy, Jackson, Miss; (2)The University of Mississippi Medical Center, Jackson, Miss.

PURPOSE: Dipeptidylpeptidase-IV (DPP-IV) inhibitors are a novel class of agents for the treatment of type 2 diabetes. Several clinical trials have been published recently detailing effects of DPP-IV inhibitors in patients with type 2 diabetes; however, variability in the degree of hemoglobin A1C (A1C) reduction and changes in body weight have complicated clinical interpretation of results.
METHODS: A systematic literature search of MEDLINE, EMBASE, CINAHL, and Web of Science from January 1966 through June 2007 was conducted to extract a consensus of clinical trial data of randomized controlled trials of DPP-IV inhibitor therapy. A random effects model meta-analysis evaluated outcome measures which included effects on A1C and body weight versus placebo. Subgroup analysis comparing DPP-IV inhibitors to sulfonylureas (SFU), metformin and thiazolidinediones (TZD) was also conducted. Studies were included if they met the following criteria: 1) randomized, controlled clinical trials, 2) well-described protocol, and 3) data reported with effect on A1C or body weight.
RESULTS: A total of 14 trials (n=3891) reported effects on A1C versus placebo, while 9 trials (n=2275) reported effect on body weight. Six trials (n=3149) were included in the subgroup analysis. DPP-IV inhibitor therapy significantly reduced A1C -0.69% (95% CI = -0.78 to– -0.60) while slightly increasing body weight 0.48 kg (95% CI = 0.04–0.92) versus placebo. Upon subgroup analysis, DPP-IV inhibitors demonstrate similar A1C reductions to SFU 0.09% (95% CI = -0.12–0.31), but significantly inferior A1C reductions compared to metformin 0.44% (95% CI = 0.26–0.62) and TZD 0.25% (95% CI = 0.05–0.45). Body weight significantly favored DPP-IV inhibitors in both the SFU -1.75 kg (95% CI = -3.41– -0.08) and TZD -1.60 kg (95% CI = -2.19– -1.01) subgroups.
CONCLUSIONS: DPP-IV inhibitors demonstrate modest reductions in A1C comparable to SFU with less weight gain than both SFU and TZD.

Gastroenterology

74. **Effect of medication reconciliation on the inappropriate use of stress ulcer prophylaxis upon discharge from an intensive care unit.** *Amy J. Zeigler, Pharm.D.*, Karen J. McAllen, Pharm.D., Martha G. Slot, Pharm.D., Jeffrey F. Barletta, Pharm.D., FCCM; Spectrum Health, Grand Rapids, Mich.

PURPOSE: Medication reconciliation (MR) is intended to limit errors of transcription, omission, duplicate therapy, and unnecessary treatment. One area where unnecessary treatment is often prescribed especially in non-ICU settings is stress ulcer prophylaxis (SUP). However, the impact of MR on SUP is largely unknown. The

objective of this study was to determine the effect of MR on the incidence of inappropriate SUP upon transfer from an intensive care unit (ICU) to a non-ICU setting and at hospital discharge.

METHODS: A retrospective before-and-after study was performed of patients who were admitted to the ICU and had SUP initiated. Patients with acid suppressive therapy prior to ICU admission, a documented gastrointestinal bleed, or those who expired were excluded. Appropriate use of SUP was defined using evidence-based guidelines developed by the American Society of Health-System Pharmacists. Appropriate use of SUP was assessed upon transfer from the ICU to a non-ICU setting and at hospital discharge. Results were compared between pre-MR and post-MR groups.

RESULTS: Data of 114 ICU patients were evaluated (53 pre-MR, 61 post-MR). There was no difference in the use of inappropriate SUP upon transfer from the ICU to a non-ICU setting in the pre-MR and post-MR groups, respectively (85% [45/53] vs. 79% [48/61], p=0.393). These results were not different when stratified by unit (MICU: pre-MR = 82% [22/27] vs post-MR = 71% [22/31], p=0.351; SICU: pre-MR = 89% [23/26] vs post-MR = 87% [26/30], p=1.000). There was no difference in the use of inappropriate SUP upon hospital discharge in the pre-MR and post-MR groups, respectively (14% [6/44] vs. 23% [10/43], p=0.247).

CONCLUSIONS: MR does not decrease the incidence of inappropriate SUP upon transfer from an ICU or at hospital discharge. Other strategies are recommended to discourage the inappropriate use of SUP in non-ICU settings.

75E. **A phase 2 double-blind randomized parallel group study of IV Methylnaltrexone in the management of Postoperative Ileus.** *Sander Binderow, M.D.*[1], Eugene Viscusi, M.D.[2], Tj Gan, M.B., B.S., FRCA[3], James Rathmell, M.D.[4], Alessandro Fichera, M.D.[5], Nancy Stambler, M.D.[6], Frank Galasso, M.D.[6], D Penenberg, M.D.[6], Robert Israel, M.D.[6]; (1)Atlanta Colon & Rectal Surgery, Atlanta, Ga; (2) Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pa; (3)Duke University Medical Center, Durham, NC; (4)Harvard Medical School, Boston, Mass; (5)University of Chicago, Chicago, Ill; (6)Progenics Pharmaceuticals, Tarrytown, NY.

PURPOSE: Postoperative ileus (POI) occurs in patients undergoing bowel resection and can lead to prolonged hospitalization. Methylnaltrexone, a quaternary derivative of naltrexone, is designed to block peripheral adverse effects of opioids while sparing central analgesic effects. We hypothesized that methylnaltrexone might improve POI outcome without affecting opioid analgesia.

METHODS: In this double-blind, randomized, placebo-controlled study, 65 patients undergoing segmental colectomies via laparotomy were randomized to receive within 90 minutes post-surgery either IV methylnaltrexone 0.3 mg/kg every 6 hours or placebo, until 24 hours after gastrointestinal (GI) recovery, discharge from the hospital, or for a maximum of 7 days. Postoperative analgesia was provided with systemic opioid analgesics. Adverse events (AEs) were monitored during and for 30 days after the study.

RESULTS: The mean time to first bowel movement was reduced by 20 hours for patients in the methylnaltrexone group compared with those receiving placebo (p=0.038; log rank, two-sided). Time to discharge eligibility was 33 hours shorter in the methylnaltrexone group compared with placebo (p=0.049; log rank, two-sided). Patient analgesic requirements and pain scores were similar in both the methylnaltrexone and placebo treatment groups. Methylnaltrexone was generally well tolerated. AEs occurred more often in the placebo group compared with the methylnaltrexone group, including nausea (63% vs 30%, respectively), vomiting (25% vs 12%, respectively), and abdominal pain (13% vs 0%), respectively).

CONCLUSIONS: In this study, IV methylnaltrexone significantly reduced time to first bowel movement and hospital discharge eligibility without affecting opioid analgesia following segmental colectomy.

Presented at the Society of Surgical Oncology's 60th Annual Cancer Symposium, Washington, D.C., March 15-18, 2007, and the American Society of Clinical Oncology's Gastrointestinal Cancers Symposium, Orlando, Fla, January 17-21, 2007.

General Surgery

76E. **Phase 3 study comparing recombinant human thrombin and bovine thrombin for surgical hemostasis.** Kenneth Renkens Jr., M.D.[1], William Chapman, M.D.[2], Fred Weaver, M.D.[3], Tracy Zhang, M.S.[4], Allan Alexander, M.D.[4], *John Pribble, Pharm.D.*[4]; (1)Indiana Spine Group, Indianapolis, Ind; (2) Washington University School of Medicine, St. Louis, Mo; (3)University of Southern California, Los Angeles, Calif; (4)ZymoGenetics, Inc., Seattle, Wash.

INTRODUCTION: Recombinant human Thrombin (rhThrombin) is being developed as a potential alternative to bovine thrombin (bThrombin) as an adjunct to surgical hemostasis. Antibodies to bThrombin product have been associated with bleeding and thromboembolic events.

METHODS: A randomized double-blind study enrolled patients undergoing spinal surgery, hepatic surgery, peripheral arterial bypass, or arteriovenous vascular access procedures. rhThrombin or bThrombin (1000 U/mL) was applied topically to bleeding sites with an absorbable gelatin sponge. The primary efficacy analysis evaluated the difference in incidence of hemostasis within 10 minutes between treatment groups. Patients were monitored for 30 days for complications and antibody formation.

RESULTS: A total of 401 patients (median age, 60 years) at 34 medical centers completed the study. Hemostasis was achieved within 10 minutes in 95.4% of patients in the rhThrombin group and 95.1% in the bThrombin group (0.3% difference; 95% CI = -3.7%–4.4%). Complications including operative mortality, adverse events, and laboratory abnormalities were similar between treatment groups and consistent with the surgical procedures performed. Forty-three (22%) patients receiving bThrombin developed anti-bovine thrombin antibodies whereas 3 (1.5%; $p<0.0001$) patients in the rhThrombin group developed anti-rhThrombin antibodies. None of the 3 patients who developed anti-rhThrombin antibodies had abnormal coagulation laboratory results or bleeding, thromboembolic, or hypersensitivity events.

CONCLUSION: Surgical hemostasis was achieved in 95% of patients at 10 minutes using either rhThrombin or bThrombin. Both treatments were well tolerated; however, rhThrombin demonstrated a superior immunogenicity profile.

Presented at the Society for the Advancement of Blood Management Annual Meeting, Jersey City, NJ, September 15-17, 2006.

Geriatrics

77. **Serum vitamin B12 concentrations among older adults with and without use of acid suppressant medications.** *J. Mark Ruscin, Pharm.D.*, Sunny A. Linnebur, Pharm.D., Robert J. Valuck, R.Ph., Ph.D.; University of Colorado Health Sciences Center, School of Pharmacy, Denver, Colo.

PURPOSE: The use of acid suppressant medications (ASM), including histamine-2 receptor antagonists and proton pump inhibitors, has been shown to reduce the absorption of food-bound vitamin B12. This study evaluated serum vitamin B12 concentrations in older community dwelling adults, comparing vitamin B12 concentrations among non-users of ASM, past users of ASM, active users of ASM for less than 12 months, and active users of ASM for 12 or more months.

METHODS: A retrospective review was conducted in 813 patients age 65 years or older with no history of gastrectomy or vagotomy, pernicious anemia, or pancreatic disease and with documented serum vitamin B12 concentrations measured between January 1, 1990, and December 31, 1998. Patient pharmacy and medical records were reviewed to identify use of ASM prior to the documented date of serum vitamin B12 studies. Patients were categorized a priori as either non-users of ASM, past users of ASM, short-term active users of ASM (less than 12 months), or long-term active users of ASM (2 months or more). Vitamin B12 concentrations were compared among the four groups using a one-way ANOVA with pairwise comparisons using Tukey's HSD statistic.

RESULTS: One-hundred twenty-four patients (15.3%) had previously used or were active users of ASM at the time vitamin B12 studies were performed. Long-term active users of ASM (mean duration 31 months) had mean ($\pm$ SD) serum vitamin B12 concentrations that were significantly lower (357 pg/mL $\pm$ 163; n=30) than non-users of ASM (495 pg/mL $\pm$ 282; n=689), p=0.042; past users of ASM (521 pg/mL $\pm$ 280; n=71), p=0.039; and short-term active users (mean duration 5 months) of ASM (563 pg/mL $\pm$ 368; n=23),p=0.041.

CONCLUSION: Active use of ASM for 12 months or more is associated with lower serum vitamin B12 concentrations, and may put older adults at increased risk for the development of vitamin B12 deficiency.

78E. **Safety and quality of life of elderly men treated for OAB with transdermal oxybutynin: impact of preexisting prostate problems.** David R. Staskin, M.D.[1], Paul V. Polishuk, M.D., M.S.[2], *Naomi V. Dahl, Pharm.D.*[3]; (1)Department of Urology, New York University School of Medicine, New York, NY; (2)Private Practice, Escondido, Calif; (3)Watson Laboratories, Morristown, NJ.

PURPOSE: The incidence of benign prostatic hyperplasia (BPH) and prostate cancer increases with age, as does the incidence of bladder problems. The Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin (MATRIX) study was assessed safety and effectiveness of transdermal oxybutynin treatment (OXY-TDS) for overactive bladder (OAB). We conducted a post hoc analysis of data from men with pre-existing prostate problems.

METHODS: This was a multicenter, open-label, prospective study in community-dwelling adults with OAB. Participants could be enrolled despite current use of BPH medication or a history of prostate cancer. All participants were treated with OXY-TDS 3.9 mg/day (2 patches/week) for 6 months or less. HRQOL was assessed at 3-monthly intervals with King's Health Questionnaire (KHQ).Changes in KHQ domain scores were calculated

from baseline to last assessment (study end). *P* values for between-group comparisons were based on ANCOVA. Adverse events were summarized descriptively.

RESULTS: Among 369 men in MATRIX, 119 (32%) had pre-existing prostate problems (67 concurrently receiving BPH medication: α-blocker and/or 5α-reductase inhibitor). These men were older than other male participants (mean age, 73 years vs 68 years; p=0.0010), but baseline diuretic use was similar (26.1% vs 20.4%; p=0.2223). A higher proportion of men with prostate problems (61.9%) than without (53.8%) had been treated previously for OAB. Baseline scores for the 2 groups were similar in all 10 KHQ domains (p≥0.1707). HRQOL improved in both groups, as was shown by mean decreases from baseline to study end in 9 of 10 KHQ domains. Changes in KHQ domain scores were similar for both groups in all 10 domains (p≥0.1016). The safety profile was good in both groups; there were no cases of urinary retention requiring catheterization.

CONCLUSIONS: Improvements in HRQOL after treatment with OXY-TDS were similar in men with or without pre-existing prostate problems. OXY-TDS was well tolerated in both groups.

Presented at the American Geriatrics Society Annual Scientific Meeting, Seattle, Wash, May 2–6, 2007.

Health Services Research

79. **Impact of pharmacist follow-up telephone calls after intensive nurse-based patient education upon hospital discharge.** *Gail M. Burniske, Pharm.D., BCPS*, Julie O'Donnell, B.A., Vk Chetty, Ph.D., Lynn Schipelliti, R.N., Mary Goodwin, R.N., Anna Johnson, B.A., David Anthony, M.D., M.Sc., Jeffrey L. Greenwald, M.D., Chris Manasseh, M.D., Steve Martin, M.D., M.Ed., Michael Paasche-Orlow, M.D., M.P.H., Kevin Casey, M.P.H., Shaula Forsythe, B.S., Brian Jack, M.D.; Boston Medical Center, Boston, Mass.

PURPOSE: Hospital discharges are complicated by adverse events within 30 days, often leading to additional hospital utilization. Studies have shown that follow-up telephone calls by a pharmacist reduce hospital utilization.

METHODS: Project RED (Re-Engineered Discharge), is an ongoing, randomized, controlled trial of adult patients admitted to the medical service at Boston Medical Center. A nurse conducts 10 activities, including medication reconciliation, scheduling follow-up appointments, and patient education prior to discharge. A pharmacist calls the patient within 4 days post-discharge to reinforce and review the discharge plan and medication regimen. This analysis compares outcomes between patients reached by the pharmacist and those not reached, and describes the pharmacist's interventions.

RESULTS: To date, 275 subjects have been enrolled in the intervention group, and attempts have been made to call 257. The average age is 49 years, and 49% are female. On average, subjects were prescribed six around-the-clock medications upon discharge. The pharmacist follow-up call was successfully conducted with 183 subjects (71%). During the post-discharge telephone call, the pharmacist was able to complete the medication regimen section of the interview for 161 subjects, leading to drug therapy interventions in 103 subjects (64%). Of those 103 subjects with an intervention, 19% were encouraged to take a prescribed medication, verbal communication with health care providers accounted for 26% of interventions, and written communication accounted for 42% of interventions. Of those subjects reached by telephone, 9.8% (18 of 183 subjects) were seen in the emergency department within 30 days of discharge compared with 20.3% (15 of 74 subjects) among those not reached by telephone (p=0.04).

CONCLUSIONS: Among subjects receiving a nurse-directed hospital discharge program, ED visits are 10.5% lower among patients whose discharge plan was reinforced by a pharmacist post-discharge. These data add to the evidence that post-discharge pharmacist involvement can improve patient outcomes.

81. **Survey item development for health literacy research.** *Julie M. Wright, Pharm.D., FCCP*[1], Dawn Charles, Medical Student[1], Darcie L. Keller, Pharm.D., BCPS[1], Karen Williams, Ph.D.[2]; (1)University of Missouri-Kansas City, School of Medicine, Kansas City, Mo; (2)University of Missouri-Kansas City, School of Dentistry, Kansas City, Mo.

PURPOSE: Health literacy (HL) is defined as a person's ability to read and understand basic information needed to make appropriate decisions regarding his or her health. Little is known about patients' feelings regarding provider evaluation of their HL status. The purpose of this project was to develop a research tool that can be used to measure how patients perceive their own HL within the medical system.

METHODS: A pilot survey was developed to test for best items to measure patient 1) comfort with provider evaluation of their HL, 2) confidence in their own HL, 3) view of the providers' role in assessing their HL. The 30-item survey with 4-point Likert scale responses was administered to 15 patients seen by a single provider. Item response distribution was used to eliminate non-discriminating items. Factor analysis of retained items was performed to assess survey reliability.

RESULTS: Eleven items were useful discriminating variables. Factor analysis of these 11 items showed that, within this pilot study, they were reliable to measure the three aspects of 1) comfort with HL assessment, 2) confidence regarding HL, and 3) provider role regarding HL. Seventy three percent of cumulative variance was accounted for by these 11 items within the construct of the 3 factors.

CONCLUSIONS: This pilot study contributed to further development of health literacy research in the clinical setting. The reliability and validity of this survey will next be tested in a large population. A survey tool was created, which will be used to measure patients' perceptions of their own HL within a large health literacy study and within the medical system.

82. **Physicians' awareness, attitudes and experience with health literacy.** *Darcie L. Keller, Pharm.D., BCPS*, Sheetal L. Karne, Medical Student, Julie M Wright, Pharm.D., FCCP; University of Missouri-Kansas City, School of Medicine, Kansas City, Mo.

PURPOSE: To evaluate physicians' awareness and attitudes regarding patients' level of health literacy (HL) and explore their experience in caring for patients with low HL.

METHODS: A 32-item questionnaire was distributed by mail to 180 Family Medicine (FM) and Internal Medicine (IM) physicians and residents practicing at an urban academic medical center.

RESULTS: Of the 43 respondents, 35% were residents, 77% were Caucasian, 60% were men, and 28% were FM. Most (93%) reported encountering patients with low HL in practice ; 20% to 60% of their patients have marginal or inadequate HL. Eighty-one percent agree it is important to assess patient HL, and 98% agree it is important to tailor communication with low HL patients. Seventy-five percent report assessing patients' HL, 63% rely on clinical impression as means of assessment, and 0% use a validated instrument. Respondents felt education and employment status were stronger predictors of patient HL than race and insurance status (p<0.01). All rated the "teach back" method as an effective strategy to improve communication with patients' with low HL; only 23% reported employing this strategy frequently. Sixty percent of physicians felt prepared to effectively communicate with patients with low HL; only 28% report any formal training. FM felt more prepared compared with IM (p<0.01). Most (88%) felt that HL training should be incorporated into medical education.

CONCLUSION: The majority of physicians surveyed care for patients' with low HL and recognize the importance of assessing patients' HL, although there wasn't any standardized method of evaluation. In addition, few physicians report using strategies to enhance communications with said patients. Although some physicians felt they were prepared to care for patients with low HL, few have received any formal training and the vast majority agreed that HL training should be incorporated into medical education.

83. **Metabolic screening frequencies for ambulatory patients taking atypical antipsychotics.** *Amy C. Dill, Pharm.D.*[1], Pamela C. Heaton, Ph.D., R.Ph.[2]; (1)University Hospital, Cincinnati, Ohio; (2)University of Cincinnati College of Pharmacy, Cincinnati, Ohio.

PURPOSE: 1) To determine whether metabolic screening parameters, including height, weight, and blood pressure, are measured and whether fasting plasma glucose/hemoglobin A1C is ordered for patients with a new prescription for an atypical antipsychotic, and 2) to determine whether the atypical antipsychotic prescribed influences the likelihood of receiving screening.

METHODS: The 2005 National Ambulatory Medical Care Survey and the outpatient department component of National Hospital Ambulatory Medical Care Survey were used to identify patients with a new prescription for an atypical antipsychotic and without a diagnosis of diabetes. Metabolic screening rates were compared among the following risk stratified groups: aripiprazole and ziprasidone (lower risk); quetiapine (medium risk); risperidone (medium risk); and olanzapine and clozapine (higher risk). A logistic regression model predicted whether the medication prescribed influenced screening rates. Covariates in the analysis included age, gender, race, and expected source of payment.

RESULTS: Few patients received metabolic screening. Only 5.6% of patients had a glucose or hemoglobin A1C measurement, whereas 42.1%, 26.8%, and 62.0% had a weight, height, and blood pressure measurement, respectively. Medication prescribed was inconsistently correlated with screening rates. Compared to aripiprazole and ziprasidone, prescriptions for risperidone were most closely correlated with monitoring (OR = 33.8, p<0.001), followed by clozapine and olanzapine (OR = 9.1, p<0.001), and finally quetiapine (OR = 2.2, p<0.001).

CONCLUSIONS: Baseline screening rates for fasting glucose/ hemoglobin A1C at private physician offices and clinics are unacceptably low for patients with a new prescription for an atypical antipsychotic compared with American Diabetes Association Guideline recommendations. Similarly, documentation of weight, height, and blood pressure are often absent.

Hematology/Anticoagulation

84. **Evaluation of INR monitoring frequency and achievement of therapeutic goals.** *Christin M. Snyder, Pharm.D.*[1], Bethany E. Helms, Pharm.D.[2], Deanne L. Hall, Pharm.D., CDE[1]; (1)University of Pittsburgh School of Pharmacy, Pittsburgh, Pa; (2)University of Pittsburgh Medical Center, Pittsburgh, Pa.

PURPOSE: The University of Pittsburgh Medical Center (UPMC) Anticoagulation Service uses an algorithm to guide warfarin management during the maintenance phase of therapy. Patients with therapeutic INR (International Normalized Ratio) measurements on two or more consecutive occasions are advised to have INR testing repeated within 2–6 weeks at the discretion of the pharmacist. This retrospective review was conducted to determine whether an increased frequency of monitoring affects INR control among patients receiving stable doses of warfarin managed by an anticoagulation clinic.
METHODS: Adult patients actively followed by the UPMC Anticoagulation Service between April 1, 2006, and September 30, 2006, were eligible for inclusion. Patients were receiving maintenance warfarin therapy. Electronic medical records were retrospectively reviewed to determine the date and result for each subsequent INR measurement. To compare the degree of INR control for patients monitored at intervals of < 21 days or ≥ 21 days, the percentage of INR measurements within the therapeutic range was calculated for each interval.
RESULTS: During the 6-month evaluation period, more than 10,000 INR results were reviewed. A total of 2222 INR results were obtained during maintenance therapy and evaluated. INR measurements taken within 21 days of the preceding test were within the target range 75.1% of the time whereas INR readings obtained at least 21 days after the antecedent INR test were within the desired goal range 79.9% of the time ($X^2 = 7.16$, p<0.001).
CONCLUSIONS: Although these findings suggest that INR monitoring at an interval of at least 21 days produced a statistically larger proportion of results within goal range, a clinically meaningful improvement of at least 10% was not realized. Moreover, these findings support the re-evaluation of the Anticoagulation Service management algorithm to reduce the frequency of INR measurements among patients receiving stable doses of warfarin.

85. **Evaluation of bivalirudin dosing requirements in patients with heparin-induced thrombocytopenia (HIT).** *Jessica C. Burch, Pharm.D.*[1], Patrick M. Klem, Pharm.D.[2], Kathryn L. Hassell, M.D.[1], Tyree H. Kiser, Pharm.D.[1]; (1)University of Colorado Health Sciences Center, Denver, Colo; (2)University of Colorado Hospital, Denver, Colo.

PURPOSE: Evaluate bivalirudin dosing requirements in patients with HIT.
METHODS: This study retrospectively evaluated patients diagnosed with HIT and treated with bivalirudin between January 1, 2004, and March 31, 2007, at University of Colorado Hospital. Patients were divided into three renal function groups for assessment of bivalirudin dosing requirements. Thrombosis and bleeding were also evaluated.
RESULTS: Thirty-seven patients were evaluated: 12 patients with creatinine clearance (CrCl) > 60 mL/minute (Group 1); 11 patients with CrCl 30–60 mL/minute (Group 2); and 14 patients with CrCl < 30 mL/minute or receiving renal replacement therapy (RRT) (Group 3). Except for renal function, characteristics were similar between groups. Patients were 50 ± 16 years, 80 ± 20 kg, and 62% male; 95% were treated in the intensive care unit. Fifty-one percent of patients achieved goal-activated partial thromboplastin time (aPTT) with initial bivalirudin doses of 0.14 ± 0.04 mg/kg/hr (median 0.15 mg/kg/hr), 0.1 ± 0.07 mg/kg/hr (median 0.08 mg/kg/hr), and 0.05 ± 0.05 mg/kg/hr (median 0.05 mg/kg/hr) in groups 1, 2, and 3 respectively. Doses remained similar over the study period and were 0.13 ± 0.04 mg/kg/hr (median 0.15 mg/kg/hr), 0.1 ± 0.06 mg/kg/hr (median 0.1 mg/kg/hr), and 0.04 ± 0.02 mg/kg/hr (median 0.03 mg/kg/hr) for groups 1, 2, and 3 respectively. aPTTs were 67 ± 22 seconds in all patients. Bivalirudin dosing requirements correlated with CrCl ($r^2 = 0.37$; p<0.0001). Therapy duration was 11 ± 13 days (median 7 days). Systemic thrombosis on bivalirudin occurred in one patient. Clinically significant bleeding occurred in 3% of patients.
CONCLUSIONS: Bivalirudin dosing requirements correlate with patient renal function. The following initial bivalirudin doses achieved goal aPTT values in the majority of patients: 0.15 mg/kg/hr for CrCl > 60 mL/minute, 0.08–0.1 mg/kg/hr for CrCl 30–60 mL/minute, and 0.03–0.05 mg/kg/hr for CrCl < 30 mL/minute or RRT.

86. **Evaluation of the pre-test probability to aid in the optimal utilization of the platelet factor 4 assay in suspected heparin-induced thrombocytopenia.** *Kristen A. Kusmierski, Pharm.D.*[1], Kimberly T. Zammit, B.S., Pharm.D.[2], Stephanie J. Seyse, B.S., Pharm.D.[2]; (1)Kaleida Health, Williamsville, NY; (2)Kaleida Health, Buffalo, NY.

PURPOSE: Heparin-induced thrombocytopenia (HIT) is a prothrombic disorder that follows exposure to heparin products. The presence of thrombocytopenia, regardless of the likelihood of true disease, may result in over-utilization of the platelet factor 4 (PF4) enzyme-linked immunosorbent assay (ELISA) as a diagnostic test. The primary objective of this study is to determine whether the pre-test probability is a useful clinical tool in the diagnosis and management of patients with suspected HIT.

METHODS: Medical records of patients in whom a PF4 ELISA was performed between July 1, 2005, and December 31, 2006, were reviewed. Patient demographics, PF4 ELISA, serotonin release assay, platelet counts, interpretation and management of thrombocytopenia, and patient outcomes were collected. The pre-test probability score was determined using a previously validated method. These scores were then correlated with the PF4 ELISA results, clinical patient outcomes, and appropriateness of empiric management to determine whether a relationship exists.
RESULTS: A total of 211 patients were identified. An interim analysis of 146 patients demonstrated that 78.1% had a negative PF4 ELISA, 17.1% had a PF4 ELISA possibly indicative of HIT, and 4.8% had a PF4 ELISA probably/definitely indicative of HIT. The likelihood of HIT was significantly different between the pre-test probability categories of low, moderate, and high (p=0.0001). No patients having a low pre-test probability were diagnosed with HIT. Of the 31 patients with a moderate or high pre-test probability score, 19.4% developed a thrombosis compared with no patients in the low pre-test probability group (p=0.0039). Management of suspected HIT was similarly inappropriate regardless of pre-test probability. Final conclusions are pending completion of data analysis.
CONCLUSIONS: Preliminary results indicate that calculation of the pre-test probability score in patients with suspected HIT may eliminate the need to obtain a PF4 ELISA and would be a useful tool for empiric management.

87. **Effect of a mandatory electronic VTE risk assessment on the ordering of VTE prophylaxis in medically ill patients.** *Toby Trujillo, Pharm.D., BCPS*, Jeffrey Greenwald, M.D., Deborah Whalen, RNCS, M.B.A., ANP, Kate Phillips, Pharm.D., Sobieraj Jerry, M.D., Taiwo Evelyn, M.D., Ansell Jack, M.D.; Boston Medical Center, Boston, Mass.

PURPOSE: Although well-established guidelines clearly mandate the use of prophylaxis to prevent venous thromboembolic (VTE) events in hospitalized medically ill patients, numerous studies continue to show the underutilization of VTE prophylaxis. We implemented mandatory electronic risk stratification on hospital admission for medical patients to increase the rate of VTE prophylaxis.
METHODS: Mandatory risk stratification was implemented within computerized physician order entry software beginning July 1, 2006. Pre- and post-order set implementation data were collected (July 1–Dec 31, 2005 vs July 1–Dec 31, 2006) with specific inclusion/exclusion criteria. Inclusion criteria included patients with acute medical illness and length of stay greater than 3 days. Exclusion criteria included an INR > 1.8, or patients on full dose anticoagulation within 24 hrs of admission.
RESULTS: 3889 and 3774 eligible patients respectively were included from the time periods prior to and after implementation of the mandatory electronic risk stratification. The rate of VTE prophylaxis increased significantly in the 6-month period after implementation compared with the same time period 1 year prior (89.7% vs 84%; p<0.005). However, this increase did not result in an appreciable change in the incidence of clinical in hospital VTE events (1.4% vs 1.3%, p= NS). In analyzing the post-implementation patient group only, there was a significant difference in the incidence of in hospital VTE events in those patients receiving prophylaxis vs. those who did not (1.3% vs 3.6%, p<0.05).
CONCLUSION: The implementation of a mandatory electronic alert on admission requiring physicians to stratify medical patients for risk of VTE increased the percentage of eligible patients receiving VTE prophylaxis. The unexpected high rates of VTE prophylaxis prior to implementation may have prevented the detection of a significant effect on clinical in-hospital VTE events. Full 1-year results will be presented.

88. **Longitudinal assessment of the clinical utility of point-of-care measurement devices for determining the International Normalized Ratio.** *Kenneth M. Shermock, Pharm.D.*[1], Jason Connor, Ph.D.[2], Jodie M. Fink, Pharm.D., BCPS[3], Lee Bragg, Pharm.D.[4]; (1) The Johns Hopkins Hospital, Baltimore, Md; (2) Berry Consultants, Noblesville, Ind; (3) The Cleveland Clinic Foundation, Cleveland, Ohio; (4) Medina General Hospital, Medina, Ohio.

PURPOSE: We conducted a randomized, longitudinal trial to identify the best of five point-of-care (POC) finger-stick technologies for monitoring patients' International Normalized Ratio (INR) on oral anticoagulation therapy (i.e., warfarin). Instead of simply comparing each device's measurements to the reference laboratory, we identified which device led to the best patient management, defined as the percent time patients' INR values remained in their individually identified target ranges (TR) over time.
METHODS: 287 patients were randomized to 1 of 5 POC devices, completed ≥ 3 visits, and were monitored for an average of 87 days. Clinicians made all warfarin dosing decisions based on POC device INR measurements. Subjects provided simultaneous INR measurements from venous blood draws that were sent to a reference laboratory. These laboratory measurements served as a gold standard to estimate the percent time each patient's INR was within their TR. A Bayesian hierarchical model with a parametric variance component for estimating

coagulation times between observed blood draws was used to estimate the mean proportion of time each patient's INR was within their TR. The analysis assessed the probability that each device was the best and worst at maintaining patients' INR values within the TR over time.

RESULTS: Two POC devices, Coaguchek S (52.2% of time in the target INR range) and Coaguchek ProDM (51.5%) proved superior to their three competitors: Hemochron Jr.(48.3%), ProTime (45.5%), and Rapidpoint (41.2%). The posterior probabilites that the Coaguchek S and Coaguchek ProDM were the superior devices were 0.58 and 0.31, respectively.

CONCLUSION: This longitudinal study offers improvement over measures of numeric agreement by assessing more clinically relevant outcomes. It provides information on how discrepancies between the POC device and gold standard may lead to compounding dosing errors during long-term management of patients' anticoagulation therapy, ultimately affecting the percent time in the TR.

89. **Association between *CYP2C9* genotype and warfarin dose requirements in African Americans.** *Kathryn M. Momary, Pharm.D., BCPS*, Nancy L. Shapiro, Pharm.D., Marlos A.G. Viana, Ph.D., Edith A. Nutescu, Pharm.D., Cathy M. Helgason, M.D., Larisa H. Cavallari, Pharm.D.; University of Illinois at Chicago, Chicago, Ill.

PURPOSE: The cytochrome P450 (CYP) 2C9 enzyme metabolizes the more potent S-isomer of warfarin. The *CYP2C9**2 (144Cys) and *3 (358Leu) alleles have been associated with lower warfarin dose requirements compared to the *1/*1 (144Arg, 358Ile) genotype in primarily Caucasian populations. However, this association has not been well studied in African Americans. In addition, the *CYP2C9**5 allele (Asp360→Glu), which occurs almost exclusively in African Americans, is associated with reduced enzyme activity and may alter warfarin dose requirements. Our primary objective was to determine whether *CYP2C9* genotype was associated with mean warfarin dose requirement in African Americans.

METHODS: Genetic samples and demographic, clinical, and laboratory data were collected from 101 African American patients on a stable warfarin dose, defined as the same dose for $\geq$ 3 consecutive clinic visits. Patients with liver dysfunction or taking potent CYP2C9 inducers or inhibitors were excluded. The *CYP2C9* Arg144Cys, Ile358Leu, and Asp360Glu genotypes were determined by PCR and pyrosequencing.

RESULTS: Compared to the *CYP2C9* *1/*1 genotype, possession of a variant *CYP2C9* allele was associated with a 38% lower mean warfarin dose requirement (48 $\pm$ 18 vs. 30 $\pm$ 13 mg/week; p=0.003). Warfarin dose requirements for individual genotypes were 31 $\pm$ 8, 29 $\pm$ 27, and 31 $\pm$ 9 mg/week for patients with *CYP2C9* *1/*2 (n=6), *1/*3 (n=3), and *1/*5 (n=2) genotypes, respectively. After multivariate analysis, age, body surface area, and possession of a variant *CYP2C9* allele were jointly associated with warfarin dose requirements. Together these factors explained 33% of the variability in warfarin dose requirements in our African American population.

CONCLUSIONS: The *CYP2C9* genotype is associated with warfarin dose requirements in African Americans. Although there are data on the effect of *CYP2C9* genotype on warfarin response in Caucasians, this study is among the first to report its contribution to warfarin dose requirements in African Americans.

90. **Assessment of vitamin K use in the inpatient treatment of excessive anticoagulation.** *Douglas L. Jennings, Pharm.D.*, Lizbeth Hansen, Pharm.D., Maria Jose Pallares, Pharm.D., Amy Thompson, Pharm.D., Kelli D Garrison, Pharm.D., Andrea M Wessell, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Guidelines from the Seventh American College of Chest Physicians (ACCP) Conference on Antithrombotic and Thrombolytic Therapy provide specific recommendations for the management of patients with supratherapeutic international normalized ratios (INRs). The purpose of this medication use evaluation was to evaluate the use of vitamin K in patients with excessive anticoagulation and to assess the appropriateness of vitamin K administration in the inpatient setting according to existing guidelines.

METHODS: A retrospective chart review was performed for randomly selected patients on warfarin therapy who received vitamin K during hospitalization from April 2005 to March 2006 of time. Data were collected on patient demographics, vitamin K dosage, route of administration, warfarin dosage, alternative therapies, and INR before and after vitamin K administration. The appropriateness of vitamin K according to ACCP guidelines was evaluated by indication, route and dosage.

RESULTS: A total of 136 patient charts were reviewed. The majority of patients (72%) had a baseline INR of less than 5, with a mean INR of 4.4 (SD 2.9). A total of 75 patients had documented bleeding events on admission, 49% of which were considered major. Average time to repeat INR was 9.7 hours (SD 6.8). Seventy-one percent of patients had an appropriate indication documented for vitamin K, 42% received an appropriate dose, and 27% received the appropriate route of vitamin K. Only 21% of patients received vitamin K for an appropriate indication, with an appropriate dose and route.

CONCLUSION: From a representative sample of patients, the current use of vitamin K at our institution for the reversal of excessive anticoagulation is inconsistent and suboptimal with regard to route, dose, and monitoring parameters. Education of both medical and pharmacy staff will be essential to improve adherence with ACCP recommendations.

91E. **Heparin-induced thrombocytopenia: are we catching it?** *Chad Hatfield, Pharm.D.*, Harminder Sikand, Pharm.D.; Scripps Mercy Hospital/Cardinal Health, San Diego, Calif.

PURPOSE: Heparin is an extensively prescribed and effective anticoagulant, although it can rarely lead to thrombocytopenia. Two types of heparin-induced thrombocytopenia (HIT) can occur (Type I and Type II). Type II is more severe, occurring in 1%–3% of patients exposed to unfractionated heparin and < 0.8% of patients receiving low-molecular-weight heparin. Establishing a diagnosis for HIT is complicated by concomitant medical conditions and therapies. The primary goal of this study is to develop and assess a Pharmacist Intervention tool to improve early diagnosis and treatment of HIT.
METHODS: This IRB-approved study includes a retrospective (18 months) and prospective analysis (6 months) to determine incidence and treatment of HIT before and after pharmacist intervention. We reviewed the diagnosis, clinical symptoms, incidence, and treatment of HIT during both phases. A laboratory-screening tool designed specifically for the prospective phase will identify patients with a 50% decrease in platelet count from baseline. This tool will capture all patients exposed to heparin or low-molecular-weight heparin.
RESULTS: The retrospective analysis identified 14 patients with Type II HIT in 4179 heparin exposures yielding an incidence of 0.33%. Preliminary results from the prospective phase yielded 185 patients with a 50% platelet drop from baseline, 28 of which had thrombocytopenia secondary to heparin. Five patients to date had Type II HIT, resulting in an incidence of 0.36%. Patients were identified in less than 8 days after initiation of heparin therapy and treated with direct thrombin inhibitors.
CONCLUSION: Given the wealth of knowledge, little is known on screening for HIT unless the patient exhibits significant thrombotic complications. The diagnosis of HIT remains a diagnosis of exclusion. The pharmacist intervention tool slightly increased the diagnosis of HIT and has been modified to facilitate better results. This study will close on June 30, 2007, and final results will be presented.
Presented at Western States Conference, Pacific Grove, Calif, May 29-June 1, 2007.

92E. **Prevalent etiologies of non-therapeutic warfarin anticoagulation in a network of pharmacist-managed anticoagulation clinics.** *Brian T. Cryder, Pharm.D.*[1], Margaret A. Felczak, Pharm.D.[1], Justine D. Rojszyk, Pharm.D.[2], Lea DelaPena, Pharm.D.[1], Sheila Allen, Pharm.D.[1], Patricia Gutierrez, Pharm.D.[2]; (1)Midwestern University, Downers Grove, Ill; (2)Advocate Health Centers, Chicago, Ill.

PURPOSE: To determine the prevailing etiologies of non-therapeutic warfarin anticoagulation episodes among patients currently enrolled in an outpatient anticoagulation clinic and compare the relative frequency in which they occur compared to therapeutic anticoagulation regimens.
METHODS: The prospective, observational cohort study was set within three pharmacist-managed anticoagulation clinics in a community outpatient health system. Patients were included if they arrived for an office visit during the 6month period from September 2006 to March 2007 and were evaluated for the presence or absence of the 14 commonly identified factors linked to non-therapeutic anticoagulation results.
RESULTS: During the study period, 5818 patient-visits were documented, producing 2887 (49.6%) non-therapeutic and 2931 (50.4%) therapeutic INR readings. The most prevalent etiologies linked to non-therapeutic INR results included change in dietary vitamin K (16.9%, OR = 6.4), noncompliance (15.0%, OR = 4.9), and initiation of therapy (9.9%, OR = 2.3). The factor with the highest predictive value of non-therapeutic INR results was a change in health status (OR = 9.5) despite its lower rate of frequency (4.9%). Despite the identification of many causative factors in this study, 40.2% of non-therapeutic INR readings had no known etiology. In the end, the lack of any study factor was a greater predictor of therapeutic anticoagulation (86.2%) than the presence of a study factor was for predicting non-therapeutic INR values (51.4%).
CONCLUSIONS: Our study demonstrated that there are many etiologies for non-therapeutic INR values that were not explained by our investigational factors. Lack of influencing factors is a stronger predictor of therapeutic INR than presence of influencing factors for non-therapeutic INR.
Presented at the Ninth National Conference on Anticoagulant Therapy, Chicago, Ill, May 3-5, 2007.

93. **Evaluation of correlation between hemoglobin measurements obtained from a point-of-care device and central lab instrumentation.** *Tyan Frazier, Pharm.D.*[1], Robert Dombrowski, Pharm.D.[2]; (1) Philadelphia College of Pharmacy, Philadelphia, Pa; (2)Baltimore VA Medical Center, Baltimore, Md.

PURPOSE: Use of a point-of-care (POC) device to determine hemoglobin (Hgb) concentrations is a convenient way to monitor erythropoietin (EPO) therapy. However, use of POC Hgb determinations to adjust EPO therapy has not been adequately reported in literature. The Baltimore Veterans Administration Medical Center (BVAMC) has an EPO clinic that uses a POC device, the Hemocue® (Hemocue Inc., Lake Forest, Calif), using blood samples obtained from finger puncture to determine Hgb concentrations. EPO therapy is initiated and adjusted based on these POC Hgb concentrations.

METHODS: To determine correlation, a linear plot was created to determine the coefficients of correlation and determination using paired Hgb samples obtained from patients seen in the BVAMCs EPO clinic between September 6, 2005, and April 12, 2006. There had to be no more than 24 hours between the time the Hemocue® and central lab Hgb concentrations were obtained. To evaluate the impact on EPO dosing, encounter notes were reviewed from visits where there was more than 10% difference between the two Hgb concentrations.

RESULTS: Eighty-three paired Hgb concentrations, measured among 34 patients, were included in the correlation study. A plot of Hemocue® versus central lab Hgb concentrations yielded a coefficient of determination and a coefficient of correlation of 0.61 and 0.78, respectively. There was more than 10% difference between Hgb concentrations in 29 of the 83 (34%) paired samples. The retrospective medical record review revealed three clearly documented cases where decisions were made based on the Hemcoue® Hgb, but had to be changed upon receiving central lab Hgb concentrations.

CONCLUSIONS: These results show that use of POC determinations of Hgb concentrations employing finger-puncture samples to adjust EPO therapy should be investigated further. Given the poor correlation, the authors suggest limiting use of the finger-puncture method for POC determinations of Hgb for anemia screening, pending further investigation.

94. **Accuracy and clinical utility of the CoaguChek XS in measuring the international normalized ratio (INR) in anticoagulated patients.** *Rex W. Force, Pharm.D., FCCP, BCPS*, Camille M. Nulph, Pharm.D., Michelle L. Mayne, Pharm.D.; Departments of Family Medicine and Pharmacy Practice and Administraion Sciences College of Pharmacy, Idaho State University, Pocatello, Idaho.

PURPOSE: Point-of-care (POC) INR testing is performed in many anticoagulation clinics. Advantages of POC testing include timely results as well as immediate decision-making and patient feedback. On October 19, 2006, reports of falsely elevated INR results led Roche Laboratories and the FDA to issue a recall of all CoaguChek strips. This effectively ended POC testing for clinics using this system until the problems could be resolved. In February 2007, Roche released the CoaguChek XS system, which is advertised as having enhanced features and safety compared with previous CoaguChek systems. Limited data are available regarding the accuracy of this system. We performed a paired analysis of the new POC system and gold standard venipuncture INR determinations.

METHODS: Consecutive patients receiving chronic anticoagulation with warfarin were studied. INRs were determined by venipuncture at our local laboratory using a Dade Behring coagulation analyzer and thromboplastin (ISI = 1.06). Simultaneously, INRs were obtained by fingerstick for CoaguChek XS. Pearson's correlations were determined. The two methodologies were analyzed by t-test. Differences ≥ 0.3 INR units or 15% were quantified. Clinically meaningful discrepancies between INRs likely leading to a change in therapy were also determined.

RESULTS: 38 patients had 86 paired INRs (total INR n=172). Mean INRs for venipuncture and CoaguChek XS were 2.37 and 2.45, respectively (p=0.00046, difference (+/- SD), 0.081 (+/- 0.21)). Values correlated well (r = 0.9590, r2 = 0.9197, y = 0.9451x+0.2113). 23.3% (20/86 pairs) varied by ≥ 0.3 INR units. 11.6% (10/86 pairs) varied by > 15%. 7.0% of the pairs (6/86 pairs) may have resulted in a different therapeutic plan.

CONCLUSIONS: The CoaguChek XS is accurate compared with venipuncture, although, on average, INR values run slightly higher. These differences may infrequently result in changes in therapy.

HIV/AIDS

95E. **Once-daily ritonavir (100 mg) boosting of fosamprenavir (FPV/r) or atazanavir (ATZ/r) with tenofovir (TDF)/emtricitabine (FTC) in antiretroviral-naive HIV-infected patients: 48-week safety/ efficacy results from COL103952 (ALERT).** Kimberly Smith, M.D.[1], Winkler G. Weinberg, M.D.[2], Edwin DeJesus, M.D.[3], Margaret A. Fischl, M.D.[4], Qiming M. Liao, Ph.D.[5], Lisa L. Ross, M.S.[5], Keith Pappa, Pharm.D.[5], *Charles T. Lancaster, B.A.*[5]; (1)Rush University Medical Center, Chicago, Ill; (2)Kaiser Permanente, Atlanta, Ga; (3)Orlando Immunology Center, Orlando, Fla; (4)University of Miami, Miami, Fla; (5)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: To evaluate the efficacy and safety of FPV/r or ATV/r combined with TDF/FTC in antiretroviral-naïve patients. Clinical data in HIV-infected patients supporting use of FPV/r 1400 mg/100 mg daily is limited.

METHODS: ALERT was an open-label, randomized study evaluating FPV/r 1400 mg/100 mg or ATV/r 300 mg/100 mg + TDF/FTC 300 mg/200 mg given once daily in patients with screening HIV RNA > 1,000 c/mL. Substitutions were permitted for TDF/FTC-related adverse events requiring discontinuation.

RESULTS: 106 patients were enrolled. Median FPV/r vs ATV/r baseline (BL) data were as follows: plasma HIV RNA viral load (VL) 4.9 vs 4.9 $\log_{10}$c/mL, Total-cholesterol 160 vs 153 mg/dL, triglycerides 120 vs 123 mg/dL, HDL-cholesterol 35 vs 38 mg/dL, and LDL-cholesterol 95 vs 97 mg/dL. Mean CD4 counts were 176 vs 205 cells/mm^3, and 36% vs 40% had glomerular filtration rate (GFR) by MDRD in the normal range ($\geq$ 90 mL/minute). Twelve patients, 8 vs 4, discontinued study early. All lipids were fasting.

Results at Wk 48	FPV/r	ATV/r	p-value
VL < 400 c/mL[ITT,MD=F]; n/N (%)	42/53 (79%)	46/53 (87%)	0.30*
VL < 400 c/mL [Obs]; n/N (%)	42/45 (93%)	46/48 (96%)	0.60*
VL < 50 c/mL [ITT,MD=F]; n/N (%)	40/53 (75%)	44/53 (83%)	0.34*
VL < 50 c/mL [Obs]; n/N (%)	40/45 (89%)	44/48 (92%)	0.66*
Mean CD4 change from BL (cells/mm^3)	+170	+183	‡
Total-cholesterol (mg/dL), median	179	181	‡
HDL-cholesterol (mg/dL), median	43	48	‡
LDL-cholesterol (mg/dL), median	99	102	‡
Triglycerides (mg/dL), median	167	133	‡

P-values were calculated using: *Cochran-Mantel-Haenszel test stratified by baseline VL (< 100,000/$\geq$ 100,000).
‡ Statistical testing was not done.

Three patients with baseline GFR 50–80 mL/minute discontinued TDF/FTC when GFR declined to < 50 mL/minute (confirmed). Treatment-related grade 2-4 adverse events occurred in 15% vs 57%, with differences driven by ATV/related hyperbilirubinemia.

CONCLUSIONS: Both regimens demonstrated comparable virologic suppression through 48 weeks. Lipid changes were similar. FPV/r had lower percentage of treatment-related Grade 2–4 adverse experiences.

Presented at 4th International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention in Sydney, Australia, July 2007.

96E. **Once-daily Abacavir/Lamivudine (ABC/3TC) and boosted Atazanavir (ATV/RTV) for antiretroviral naive HIV-1 infected subjects: 48-week results from COL102060 (SHARE).** Richard Elion, M.D.[1], Edwin DeJesus, M.D.[2], Michael Sension, M.D.[3], Daniel S. Berger, M.D.[4], William J. Towner, M.D.[5], Gary Richmond, M.D.[6], Linda H. Yau, Ph.D.[7], *Belinda Ha, Ph.D.*[7]; (1)George Washington University, Washington, DC; (2)Orlando Immunology Center, Orlando, Fla; (3)Comprehensive Care Ctr, Fort Lauderdale, Fla; (4)Northstar Medical Center, Chicago, Ill; (5)Kaiser Permanente S. California, Los Angeles, Calif; (6)Broward General Medical Center, Fort Lauderdale, Fla; (7)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: To assess the efficacy and safety of a once-daily (QD) regimen consisting of the co-formulation of abacavir/lamivudine (ABC/3TC) and atazanavir plus ritonavir (ATV+RTV) in antiretroviral (ART)-naïve subjects with plasma HIV-1 RNA >5,000 copies/mL.

METHODS: In this open-label, multicenter study, subjects received ABC 600 mg/3TC 300 mg and ATV 300 mg+RTV 100 mg QD. Drug switches were permitted for ABC hypersensitivity and ATV-related hyperbilirubinemia. Primary end points were proportion of subjects achieving HIV-1 RNA < 50 copies/mL at week 48 and treatment discontinuation due to study drugs.

RESULTS: 111 subjects were treated. Median baseline (BL) characteristics were: HIV RNA 5.1 $\log_{10}$c/mL (56% had HIV RNA $\geq$ 100,000 c/mL), CD4+ 207 cells/mm^3 (47% had CD4+ < 200 cells/mm^3), triglycerides 120 mg/dL, cholesterol 165 mg/dL, HDL-cholesterol 31 mg/dL, and LDL-cholesterol 103 mg/dL. At week 48, the proportion of subjects achieving HIV-1 RNA < 50 copies/mL was 77% (85/111) by ITT missing=failure or switch included response rate and 90% (85/94) by ITT-observed response rate. Drug substitutions occurred in 8 (7%) subjects for suspected ABC hypersensitivity reaction (HSR) and in 6 (5%) subjects for ATV-related toxicities; only 1 subject discontinued study due to ABC HSR. Treatment-emergent drug resistance was rare, and no subject had virus that developed reduced susceptibility to ATV. Median fasting lipids at week 48 were 174 mg/dL for triglycerides, 198 mg/dL for total cholesterol, 46 mg/dL for HDL-cholesterol, and 115 mg/dL for LDL-cholesterol.

CONCLUSIONS: ABC/3TC and ATV+RTV QD is an effective, well-tolerated regimen in ART-naïve subjects through 48 weeks. Further study is under way of ABC/3TC+ATV without RTV as maintenance regimen in virologically suppressed subjects to evaluate the impact on fasting lipid levels.
Presented at the International AIDS Society Meeting in Sydney, Australia, July, 2007.

97. **Time to onset of abacavir hypersensitivity in patients: comparison based on presence or absence of the *HLA-B*5701* allele.** *Mark S. Shaefer, Pharm.D.*, Rukmini B Balu, Ph.D., Cindy H. Brothers, MSPH, Britt S Stancil, B.S., Mike M Mosteller, Ph.D., Arlene R. Hughes, Ph.D., Paul G Wannamaker, B.S.; GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: Hypersensitivity to abacavir (ABC HSR) is a multiorgan clinical syndrome with a reported incidence of about 8% from 9 recent clinical trials. Symptoms occur within the first 6 weeks of therapy in 89% of cases (median onset 9 days). The objectivewas to compare time to onset of ABC HSR in patients who were either *HLA-B*5701* positive or negative.
METHODS: Study ABC107442 (SHAPE) was a retrospective case-control study to determine the sensitivity of *HLA-B*5701* for ABC HSR in White and Black patients. Subjects with clinically suspected ABC HSR were identified through chart reviews. Clinical symptoms and timing of ABC HSR were collected at the time of the clinical diagnosis. All subjects with clinically suspected ABC HSR underwent *HLA-B*5701* determination and abacavir skin patch testing for immunologic confirmation of the clinical diagnosis.
RESULTS: In SHAPE, 42 of 130 White (32.3%) and 5 of 69 (7.2%) Black cases that met the criteria for clinically-suspected ABC HSR were immunologically-confirmed. All 42 White cases with immunologically-confirmed ABC HSR were *HLA-B*5701* positive (sensitivity = 100%; OR = 1945; 95% CI = 110–34352). Among Blacks, 5/5 immunologically-confirmed ABC HSR cases were *HLA-B*5701* positive (sensitivity 100%; OR = 900; 95% CI = 38–21045). Median time to onset of the first symptom of HSR was 7 days in *HLA-B*5701* positive patients (range 0–34 days). In those negative for *HLA-B*5701*, the median time (range) to onset of symptoms was 7 days (0–469 days).
CONCLUSION: Sensitivity of *HLA-B*5701* was 100% for immunologically-confirmed ABC HSR in Blacks and Whites. Onset of ABC HSR occurred within 5 weeks in all patients positive for the *HLA-B*5701* allele.

98E. **Safety and efficacy of fosamprenavir used during pregnancy in a clinical practice (COL108577).** *Claudia Martorell, M.D., M.P.H.*[1], Eileen Theroux, R.N.[2], Jane Garb, M.S.[2], Debra Kronschnabel, Pharm.D.[3], Katrina Oie, Ph.D.[4]; (1)The Research Institute, Springfield, Mass; (2)Baystate Medical Center, Springfield, Mass; (3)GlaxoSmithKline, Canton, Conn; (4)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: Prospective safety and efficacy data about fosamprenavir use during pregnancy are unavailable. This study provides needed observational data until prospective trials are undertaken.
METHODS: COL108577 is a retrospective, observational case-series of all HIV-positive pregnant women from one clinical practice who delivered while taking fosamprenavir. Abstracted chart data include: antiretroviral regimen; maternal age, CD4+ T-cell count, viral load; infant weight/height, APGAR scores, HIV status; delivery mode/time; adverse events. Baseline is last observation before fosamprenavir initiation.
RESULTS: Seven women were included. Median baseline age was 33 years (range 20–43). Six were HAART-naïve at baseline. Fosamprenavir regimens included ritonavir-boosting (n=5), zidovudine/lamivudine (n=5), tenofovir/emtricitabine (n=2), and didanosine/emtricitabine (n=1).

Variable (N=7 for all)	Mean	Standard Deviation	Median	Range
Viral Load (copies/mL) at: --Baseline --Delivery[1]	75178 N/A[2]	94234 N/A[2]	18595 <50[2]	<50–239786 <50–1300
CD4 Count (cells/mm³) at: --Baseline --Delivery[1]	442.3 509	192.7 191.6	415 499	153–714 233–787
Wks on FPV During Pregnancy	18.8	3.2	20.0	14–22.3
Gestation (weeks)	37 4/7	2.1	37 1/7	35 4/7–42
Birth Weight (grams)	2914.7	691.7	2923	2175–4216
Birth Height (cm)	49.4	5.0	48.9	44.5–58.4

APGAR Score (mean of 3 readings)	8.4	0.6	8.7	7.3–9

[1]At/near delivery; [2]Actual viral loads: <50 (n=5), 63 (n=1), 1300 (n=1)

Delivery modes were: 42.9% vaginal, 42.9% scheduled c-section, 14.3% emergent C-section. The regimens were well-tolerated. No hepatic, renal, or pancreatic abnormalities were observed in mothers. There were no CNS abnormalities, sometimes of concern with sulfonamide-containing products, nor other adverse events seen in the infants. All infants were HIV-negative at month 4 testing.

CONCLUSIONS: Fosamprenavir-based regimens were well-tolerated in this cohort of pregnant women, who responded virologically and immunologically after regimen initiation. Good birth outcomes and no significant adverse events were reported in the infants.

Presented as an abstract on CD-ROM only at the 4th International AIDS Society Conference, Sydney, Australia, July 2007. Abstract Ref. No. A-042-0132-01999.

99. **Evaluation of a pharmacy implemented medication reconciliation strategy directed at anti-retroviral therapy in HIV/AIDS patients admitted to an academic medical center.** *Megan A. Corrigan, Pharm.D.*, Christopher W. Crank, Pharm.D., Kendra M. Damer, Pharm.D., Beverly E. Sha, M.D.; Rush University Medical Center, Chicago, Ill.

PURPOSE: Anti-retroviral therapy (ART) for Human Immunodeficiency Virus (HIV) is commonly associated with hospital-based medication errors due to complex regimens, drug interactions, and unfamiliarity with ART. The primary outcome examined was the difference in appropriateness of ART 48 hours after admission between standard practice and a pharmacist-driven process.
METHODS: We prospectively compared medication reconciliation by housestaff/attendings (standard practice) versus pharmacist driven medication reconciliation of HIV therapy. Appropriate therapy was defined as treatment in accordance with published guidelines, proper dosing, and avoidance of potential drug interactions. HIV patients taking ART between October 2006 and April 2007 at Rush University Medical Center were enrolled. Twenty-one patients were included in the assessment of the standard medication reconciliation process (Phase 1). Twenty patients were included in the pharmacist-driven process, which consisted of a pharmacist obtaining a formal medication history of ART and opportunistic infection prophylaxis within 24 hours of admission (Phase 2).
RESULTS: There were no significant differences in baseline characteristics between the two phases. In Phase 1, there were 17 errors in 11 patient regimens at 48 hours. In Phase 2, there was 1 error at 48 hours after 28 interventions were recommended within 24 hours of admission. Phase 2 was associated with a statistically significant reduction in medication regimens with errors at 48 hours (p=0.001, 2-sided Fisher's exact test). Logistic regression demonstrated that the presence of a pharmacist-driven medication history was associated with an increased likelihood of an appropriate regimen (p=0.006; OR = 20.9; 95%CI = 2.3–185.9). The mean time to pharmacist-driven medication history was 17 hours, and the mean time to perform medication histories was 19.75 minutes.
CONCLUSIONS: Transitions in care are associated with an increased risk of medication errors. In this analysis, pharmacist-driven medication reconciliation was associated with a decrease in errors in a high-risk patient population.

100E. **Long-term efficacy of fosamprenavir (FPV) 1400 mg once daily (QD) Boosted by ritonavir (RTV) 100 mg qd in antiretroviral (ARV)-naïve HIV+ patients and ARV-experienced patients switched to FPV/RTV due to intolerance to prior regimens: BOLD 100 (COL109766).** *Gary Blick, M.D.*[1], Paola Greiger-Zanlungo, M.D.[2], Veronica Plasencia, M.D.[1], Scott Gretz, B.A.[1], Trish Garton, APRN[1], Deborah Dupree, B.A.[2], Gary Pakes, Pharm.D.[3], Qiming Liao, Ph.D.[3]; (1)Circle Medical LLC, Norwalk, Conn; (2)Mt. Vernon Hospital, Mt. Vernon, NY; (3)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: No study to date has assessed the long-term efficacy/safety of ARV regimens containing FPV 1400 mg QD boosted by RTV 100 mg QD (half the currently recommended QD boosting dose).
METHODS: In a retrospective database study at two HIV treatment centers, medical records were accessed for all HIV+ adults who were started on FPV/RTV 1400 mg/100 mg QD-based regimens between January 2004 and January 2006. At baseline (BL), patients had to have a viral load (VL) ≥ 1,000 copies/mL, any CD4 count, and no active AIDS-related infections/complications/malignancies.
RESULTS: Data were available for 20 ART-naïve patients (median age 50.4 years; non-Caucasian 50%; females 50%; BL VL 4.9 $\log_{10}$ copies/mL; median CD4 count 327 cells/mm^{3}; duration HIV+ 5.3 years); 30 PI-naïve, ARV-experienced patients (median age 49.2 years; non-Caucasian 63%; females 23%; BL VL 3.3 $\log_{10}$ copies/mL; median CD4 count 339 cells/mm^{3};duration HIV+ 10.2 years); and 25 PI-experienced patients (median age 48.8 years; non-Caucasian 35%; females 25%; BL VL 2.6 $\log_{10}$ copies/mL; median CD4 count 342 cells/mm^{3};

duration HIV+ 14 years; prior treatment commonly lopinavir/RTV-based (mean, 23.4 months), atazanavir-based (mean, 12.0 months), or efavirenz-based (5.9 months). Nucleoside backbones were generally tenofovir/emtricitabine, abacavir/lamivudine, abacavir/lamivudine/zidovudine, or tenofovir/lamivudine. Efficacy results (as-treated) showed that virologic suppression (VL < 50 copies/mL) was achieved and maintained in 100% of the ARV-naïve group (median 2.4 years; range 1.5–3.2 years), 87% of PI-naïve patients (2.4 years; 1.2–3.4 years), and 88% of PI-experienced patients (2.2years; 1.0–3.2years); median CD4 cell count increased above BL by 181,142, and 109 cells/mm^3; and virologic failure (VL decrease to < 400 copies/mL, then increase to ≥ 400 copies/mL on two consecutive occasions, or not achieving VL < 400 copies/mL by week 48) occurred in 0%,7%,12%, respectively. Adverse events reported were Grade 1–2 diarrhea (30%,13%,8%), nausea (20%,7%,0%), and vomiting (10%,3%,0%). Median fasting lipid changes from BL were: total-cholesterol +15,-11,+2mg/dL; LDL-cholesterol +3,-11,+3mg/dL; HDL-cholesterol +6,+2,+5; triglycerides +27,-27,-41 mg/dL, respectively.
CONCLUSIONS: FPV/RTV 1400/100 mg QD remained effective and generally well-tolerated long-term (over up to 3.4 years) in all ART-naïve and most ARV-experienced HIV+ patients.
Presented in part at the 4th International AIDS Society Conference on HIV Pathogenesis, Prevention, and Treatment, Sydney, Australia, July 2007.

101E. **The KLEAN Study: Similarity of virologic response and immunologic recovery in antiretroviral treatment (ART)-naïve subjects receiving fosamprenavir/ritonavir (FPV/r) or lopinavir/ritonavir (LPV/r) by baseline viral load and CD4+ cell count over 48 weeks.** *Joseph Gathe Jr., M.D.*[1], Christine Katlama, M.D.[2], Louis Sloan, M.D.[3], Nathan Clumeck, M.D., Ph.D.[4], Nicholas C. Bellos, M.D.[5], Jean-Guy Baril, M.D.[6], Linda Yau, Ph.D.[7], Lisa G. Patel, Pharm.D.[7], Manoli Vourvahis, Pharm.D.[7]; (1)Therapeutic Concepts, PA, Houston, Tex; (2)APHP-Groupe Hospitalier Pitié-Salpêtrière, Paris, France; (3)North Texas IDC, Dallas, Tex; (4)CHU Saint-Pierre, Brussels, Belgium; (5)Southwest Infectious Disease Associates, Dallas, Tex; (6)Clinique Médicale du Quartier Latin, Montréal, Quebec; (7)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: KLEAN was a randomized, open-label study that demonstrated non-inferiority of FPV/r BID to LPV/r BID, each with abacavir/lamivudine.
METHODS: Virologic response [Time to Loss of Virologic Response (TLOVR)] was evaluated by stratification of baseline (BL) HIV-1 RNA (VL) [< or ≥ 100,000 c/mL] and CD4+ cell counts (< or ≥ 50 cells/mm^3) in a combined analysis. Immunologic recovery was assessed and stratified by baseline CD4+ < 50, 50–< 200, or ≥ 200 cells/mm^3.

RESULTS:

TLOVR at Week 48		Overall Response	High VL/ Low CD4+	Low VL/ High CD4+	Low VL/ Low CD4+	High VL/ High CD4+
<400 c/mL	FPV/r; %(n)	73 (434)	75 (52)	71 (182)	53 (15)	75 (185)
	LPV/r; %(n)	71 (444)	73 (62)	69 (191)	78 (18)	73 (173)
<50 c/mL	FPV/r; %(n)	66 (434)	65 (52)	68 (182)	53 (15)	64 (185)
	LPV/r; %(n)	65 (444)	68 (62)	63 (191)	78 (18)	65 (173)

Consistent response rates for VL < 400 c/mL and < 50 c/mL were seen across combined BL VL/CD4+ strata (within 3% of the overall response rate for both arms), except the low VL/low CD4+ arm, which included few subjects (n=33). Median increases in CD4+ count (cells/mm^3, observed analysis) for the FPV/r and LPV/r groups respectively were as follows: overall population: 176 and 191; BL CD4+ < 50: 159 and 173; BL CD4+ 50–< 200: 176 and 172; BL CD4+ ≥ 200: 196 and 213.
CONCLUSION: Subjects receiving FPV/r or LPV/r BID had consistent response rates < 400 and < 50 c/mL across BL VL/CD4 strata at 48 weeks. The median CD4+ cell count increases at Week 48 were similar between treatment arms and strata. Slightly higher CD4+ cell count increases were seen in those subjects with higher BL CD4+ cell counts. The observed benefits of FPV/r BID are similar to that of LPV/r BID in this ART-naïve HIV population.
Presented at the Molecular and Cellular Determinants of HIV Pathogenesis, Keystone Symposia, Whistler, British Columbia, Canada, March 25-30, 2007.

102E. Darunavir in combination with other medications: pharmacokinetic interactions. *James D. Scott, Pharm.D., M.Ed., B.S.*[1], Tony Vangeneugden, M.Sc.[2], Star Seyedkazemi, Pharm.D., B.S.[3], Joseph Mrus, M.D.[3], Vanitha Sekar, Ph.D.[4]; (1)Western University of Health Sciences, Pomona, Calif; (2)Tibotec BVBA, Mechelen, Belgium; (3)Tibotec Therapeutics, Bridgewater, NJ; (4)Tibotec Inc., Yardley, Pa.

PURPOSE: We present data on pharmacokinetic interactions between darunavir (PREZISTA™) co-administered with low-dose ritonavir (darunavir/r) and other medications commonly used in HIV-infected patients.
METHODS: The potential for interactions was studied when darunavir/r was co-administered with: atazanavir, indinavir, lopinavir/r, saquinavir/r, efavirenz, nevirapine, etravirine (TMC125), enfuvirtide, tenofovir, atorvastatin, omeprazole, ranitidine, sildenafil, clarithromycin, sertraline, paroxetine, ethinyl estradiol, norethindrone, methadone, ketoconazole, pravastatin, and digoxin. Maraviroc pharmacokinetic interaction studies were conducted by Abel et al (IWCPHIV 2007). Effect on exposure (AUC) is presented as the least squares mean ratio.
RESULTS: Darunavir/r increased exposure of efavirenz (1.21), nevirapine (1.27), tenofovir (1.22), indinavir/r (1.23), lopinavir/r (1.09), maraviroc (4.05), ketoconazole (3.12), clarithromycin (1.57), atorvastatin (0.85 [AUC for 10 mg atorvastatin in the presence of darunavir/r increased relative to AUC for 40 mg atorvastatin when dosed alone]), sildenafil (0.97), pravastatin (1.81), and digoxin (1.77), and decreased exposure to etravirine (0.63), sertraline (0.51), methadone (0.84), ethinyl estradiol (0.56), and norethindrone (0.86). Exposure to atazanavir/r or saquinavir/r did not change. Darunavir exposure increased when combined with tenofovir (1.21), indinavir/r (1.24), nevirapine (1.24), and ketoconazole (1.42); decreased when combined with efavirenz (0.87), saquinavir/r (0.74), and lopinavir/r (0.62); and was unchanged when combined with other commonly co-administered medications.
CONCLUSIONS: Darunavir/r can be combined with many agents with no darunavir/r dose adjustments. Some co-administered agents (atorvastatin, pravastatin, digoxin, and maraviroc) may require dose adjustments. When administering atorvastatin in patients receiving darunavir/r, start with lowest atorvastatin dose and titrate as necessary. When co-administration of pravastatin or digoxin with darunavir/r is required, titrate for desired clinical effect, monitor for toxicity, and follow digoxin serum concentrations. In patients receiving darunavir/r and maraviroc, decrease maraviroc dose by 50%. Combining darunavir with lopinavir/r or saquinavir/r is not recommended. Additional contraception should be used when oral contraceptives are combined with darunavir/r. Drug interactions with darunavir/r are well characterized and manageable.
Presented at the American Conference for the Treatment of HIV (ACTHIV), Dallas, Tex, May 31–June 3, 2007.

103E. TMC125 in combination with medications commonly used in HIV infection: summary of drug-drug interactions. *Tiffany Surles, Pharm.D.*[1], Monika Schöller-Gyüre, M.D.[2], Richard M. Hoetelmans, Ph.D.[2], Monika Peeters, M.Sc.[2], Brian Woodfall, M.D.[2], James Witek, M.D.[1], Thomas N. Kakuda, Pharm.D.[3]; (1)Tibotec Therapeutics, Bridgewater, NJ; (2)Tibotec BVBA, Mechelen, Belgium; (3) Tibotec Inc., Yardley, Pa.

PURPOSE: TMC125 (etravirine; ETR), a next-generation NNRTI with demonstrated activity in treatment-experienced HIV-infected patients, including those with NNRTI resistance, is a substrate and weak inducer of CYP3A4 and a substrate and weak inhibitor of CYP2C9 and CYP2C19. Pharmacokinetic interactions between TMC125 and other medications commonly used in HIV-infected patients are summarized.
METHODS: Pharmacokinetic studies were conducted: steady-state two-way interaction studies with TMC125 and rifabutin, clarithromycin, atorvastatin, didanosine, tenofovir, elvitegravir/ritonavir, raltegravir, atazanavir and ritonavir-boosted (/r) protease inhibitors atazanavir, darunavir, lopinavir, and tipranavir; one-way effect of nevirapine, efavirenz, omeprazole, and ranitidine at steady-state on single-dose TMC125; one-way effect of steady-state TMC125 on steady-state fosamprenavir/r, lopinavir/saquinavir/r, methadone, ethinyl estradiol and norethindrone (oral contraceptive), and single-dose sildenafil and saquinavir.
RESULTS: TMC125 had no clinically relevant effect on rifabutin, atorvastatin, didanosine, tenofovir, elvitegravir/r, raltegravir, methadone, ethinyl estradiol and norethindrone, saquinavir, and the boosted protease inhibitors atazanavir, darunavir, lopinavir (with or without saquinavir), or tipranavir. TMC125 increased exposure to fosamprenavir by 69%, and decreased exposure to sildenafil by 57% and its active metabolite, *N*-desmethyl sildenafil, by 41%. Clarithromycin exposure decreased 39%, but active metabolite 14-OH-clarithromycin increased by 21%; C_{min} of unboosted atazanavir decreased by 47%. No clinically relevant changes in TMC125 exposure were observed when combined with rifabutin, clarithromycin, atorvastatin, didanosine, tenofovir, elvitegravir/r, raltegravir, atazanavir, atazanavir/r, darunavir/r, lopinavir/r, and omeprazole or ranitidine. TMC125 exposure decreased 76% with tipranavir, 55% with nevirapine, and 41% with efavirenz. When co-administered with fosamprenavir/r, lopinavir/saquinavir/r, methadone, ethinyl estradiol and norethindrone, sildenafil or saquinavir, TMC125 pharmacokinetic were comparable to historical controls.
CONCLUSIONS: TMC125 can be combined with many drugs without dosage adjustment. Dose adjustments may be considered for fosamprenavir and sildenafil. TMC125 is not recommended in combination with

efavirenz, nevirapine, tipranavir/r, full-dose ritonavir, and unboosted protease inhibitors. Use of an alternative to clarithromycin is recommended when treating *Mycobacterium avium* complex.
Presented at the American Conference for the Treatment of HIV (ACTHIV), Dallas, Tex, May 31–June 3, 2007.

Infectious Diseases

104. **Utility of doxycycline (DOX) for multidrug-resistant (MDR)** *Acinetobacter baumannii* **(ACN) in Thailand.** *David S. Burgess, Pharm.D., FCCP*[1], Michael F. Carden, B.A.[2], Surakit Nathisuwan, Pharm.D., BCPS[3], Pitak Santanirand, Ph.D.[4], Kumthorn Malathum, M.D.[4]; (1)Center for Advancement of Research and Education in Infectious Diseases, University of Texas at Austin College of Pharmacy, San Antonio, Tex; (2)University of Texas Health Science Center at San Antonio, San Antonio, Tex; (3)Faculty of Pharmacy, Mahidol University, Bangkok, Thailand; (4)Faculty of Medicine at Ramathibodi Hospital, Bangkok, Thailand.

BACKGROUND: Multidrug-resistant (MDR) *Acinetobacter baumannii* has been reported worldwide and continues to increase. Because limited new antimicrobials are being developed for MDR gram-negative bacteria, some data suggest that older drugs such as DOX have activity against these organisms. Therefore, we evaluated the in vitro activity of DOX against MDR ACN via time-kill methodology.
METHODS: In 2006, 48 non-duplicate clinical isolates of ACN were collected at Ramathibodi Hospital, Bangkok, Thailand. MICs were determined against DOX, meropenem (MER), amikacin (AMK), and ciprofloxacin (CIP) according to CLSI (M7-A7). All isolates were screened for metalo-ß-lactamase (MBL) using the MBL E-strip. Time-kill curves were performed in duplicate against DOX at 4 mcg/mL using a standard inoculum. Isolates (N=7) were selected based on DOX MICs (MIC ranged 1–64). Bacterial densities were determined at 0, 2, 4, 6, 8, 12, and 24 hours.
RESULTS: The MIC50, MIC90 and %S were: DOX (4, 64, 50%), MER (64, 128, 6%), AMK (128, > 128, 0%), and CIP (64, 128, 4%). Overall, 83% were positive for MBL. DOX was bacteriostatic against MDR ACN with MICs = 1 for the entire 24 hrs. For isolates with MICs 4–16, DOX was bacteriostatic over the first 8-12 hrs before regrowth occurred by 24 hours. Kill curves for MDR ACN with DOX MICs = 64 resembled the growth controls.
CONCLUSIONS: According to our results, DOX appears to be a viable option for MDR ACN. Further investigation of DOX and combinations seem to be warranted for the treatment of MDR ACN.

105. **Evaluation of methodology in meta-analyses in the infectious disease (ID) literature.** *Supriya A. Bavadekar, Ph.D.*, Eve C. Elias, Pharm.D., Katie J. Suda, Pharm.D.; University of Tennessee Health Science Center, Memphis, Tenn.

PURPOSE: Health care professionals are using meta-analyses increasingly to make patient care decisions even though these studies are known to have methodological weaknesses. However, a study has not been conducted to determine if a detailed search of secondary databases was completed to identify studies for inclusion in the meta-analyses. The aim of this study was to examine the sources used for location and selection of studies, and the usage of study quality validation tools (SQVT) in ID meta-analyses.
METHODS: A Medline search using "meta-analyses" and "bacterial infections and mycoses" as MeSH terms limited to humans, English, and publication in the last 10 years was conducted to retrieve relevant meta-analyses. Articles were examined for language restrictions, sources searched for identification of studies constituting the meta-analyses, and prevalence of utilization of SQVT. A Fischer's Exact test was used for statistical analysis; $p < 0.05$ was considered significant.
RESULTS: Out of 27 meta-analyses selected and analyzed, 37% restricted their search to English. 96% reported usage of Medline, whereas usage of EMBASE, IPA, CINAHL, and Cochrane was found to be 30%, 0%, 7%, and 19%; respectively. Only 35% of the meta-analyses searched more than one database. Only 4% reported using clinical trial registries, while none reported use of any other Internet search engine. Further, searches of references of published studies and meeting abstracts were 48% and 19%, respectively. Only 19% of the reports evaluated the study quality. Meta-analyses that searched multiple databases utilized the SQVT and searched references of published studies more frequently ($p < 0.05$ for all).
CONCLUSIONS: This study has identified several inadequacies in ID meta-analyses in terms of sources used for identification of relevant studies and SQVT used for determining individual study methodology quality. Surprisingly, few studies limited their search to English. Correction of these flaws is imperative to make meta-analyses clinically robust.

106E. Levofloxacin (LEV) and cefepime (CFP) alone and in combination against multidrug-resistant ESBL *E. coli* and *Klebsiella* sp. *David S. Burgess, Pharm.D., FCCP*[1], Michael F. Carden, EMT[2]; (1) Center for Advancement of Research and Education in Infectious Diseases, University of Texas at Austin College of Pharmacy, San Antonio, Tex; (2)University of Texas Health Science Center at San Antonio, San Antonio, Tex.

PURPOSE: Fluoroquinolones (FQs) and fourth-generation CEPHS are commonly used as empiric therapy. However, infections due to ESBL producing organisms continue to increase worldwide. Because controversy exists for the appropriate breakpoint for CEPHs against ESBL organisms and the utility of FQ in these infections, we assessed the activity of LEV and CFP alone and in combination against MDR ESBL-producing organisms.
METHODS: MICs were determined for 83 ESBL positive clinical isolates (40 *E. coli*, 27 *K. pneumoniae*, 16 *K. oxytoca*) using CLSI methodologies. Time-kill curves were performed against 14 representative isolates based on the MICs for LEV. Kill curves were performed using a standard inoculum in duplicate for LEV (4 mcg/mL) and CFP (16 mcg/mL) alone and in combination. Samples were obtained at 7 timepoints over 24 hrs to determine bacterial densities.
RESULTS: The MIC50, MIC90, and %S were: LEV (16, >32, 26%) and CFP (8, 32, 59% for MIC ≤ 8 and 27% for MIC ≤ 2). For LEV susceptible isolates (n=5), LEV reached and maintained bactericidal activity over the 24 hours. For LEV resistant isolates (n=9), the curves resembled the growth control. For CFP, the kill curves could be divided into 4 separate groups. For isolates with CFP MICs ≤ 2 (n=4), CFP reached and maintained bactericidal activity for the 24 hours. For those isolates with MICs 4–16 (n=5), CFP reached bactericidal but regrowth occurred by 24 hours. For isolates with CFP MICs of 32 (n=2), CFP was bacteriostatic and regrowth occurred; whereas those isolates with ≥ 64 (n=3) resembled the growth control. The combination of LEV and CFP did not produce any antagonism or synergy for any isolate.
CONCLUSIONS: This study supports the current CLSI breakpoints for LEV and suggests that CFP breakpoint should be ≤ 2 for ESBL organisms. Finally, the combination of LEV and CFP does not provide any additional benefit.
Presented at the 47th ICAAC, Chicago, Ill, September 17-20, 2007.

107E. In vitro activity of colistin (COL) against multidrug-resistant (MDR) *Acinetobacter baumannii* (ACN). *David S. Burgess, Pharm.D., FCCP*[1], Michael F. Carden, EMT[2], Surakit Nathisuwan, Pharm.D., BCPS[3], Pitak Santanirand, Ph.D.[4], Kumthorn Malathum, M.D.[4]; (1)Center for Advancement of Research and Education in Infectious Diseases, University of Texas at Austin College of Pharmacy, San Antonio, Tex; (2)University of Texas Health Science Center at San Antonio, San Antonio, Tex; (3)Faculty of Pharmacy, Mahidol University, Bangkok, Thailand; (4)Faculty of Medicine at Ramathibodi Hospital, Bangkok, Thailand.

PURPOSE: Infections caused by MDR-ACN are now a serious threat in tertiary-care settings worldwide, especially in Southeast Asia. Treatment of such infection is a major challenge. In many countries, COL has become the only viable option against MDR-ACN despite limited information on its efficacy. The objective of this study was to evaluate the in vitro killing activity of COL against MDR ACN.
METHODS: Forty-eight clinical isolates of MDR-ACN were collected from a tertiary care hospital in Thailand. MICs were determined against COL, meropenem (MER), imipenem (IMI), cefepime (CFP), piperacillin/tazobactam (PTZ), amikacin (AMK), and levofloxacin (LEV) according to CLSI guidelines. All isolates were screened for metalo-ß-lactamase using the MBL E-strip. For 19 isolates, time-kill curves were performed against COL at 4 mcg/mL using a standard inoculum. These isolates were selected based on MICs to COL. Bacterial densities were determined at 0, 2, 4, 6, 8, 12, and 24 hours.
RESULTS: The MIC50, MIC90 and %S were: COL (0.5, 1, 100%), MER (64, 128, 6%), IMI (128, < 128, 2%), CFP (128, 128, 0%), PTZ (1024, 2048, 0%), AMK (128, > 128, 0%), and LEV (8, 32, 6%). Overall, 83% were positive for MBL. For isolates with COL MIC's ≤ 0.25 (n=5), COL was able to achieve ≥ 3 log decrease in CFU/mL within 4-6 hr and maintained bactericidal activity for the entire 24 hours. However isolates with MICs of 0.5–2 (n=14), COL displayed rapidly bactericidal activity but regrowth was observed for all isolates by 24 hrs.
CONCLUSIONS: COL possesses a rapid and sustained bactericidal activity against MDR-ACN with MICs ≤ 0.25. Nevertheless, such effect was not seen with MDR-ACN with MIC ≥ 0.5. Therefore, COL may not be reliable as monotherapy against MDR-ACN with MIC ≥ 0.5. Further investigation for COL in combination with other agents is warranted.
Presented at the 47th ICAAC, Chicago, Ill, September 17-20, 2007.

108. **Impact of oseltamivir for the treatment of influenza on secondary complications and health care costs.** *John G. Gums, Pharm.D.*[1], William A. Blumentals, Ph.D.[2], Elise M. Pelletier, M.S.[3]; (1)University of Florida, Gainesville, Fla; (2)Roche Laboratories, Nutley, NJ; (3)Pharmetrics, Watertown, Mass.

PURPOSE: To assess the impact of oseltamivir (Tamiflu®) on secondary infectious disease complications and health care costs in a managed care population.
METHODS: This retrospective cohort study used health insurance claims data (PharMetrics Patient-Centric Database) from October 1, 2001, through March 31, 2006, to identify patients diagnosed with influenza. Influenza patients prescribed oseltamivir within 1 day of diagnosis were propensity matched in a 1:1 ratio with those not prescribed antiviral therapy. Clinical outcomes assessed over 30 days included frequency of diagnosis with pneumonia and otitis media and rates of hospitalization for any reason. Comparisons of the frequency of pneumonia, otitis media, and hospitalization were expressed in terms of odds ratios (OR) and 95% confidence intervals (CI). Inpatient, outpatient, and pharmacy costs within 30 days of influenza diagnosis also were analyzed.
RESULTS: Propensity matching resulted in 45,751 patients in each group. Patients receiving oseltamivir had a statistically significant reduction in the risk of diagnosis of pneumonia by 11% (OR = 0.89; 95% CI = 0.80–1.00), of diagnosis of otitis media by 16% (OR = 0.84; 95% CI = 0.77–0.91) and of hospitalization by 29% (OR = 0.71; 95% CI = 0.62–0.83). Patients prescribed oseltamivir had significantly lower total healthcare costs compared with controls (mean [SD]; \$500 [2997] vs. \$510 [3265], p<0.0001). The costs of hospitalizations and outpatient care were lower in patients receiving oseltamivir (\$108 [2726] vs. \$134 [3030], p<0.0001, and \$270 [1049] vs. \$302 [936], p<0.01, respectively); however, pharmacy costs were higher in the oseltamivir cohort (\$122 [277] vs. \$74 [346], p<0.0001).
CONCLUSION: Oseltamivir reduced the risk of influenza-related secondary complications and was cost-effective for the treatment of influenza.

109E. **In vivo efficacy of doripenem human-simulated exposures against *Pseudomonas aeruginosa*.** *Aryun Kim, Pharm.D.*, Mary A Banevicius, B.S., David P Nicolau, Pharm.D., FCCP; Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, Conn.

PURPOSE: Doripenem (DOR) is an investigational broad-spectrum carbapenem with activity against a wide range of Gram-negative pathogens, including non-fermenting bacteria such as *P. aeruginosa* (PSA). The purpose of the study was to evaluate human-simulated exposures of DOR against PSA isolates with a wide range of MICs.
METHODS: Clinical PSA isolates with DOR MICs (µg/mL) 0.125–16 were used. The pharmacokinetic profile of DOR in mice was assessed to design regimens that approximated the free time above MIC ($fT > MIC$) observed with DOR 500 mg every 8 hours given as either a 1 hour or 4 hour IV infusion in humans. DOR 10, 15, 2.5, 1.25, 0.5, 0.25 mg/kg dosed subcutaneously in mice at 0, 0.5, 2.5, 4, 5.5, 7 hours in three 8-hour intervals best depicted the human $fT > MIC$ of 1 hour infusion regimen, whereas DOR 5.5, 2.25, 4.5, 4.5, 4.5, 4.5, 0.75, 0.375 mg/kg at 0, 0.5, 1.5, 2.5, 3.5, 4.5, 6, 7.5 hours simulated the human $fT > MIC$ of 4 hour infusion regimen. A neutropenic murine thigh model was used to examine the antibacterial effects of simulated DOR 1-hour and 4-hour infusions against 24 and 11 isolates, respectively.
RESULTS: The simulated 1-hour infusion provided bactericidal effects for PSA with MIC ≤ 2. Variable kill was noted for isolates with MICs 4–8, while regrowth was observed with MIC=16. Maximal antibacterial kill was associated with DOR exposures ≥ 40% $fT > MIC$; bacteriostatic effects were noted ≈20% $fT > MIC$. The 4-hour infusion regimen displayed similar kill for MIC ≤ 2, and enhanced activity for 2 of 4 PSA with MIC = 4. Given that the 4-hour regimen yields negligible $fT > MIC$ for MIC ≥ 8, regrowth was generally observed.
CONCLUSIONS: Simulated doses of DOR 500 mg every 8 hours infused over 1 hour demonstrated antibacterial kill for PSA with MICs 0.125–8. Exposures ≥ 40% $fT > MIC$ resulted in the most pronounced bactericidal effects while kill was variable for ≈20%–30% $fT > MIC$. Doses infused over 4-hour enhanced efficacy against selected pseudomonal isolates with MIC = 4.
Presented at Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, Ill, September 17-20, 2007.

110. **Steady-state pharmacodynamics of meropenem 500 mg every 6 hours versus 1 gram every 8 hours in hospitalized patients.** Christian Cheatham, Pharm.D.[1], *Michael B. Kays, Pharm.D.*[2], David W. Smith, Pharm.D.[3], Matthew F. Wack, M.D.[4], Kevin M. Sowinski, Pharm.D.[2]; (1)St. Francis Hospitals and Health Centers, Beech Grove, Ind; (2)Purdue University School of Pharmacy, Indianapolis, Ind; (3) Clarian Health Partners, Inc., Methodist Hospital, Indianapolis, Ind; (4)Infectious Diseases of Indiana, Indianapolis, Ind.

PURPOSE: Previous studies have compared the pharmacodynamics of meropenem 500 mg every 6 hours (q6h) and 1 gram every 8 hours using pharmacokinetic data from volunteers. The objective was to compare the

steady-state pharmacodynamics of meropenem 500 mg q6h and 1 gram q8h using pharmacokinetic data from hospitalized patients.

METHODS: Meropenem 500 mg q6h, infused over 30 minutes, was administered to hospitalized patients with a suspected or proven bacterial infection and creatinine clearance > 60 mL/minute. At steady state, serial blood samples were obtained, and meropenem concentrations were determined by HPLC. Pharmacokinetic parameters were estimated using ADAPT II (release 4), and 10,000 patient Monte Carlo simulations were performed for 500 mg q6h and 1 g q8h against *E. coli*, *K. pneumoniae*, Enterobacter species, *S. marcescens*, Citrobacter species, *P. aeruginosa*, and Acinetobacter species (MYSTIC 2004-2005, USA). The cumulative fraction of response (CFR) of $fT > MIC \geq 40\%$ was calculated for each regimen, and the results were compared.

RESULTS: Nine patients completed the pharmacokinetic study. Demographic data (mean ± SD) were as follows: age, 43 ± 16 years; weight, 87 ± 23 kg; CrCl, 89 ± 13 ml/min. Meropenem pharmacokinetic parameters (mean ± SD) were as follows: Cmax, 28.8 ± 10.9 µg/ml; Cmin, 2.2 ± 1.4 µg/ml; Cls, 10.9 ± 3.0 L/hr; Vss, 32.1 ± 10.5 L; half-life, 2.3 ± 1.1 h. The CFR for both regimens was very similar for all bacterial species evaluated, differing by ≤ 2.8%. The CFR was ≥ 97.4% for both regimens against the enteric bacteria. The CFR for *P. aeruginosa* was 90.4% for 500 mg q6h and 92.8% for 1 g q8h. For Acinetobacter species, the CFR was 82.9% and 85.7% for 500 mg q6h and 1 g q8h, respectively.

CONCLUSIONS: Using pharmacokinetic data from hospitalized patients, meropenem pharmacodynamics are comparable at 500 mg q6h and 1 g q8h against common gram-negative nosocomial pathogens.

111. Cost drivers for nosocomial vancomycin-resistant enterococcus infections (NVREIs). Cassandra D. Salgado, M.D., M.S., Patrick D. Mauldin, Ph.D., Valerie L. Durkalski, Ph.D., *John A. Bosso, Pharm.D.*; Medical University of South Carolina, Charleston, SC.

PURPOSE: NVREIs have been associated with increased length of stay (LOS) and higher cost of care. We describe cost drivers for 19 adult patients with NVREI at our hospital from 2000 to 2005.
METHODS: Patient characteristics (infection, receipt of chemotherapy, neutropenia, TPN, surgery, and antibiotics); total hospital, ICU, and drug cost; and LOS for each patient was recorded. Cost of each hospitalization was calculated as the product of billed charges for the hospital episode and the hospital's overall cost-to-charge ratio for that year from the Medicare cost report. The effect that patient characteristics had on total hospital and ICU cost and LOS were analyzed. Categorical and continuous variables were assessed using t-tests and Pearson correlation analysis, respectively. Equality of variances was assessed.
RESULTS: The mean total hospital cost for patients with NVREI was $115,260. There was no significant correlation between total cost and any patient characteristic. Mean drug cost for patients with NVREI was $37,171. Central line-associated bloodstream infection (CLABSI) was identified as a cost driver for significantly increased drug cost (p=0.0045), and surgery was associated with significantly decreased drug cost (p=0.0045). Mean LOS for patients with NVREI was 38.7 days. There was no significant correlation between LOS and any patient characteristic. Mean ICU cost among 12 patients with NVREI was $24,681. There was no significant correlation between ICU cost and any patient characteristic. Quinolones were the only antibiotics associated with increased total hospital cost, ICU cost, drug cost, and LOS (Pearson coefficients of 82%, p<0.0001, 90%, p<0.0001, 59% p=0.008, and 82%, p<0.0001, respectively).
CONCLUSIONS: In this pilot study of patients with NVREI, CLABSI was identified as a cost driver for significantly increased drug cost, whereas surgery was associated with decreased drug cost. Most antibiotics do not appear to be significant cost drivers among these patients.

112E. Characteristics and costs associated with nosocomial MRSA and VRE infections. *John A. Bosso, Pharm.D.*, Cassandra D. Salgado, M.D., M.S., Valerie L. Durkalski, Ph.D., Patrick D. Mauldin, Ph.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Infections due to MRSA and VRE have been associated with prolonged length of hospital stay (LOS) and increased health care costs. We assessed patient characteristics, LOS, and costs associated with the care of adult patients with nosocomial MRSA or VRE infections at our tertiary care hospital from 2000 to 2005.
METHODS: Patient characteristics, including type and number of infections; receipt of ICU care, chemotherapy, or TPN; diabetes; neutropenia; transplantation; surgery; and antibiotics used were recorded as well as LOS and total hospital, ICU, and drug costs. Cost of each hospitalization was calculated as the product of billed charges for the hospital episode and the hospital's overall cost-to-charge ratio, from the Medicare cost report. Patient characteristics and costs of care of MRSA-infected patients were compared to those of VRE-infected patients. Continuous and categorical variables were analyzed using t-tests, Fisher Exact test or Chi-square statistic, as appropriate.
RESULTS: 206 patients developed nosocomial MRSA (187) or VRE (19) infections over the study period. There were no statistical differences in total hospital cost, ICU cost, drug cost, or LOS between the two groups. The

mean total hospital cost for MRSA-infected patients was $110,493 and for VRE-infected patients was $115,260. Ciprofloxacin use was significantly higher (p=0.0233) among MRSA-infected patients (1.52 ddd/1000 vs 0.67 ddd/1000 pt days) as was the proportion with surgery (52% vs 21%, p=0.008). The proportion of patients with a central line-associated bloodstream infection, who received chemotherapy or who had neutropenia, was significantly higher among VRE-infected patients than among MRSA-infected patients (78% vs 29%, p<0.0001, 15% vs 3%, p=0.04, 31% vs 2%, p<0.0001, respectively).

CONCLUSIONS: Risk factors for nosocomial MRSA and VRE infections may be different among patients at our hospital; however, LOS and cost of care do not appear to differ appreciably.

Presented at Annual Meeting of the Infectious Diseases Society of America, San Diego, Calif, October 4-7, 2007.

113E. **Efficacy of antimicrobials for acute exacerbation of chronic bronchitis episodes.** *Christopher J. Destache, Pharm.D., FCCP*, Mark A. Malesker, Pharm.D., FCCP, Julie A. Chang, M.D., Lee E. Morrow, M.D., FCCP, Dan Schuller, M.D., FCCP; Creighton University Medical Center, Omaha, Neb.

PURPOSE: Efficacy of antimicrobials for managing acute exacerbations of chronic bronchitis (AECB) episodes to prevent hospitalizations and slow decline in pulmonary function in patients with chronic obstructive pulmonary disease (COPD) is controversial.

METHODS: Medical records of COPD patients seen in an outpatient Pulmonary Clinic were retrospectively reviewed to capture AECB episodes and antimicrobial selection. Antimicrobial failure was defined as an AECB episode that did not respond to therapy and that necessitated a new antimicrobial prescription within 14 days.

RESULTS: A total of 1185 medical records were reviewed; 42 patients had 103 episodes between January 1, 2000, and June 30, 2006. Each patient averaged 2.5 exacerbations (range 1–19), which required antimicrobial therapy with or without corticosteroids. Mean (± SD) age, weight, and body mass index were 59.9 ± 10.1 years, 169.6 ± 54.9 pounds, and 28.1 ± 8 kg/m2. Fifty one episodes (49%) were patients receiving home oxygen. A total of 86% and 54% of AECB episodes were patients receiving inhaled or combination inhaled and oral corticosteroids. Mean antimicrobial therapy was 8.6 ± 4.0 days. Overall, 80% of episodes were successfully treated. Antimicrobial failure rates were significantly higher (p<0.05) with macrolides (azithromycin or clarithromycin 39%) compared with fluoroquinolones (levofloxacin and moxifloxacin 18%). AECB episodes treated with amoxicillin/clavulanate had an intermediate failure rate (25%). Significantly more AECB episodes were successful if the patient was seen in the clinic compared with a phone-in prescription (76% vs. 26%, p<0.05).

CONCLUSIONS: AECB episodes given fluoroquinolones were treated successfully more often than those treated with other antimicrobial categories.

Presented at Annual Meeting of the American College of Chest Physicians, Chicago, Ill, October 20-25, 2007.

114. **Daptomycin for treatment of vancomycin-resistant *Enterococcus* bloodstream infections.** *Benjamin D. Brielmaier, Pharm.D.*[1], Richard M. Reichley, R.Ph.[1], Ed Casabar, Pharm.D.[1], Nathan A. Ledeboer, Ph.D.[2], Gourang P. Patel, Pharm.D.[3], Christopher W. Crank, Pharm.D., BCPS[3], John A. Segreti, M.D.[3], David J. Ritchie, Pharm.D., FCCP, BCPS[4]; (1)Barnes-Jewish Hospital, St. Louis, Mo; (2)Washington University School of Medicine, St. Louis, Mo; (3)Rush University Medical Center, Chicago, IL; (4)Barnes-Jewish Hospital and St. Louis College of Pharmacy, St. Louis, Mo.

PURPOSE: Bloodstream infections (BSIs) due to vancomycin-resistant *Enterococcus* (VRE) are a significant source of morbidity and mortality. Existing treatment options are limited and are commonly associated with adverse effects and drug interactions. Daptomycin possesses *in vitro* activity against VRE and an apparent favorable safety profile; however, clinical data are limited. We describe our experience with daptomycin for treatment of VRE BSIs.

METHODS: Patients receiving daptomycin for VRE BSIs (≥ 2 positive blood cultures and evidence of infection) from 2003-2006 were retrospectively evaluated. Patient, microbiologic, and drug administration data were collected. A favorable treatment outcome was defined as clinical response and documented or presumed microbiologic eradication.

RESULTS: Sixty-seven patients were identified. Patients had a median of three positive blood cultures (range 2–23) (85.1% *E. faecium*, 11.9% *E. faecalis*, 3.0% *E. faecium* and *E. faecalis*). The mean initial dose of daptomycin was 5.49 mg/kg every 24–48 hours. Seven patients (10.4%) had subsequent dose escalations (mean 7.1 mg/kg). Patients were bacteremic for a median of 1.0 day (range 0–20) after starting daptomycin. Fifteen patients (22.4%) had persistent bacteremia (≥ 5 days of positive cultures on daptomycin). BSIs were most commonly line-related (50.7%). Common patient characteristics were acute renal failure (47.8%), neutropenia (44.8%), ICU status (43.3%), solid organ or bone marrow transplantation (41.8%), hemodialysis or continuous renal replacement therapy (37.3%), and mechanical ventilation (34.3%). Two patients (3.0%) had creatinine phosphokinase elevations. Favorable treatment outcomes were observed in 49.3% of patients with a crude in-hospital mortality

rate of 46.3%. Favorable outcome rates were higher in patients with dose escalations than in those receiving the same dose throughout therapy [5/7 (71.4%) versus 28/60 (46.7%)].
CONCLUSIONS: Daptomycin is a viable, well-tolerated treatment option for VRE BSIs, although overall mortality remains high. The most appropriate daptomycin dose for optimal outcomes in VRE BSIs is unknown and merits future research.

115. **Heterogeneous variations in gram-negative pathogen susceptibility to fluoroquinolones within the State of Florida from 1997-2005: results from the Antimicrobial Resistance Management (ARM) program.** *Shawn D. Anderson, Pharm.D.*, John G. Gums, Pharm.D.; University of Florida, Gainesville, Fla.

PURPOSE: To prevent antimicrobial resistance, the CDC recommends diagnosing and treating infection effectively by targeting the pathogen and using antimicrobials wisely based on local data. Using data from the ARM program, this study examined the intrastate susceptibility patterns of select gram negative pathogens to fluoroquinolone antibiotics.
METHODS: Florida hospitals were grouped into North/Panhandle, Central, and South regions for comparison. Select gram negative organisms in the ARM database were identified to determine susceptibility rates to fluoroquinolone antibiotics between 1997 and 2005. Antibiograms and sensitivity reports for isolates of *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, and Serratia marcescens* were reviewed for susceptibility to fluoroquinolones (ciprofloxacin and levofloxacin).
RESULTS: In all regions, *E coli* isolate sensitivity decreased to ciprofloxacin (n=135,509) and levofloxacin (n=94,663), with the greatest decreases seen for ciprofloxacin (96%–71%) and levofloxacin (94%–71%) in the South. *K pneumoniae* isolate sensitivity remained relatively stable to ciprofloxacin (n=42,370) and levofloxacin (n=29,486) in all regions, with the exception of decreased susceptibility to ciprofloxacin in the Central region (98%–92%). Reduced *P mirabilis* susceptibility to ciprofloxacin (n=29,877) and levofloxacin (n=21,939) occurred in all regions although the South exhibited the highest susceptibilities to ciprofloxacin (90%–80%) and levofloxacin (87%–85%). For the most part, *P aeruginosa* susceptibility to ciprofloxacin (n=73,036) and levofloxacin (n=45,952) remained stable in all regions, with the lowest susceptibilities to levofloxacin in the North (64%–53%). For *S marcescens*, susceptibilities to ciprofloxacin (n=8,280) and levofloxacin (n=6,485) remained stable in the North and Central regions, while decreasing in the South: 90%–80% for ciprofloxacin and 98%–92% for levofloxacin.
CONCLUSIONS: Data from the ARM Program can assist in identifying and screening for heterogeneous differences in antimicrobial susceptibility, allowing resources to be directed to a local area with an identified resistance issue.

116. **Pharmacodynamic evaluation of levofloxacin 500 mg and 750 mg once daily using sex-specific pharmacokinetic and MIC data.** *Michael B. Kays, Pharm.D.*[1], Brian R. Overholser, Pharm.D.[1], Ronald N. Jones, M.D.[2], Kevin M. Sowinski, Pharm.D.[1]; (1)Purdue University School of Pharmacy, Indianapolis, Ind; (2)JMI Laboratories, North Liberty, Iowa.

PURPOSE: Levofloxacin pharmacokinetics differ significantly between men and women, but the pharmacodynamic significance of these findings is unknown. The objective was to evaluate the pharmacodynamics of levofloxacin 500 mg and 750 mg once daily using sex-specific pharmacokinetic and MIC data.
METHODS: Levofloxacin pharmacokinetic data for men and women were obtained from a study published by our research group. MICs for isolates recovered from men and women were obtained from the SENTRY Antimicrobial Surveillance Program (2004-2005) for *E. coli* (n=944 [men]; n=1374 [women]), *K. pneumoniae* (n=576 [men]; n=496 [women]), Enterobacter species (n=473 [men]; n=319 [women]), *S. marcescens* (n=239 [men]; n=169 [women]), *P. aeruginosa* (n=758 [men]; n=494 [women]), Acinetobacter species (n=187 [men]; n=142 [women]), and *S. pneumoniae* (n=1367 [men]; n=783 [women]). Monte Carlo simulations (10,000 subjects) were performed using the pharmacokinetic and MIC data for men and women. The cumulative fraction of response (CFR) was calculated for levofloxacin 500 mg and 750 mg once daily against the gram-negatives (AUC_{24}/MIC $\geq$ 87) and *S. pneumoniae* ($fAUC_{24}$/MIC $\geq$ 33.7).
RESULTS: For the enterics and *P. aeruginosa*, the CFR was 1.1%–6.7% greater in women for the 500 mg dose and 0.4%–6.7% greater in women for the 750 mg dose. For Acinetobacter species, the CFR was 4.9% and 6.3% greater in men at 500 mg and 750 mg, respectively. For *S. pneumoniae*, the CFR was 45.3% greater in women (42.0% for men, 87.3% for women) for the 500 mg dose. At the 750 mg dose, the CFR was 2.6% greater in women (96.0% for men, 98.6% for women).
CONCLUSIONS: Sex-related differences in levofloxacin pharmacokinetics result in minimal pharmacodynamic differences between men and women for the gram-negative pathogens evaluated. For *S. pneumoniae*, the CFR was

substantially greater in women at the 500 mg dose, suggesting that levofloxacin 750 mg should be used to treat pneumococcal infections, especially in men.

117. Outcomes associated with *Clostridium difficile*-associated diarrhea in patients who received gastric acid suppression. *Paul Juang, Pharm.D.*[1], Heather Kohlhaas, Pharm.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, Mo; (2)Missouri Baptist Medical Center, St. Louis, Mo.

PURPOSE: The incidence and severity of *Clostridium difficile*-associated disease (CDAD) is increasing, and recently it has been speculated that decreasing gastric acidity might increase the risk of CDAD. However, no studies to date have examined the outcomes of patients with CDAD on gastric acid suppressants. The purpose of this study is to determine whether there are outcome differences associated with CDAD in inpatients who received gastric acid suppressants (GAS) versus those who did not.
METHODS: Single-center, retrospective chart audit of hospitalized patients with positive *Clostridium difficile* toxin assay and associated disease. The primary outcome was length of hospital stay and duration of antibiotic treatment for CDAD. Secondary outcomes were discharge disposition, mortality, and timing of CDAD.
RESULTS: Fifty patients with CDAD were identified with 33 receiving GAS and 17 who did not. No significant differences were observed in the baseline characteristics between groups except that a greater number of patients in the GAS group carried a neurological disease history. There was no difference between groups in regard to time from admission until diagnosis of disease, duration until initiation of antibiotics after admission, length of antibiotic use until CDAD and discharge disposition. Patients receiving GAS had a longer length of hospital stay than those in the control group (14.6 vs. 9.5 days, p=0.012) as well as a longer duration of CDAD treatment (7.9 vs. 4.3 days, p<0.001). The mortality rate was higher in the GAS patients compared to controls, however, this was not statistically significant. Patients receiving GAS had a longer duration of antibiotic use compared with controls, however, this was not statistically significant.
CONCLUSION: Concomitant use of GAS in patients with CDAD may increase hospital morbidity. This trial was not adequately powered to determine whether there is an increase risk of CDAD in patients who receive GAS.

118. Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CMRSA): Vancomycin (VAN) Susceptibility Trends at a Veteran Affairs Healthcare System. Pamela A. Moise, Pharm.D.[1], *Caroline K. Sul, Pharm.D.*[2], Scott T. Johns, Pharm.D.[2], John S. Andrews, M.D., M.S.[3], George Sakoulas, M.D.[4]; (1)University of the Pacific/VA San Diego Healthcare, San Diego, Calif; (2)VA San Diego Healthcare, San Diego, Calif; (3)Pfizer Inc., La Jolla, Calif; (4)New York Medical College., Valhalla, NY.

PURPOSE: Recent studies have demonstrated increases in VAN MICs among clinical *S. aureus* isolates under increasing VAN selection pressure, with consequences on VAN treatment efficacy. Due to the emergence of CMRSA, and now with a case of VAN-resistant CMRSA in California, it is anticipated that clinicians would be interested in VAN MIC trends in the community setting. We evaluated VAN MICs of MRSA isolates from patients with community onset infections (as defined by CDC).
METHODS: Patients who received systemic antibiotic therapy targeted against CMRSA in the years 1998-2006 at the VA San Diego Healthcare System were analyzed retrospectively for MRSA VAN MIC (Vitek), site of infection (blood, respiratory, wound), and previous IV VAN use (within 30 days prior to MRSA culture).
RESULTS: 79 unique patients with clinically significant CMRSA were analyzed from 1998 to 2006. The median age was 55 (range 33–83) years. VAN MICs were 0.5 (43%), 1.0 (48%), and 2.0 mcg/mL (9%). CMRSA showed an increase in VAN MIC in 2004-2006 compared with 2001-2003 (p<0.005). 36% of CMRSA in 2001-2003 had VAN MIC of > 1.0 mcg/mL; and 90% of CMRSA in 2004-2006 did. 3% of patients with CMRSA had prior VAN use.
CONCLUSIONS: VAN MICs in patients with CMRSA were significantly higher in more recent years. Evaluations of the VAN MIC creep among clinical CMRSA may be confounded by the potential increase use of VAN in the community, and the spread of CMRSA in the community. In light of these findings, quantitative VAN MIC's should be considered on an individual case basis.

119. Antibiotic exposures and treatment outcome assessment for *Clostridium difficile*-associated diarrhea in a large urban teaching community hospital. *Lisha C. Kronmann, Pharm.D.*[1], Molly L. Marten, M.P.H.[2], Donna L. Agan, Ed.D.[2], Karl C. Kronmann, M.D., M.P.H.[3], Harminder Sikand, Pharm.D.[1]; (1)Scripps Mercy Hospital/Cardinal Health, San Diego, Calif; (2)Scripps Mercy Hospital, San Diego, Calif; (3)Balboa Naval Medical Center, San Diego, Calif.

OBJECTIVE: *Clostridium difficile*-associated diarrhea (CDAD) is a growing problem nationally. The purpose of this IRB-approved study was to evaluate antibiotic risk factors and efficacy of treatment regimens at our institution. The results of this study will guide prevention, diagnosis, and treatment protocols.

METHODS: A medical record review of all *Clostridium difficile* toxin positive patients identified from January 2006 thru July 2006 was conducted. The primary end point was to measure antibiotic exposure prior to diagnosis of CDAD. The secondary end points were appropriateness of CDAD treatments and patient outcomes. Patient's medical histories were analyzed for exposure type (community versus nosocomial), antibiotic use, indication, CDAD treatment regimen, timing of diagnosis, number of toxin tests to positive result, and patient outcome (death, colectomy, recurrence, or no recurrence).

RESULTS: A total of 98 patients with CDAD were identified. The incidence during this time period was 8.5 cases per 1000 admissions. The most prevalent antibiotic exposures were cephalosporins (57.1%), levofloxacin (48.9%), vancomycin (39.8%), piperacillin/tazobactam (31.6%), and clindamycin (20.4%). Initial treatment regimens were appropriate in 84.7% of cases. Thirty percent of the patients treated initially with an inappropriate regimen had severe outcomes (colectomy or death) versus 9.6% in the appropriate treatment group. The difference in outcomes trended toward statistical significance ($p=0.09$). Sensitivity analysis indicated that to achieve 90% sensitivity, an initially negative toxin test should be repeated two additional times.

CONCLUSION: Cephalosporins and fluoroquinolones were the most common antibiotics used in our population and are risk factors for CDAD per current medical literature. Results suggest that initial inappropriate CDAD regimens may potentially lead to higher morbidity and mortality and support the need for CDAD-related protocols. Our data also suggests that enzyme immunoassay toxin tests should be performed at least 3 times to confidently rule out CDAD in our population.

120. **Outpatient use of newer macrolides and fluoroquinolones.** *Makiko Iwasawa, Pharm.D.*, Jeff King, Pharm.D.; Robert M. Mowers, Pharm.D., Cinda Christensen, Pharm.D., Javeed Siddiqui, M.D., Hien Nguyen, M.D.; University of California Davis Health System, Sacramento, Calif.

PURPOSE: Appropriate use of antibiotics is essential to improve patient outcomes and prevent antibiotics resistance. Outpatient utilization patterns of broad-spectrum antibiotics at UC Davis Health System (UCDHS) are unknown. The purpose of this study is to determine how oral macrolide and fluoroquinolone (FQ) antibiotics are being used in the outpatient arena. After reviewing the current utilization patterns, we plan to develop educational programs promoting optimal antibiotics selection.

METHODS: Retrospective prescription claim data from managed care plans was analyzed to obtain all prescriptions filled for oral FQ and macrolides between July 1, 2005, and June 30, 2006. Prescriptions were written by the UCDHS Primary Care Network physicians. Fifty prescriptions from each antibiotic class were selected randomly and reviewed for indication, dosing, length of therapy, and contraindications. Previous antimicrobial histories were collected for a 6-month time period. Antibiotic use was compared to national consensus guidelines and reviewed by an Infectious Disease physician and pharmacist for appropriateness.

RESULTS: Of the FQ reviewed, the prescribed indications include uncomplicated urinary tract infection (UTI) (40%), acute sinusitis (18%), and acute bronchitis (8%). The mean duration of therapy for acute cystitis was 5.8 days despite IDSA guidelines of 3 days. The second most prescribed indication of FQ use was sinusitis although nearly all cases of acute sinusitis resolve without antibiotics. Of the macrolides reviewed, the prescribed indications include acute bronchitis (40%), acute sinusitis (22%), and acute otitis media (8%). More than 90% of acute bronchitis is viral, and antibiotic drug use is not recommended.

CONCLUSIONS: The results show that FQ and newer macrolides are overprescribed at UCDHS primary care clinics. To improve appropriate antibiotic utilization, a newer approach to promote appropriate antibiotic use will be necessary.

121. **Relationship between broad-spectrum antimicrobial consumption and antimicrobial resistance among gram-negative hospital isolates in a tertiary-care hospital of Thailand.** *Surakit Nathisuwan, Pharm.D., BCPS*[1], Sumaiporn Praisukhwisal, M.S.[1], Kumthorn Malathum, M.D.[2], Pitak Santanirand, Ph.D.[2], Piriyaporn Chongtrakool, Ph.D.[2]; (1)Faculty of Pharmacy, Mahidol University, Bangkok, Thailand; (2)Faculty of Medicine at Ramathibodi Hospital, Bangkok, Thailand.

PURPOSE: This retrospective study was conducted to assess the relationships of resistance rates of *E. coli* (EC), *K. pneumoniae* (KP), *P. aeruginosa* (PA) and *Acinetobacter* spp. (AC) and consumption of broad spectrum antibiotics during 1994–2005, at a tertiary-care hospital in Bangkok, Thailand.

METHODS: Hospital isolates of organisms of interest and their susceptibility patterns during 1994–2005 were collected. Consumption of broad-spectrum parenteral antibiotics from the same period were also collected and analyzed. Correlation between antibiotic consumption and resistance were analyzed by Pearson's correlation. Autoregressive integrated moving average (ARIMA) model was used to predict the incidence trend of resistance rates through the fourth quarter of 2010.

RESULTS: Antimicrobial agents with highest volume of use were cephalosporins (181 DDD/1000 patient-days), especially ceftriaxone (102 DDD/1000 patient-days) followed by carbapenems (54.56 DDD/1000 patient-days). Strong relationship were evident for ceftriaxone-resistant EC vs cephalosporins consumption ($r = 0.7694$; $p<0.0001$) and imipenem-resistant AC vs carbapenems consumption ($r = 0.9098$; $p<0.0001$). Ceftriaxone appeared to drive the major resistance among EC, but with little effect on KP. For cefoperazone/sulbactam-resistant AC and sulbactam consumption, a moderate relationship was found ($r = 0.5965$; $p=0.0021$). Fluoroquinolones consumption also showed a moderate relationship with ceftriaxone-resistant EC ($r = 0.6690$; $p<0.0001$). For PA, a decreasing trend in resistance was observed that coincided with reduced consumption of ceftazidime. Results from 5-year prediction demonstrated increased resistance in most organisms of interest, especially ceftriaxone-resistant EC (11 isolates/1000 patient-day; 95% CI = 4.64–43.08), cefoperazone/sulbactam-resistant AC (7.62 isolates/1000 patient-day; 95% CI = 1.58–23.34), and imipenem-resistant AC (2.65 isolates/1000 patient-days, 95% CI = 1.51–3.79), respectively.

CONCLUSION: Resistance among gram-negative organisms showed strong relationship with antimicrobial consumption. Prudent antimicrobial use, especially for cephalosporins and carbepenems is urgently needed to prevent such a dramatic increase in resistance in the near future.

122. **Identifying risk factors for *Clostridium difficile*-associated disease following a formulary change from levofloxacin to moxifloxacin.** *Jason J. Schafer, Pharm.D.*, Stacey L. Heberlig, Pharm.D., BCPP; The University of Pittsburgh Medical Center, St. Margaret Hospital, Pittsburgh, Pa.

PURPOSE: Identify risk factors for *Clostridium difficile*-associated disease (CDAD) in a community hospital where incidence doubled from 0.92 to 1.85 cases/1000 patient days in the year following a formulary change from levofloxacin to moxifloxacin.

METHODS: A 1:1 matched case-control study examined exposures for all cases of hospital-acquired CDAD over the 2 year period. Case inclusion criteria were CDAD signs and symptoms and a positive C. difficile toxin assay > 48 hours following hospital admission. Patients without CDAD were matched to cases using admission date (+/-1 day), medical service, and length of stay (at least as long as the case to acquire CDAD). Data collected include demographics, intensive care (IC) exposure, medical/surgical history, antibiotic exposure (within 6 weeks of CDAD diagnosis), and concurrent medications. A paired t-test was used to detect differences in age and length of hospital stay (LOS) between groups. Potential factors associated with CDAD were identified by matched univariate analysis and Chi-Square testing.

RESULTS: One hundred twenty-six cases were included and matched to controls. Age, LOS, presence of co-morbidities, and concomitant medications were similar for the two groups. Factors associated with CDAD cases included IC exposure (OR = 1.9, $p=0.032$), surgery (OR = 2.5, $p=0.005$), gastrointestinal surgery (OR = 2.5, $p=0.003$), and prior antibiotic exposure (OR = 2.9, $p=0.007$). Cases were also more commonly exposed to more than 1 antibiotic drug (OR = 3.1, $p=0.005$). Antibiotics associated with cases were aminopenicillins (OR = 3.5, $p=0.018$), azithromycin (OR = 2.0, $p=0.031$), levofloxacin (OR = 3.0, $p=0.014$), the cephalosporins (OR = 3.0, $p=0.0001$), cefazolin (OR = 4.5, $p=0.0006$), ceftriaxone (OR = 2.1, $p=0.039$), cefepime (OR = 10.5, $p=0.001$) and piperacillin-tazobactam (OR = 1.9, $p=0.047$). Moxifloxacin was not a factor associated with CDAD cases in this population (OR = 1.7, $p=0.11$).

CONCLUSION: The formulary change from levofloxacin to moxifloxacin was likely not associated with the increased incidence of CDAD following the switch. All variables associated with CDAD cases identified by univariate analysis will be evaluated by multiple logistic regression.

123E. **Outcomes with daptomycin as first-line therapy (FLT) for *Staphylococcus aureus* infections.** George Sakoulas, M.D.[1], *Jack Brown, Pharm.D.*[2], Lawrence V. Friedrich, Pharm.D.[2], Kenneth Lamp, Pharm.D.[2]; (1)New York Medical College, Valhalla, NY; (2)Cubist Pharmaceuticals, Lexington, Mass.

PURPOSE: Vancomycin treatment outcomes for infections due to either methicillin-resistant or methicillin-susceptible *S. aureus* (MRSA, MSSA) are considered suboptimal by many clinicians. Effective agents are needed for empiric and first-line therapy for infections due to these organisms given the rapidly increasing incidence of MRSA infections. The purpose of this analysis was to evaluate outcomes in patients receiving daptomycin as FLT.

METHODS: Patients receiving daptomycin as FLT for *S. aureus* and evaluable for outcome were selected from a registry (The Cubicin® Outcomes Registry and Experience; COREsm, 2005 and 2006 program years. Outcomes were assessed as cure, improved, or failure at the end of daptomycin therapy. Success was defined as cure + improved.

RESULTS: 189 patients from 44 sites representing 20% of all evaluable patients with *S. aureus* in the registry met the criteria for inclusion. 24% of patients were ≥ 66 years of age, 31% had diabetes, and 26% had an initial CrCl < 30 mL/minute. 68% of patients were located in the community 48 hours before the start of daptomycin therapy;

14% received daptomycin in an ICU. Clinical success was achieved in 95% of patients. Success rates by diagnosis were: osteomyelitis 100% (n=28), complicated skin infection (SI) 99% (n=75), uncomplicated SI 98% (n=40), bacteremia 86% (n=29), infective endocarditis 67% (n=6). Success rates by pathogen were: MSSA 90% (n=41), MRSA 96% (n=127), *S. aureus* (methicillin susceptibility unreported) 100% (n=20), glycopeptide-intermediate *S. aureus* 100% (n=1). Concomitant antibiotics were used in 37% of patients including rifampin (16%), quinolones (14%), and vancomycin (10%). Adverse events (AEs) possibly related to daptomycin were reported in 6 patients (3.2%).

CONCLUSIONS: These data support the use of daptomycin as FLT for multiple infection types caused by MRSA and MSSA. Further prospective studies are needed to evaluate daptomycin efficacy outside of its labeled indications.

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124. **Correlation of vancomycin MICs to linezolid and oxacillin MICs in clinical MRSA blood isolates.** *Roger L. White, Pharm.D.*; South Carolina College of Pharmacy, Charleston, SC.

PURPOSE: It is increasingly evident that a vancomycin (V) MIC creep is occurring in MRSA. Some studies have shown an increase in V MICs affecting daptomycin (D) MICs. These studies were performed on glycopeptide-resistant *Staphylococcus aureus* (GISA) isolates; thus, extrapolation of the findings to V susceptible isolates may be inappropriate.

METHODS: E test MICs were performed on 5 years (2001-05) of MRSA isolates with V, D, linezolid (L), and oxacillin (O). D was included as a cell-wall active antibiotic, L as a non cell-wall active control, and O to verify the classification of MRSA. All isolates (1/patient) were from a single institution. MICs above the highest concentration were rounded upward to the next Etest dilution. Nonparametric regression (Spearman's rho) was used to assess the association between MICs of V and D, L, and O. Parametric correlations were also performed on log MICs. Assessments were performed for all years combined and by individual years. $P<0.05$ was considered statistically significant.

RESULTS: 662 isolates were studied (n=108,126,143,154,131 for 2001-05, respectively). MICs (mg/L) were: 0.25–2.0 for V, 0.19–0.75 for D, 0.25–4 for L, and 4– > 256 for O. Rounding of MICs only occurred with O (11% of isolates). For all years combined, nonparametric correlations with V MICs were: D (r=0.047, p=0.2241), L (r=0.2070, p<0.0001), O (r=0.3530, p<0.0001). Results from individual years and with parametric correlations of log MICs were similar.

CONCLUSIONS: D MICs were poorly correlated with V MICs for clinical MRSA isolates; however, significant correlations were found between V and both L and O MICs. As the prevalence of MRSA increases and MICs to O increase, associated increases in V and L MICs may have implications for therapy.

125. **Impact of MIC creep of vancomycin against clinical MRSA blood isolates on Monte Carlo analysis target attainment.** *Roger L. White, Pharm.D.*; South Carolina College of Pharmacy, Charleston, SC.

PURPOSE: Vancomycin (V) MRSA MICs are increasing in some institutions. This MIC creep may affect the pharmacodynamics (PD), and thus the efficacy, of V. Monte Carlo (MC) analysis can assess the potential impact of MIC creep on patient population PD over time.

METHODS: V MICs (Etest) were determined for MRSA blood isolates (n=662) from a single institution from 2001 to 2005. Population PK (CrCl vs. Cl regressions), and a tertiary-care hospital CrCl distribution were used to simulate the variability in patient PK profiles. Total serum AUCs were simulated for: V 1 g and 2 g (intervals per Matzke nomogram). MC (10,000 simulations) was performed for each regimen and study year and percent target attainment (TA) for V at AUC/MIC $\geq$ 350 and $\geq$ 400 was assessed. PD target values are based on published microbiological and clinical end points in patients. To assess the impact of continual MIC creep, MIC distributions through year 2010 were simulated using the 2005 MIC distribution as the index year. The rate of increase in MICs was assumed to be the same as that observed from 2001 to 2005.

RESULTS: MICs (mg/L) were 0.25–2 for V and increased over the study period (geometric mean 0.6 in 2001, 0.9 in 2005). Median (range) AUCs were: V 1g = 531 (362–776), V 2g = 1062 (724–1552). At AUC/MIC $\geq$ 400 ($\geq$ 350), TA declined from 99.4% (100%) to 92.3% (96.4%) from 2001 to 2005. In the simulated MIC distributions at AUC/MIC $\geq$ 400, TA declined to 53% in 2007 and 27% in 2010 (when geometric mean was 1.7) for the V 1g dosing regimen. With the 2 g regimen, TA rates were $\geq$ 87% through 2010.

CONCLUSION: In this MRSA population, 2001-2005 TA rates were $\geq$ 90% for V. However, if the rate of MIC creep continues, TA for V 1 g dosing will decline precipitously and higher doses may be needed to increase the likelihood of efficacy.

126E. Post-marketing experience: daptomycin use in patients with prosthetic device osteomyelitis.
Lenore Tominna, Pharm.D., *Kenneth Lamp, Pharm.D.*, Lawrence V. Friedrich, Pharm.D.; Cubist Pharmaceuticals, Lexington, Mass.

PURPOSE: Joint replacement surgery is increasing, and infection is frequently due to multidrug-resistant gram-positive bacteria. A phase 2 study evaluating the safety and efficacy of daptomycin vs. comparators for osteomyelitis associated with an infected prosthetic joint due to methicillin-resistant *Staphylococcus aureus* (MRSA) and/or coagulase-negative staphylococci (CoNS) is under way; however, results are years away.
METHODS: The real-world experience of daptomycin for prosthetic device osteomyelitis was assessed. Evaluable (cure, improved, failure) patients were identified in a registry (The Cubicin Outcomes Registry and Experience, COREsm, 2006 program year). Outcomes were defined using protocol defined criteria at the end of daptomycin therapy (EOT).
RESULTS: Forty of 161 osteomyelitis patients met inclusion criteria. The reported clinical success (cure plus improved) at EOT was 90% (9/9 with temporary prosthetic devices, 27/31 with permanent prosthetic devices); however, adjuvant surgical interventions were not collected. Patients were 55% female and 53% $\geq$ 66 years. Diabetes was common (30%). 80% of patients received antibiotic drugs prior to starting daptomycin; vancomycin being most common (58%). Of 29 patients with positive cultures, common pathogens were *S. aureus*, 45% (47% MRSA), CoNS, 31%, and *Enterococcus* sp., 14%. The median (range) daptomycin dose was 6 mg/kg (3–8; 63% $\geq$ 6 mg/kg), and the median (range) duration was 39 days (4–90 days). 50% of patients received concomitant antibiotics with daptomycin, most frequently quinolones (40%). Median time to clinical response was 9 days (range 1–21; reported in 19 patients). Eight adverse events (AEs) in 5 patients (including 3 serious AEs in 1 patient) were reported as possibly related to daptomycin. All of these AEs were mild or moderate in severity and resolved.
CONCLUSIONS: Daptomycin appears to be a useful adjunct in treating patients with prosthetic device-associated osteomyelitis. Further studies with followup assessments are warranted to determine whether daptomycin is effective and well tolerated for these patients.
Submitted to ICAAC 07, 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Chicago, Ill, September 17-20, 2007.

127E. Does it matter which aminoglycoside is used in combination with cefepime (CFP) or piperacillin/ tazobactam (PTZ) vs ESBL-producing bacteria? *David S. Burgess, Pharm.D., FCCP*[1], Michael F. Carden, EMT[2]; (1)Center for Advancement of Research and Education in Infectious Diseases, University of Texas at Austin College of Pharmacy, San Antonio, Tex; (2)University of Texas Health Science Center at San Antonio, San Antonio, Tex.

PURPOSE: Multidrug-resistant (MDR) ESBL-producing organisms are increasingly common causes of infection. Since options for treating these MDR organisms are limited, we assessed the in vitro activity of GEN, TOB, and AMK in combination with PTZ and CFP against molecularly characterized MDR ESBL producing organisms.
METHODS: MICs were performed using CLSI standards. ESBL-encoding genes were identified using PCR and sequencing. Time-kill curves were performed using a standard inoculum and the following concentrations (mcg/ mL): GEN (4), TOB (4), AMK (16), PTZ (40/5), and CFP (16). Bacterial densities were determined at 0, 2, 4, 6, 8, 12 and 24 hours.
RESULTS: The MICs for each isolate are displayed.

Isolate	GEN	TOB	AMI	PTZ	CFP
5	128	128	64	16	128
9	128	128	32	256	>256
12	>128	64	32	512	256
32	128	16	32	128	128

None of the antibiotics alone reached bactericidal activity. For combination therapy, PTZ + AMK and CFP + AMK displayed synergy and maintained bactericidal activity over the entire 24-hour period against all isolates. However, the activity of PTZ in combination with GEN or TOB was highly variable and not associated with susceptibility pattern or genotype. Only PTZ + GEN vs 5 and 32 and PTZ + TOB vs 5 was synergistic and bactericidal. All other combinations of PTZ displayed indifference. No CFP combinations with either GEN or TOB were synergistic or able to maintain bactericidal activity. No combination was antagonistic.
CONCLUSION: Only AMK combinations were synergistic and bactericidal over the 24-hour period against all isolates regardless of susceptibility or genotype. The specific aminoglycoside used has a major impact on the in vitro activity and should be further evaluated.

Presented at the 47th ICAAC, Chicago, Ill, September 17-20, 2007.

128E. Trends in US hospital admissions for skin and soft tissue infections (SSTIs), 2000–2004: estimates from the healthcare cost and utilization project (HCUP) national inpatient sample (NIS).
Charu Taneja, M.P.H.[1], Marcus J. Zervos, M.D.[2], John S. Edelsberg, M.D., M.P.H.[1], Nadia Z. Haque, Pharm.D.[2], Carol L. Manierski, Pharm.D.[2], *James Spalding, Pharm.D.*[3], Gerry Oster, Ph.D.[1]; (1)Policy Analysis Inc., Brookline, Mass; (2)Henry Ford Health System, Detroit, Mich; (3)Astellas Pharma US, Inc., Deerfield, Ill.

PURPOSE: *S. aureus* is a common etiologic organism in skin and soft tissue infections (SSTIs). Although methicillin-resistant *S. aureus* (MRSA) has been common among hospitalized patients, reports of community-acquired MRSA (CA-MRSA) skin infections have been increasing. It is unknown whether this is reflected in trends in US hospital admissions for SSTIs.
METHODS: Using data from the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP NIS), an approximate 20% random sample of all US community hospitals, we identified all patients admitted to the hospital from 2000 to 2004 with a principal diagnosis of complicated or uncomplicated SSTI. For purposes of comparison (i.e., to determine whether changes in SSTI admissions reflect general trends in hospitalizations for CA infections), we also identified all admissions for bacterial pneumonia (BP). Changes in admission rates over this period were then examined.
RESULTS: Total SSTI admissions to US hospitals increased by about 195,000 (29%) from 2000 to 2004, while BP admissions fell by 2.5% (Table). The increase in SSTI admissions was higher among younger (< age 65) vs older patients (37% vs 14%), and in urban vs rural hospitals (32% vs 11%).
CONCLUSIONS: The number of admissions to US hospitals for SSTIs has increased substantially in recent years. Although not necessarily attributable exclusively to MRSA, our finding is consistent with increasing numbers of serious infections due to CA-MRSA.

Principal diagnosis	2000	2001	2002	2003	2004	Change, 2000–2004 (%)
SSTI	674,939	701,672	757,858	810,768	869,777	194,838 (28.9%)
BP	1,202,387	1,177,972	1,229,204	1,272,686	1,172,304	-30,083 (-2.5%)
SSTI = skin and soft tissue infection; BP = bacterial pneumonia.						

Presented at the Infectious Diseases Society of America, San Diego, Calif, October 4-7, 2007 (submitted).

129. In vitro activity of piperacillin/tazobactam (PTZ), cefepime (CFP), and meropenem (MER) against ESBL-producing CTX-M-15 and SHV-12. *David S. Burgess, Pharm.D., FCCP*[1], Michael F. Carden, EMT[2], Brian L. Wickes, Ph.D.[2], Christopher R. Frei, Pharm.D., M.Sc., BCPS[3], James S. Lewis, Pharm.D.[4], James Jorgensen, Ph.D.[2]; (1)Center for Advancement of Research and Education in Infectious Diseases, University of Texas at Austin College of Pharmacy, San Antonio, Tex; (2)University of Texas Health Science Center at San Antonio, San Antonio, Tex; (3)The University of Texas at Austin College of Pharmacy and The University of Texas Health Science Center at San Antonio, San Antonio, Tex; (4) University Health System, San Antonio, Tex.

PURPOSE: Much debate exists regarding the clinical utility of PTZ and CFP for ESBL infections. Therefore, we assessed the in vitro activity of PTZ, CFP, and MER against molecularly characterized MDR ESBL-producing organisms.
METHODS: CLSI methodologies were used to determine MICs for 88 ESBL positive clinical isolates from our institution between 2000 and 2006. ESBL-encoding genes were identified using PCR and sequencing. Time-kill curves were performed using a standard inoculum for 13 isolates (5 CTX-M-15, 8 SHV-12) with the following antimicrobial concentrations (mcg/mL): PTZ (40/5), CFP (16), and MER (4). At various timepoints (0, 2, 4, 6, 8, 12 and 24 hours), samples were collected and plated to determine bacterial densities. A 3-$\log_{10}$ reduction in colony-forming units from the starting inoculum was considered bactericidal.
RESULTS: Of the 88 isolates, the 2 most common genotypes were CTX-M-15 (35%) and SHV-12 (23%). The MIC50, MIC90, and %S were as follows: PTZ (CTX-M-15: 16, 32, 74%; SHV-12: 8, 512, 65%), CFP (CTX-M-15: 32, 128, 29%; SHV-12: 4, 32, 65%), and MER (CTX-M-15: 0.25, 1, 100%; SHV-12: 0.125, 0.5, 100%). MER was bactericidal against each isolate regardless of genotype. For SHV-12, PTZ reached bactericidal activity against 4/8 isolates and was able to maintain this activity over 24 hrs against 3/8 isolates. CFP reached bactericidal activity against 6/8 SHV-12 isolates and maintained bactericidal activity for 4/8 isolates. For CTX-M-15 isolates, CFP was not bactericidal, while PTZ reached and maintained bactericidal activity against 1 isolate.

CONCLUSIONS: MER was equally active against CTX-M-15 and SHV-12. Although neither PTZ nor CFP were bactericidal against CTX-M-15, both were bactericidal against half of the SHV-12 organisms. Further investigation into gene-specific therapy is warranted.

130. **Relationship of clinical responses to vancomycin MICs of baseline pathogens in the ATLAS studies.** G. Ralph Corey, M.D.[1], Martin E. Stryjewski, M.D.[1], Alan Hopkins, Ph.D.[2], Michael M. Kitt, M.D.[2], *Steven L. Barriere, Pharm.D.*[2]; (1)Duke Clinical Research Institute and Duke University Medical Center, Durham, NC; (2)Theravance, Inc., South San Francisco, Calif.

PURPOSE: Telavancin (TLV) is a novel lipoglycopeptide antibiotic drug with a multifunctional mechanism of action against gram-positive pathogens, including methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* (MRSA and MSSA, respectively). The ATLAS program (**A**ssessment of **T**e**LA**vancin in complicated **S**kin and Skin Structure Infections [cSSSI]) compared TLV (10 mg/kg IV every 24 hours) with vancomycin (VAN; 1 g IV every12 hours) in parallel, randomized, double-blind trials that included more than 1800 patients with cSSSI for 7–14 days. This subanalysis was performed to determine whether the efficacy of TLV or VAN was reduced against MRSA and/or MSSA with increasing VAN MIC.
METHODS: This analysis of ATLAS patients with cSSSI due to *S. aureus* (SA) examined the association of clinical outcome with the VAN MICs.
RESULTS: VAN MICs were determined for clinical strains of *S.aureus* isolated from 433 patients in the TLV group and 452 patients in the VAN group. The distributions of VAN MICs for clinical strains of *S.aureus* were similar between the two groups. (Table). There was no significant effect on cure rates in the TLV group by higher VAN MIC of either MSSA or MRSA. There appeared to be a trend to lower response rates in the VAN group versus MRSA with higher MIC, but the number of patients was small.
CONCLUSIONS: TLV is at least equivalent to VAN for the treatment of cSSSI produced by *S.aureus*. In addition, efficacy of TLV is not diminished against organisms with elevated VAN MICs.

Cure rates in patients treated with TLV or VAN (by VAN MIC)

Treatment Group	Pathogen	Vancomycin MIC (µg/ml)		
		0.5	1	2
TLV	MSSA n/N, (%)	64/72 (88.9)	85/97 (87.6)	1/1 (100)
	MRSA n/N, (%)	52/59 (88.1)	184/202 (91.1)	2/2 (100)
	MSSA n/N, (%)	59/69 (85.5)	84/96 87.5)	1/1 (100)
VAN	MRSA n/N, (%)	58/71 (81.7)	187/209 (89.5)	4/6 (66.7)

131. **Treatment outcomes of hepatitis C following liver transplantation in a pharmacist-run outpatient clinic.** *Gregory A. Smallwood, Pharm.D.*[1], Carlos Fasola, M.D.[2], Andrei C. Stieber, M.D.[2], Thomas Heffron, M.D.[2]; (1)Emory Healthcare, Atlanta, Ga; (2)Emory University School of Medicine, Atlanta, Ga.

PURPOSE: The leading reason for liver transplantation in the United States is currently complications of chronic hepatitis C viral (HCV) infection. Following liver transplantation, HCV recurs universally within the graft. The aim of this study is to evaluate outcomes of a treatment protocol using pegylated interferon α-2A and ribavirin in a pharmacist-run HCV treatment clinic following liver transplantation.
METHODS: Patients with biopsy-proven recurrence of HCV following liver transplantation were directed to a pharmacist-run, protocol-driven, post-transplant outpatient treatment clinic. This is an IRB-approved review study of outcomes.
RESULTS: Of the 67 patients treated, 79.1% (53/67) had a biochemical response by month 3. At 3 months there was a decrease in ALT [123 (± 79) u/L vs. 69.3 (± 90) u/L; p=0.002], total bilirubin [1.7 (± 0.8) ng/dL vs. 1.1 (± 0.6) mg; p=0.05], viral load (2.2 X 106 vs. 0.7 X 106, p=0.02) and AST [156 (± 221) u/L vs 62 (± 78); p=0.002). Viral clearance during treatment was 41.7% (28/67) at 3 months, end of treatment clearance was 51.7% (30/58), and sustained virological response(SVR) was 32.6 % (14/43). Nonresponders (n=32) to previous interferon treatments were evaluated and achieved a SVR similar to naïve patients [30 % vs. 34.7 %; p=NS). Nonresponders had earlier recurrence of HCV by biopsy [181.1 (± 236) days vs. 303.4 (± 327) days; p=0.031]. Only 16.4% (10/61) had to have dose interruption with two patients having rejection. Progression of biopsy results maintained Schuler biopsy scoring. Patient/graft 3-year survival was 75.9% ± 0.5.
CONCLUSIONS: Hepatitis C following liver transplantation can safely be treated with pegylated interferon under a pharmacist-run, protocol-driven clinic to obtain similar viral clearance to that reported in the nontransplant population.

132E. **Evaluation of Etest GRD for detecting reduced vancomycin susceptibility among clinical Isolates of _Staphylococcus aureus_.** _Vanthida Huang, Pharm.D._[1], Fred C. Tenover, Ph.D.[2], John E. McGowan Jr., M.D.[3]; (1)Mercer University College of Pharmacy and Health Sciences, Department of Pharmacy Practice, Atlanta, Ga; (2)Centers for Disease Control and Prevention, Division of Healthcare Quality Promotion, Atlanta, Ga; (3)Rollins School of Public Health of Emory University, Department of Epidemiology, Atlanta, Ga.

PURPOSE: Vancomycin heteroresistance (VHR) among _S. aureus_ strains is difficult to detect, but may result in vancomycin failure. We investigated the ability of the Etest Glycopeptide Resistance Detection (GRD) vancomycin/teicoplanin (VA/TP) test to detect hetero-vancomycin intermediate _S. aureus_ (hVISA) and VISA phenotypes using well characterized control strains and a series of _S. aureus_ isolates for which the broth microdilution (BMD) vancomycin MICs were 4 µg/ml.
METHODS: 51 clinical isolates of _S. aureus_ (for 48, VA MICs = 4 µg/ml; for 3, MICs < 2 µg/ml), previously characterized by BMD and VA population analysis, were obtained from CDC, ICARE, and NARSA strain collections. _S. aureus_ ATCC 29213 (susceptible), Mu3 (hVISA), Mu50 (VISA), NRS 13 (hVISA), and 9AJ57 (hVISA) were included as controls. Detection of VHR was performed using standard VA Etest on Mueller-Hinton agar (BDDS) and investigational Etest GRD VA/TP strips on blood agar plates.
RESULTS: All 5 controls were correctly classified as VA susceptible, hVISA, or VISA. 38 of 51 (75%) isolates were hVISA/VISA by Etest GRD at 24 h. The VA MICs of the 38 isolates using the standard VA Etest at 24 hours were < 4 µg/ml; thus, they were hVISA according to the package insert. However, using Clinical and Laboratory Standards Institute (CLSI) breakpoints and rounding up Etest MIC results of 3–4 µg/ml, 29 of 38 (76%) isolates were VISA. At 48 hours, 4 more hVISA/VISA (total=42) were detected, including 2 VISA and 2 hVISA using CLSI breakpoints.
CONCLUSIONS: Etest GRD strips identified 9 hVISA isolates at 24 hours that would have been called VA susceptible using the standard Etest method and current CLSI breakpoints. Using previous CLSI breakpoints (< 4 µg/ml, susceptible), 38 hVISA isolates were identified. Four additional hVISA/VISAs were detected at 48 hours. Thus, Etest GRD enhances detection of VHR among _S. aureus_ isolates.
Presented at 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Chicago, Ill, September 17-20, 2007.

133E. **Impact of a network-wide clinical pathway on health outcomes for hospitalized patients with community-acquired pneumonia (CAP).** _Christopher R. Frei, Pharm.D., M.Sc., BCPS_[1], Theresa C. Jaso, Pharm.D.[2], Marcos I. Restrepo, M.D., M.Sc.[3], Eric M. Mortensen, M.D., M.Sc.[3], Phyllis Mosby, R.N.[4], Vanja Sikirica, Pharm.D.[5]; (1)University of Texas at Austin and University of Texas Health Science Center at San Antonio, San Antonio, Tex; (2)University of Texas at Austin and Seton Family of Hospitals, Austin, Tex; (3)University of Texas Health Science Center, Veterans Evidence-Based Research Dissemination and Implementation Center and South Texas Veterans Health Care System, San Antonio, Tex; (4)Seton Family of Hospitals, Austin, Tex; (5)Ortho-McNeil Janssen Scientific Affairs, Raritan, NJ.

PURPOSE: In 2005, a six-hospital Texas health-system instituted a voluntary, system-wide, clinical pathway for CAP patients. Pathway antibiotics were consistent with the 2007 IDSA/ATS CAP guidelines, including the newly recommended levofloxacin 750 mg. The study objective was to determine the impact of the pathway on patient length of stay (LOS) and health outcomes.
METHODS: Data were extracted from medical charts for adults (≥ age 18) with a principal CAP diagnosis and positive chest x-ray between Jan 2005 and Dec 2006. Patients with health care-associated pneumonia or admitted directly to the ICU were excluded. Pathway and non-pathway cohorts were assigned according to antibiotics received within 48 hours of admission. Pathway antibiotics included levofloxacin 750 mg monotherapy or ceftriaxone 1 g plus azithromycin 500 mg daily. LOS and health outcomes were assessed using Cox proportional hazard and logistic regression models. Receipt of pathway antibiotics was the independent variable, and Pneumonia Severity Index (PSI) risk class was a covariate.
RESULTS: Overall, 195 patients satisfied study criteria; 77% were PSI risk class III-V, and 52% received pathway antibiotics. Pathway (n=101) and non-pathway (n=94) cohorts were similar with respect to age, gender, comorbidities, pre-admission antibiotics, PSI score, and processes of care. Receipt of pathway antibiotics was independently associated with decreased LOS (p=0.04). LOS for pathway and non-pathway groups was [mean (SD) and median (25th–75th percentile)]: 5.2 (5.4) vs. 6.7 (6.5) and 4 (3-6) vs. 5 (3-7). Duration of IV antibiotics was not statistically different (p=0.39): 4.3 (2.4) vs. 5.6 (4.9) and 4 (3-5) vs. 4 (3-6). No patients expired during hospitalization.
CONCLUSIONS: Pathway antibiotics were associated with shorter length of hospital stay among hospitalized CAP patients.

134. **Genotype-specific clinical outcomes among patients infected with extended-spectrum beta-lactamase (ESBL)-producing bacteria.** *Christopher R. Frei, Pharm.D., M.Sc., BCPS*[1], Brian Wickes, Ph.D.[2], David S. Burgess, Pharm.D.[1], Nathan P. Wiederhold, Pharm.D.[1], James S. Lewis, Pharm.D.[3], Michael F. Carden, Sr.Res.Assist.[2], Daniel E. Zamarripa, Pharm.D.[1], Yifan Yu, Pharm.D.[1], James H. Jorgensen, Ph.D.[2]; (1)University of Texas at Austin and University of Texas Health Science Center at San Antonio, San Antonio, Tex; (2)Univsity of Texas Health Science Center at San Antonio, San Antonio, Tex; (3)University of Texas at Austin, University of Texas Health Science Center at San Antonio, and University Health Systems, San Antonio, Tex.

PURPOSE: Few ESBL studies have reported genotype-specific results. Our objective was to discern the impact of ESBL genotype on antimicrobial activity and patient outcomes.
METHODS: We obtained all available ESBL isolates recovered from patients at University Hospital between 1/1/00 and 12/31/06. DNA was extracted, amplified, and sequenced to determine the ESBL genotype. Susceptibility testing was conducted to determine gene- and species-specific MICs. Clinical data were extracted from medical charts. Clinical failure was defined as 14-day mortality, persistent fever, or positive cultures despite 48 hours of antibiotic therapy.
RESULTS: Forty-six adult inpatients had 51 ESBLs: 23 *E. coli*, 17 *K. pneumoniae*, 8 *K. oxytoca*, and 3 *Enterobacter* spp. ESBLs were from urine (45%), blood (28%), sputum (15%), and other (12%). Nine ESBL types were identified: 53% CTXM-8, 14, 15, or 16; 42% SHV-2, 5, or 12; and 5% TEM-10 or 15. MIC_{90} and percent susceptible were uniform for meropenem (MEM) regardless of genotype while other antimicrobials varied by genotype. Patients frequently received empiric regimens that contained piperacillin-tazobactam (PTZ, 34%), extended-spectrum cephalosporins (ESC, 18%), or fluoroquinolones (FQ, 37%). Clinical cure (%) for PTZ, ESC, and FQ was: CTXM (20, 0, 22), SHV (14, 25, 20), TEM (0, n/a, n/a), *E. coli* (13, 0, 9), *Klebsiella* spp. (25, 33, 67), blood (0, 0, 20), sputum (0, 0, 0), urine (33, 0, 29). Isolate susceptibility was not predictive of clinical cure.
CONCLUSIONS: MEM was the only antimicrobial that displayed uniform in vitro activity, regardless of ESBL genotype. Clinical cure rates were poor for PTZ, ESC, and FQ. PTZ patients faired better than ESC patients against CTXM and *E. coli* ESBLs. In contrast, ESC patients faired better than PTZ patients against SHV and *Klebsiella* spp. ESBLs.

135. **The transcription factor Mrr1p controls expression of the *MDR1* efflux pump and mediates multidrug resistance in *Candida albicans*.** Joachim Morschhäuser, Ph.D.[1], Katherine Barker, Ph.D.[2], Teresa Liu, B.S.[2], Ramin Homayouni, Ph.D.[3], Julia Blaß, B.S.[1], *P. David Rogers, Pharm.D., Ph.D.*[2]; (1) Universität Würzburg, Würzburg, Germany; (2)University of Tennessee Health Science Center, Memphis, Tenn; (3)University of Memphis, Memphis, Tenn.

PURPOSE: Constitutive overexpression of the *MDR1* gene, which encodes a multidrug efflux pump of the major facilitator superfamily, is a frequent cause of resistance to fluconazole and other toxic compounds in clinical *Candida albicans* strains, but the mechanism of *MDR1* up-regulation has not been resolved. Our objective was to elucidate this mechanism.
METHODS: Using genome-wide gene expression analysis, we identified a zinc cluster transcription factor, designated as Mrr1p (multidrug resistance regulator), that was coordinately upregulated with *MDR1* in drug-resistant, clinical *C. albicans* isolates. The gene encoding *MRR1* was disrupted in two such clinical isolates. *MRR1* alleles from both resistant isolates were introduced into a drug susceptible *C. albicans* strain. These strains were assessed for azole susceptibility and *MDR1* expression. *MRR1* alleles were subjected to sequence analysis.
RESULTS: Inactivation of *MRR1* in two drug-resistant isolates abolished both *MDR1* expression and multidrug resistance. Sequence analysis of the *MRR1* alleles of matched drug-sensitive and drug-resistant *C. albicans* isolate pairs showed that the resistant isolates had become homozygous for *MRR1* alleles containing single nucleotide substitutions that caused amino acid exchanges in the encoded protein. Introduction of these mutated alleles into a drug-susceptible *C. albicans* strain resulted in constitutive *MDR1* overexpression and multidrug resistance.
CONCLUSIONS: We have identified the central regulator of *MDR1* expression in *C. albicans* and elucidated the molecular basis of a major mechanism of multidrug-resistance development in clinical *C. albicans* strains.

136E. **Identification of differentially expressed proteins in association with azole resistance in clinical isolates of *Candida albicans*.** Chris Hoehamer, Ph.D., George Hilliard, Ph.D., *P. David Rogers, Pharm.D., Ph.D.*; University of Tennessee Health Science Center, Memphis, Tenn.

PURPOSE: *Candida albicans* is a fungal pathogen and cause of oropharyngeal candidiasis (OPC), the most frequent opportunistic infection among AIDS patients. Azoles have been proven effective in the management of OPC; however, treatment failures have occurred due to azole-resistant *C. albicans*. In an effort to identify novel mechanisms of azole resistance, we examined changes in the proteomic profiles of six matched sets of *C. albicans* isolates representing the acquisition of azole resistance.

METHODS: Isolates were obtained from AIDS patients with OPC who failed azole therapy. The azole-resistant isolates used in this study have been shown to overexpress MDR1 or both CDR1 and CDR2. Isolates were grown in YPD. The cytosolic protein fraction was subjected to 2D PAGE. Proteins were analyzed with PDQuest. Spots differentially expressed by at least 1.5-fold were excised and analyzed by MALDI-TOF MS. By searching a database constructed from *C. albicans* ORF products, proteins were identified. Changes in mRNA abundance for selected proteins were measured by real-time RT-PCR.

RESULTS: We identified 52 differentially expressed proteins in these isolates. In the three sets that overexpress Mdr1p, we identified 37 proteins. Among these were Gap1p, Eno1p, Gnd1p, Pdc11p, Adh1p, Ifd4p, Ifd5p, Ifd6p, Ssb1p, Ipf 5987p, Ipf17186p and Grp2p. In the three sets that overexpress both Cdr1p and Cdr2p, we identified 15 proteins including Gap1p, Eno1p, Gnd1p, Adh1p, Atp2p, Ilv5p, Ynk1p, and Ssb1p. The proteins identified common to both groups of isolates were Gap1p, Eno1p, Gnd1p, Adh1p, and Ssb1p.

CONCLUSIONS: Several proteins are co-regulated with Mdr1p or Cdr1p and Cdr2p, some of which potentially play a role in azole resistance in *C. albicans*. Of particular interest were the metabolic enzymes and Ssb1p. These data demonstrate that glycolytic enzymes and proteins involved with cell stress are co-regulated with Mdr1p or Cdr1p and Cdr2p in association with azole resistance.

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137. Effect of daptomycin-dosing frequency on outcomes in patients undergoing hemodialysis with bacteremia (BAC) or skin and skin structure infections (SSSI). *Brian J. Donovan, Pharm.D.*[1], Bruce A. Mueller, Pharm.D.[2], Jason A Crompton, Pharm.D.[1], Kenneth C Lamp, Pharm.D.[1]; (1)Cubist Pharmaceuticals, Lexington, Mass; (2)University of Michigan College of Pharmacy, Ann Arbor, Mich.

PURPOSE: Describe the outcomes of hemodialysis patients given daptomycin.

METHODS: Data were collected retrospectively as part of an ongoing registry (The Cubicin® Outcomes Registry and Experience; CORE[sm], 2005 and 2006 program years). Hemodialysis patients (excluding any continuous dialysis) with BAC or SSSI, evaluable for outcome (cure, improved, failure) and receiving > 1 daptomycin dose, were analyzed. Patients were categorized based on their final daptomycin frequency; every 48 hours (Q48H, approved hemodialysis regimen), 3 times per week (3x/wk), and every 24 hours (Q24H). Outcomes were assessed at the end of daptomycin therapy.

RESULTS: 116 hemodialysis patients from 38 sites, primarily teaching hospitals, were included. Success was reported in 89% of pts; 88% Q48H (n=81); 95% 3x/wk (n=22); 85% Q24H (n=13); p=0.5. In patients with bacteremia ± SSSI, success rates were 88% Q48H (n=59), 94% 3x/wk (n=17), and 83% Q24H (n=6); p=0.7. In patients with only SSSI, success rates were 86% Q48H (n=22), 100% 3x/wk (n=5), and 86% Q24H (n=7); p=0.7. There were no differences in either the pathogen types or those without pathogens between the dosing groups. Only two differences in patient characteristics were identified (neither affected outcomes); cancer rates; 11% Q48H; 24% 3x/wk; 38% Q24H (p=0.02) and median (min,max) daptomycin dose; 6 mg/kg (3,9.5) Q48H; 5.3 mg/kg (3, 14.8) 3x/wk; 4 mg/kg (2,7) Q24H (p<0.005). 8 pts had an adverse event (AE) possibly related to daptomycin; 6/81 (7%) Q48h, 1/22 (5%) 3x/wk, 1/13 (8%) Q24h, (p=0.9).

CONCLUSION: The use of daptomycin 3x/wk is an unapproved dosing regimen, but would simplify treatment of hemodialysis patients if effective and well tolerated. The dosing groups had similar patient characteristics other than the differences in dose and cancer rates. Daptomycin appeared to produce equivalent success and AE rates with differing dosing schedules. These data require confirmation via prospective clinical trials.

138. Lebanese resistance surveillance of community uropathogens. *Oussayma Moukhachen, Pharm.D., BCPS*[1], Rony Zeenny, Pharm.D.[2], Claude Afif, M.D.[3]; (1)Massachusetts College of Pharmacy, Boston, Mass; (2)Lebanese American University, Byblos, Lebanon; (3)University Of Balamand-St George Hospital University Medical Center, Ashrafieh, Lebanon.

PURPOSE: To assess Lebanese national rates of antimicrobial resistance among aerobic uropathogens isolates recovered from community patients.

METHODS: In a retrospective design, community laboratories, distributed throughout Lebanon, were requested to provide antibiotic resistance results on all uropathogens recovered from patients in the community between 2001 and 2004. Data analyzed were obtained from 30% of the 125 operating community laboratories.

RESULTS: Out of 21342 isolates, 83% were gram-negative pathogens with *E.coli* being the most predominant 13960 (65.4%) of overall pathogens, followed by *P. mirabilis* 962 (4.5%), *Klebsiella* spp 862 (4%), and *Enterobacter* spp. 516 (2.5%). *S. saprophyticus* and *Enterococci* spp. were the most reported among gram-positive isolates with 648 (3%) and 1429 (6.6%) respectively of overall pathogens. Over the study period, although most antimicrobials had an absolute increase in their antimicrobial activity against *E.coli*, ciprofloxacin and third-generation cephalosporin had an absolute decrease of antimicrobial activity by 3% and 5.5% respectively. In addition, among gram-negative uropathogens, one constant was the absolute loss in activity of ciprofloxacin and other fluoroquinolones (levofloxacin, norfloxacin, ofloxacin) ranging from 0.4 % against *K. pneumoniae* to 4.92% against *P.mirabilis*. On average, nationally 52% *E.coli* strains were resistant to amoxicillin/ampicillin, 42.6% to amoxicillin/clavulanate, 28% to first-generation cephalosporin, 17% to 2nd generation, 47.5% to cotrimoxazole, 16.32% to nitrofurantoin, and 15.7% to ciprofloxacin. Our data showed inter-regional variation in the resistance rates to amoxicillin/clavulanate and cotrimoxazole with Beirut having the highest whereas the South had the lowest rate.

CONCLUSIONS: Our study constitutes the first national surveillance study for community uropathogens prevalence and resistance upon which national antibiotic prescription practice guidelines should be developed. Two findings are pivotal for the empirical treatment of community-acquired urinary tract infections: 1) high *E.coli* resistance rates to Ampicillin/amoxicillin, amoxicillin+clavulanate, and Cotrimoxazole and 2) the steady decline in the fluoroquinolones activity.

139. **Does Depression Impact Sustained Virologic Response in Hepatitis C Patients?** *Regan C. Cullen, Pharm.D.*, Nasreen Khan, Ph.D., Sanjeev Arora, M.D., Rocsanna Namdar, Pharm.D.; University of New Mexico Health Sciences Center, Albuquerque, NM.

PURPOSE: The effect of depression on sustained virologic response (SVR), undetectable viral load 6 months after the end of treatment (ET), in hepatitis C virus (HCV) infected patients has not been defined. The purpose was to estimate: a) the effect of depression on SVR, and b) the factors involved in the development of depression.
METHODS: A retrospective chart review was conducted in HCV patients receiving treatment (pegylated interferon and ribavirin) at the University of New Mexico Health Sciences Center. Data was extracted on patients' demographics, SVR, and depression. The Center for Epidemiological Studies Depression Scale (CES-D) was used to determine the presence and development of depression. Multiple Logistics regression analysis was performed to assess the relationship between SVR and depression. Eligible patients were treatment naïve, adults, and 6 months past their ET; 694 patients were screened, and 108 patients were eligible for inclusion.
RESULTS: Forty percent of the sample was female, mean age was 46 years, 55% were of Hispanic descent, and 63% had genotype 1. Twenty-four percent had baseline depression, and among those not depressed 41% developed depression during the course of treatment. Regression analysis of the first study objective indicated the odds of achieving SVR were lower in depressed compared to non-depressed patients (OR = 0.50; 95% CI = 0.13–2.01). Patients achieving SVR had lower odds of developing depression (OR = 0.26; 95% CI = 0.18–3.04). However, these results were not statistically significant.
CONCLUSION: The impact of depression may be important for clinicians to assess when evaluating a patient's eligibility for HCV treatment, as depression may diminish chances of optimal clinical response; however, larger studies are necessary.

140. **Characterization of extended-spectrum beta-lactamase enzyme (ESBL) in *E. coli* and *K. pneumoniae* and their responses to combinations of piperacillin/tazobactam (PTZ) plus amikacin (AMK) or ciprofloxacin (CIP) versus meropenem (MER).** *Surakit Nathisuwan, Pharm.D., BCPS*[1], Panjarat Suntarasamit, M.S.[1], Chanpen Wiwat, Ph.D.[1], Kumthorn Malathum, M.D.[2], Pitak Santanirand, Ph.D.[2], Michael F. Carden, B.A.[3], David S. Burgess, Pharm.D., FCCP[3]; (1)Faculty of Pharmacy, Mahidol University, Bangkok, Thailand; (2)Faculty of Medicine at Ramathibodi Hospital, Bangkok, Thailand; (3) University of Texas Health Science Center at San Antonio, San Antonio, Tex.

BACKGROUND: Carbapenems are generally recommended as the treatment of choice for serious infection caused by ESBL-producing organisms. However, increased use of carbapenems is associated with emergence of imipenem-resistant organisms. The objective of this study was to compare the in vitro activity of PTZ plus AMK or CIP versus MER against clinical isolates of gene-specific ESBL organisms.
METHOD: In 2005-2006, 36 clinical isolates of ESBL *E. coli* (n=27) and *K. pneumoniae* (n=9) were collected at Ramathibodi Hospital. MICs were determined against MER, PTZ, AMK and CIP according to CLSI guidelines. ESBL-encoding genes were identified using PCR and sequencing. Time-kill curves were performed in duplicate using a standard inoculum. Bacterial densities were determined at 0, 4, 8, and 24 hours.
RESULTS: The MIC50, MIC90, %S was: PTZ (8, 128, 75%), AMK (16, 128, 65%), CIP (64, > 64, 15%), and MER (0.5, 1, 100%). The most prevalent ESBL genes were: CTX-M (86%), TEM (58%), VEB (56%), and SHV (14%)

with 31/36 isolates carrying multiple genes. From time-kill studies, PTZ plus AMK achieved and maintained bactericidal activity over the entire 24 hours in all isolates whereas PTZ plus CIP provided bactericidal activity in only 13 isolates. Compared to MER, PTZ plus AMK provided identical bactericidal activity, maximum killing rate, and time to 99.9% killing. However, PTZ plus CIP was significantly inferior to MER.

CONCLUSION: PTZ plus AMK may have the potential to be an attractive alternative to MER for the treatment of infection caused by ESBL-*E. coli* and *K. pneumoniae*. Randomized, controlled trials are warranted to confirm this hypothesis.

141. **Tigecycline in the treatment of *Acinetobacter* infections.** *Jason C. Gallagher, Pharm.D.*, Heather M. Rouse, Pharm.D. candidate; Temple University, Philadelphia, Pa.

PURPOSE: Antimicrobial resistance among gram-negative organisms continues to rise. Tigecycline is a glycylcycline, the first in a new class of tetracycline-related agents. Because infections caused by *Acinetobacter baumanni* often have a limited susceptibility patternand tigecycline is reported to have in vitro activity against this organism, clinicians at our institution have used tigecycline for *Acinetobacter* infections. This study was performed to describe the efficacy and safety of tigecycline for this use at our institution.

METHODS: Records of patients who received tigecycline since its approval were reviewed. Patients were included if *Acinetobacter* was cultured and the tigecycline was used for the treatment of the *Acinetobacter* infection. Data collected included demographic, microbiological, laboratory, and clinical information to observe efficacy and toxicity. Outcomes of cure and improvement were considered positive, and death within 7 days and worsening were considered negative.

RESULTS: Twenty-eight patients received tigecycline for *Acinetobacter* infection during the study period. These patients received tigecycline 29 times. Tigecycline was started an average of 33 days into the hospital stay, for a mean of 10.6 days. Patients had an average length of stay of 53 days. All patients received 50 mg IV every 12 hours after a loading dose. Pneumonia was the most common indication for tigecycline (n=15), followed by bacteremia (n=10), and wound infections and UTI (n=3 each). Bacteremia was often noted concomitantly with pneumonia. Positive outcomes were seen in 8 episodes (27.6%), negative outcomes in 18 (62.1%), and little clinical change in 3 (10.3%). Susceptibility testing was performed 11 times with an average MIC of 4.4. Nausea/vomiting was the most common adverse effect deemed likely with tigecycline.

CONCLUSIONS: Tigecycline is a new agent for the treatment of gram-positive and gram-negative infections. More supportive data is needed before its utility in the treatment of *Acinetobacter* infections can be advocated.

Insomnia

142. **Zolpidem extended-release 12.5 mg in adult patients with primary insomnia displays efficacy in multiple sleep measurements over 6 months.** *Gary Zammit, Ph.D.*[1], Andrew Krystal, M.D.[2], Milton Erman, M.D.[3], Christina Soubrane, M.D.[4], Thomas Roth, Ph.D.[5]; (1)Clinilabs Inc., New York, NY; (2) Duke University Hospital, Trent Drive, Durham, NC; (3)Pacific Sleep Medicine Services, San Diego, Calif; (4)sanofi-aventis Clinical Development, Chilly-Mazarin, France; (5)Henry Ford Hospital Sleep Disorders Center, Detroit, Mich.

PURPOSE: The efficacy and safety of zolpidem extended-release, a non-benzodiazepine hypnotic, taken "as needed," 3–7 days/week, was evaluated for 6 months in chronic insomnia patients.

METHODS: This was a multicenter, double-blind, placebo-controlled trial in 1025 randomized chronic primary insomnia patients (ages 18–64). Zolpidem extended-release 12.5 mg or placebo was taken "as needed," 3–7 days/week for 24 weeks followed by a 1-week treatment discontinuation period. Efficacy was measured by Patient Global Impression (PGI) and Clinical Global Impression scales every 4 weeks, and by daily morning questionnaires evaluating patient-reported total sleep time (TST), sleep onset latency (SOL), quality of sleep (QoS) and next-day functioning (morning sleepiness and ability to concentrate). Tablets taken/month and safety and tolerability were also assessed.

RESULTS: A total of 436/674 (64.7%) zolpidem extended-release patients and 184/351 (52.4%) placebo patients completed the study. Compared with placebo, zolpidem extended-release treated patients reported significant improvements in each item of the PGI scale (treatment aid to sleep, time to fall asleep, TST and medication strength) throughout the treatment period (p<0.0001 for all assessments/timepoints). Similar findings for improved insomnia severity with zolpidem extended-release were reported by clinicians (p<0.0001 versus placebo, Weeks 4–24). Morning questionnaires demonstrated significant and sustained reductions in TST, SOL and QoS (p<0.0001, Months 1–6) as well as a significant increase in ability to concentrate (p<0.002 each month) and reduced morning sleepiness (p<0.0001 each month) with zolpidem extended-release versus placebo. Mean monthly tablet intake was stable in the zolpidem extended-release group (range 18.9–20.1 tablets/month).

Zolpidem extended-release was well tolerated; most frequent adverse events for zolpidem extended-release/ placebo were headache (10.5%/9.5%), anxiety (6.3%/2.6%), and somnolence (5.7%/2.0%).
CONCLUSIONS: Chronic insomnia patients reported sustained efficacy during 6 months of zolpidem extended-release treatment, taken "as needed" 3–7 nights/week. Zolpidem extended-release was well tolerated, and patients maintained a stable tablet intake.

143. **Improved insomnia symptoms, quality of life, and daily functioning in patients with comorbid generalized anxiety disorder and insomnia following concomitant zolpidem extended-release 12.5 mg and escitalopram treatment.** *Greg Asnis, M.D.*[1], Ram Shrivastava, M.D.[2], Bruce Lydiard, M.D., Ph.D.[3], Bijan Bastani, M.D.[4], David Sheehan, M.D., M.B.A.[5], Thomas Roth, Ph.D.[6], Maurizio Fava, M.D.[7]; (1)Montefiore Medical Center, Psychiatry Department, New York, NY; (2)Eastside Comprehensive Medical, New York, NY; (3)South East Health Consultants, Charleston, SC; (4)North Coast Clinical Trials, Beachwood, Ohio; (5)University of Southern Florida, Tampa, Fla; (6)Henry Ford Hospital Sleep Disorders Center, Detroit, Mich; (7)Massachusetts Medical Center, Depression Clinical and Research Program, Boston, Mass.

PURPOSE: To assess the effect of zolpidem extended-release 12.5 mg, taken concomitantly with a selective serotonin reuptake inhibitor (escitalopram), on patient-reported sleep measures, as well as anxiety symptoms, quality of life (QoL) and related outcomes, in patients with comorbid generalized anxiety disorder (GAD) and chronic insomnia.
METHODS: This multicenter, double-blind, parallel-group, placebo-controlled trial randomized adults (ages 21–64) with GAD-associated insomnia to either nightly zolpidem extended-release 12.5 mg or placebo; all patients received open-label, escitalopram 10 mg treatment. Efficacy was assessed at Weeks 1, 2, 4, 6, and 8 using patient-reported morning sleep questionnaires, which evaluated total sleep time (TST), sleep onset latency (SOL), wake time after sleep onset (WASO), anxiety symptoms and QoL measures. Clinical Impression and Severity of Mental Illness and Patient Global Impression (PGI) of Insomnia Symptom scales monitored medication-response ratings.
RESULTS: A total of 381 patients were included (zolpidem extended-release/placebo = 191/190). For zolpidem extended-release versus placebo, respectively, patients reported significantly improved TST (106.0 vs 68.2 min), SOL (–55.1 vs –26.8 min) and WASO (–40.7 vs –28.8 min; $p<0.0001$ for each assessment/each visit). Healthcare resource utilization, anxiety symptoms, disability due to anxiety and insomnia, QoL in relation to cognitive function, life enjoyment and satisfaction were not significantly different from placebo after 8 weeks. However, clinical impressions of mental illness severity, PGI medication response ratings, SOL, sleep quality, and medication strength were significantly better with zolpidem extended-release versus placebo. In addition, zolpidem extended-release treated patients reported significantly improved QoL and measures of daily functioning, including mental and social wellbeing, physical activity, energy, and motivation. Zolpidem extended-release was safe and well tolerated; treatment-emergent adverse effects were similar between groups.
CONCLUSIONS: Zolpidem extended-release with concurrent escitalopram 10 mg was safe and effective in patients with GAD-associated insomnia, and improved insomnia symptoms and several other aspects of QoL and daily functioning.

Managed Care

144. **Evaluation of use of antidotes in Changi General Hospital (CGH): flumazenil, naloxone and protamine sulphate.** *Serene Yeow, B.Sc., (Pharm)(Hons)*, Jonathan Seah, B.Sc., (Pharm)(Hons), Jing Jing Wong, B.sc., (Pharm); Changi General Hospital, Singapore, Singapore.

PURPOSE: This study was carried out to 1) track the usage pattern of three antidotes: flumazenil, naloxone and protamine sulphate; 2) assess the appropriateness of use of these drugs in terms of indications, dosage and monitoring; and 3) explore the use of antidotes as trigger tools to track adverse drug reactions (ADR) and/or medication errors.
METHODS: A retrospective review of case notes of patients who were issued the antidotes from August 1 to December 31, 2006.
RESULTS: A total of 42 cases were reviewed. 33 (78.6%) cases involved flumazenil, 4 (9.5%) cases involved naloxone, 3 (7.1%) cases involved both flumazenil and naloxone, and 2 (4.8%) cases involved protamine sulphate. The most common indication for flumazenil was the reversal of benzodiazepine (BZ) effects in sedation and general anaesthesia (66.7%). Generally, the administration of flumazenil followed dosing guidelines. However, in some cases, the drug was not given in divided doses as recommended. Naloxone was given mainly for reversal of opioid depression (57.0%), followed by for diagnosis of opioid overdose (43.0%). The dosing of naloxone was generally appropriate. Monitoring of parameters (respiratory rate, heart rate, blood pressure) was either not done

or not documented for several patients. Protamine sulphate was used in two cases for the treatment of heparin overdose. Overall, antidote use was linked to ADR or medication error in 40.0% of the cases for flumazenil, 57.0% for naloxone and 100.0% for protamine.

CONCLUSION: The use of antidotes in CGH was generally appropriate. They were mainly used for registered indications, although reasons for use were not well documented in some cases. More attention should be paid to dosing regimens, especially for flumazenil and protamine. Improvements in the monitoring process and better documentation are required. The results do suggest that tracking these antidotes (especially naloxone and protamine) may reveal undetected ADRs or medication errors

Medication Safety

145. **Computerized pharmacy order entry and the occurrence of new types of medication errors: sulfadiazine and sulfasalazine as a case example.** *David Parra, Pharm.D., BCPS*, Lisa Korman, Pharm.D., Amy Colon, B.S., Roy Coakley, M.S.; Veterans Affairs Medical Center, West Palm Beach, Fla.

BACKGROUND: Implementation of computerized order entry systems has been advocated as a major advance in the prevention of medication errors. However, although implementation of such systems may reduce traditional types of medication errors, other previously unanticipated new types of errors may be generated. An example of this is where similarly spelled medications with similar dosage strengths appear in close proximity to each other on the medication order dialog presented to the provider upon order entry.

PURPOSE: Describe a medication error involving sulfadiazine and sulfasalazine that was uncovered during reconciliation of a patient's medication profile and the results of a subsequent evaluation into the nature and magnitude of this error across several medical centers utilizing computerized order entry systems.

METHODS: A retrospective evaluation was performed on all patients receiving sulfadiazine across six medical centers and their associated outpatient clinics to evaluate appropriateness and intent of therapy, with confirmation by the patient's prescribing provider.

RESULTS: A total of 16 patients were identified with an active prescription for sulfadiazine across the six medical centers. Similar medication selection (prescribing) errors occurred at four of the six facilities. Of the 16 patients receiving sulfadiazine 5 (31%) carried a diagnosis of ulcerative colitis and were receiving sulfadiazine in error. No adverse outcomes were reported. Sulfadiazine was discontinued, and the patients were switched to sulfasalazine. Processes were implemented to minimize these selection errors in the future and will be periodically reviewed.

CONCLUSION: Although computerized order entry may minimize some errors, others may be generated demonstrating the need to prospectively anticipate and circumvent various types of error as well as implement screening mechanisms to identify unanticipated errors which may have occurred. Widespread sharing and recognition of these errors amongst health care systems should minimize the risk of them being repeated.

146. **Determining the impact of a pharmacist assisting in the medication reconciliation process.** Talia B. Kleeb, Pharm.D.[1], *Nima M. Patel, Pharm.D., BCPS*[2], Mirza Perez, Pharm.D., BCPS[2]; (1)Temple University Hospital, Philadelphia, Pa; (2)Temple University School of Pharmacy, Philadelphia, Pa.

PURPOSE: To determine whether a pharmacist rounding with an internal medicine team can improve accuracy of the medication reconciliation by decreasing the number of discrepancies between home and inpatient medications.

METHODS: Patients admitted directly to a medicine team with a pharmacist were eligible for this prospective, non-randomized study. Adult patients were included who were taking at least three chronic medications and who spoke English. Patients transferred to the service who were unable to give a medication history or were unable to be interviewed by the pharmacist within 48 hours of admission were excluded. Physicians completed the patient's medication history, and a pharmacist interviewed the patient afterward. Discrepancies in medication reconciliation were classified as appropriate or inappropriate. Inappropriate discrepancies without reasonable cause were recorded and categorized according to type of discrepancy such as omission or incorrect dose, route, or frequency. All inappropriate discrepancies were further categorized according to the National Coordinating Council for Medication Error Reporting and Prevention Index.

RESULTS: Forty-five patients were included, the majority being African American (76%) and female (67%). Patients were taking an average of seven medications. To obtain medication history, the patient's community pharmacy was called 38% of the time, and the patient had the medication bottles or a list of medications 33% of the time. The total number of discrepancies was 130. The number of inappropriate discrepancies was 74, with a mean of 1.6 per patient. Most inappropriate discrepancies were due to omission of a medication (69%). There is a moderate correlation ($r = 0.62$) between the number of inappropriate discrepancies and number of medications.

Discrepancies contributed to temporary harm in 18% of the cases. Most errors (70%) led to no harm but required increased monitoring.

CONCLUSION: A pharmacist rounding with a medicine team was able to improve the accuracy of medication reconciliation and decrease adverse events due to medication errors.

147. **Where is the continuity between medication lists and progress notes? A study of the potential for adverse events in an internal medicine residents' continuity clinic.** *Stuart J. Beatty, Pharm.D.*[1], James F. Lamb, M.D.[2], Ty D. Huebert, M.D.[2], Anne H. Metzger, Pharm.D.[1], Jennifer A. Woyach, M.D.[2], Rajesh Balkrishnan, Ph.D.[1]; (1)The Ohio State University College of Pharmacy, Columbus, Ohio; (2)The Ohio State University Medical Center, Columbus, Ohio.

PURPOSE: To determine the accuracy of medication lists at an internal medicine residents' continuity clinic by evaluating the differences between medication lists and progress notes, and to identify correlation(s) between these differences and demographic parameters.
METHODS: One hundred fifty of the 2005 total patients visiting The Ohio State University Internal Medicine Residents' Continuity Clinic between July 1, 2005, and June 30, 2006, were randomly selected. Inclusion criteria were patients on at least one medication with two or more visits during the 1-year time interval. Variables collected included demographic data, medication list documentation, and progress note medication documentation.
RESULTS: Of the 150 patients identified, 45 were excluded due to lack of visits, lack of medications, or chart unavailability, leaving 105 patients for data analysis. Nineteen of 105 (18.1%) patient charts did not include a medication list, and 41 of 105 (39.0%) did not include medication allergy history. A total of 708 medications were documented on medication lists (6.52 ± 5.29 medications per patient), of which 97 (13.7%) were non-prescription products (OTC or herbal). Of the 708 medications, 148 (20.9%) were not documented in patient progress notes. In contrast, 918 medications were documented in patient progress notes (9.03 ± 6.87 medications per patient), of which 338 (36.8%) were not documented on patient medication lists. Preliminary analysis indicates the number of visits (p=0.011) and type of insurance (p=0.049) were correlated with medication discrepancies between the progress notes and medication lists.
CONCLUSION: Patient charts reviewed indicate that a high number of discrepancies exist between medication lists and progress notes, with a sizeable number of charts not including a medication list and/or medication allergy history. In addition, OTC and herbal products appear underreported in medication lists. Study results indicate a lack of continuity, leading to potential medication-related adverse events and subsequent negative patient outcomes.

148. **The prevalence of supratherapeutic acetaminophen dosing in adults in a community teaching hospital.** *Sheri N. Ober, Pharm.D.*; Carilion Medical Center, Roanoke, Va.

PURPOSE: Acetaminophen is commonly administered to hospitalized patients in various forms. The numerous available products containing acetaminophen present a barrier to effective tracking of total acetaminophen administered per 24-hour period. After a random controlled-substance audit found excessive single-patient removals of hydrocodone/acetaminophen from an automated dispensing cabinet (ADC), the prevalence of supratherapeutic dosing at the hospital was investigated.
METHODS: Acetaminophen ADC removals for adult inpatients in excess of 4 g per patient per day were retrospectively extracted from a database for a 3-month period of 2006. Charting and administration data were verified via the electronic medication administration record for these patients. Excessive dosing was counted by nursing unit and by drug product administered.
RESULTS: There were 148 instances of patients receiving over 4 g per day. Eighty-six percent of the instances involved a single day of excessive administration for a given patient. Hydrocodone/acetaminophen and propoxyphene/acetaminophen were involved in 63.5% and 28.4% of the instances, respectively. Prevalence varied greatly by nursing unit.
CONCLUSIONS: Causes for the excessive dosing were examined and have been addressed through the Medication Safety Committee. Staff education, changes to preprinted order forms, and product interchanges were instituted. A re-examination is planned for a 3-month period of 2007.

149E. **Safety and tolerability of the combination of amlodipine besylate and olmesartan medoxomil.** *Shashank Rohatagi, Ph.D.*[1], Stephen Haworth, M.D.[1], Reinilde Heyrman, M.D.[1], James Lee, Ph.D.[1], Robert Noveck, M.D.[2], Jean-Francois Marier, Ph.D.[3], Igor Rubets, Ph.D.[3], Daniel Salazar, Ph.D.[1]; (1) Daiichi Sankyo, Inc., Parsippany, NJ; (2)MDS Pharma Services, Neptune, NJ; (3)MDS Pharma Services, Montreal, Quebec, Canada.

PURPOSE: Many hypertensive patients need more than one antihypertensive agent; combining agents with different mechanisms of action may improve efficacy vs monotherapy. The purpose of this presentation is to summarize the safety data from 5 phase I clinical trials (n=23–30) for the combination of amlodipine besylate (AB) and olmesartan medoxomil (OM).

METHODS: The pharmacokinetics of a novel fixed-dose combination of AB and OM were compared with free combination of these agents (AB + OM) or monotherapy in phase 1 studies in 200 healthy volunteers. Safety/ tolerability data for AB/OM single- or multiple-dose studies of randomized, open-label, crossover design are presented.

RESULTS: Treatment-emergent adverse events (TEAEs) occurred in 10%–60% of volunteers, and possibly or probably study-drug-related AEs were reported in 0%–30% of volunteers. Most TEAEs were of mild severity; the most common was headache. In one large study (Study 112; n=60), the most frequent TEAEs were headache, dizziness, cough, and pharyngolaryngeal pain, reported in 36.7%, 13.3%, 11.7% and 11.7% of volunteers, respectively. In two studies (110, 111), headache was the only possibly drug-related AE; headache and dizziness were the only possibly or probably drug-related AEs in Study 112. There were no severe AEs for the fixed- or free-dose combination of AB + OM. One volunteer given a single dose of AB 10 mg + OM 40 mg discontinued due to a non-drug related AE (Study 111). In Study 109, a volunteer discontinued due to a positive serum pregnancy test and later had a spontaneous abortion classified as a serious, unlikely drug-related AE. There were few clinically significant laboratory abnormalities (0–6 volunteers in individual studies). Generally, there were no clinically significant ECG abnormalities.

CONCLUSIONS: The fixed-dose combinations of AB/OM appear to be safe and well-tolerated in healthy volunteers. Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, May 19-22, 2007, Chicago, Ill.

150. **Patient-reported outcomes in patients with Stage 2 hypertension treated with olmesartan medoxomil/hydrochlorothiazide or benazepril/amlodipine besylate.** *Henry Punzi, M.D.*[1], Dean Kereiakes, M.D.[2], Joel Neutel, M.D.[3], Findlay Walker, M.D.[4], Robert Dubiel, Pharm.D.[4], Jianbo Xu, M.S.[4]; (1)Punzi Medical Center and Hypertension Research Institute, Carrollton, Tex; (2)The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, Ohio; (3)Orange County Research Center, Tustin, Calif; (4)Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: Most patients with Stage 2 hypertension require combination antihypertensive therapy; however, some blood pressure-lowering combinations may improve patient outcomes (e.g., fewer side effects or better quality of life [QoL]).

METHODS: Patient-reported outcomes were assessed in patients with Stage 2 hypertension treated with an olmesartan medoxomil (OM)-based regimen: OM 20 mg (weeks 0–2), OM 40 mg (weeks 2–4), OM 40 mg/ hydrochlorothiazide (HCTZ) 12.5 mg (weeks 4–8), and OM 40 mg/HCTZ 25 mg (weeks 8–12) following a 3–4-week placebo run-in vs. a benazepril (BEN)-based regimen titrated at same intervals: BEN 10 mg, BEN 20 mg, BEN 20 mg/amlodipine besylate (AML) 5 mg, and BEN 20 mg/AML 10 mg. Patients completed a questionnaire evaluating adverse effect severity, physical impairment, and QoL at day 0, weeks 4 and 12 or study end.

RESULTS: Most patients in the OM and BEN groups were not bothered by adverse effects at baseline (OM 82.2%; BEN 78.5%), week 4 (OM 82.8%; BEN 83.1%) or week 12 (OM 88.3%; BEN 81.6%). Patient-reported that "bothersome" adverse effects evaluated in the questionnaire included headache, coughing, dizziness, and leg swelling. The most marked changes in patient-reported adverse effects were a decrease in headache in both groups (43% of days over the 2 weeks prior to treatment [baseline] in both groups vs 24% (OM) and 29% (BEN) at week 4 and 26% (OM/HCTZ) and 22% (BEN/AML) at week 12), increased cough with BEN regimen (17% of days [baseline] vs 31% and 32% at weeks 4 and 12) and increased dizziness with OM regimen (6% at baseline vs 8% and 20% at weeks 4 and 12). At 4 and 12 weeks, 29%–30% of patients rated their QoL as moderate; 66%–70% rated it high across both regimens. Most patient-reported that adverse effects were mild to moderate in severity, and physical condition scores were generally high.

CONCLUSIONS: OM±HCTZ and BEN±AML are well-tolerated with a positive impact on patient-reported outcomes.

151. **An approach to continuous improvement of clinical decision support for medications.** *James M. Hoffman, Pharm.D., M.S.*, Donald K. Baker, Pharm.D., M.B.A., Jerry L. Shenep, M.D., Joe Mirro, M.D.; St. Jude Children's Research Hospital, Memphis, Tenn.

PURPOSE: Clinical decision support (CDS), particularly computerized alerts, is cited as a compelling benefit of computerized provider order entry (CPOE). However, if too many alerts are presented, "alert fatigue" may result in clinicians disregarding alerts. We sought to minimize nuisance alerts while maintaining clinically important alerts. The purpose of this analysis is to present an approach to continuous improvement of CDS.

METHODS: Before implementation of an integrated CPOE pharmacy eMAR system, a clinician group made decisions prospectively to decrease the likelihood of alert fatigue. Given the intense therapy our patients receive, drug interaction alerts were set to display only at the highest severity level, and duplicate therapy alerts were disabled. To facilitate assessment and careful consideration, override reasons were required. Each interaction, allergy, duplicate therapy, and rule event that fired, regardless of whether it is displayed, was analyzed from September to December 2006.

RESULTS: Without restrictions, 383,400 alerts would have been displayed over the 4-month period, roughly 150 alerts per attending physician per day. Initial filtering decisions resulted in 6.5% (24,914) of the alerts actually being displayed; the majority of these alerts were drug-drug interactions (72%), with the primary reason for override being "drug clinically indicated." Override reasons for allergy warnings were primarily distributed between "tolerated in past" (40%), "drug clinically indicated" (37%), and "premed/alter infusion" (21%). An informal review process resulted in 49 alert modifications, and a formal review process for alert modifications is now in use.

CONCLUSIONS: Our efforts to limit the number of alerts presented to clinicians so that only the most important alerts are presented were successful. Reasons for alert override are useful to evaluate and to improve alerts. To maximize the safety benefits of alerts and other CDS, institutions should continuously evaluate alerts and establish a formal review process for problematic alerts.

Nephrology

152. **Cefepime hemodialysis clearance in patients can be accurately predicted from in vitro dialytic experiments.** *Donald F. Brophy, Pharm.D.*, Lena Maynor, Pharm.D., Daniel Carl, M.D., Todd W.B. Gehr, M.D., Elizabeth B.D. Ripley, M.D., Gary R, Matzke, Pharm.D.; Virginia Commonwealth University School of Pharmacy, Richmond, Va.

PURPOSE: In vitro techniques to assess drug clearance (CL) during hemodialysis (HD) can predict what occurs in the in vivo setting. This method can allow for rapid evaluation of drugs without unnecessarily exposing subjects to potentially toxic medications.

METHODS: In vitro HD was conducted using a high-flux Fresenius 180 dialyzer, a 5-Liter phosphate buffered saline solution containing urea 100 mg/dL, creatinine 10 mg/dL, and cefepime 100 mg/L. The solution flow rate (Qs) was 300 mL/minute; the dialysate (Qd) and ultrafiltration (UF) flow rates were 600 and 0 mL/minute, respectively. The Qs of 300 mL/minute was set to simulate the dialysis plasma flow rate for a typical patient with a blood flow rate (Qb) of 450 mL/minute and a hematocrit of 35%. In vivo dialysis was conducted in 5 patients following a 1 g dose of cefepime 30 minutes before HD using Qb 500 mL/minute and the same Qd, UF, and filter as above. Arterial (Ca), venous (Cv) and dialysate (Cd) cefepime concentrations were simultaneously obtained during dialysis at Qb 500 mL/minute. Cefepime concentrations were measured using a validated HPLC assay. In vitro dialytic clearance (CLd) was determined as $[(Ca – Cv / Ca) \cdot Qs]$; In vivo plasma clearance (CLp) was determined as $[Ca – Cv / Ca] \cdot [Qb \cdot (1\text{-hematocrit})]$.

RESULTS: The plasma flow rate for the patients was calculated as 304 ± 13 mL/minute which provided a valid comparison to the in vitro Qs of 300 mL/minute. The in vitro cefepime CLd of 196.4 mL/minute at Qs 300 mL/minute was similar to the in vivo cefepime CLp values of 191.8 ± 24.6 at Qb 500 mL/minute.

CONCLUSIONS: This in vitro model reliably predicts cefepime CL in HD patients. This model may be useful in dosage regimen design for various dialyzer and hemodialysis prescription combinations.

153. **An evaluation of nephrotoxicity of liposomal Amphotericin B.** *Gourang Patel, Pharm.D.*, Christopher Crank, Pharm.D., Mira Loh-Trivedi, Pharm.D., Robert Balk, M.D.; RUSH University Medical Center, Roselle, Ill.

PURPOSE: Selection of the appropriate antifungal agent requires consideration of the adverse effect profile with respect to the patient. Renal function is an important consideration when selecting polyene antifungal therapy. Although the lipid formulations of amphotericin B minimize the risk of nephrotoxicity, the potential still exists. This investigation of liposomal amphotericin B (L-AMB) was conducted to determine the incidence and factors associated with the development of nephrotoxicity.

METHODS: A retrospective review was conducted of 100 consecutive patients receiving L-AMB at doses of 1, 3, and 5 mg/kg. Nephrotoxicity was defined as an increase in serum creatinine of 0.5 mg/dL or an increase of 50% from baseline. Patients were included if they were 18 years of age or older and received L-AMB at one of the indicated doses. Patients were excluded if they had developed renal dysfunction prior to L-AMB administration. Baseline demographics were collected including age, gender, baseline serum creatinine, immunosuppression regimen, intravenous (IV) contrast exposure, concomitant nephrotoxins, and length of L-AMB treatment.

RESULTS: 75 patients were included based upon the predefined inclusion/exclusion criteria. Overall, 56% (42/75) of patients developed nephrotoxicity. Hematology/oncology patients composed 79% (59/75) of the total population. Of the patients that developed nephrotoxicity, 74% (31/42) were exposed to IV contrast, and 90% (38/42) were receiving nephrotoxins concurrently. Age, cumulative dose, concomitant nephrotoxins, and IV contrast exposure were associated with increased nephrotoxicity ($p<0.001$).
CONCLUSION: The development of nephrotoxicity with L-AMB was common and often multifactorial. Lipid amphotericin B products are associated with lower rates of nephrotoxicity than conventional amphotericin; however, in this analysis L-AMB was associated with a high incidence of nephrotoxicity.

155. **Differences in cefazolin and cefepime clearance in hemodialysis.** *Lena Maynor, Pharm.D.*, Daniel Carl, M.D., Gary R. Matzke, Pharm.D., Todd W.B. Gehr, M.D., Donald F. Brophy, Pharm.D.; Virginia Commonwealth University School of Pharmacy, Richmond, Va.

PURPOSE: Cefazolin and cefepime are routinely prescribed for infected hemodialysis (HD) patients. Few studies have evaluated their dialytic plasma clearance (CL_p) using contemporary high-flux dialysis membranes. This study was conducted to characterize the influence of dialysis prescription variability on HD drug clearance.
METHODS: Five chronic HD patients received a single 1 gram IV dose of cefazolin and cefepime before HD. HD was performed with a high-flux Fresenius 180 dialyzer. The dialysis blood flow rate (Q_b) was sequentially increased from 100 mL/minute to 500 mL/minute and allowed to equilibrate for 15 minutes prior to the determination of CL_p; the dialysate flow rate was 600 mL/minute. Arterial (C_a), venous (C_v), and dialysate (C_d) concentrations were simultaneously obtained for urea, creatinine, cefazolin, and cefepime. Cefazolin and cefepime concentrations were measured using a validated HPLC assay. CL_p was determined as $[C_a - C_v / C_a] \cdot [Q_b \cdot (1\text{-hematocrit})]$.
RESULTS: Urea, creatinine and cefepime CL_p were positively correlated with Q_b. Cefazolin, which is > 80% protein bound, is not affected by increasing Q_b.

Mean (S.D.) Solute Clearance (mL/min)			
	Q_b 100 mL/min	Q_b 300 mL/min	Q_b 500 mL/min	r^2
Urea	100.0 (0)	274.0 (7.2)	403.6 (11.2)	0.99
Creatinine	88.2 (4.9)	244.7 (11.0)	359.3 (17.3)	0.99
Cefepime	60.1 (2.6)	120.5 (33.2)	191.8 (24.6)	0.99
Cefazolin	42.3 (7.7)	52.7 (16.0)	48.5 (44.5)	0.28

CONCLUSIONS: Cefepime CL_p is highly bloodflow-rate dependent whereas the CL_p of cefazolin is not. The cefepime CL_p values obtained in our study are about 20% higher, but consistent with those previously reported with high efficiency HD. Cefazolin CL_p was not dramatically enhanced with the use of this high flux dialyzer. Clinicians should not assume that all cephalosporins are cleared similarly by HD. Changes in Q_b and plasma protein binding can have significant effects on drug clearance.

156. **Modification of diet in renal disease (MDRD) GFR-based potassium (K) replacement protocol effectively and safely corrects hypokalemia.** *Scott A. Chapman, Pharm.D.*[1], Tony Kaufenberg, Pharm.D.[2], Patty Anderson, R.N.[3], Anwar Khokhar, M.D.[4], Christian G. Schrock, M.D.[5]; (1)University of Minnesota College of Pharmacy and North Memorial Medical Center, Minneapolis, Minn; (2) North Memorial Medical Center, Robbinsdale, Minn; (3) North Memorial Medical Center, Robbinsdale, Minn; (4)North Memorial Medical Center, Robbinsdale, Minn; (5)North Memorial Medical Center, Robbinsdale, Minn.

PURPOSE: To evaluate the efficacy and safety of a new K replacement protocol where K dosing regimens are determined by MDRD GFR and serum K deficiency (Kdef).
METHODS: K replacement dosing regimens are based on MDRD GFR > 70 mL/minute/1.73 m^2, 40–70 mL/minute/1.73 m^2, or < 40 mL/minute/1.73 m^2 and Kdef determined by prescriber defined goal K minus serum K. Default goal K was 3.5. Goal K was 4.0 in pts with cardiovascular disease. Serum K, MDRD GFR, and K replacement doses prescribed were collected. K replacement protocol was evaluated by determining goal K, Kdef, change in K following replacement (ΔK), K dose to reach goal (Kdose), and K > 5 mEq/L following replacement.
RESULTS: Over the first month of implementation, K replacement was ordered in 368 patients. 253 patients receiving at least one K replacement protocol dosing regimen were reviewed. 138 patients were excluded for failure to follow the protocol. 115 patients whose goal K was 3.5 (36 patients), 3.7 (2 patients), or 4.0 (77 patients) mEq/L required 140 protocol initiations (1.2/patient). 105 (75%) protocol initiations required one dosing regimen, while 31 (22.1%) required more than one dosing regimen (range 2–6) to achieve goal K. 4 (2.8%) did not achieve

goal K. A total of 185 K replacement dosing regimens (1.6/patient) were evaluated. MDRD GFR was > 70 mL/minute/1.73 m² in 99, 40–70 mL/minute/1.73 m² in 63, and < 40 mL/minute/1.73 m² in 23 dosing regimens.

MDRD (m±SD) Kpre Kdef K Kpost Kdose

>70(101.3±23.0)	3.4±0.3	0.39±0.28	0.53±0.38	3.9±0.5	52±37
40-70(55.5±8.0)	3.5±0.3	0.44±0.28	0.46±0.36	3.9±0.4	44±28
<40 (26.5±9.0)	3.3±0.3	0.6±0.27	0.59±0.39	3.9±0.4	36±15
Total	3.4±0.5	0.4±0.28	0.51±0.37	3.9±0.6	48±33

No patient reached a serum K greater than 5 mEq/L following K replacement dosing regimen.
CONCLUSION: Our K replacement dosing regimens based on MDRD GFR and Kdef consistently corrected K depletion without resulting in hyperkalemia.

157. **Long term outcomes of darbepoetin in hemodialysis patients following conversion from epoetin.** *Lisa M. Mueller, Pharm.D.*, Madeline Pahl, M.D., Renee Weng, Pharm.D.; UC-Irvine, Orange, Calif.

PURPOSE: Darbepoetin has a half-life significantly longer than epoetin, allowing for decreased frequency of administration. Some dialysis centers switched to darbepoetin with the hope that the decreased frequency of administration would lower the cost of maintaining hemoglobin (Hb) in their patients. UC Irvine Dialysis Center converted in February 2005. The manufacturer supplies recommendations for converting patients from epoetin to darbepoetin. This study compares the darbepoetin dosage required to maintain Hb to the manufacturer's recommendation and the cost of maintaining Hb using darbepoetin in place of epoetin.
METHODS: Medical records of all patients receiving hemodialysis at the time of conversion from epoetin to darbepoetin were reviewed. The study period was from 12 weeks before conversion to 52 weeks following conversion. Data collected included epoetin/darbepoetin dosage, Hb, serum ferritin, iron saturation, and demographic information. Cost information was calculated using the center's acquisition cost for both drugs.
RESULTS: Average Hb was 11.8 g/dL in the 12 weeks before conversion, and following darbepoetin dose titration was also 11.8 g/dL after about 1 year on darbepoetin. The average darbepoetin dosage that was required to maintain Hb after about 1 year was 49 mcg, which is 22.5% greater than the initial dose recommendation in the manufacturer's guidelines. The weekly medication cost of darbepoetin began at 20% lower than epoetin and rose to 14% greater than epoetin by the end of the study.
CONCLUSIONS: Following dose titration, darbepoetin was able to maintain Hb as well as epoetin. The darbepoetin dose that was required to maintain an average Hb of 11.8 g/dL exceeded the manufacturer's guidelines on converting from epoetin suggesting that the guidelines underestimate the dose requirements.

Neurology

158. **Effect of viagra® on neurodegenerative diseases**. *Muralikrishnan Dhanasekaran, Ph.D.*, Subramaniam Uthayathas, M.S., Koodeswaran Parameshwaran, M.S., Senthikumar Shanmugam, M.S., Vishnu Suppiramaniam, Ph.D.; Harrison School of Pharmacy, Auburn, Ala.

PURPOSE: This study focused on the effects of Viagra® on neurodegenerative diseases. We investigated the effects of sildenafil, active ingredient of Viagra®, on its possible role in: 1) Parkinson's disease therapy, and 2) hippocampal dependent memory.
METHODS: Three-month-old male C57BL/6 mice were used in both Parkinson's study and memory test. Mice were intraperitoneally (i.p.) injected with sildenafil (10 mg/kg) every 16 hours, 30 minutes prior to administration of 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP). Behavioral changes were recorded immediately after the toxin administration. Substantia nigra and striatum were dissected out 6 days after the last injection, and monoaminergic neurotransmitters were analyzed using HPLC–ECD. For the memory test, mice were injected (i.p.) with sildenafil (0.5, 1, and 2 mg/kg), immediately after the first trial of object recognition task and Y maze, and tested for the retention of memory. In another experiment, mice were treated (i.p.) with different doses of sildenafil (0.5, 1, and 2 mg/kg) and placed in open field for 5 minutes to test for anxiety, early indicator of memory dysfunction. Latent time from center, distance traveled, and number of fecal boli excreted were recorded.
RESULTS: Sildenafil did not have neuroprotective effect against MPTP-induced neurotoxicity. With regard to memory, discrimination index of object exploration was high in 1 mg/kg and 2 mg/kg treatment compared to the control. Both object memory and spatial memory were enhanced by the administration of sildenafil (1mg/kg). Open field test suggest the absence of anxiety after administration of sildenafil. CONCLUSION: Sildenafil may not have beneficial effects on nigral dopaminergic neurons. However, there is a huge demand for therapeutically safe and effective drugs for the memory enhancement. Current results reveal that sildenafil (moderate level/

dose) may be beneficial for memory enhancement. Further studies need to be carried out to elucidate the memory enhancing mechanisms of sildenafil.

159E. Safety of concomitant therapy with rasagiline and antidepressants in Parkinson Disease.
Jack J. Chen, Pharm.D.[1], Michel Panisset, M.D.[2], Steven Schwid, M.D.[3], William Ondo, M.D.[4], Cheryl Fitzer-Attas, Ph.D.[5]; (1)Loma Linda University, Loma Linda, Calif; (2)CHUM - Hôtel-Dieu de Montréal, Montreal, Quebec; (3)University of Rochester, Rochester, NY; (4)Baylor College of Medicine, Houston, TX; (5)Teva Pharmaceutical Industries, Ltd, Petach Tikva, Israel.

PURPOSE: The objective was to assess the safety of combining antidepressant therapy with rasagiline therapy in patients with Parkinson's disease (PD) Certain serotonergic drugs, when used in combination, may trigger a potentially serious serotonin toxicity (ST) characterized by major adverse events (AEs) (confusion, fever/hyperthermia, diaphoresis, myoclonus, hypertonia, tremor, shivering, and hyperreflexia) along with other minor psychic, autonomic, and neuromuscular AEs. Such ST has not been reported to date with rasagiline, a novel, selective, and irreversible MAO-B inhibitor now in use for the treatment of PD.
METHODS: All records of PD patients who had taken antidepressants concomitantly with rasagiline in rasagiline clinical trials were assessed for 15 AEs suggestive of ST. The incidence rates of the selected AEs in these patients were compared with incidence rates in patients taking rasagiline only, using a Fisher Exact 2-tailed test. Possible combinations of AEs suggestive of ST were analyzed.
RESULTS: From a total of 1361 patients who ever took rasagiline in controlled clinical trials, 323 were noted to have taken a concomitant antidepressant, for a median time of 367 days (range 1–3067 days). The most common exposures were to amitriptyline (n=112), sertraline (n=75), paroxetine (n=70), trazodone (n=60), and citalopram (n=34). Rate ratios indicated that sleep disorder (10.1 vs 6.3; p=0.0005), dyspnea (2.9 vs 1.6; p=0.03), and confusion (2.9 vs 1.5; p=0.02) occurred significantly more frequently in patients taking rasagiline plus antidepressant than in patients taking rasagiline alone; these are all known AEs of antidepressants and symptoms of depressive disorders. Termination rates were similar with and without antidepressants, and no apparent cases of ST were identified.
CONCLUSIONS: Use of antidepressants in PD patients taking rasagiline does not appear to cause any unexpected AEs or increase the rate of termination. Antidepressants appear to be safe for use in conjunction with rasagiline for PD.
Presented at the Movement Disorders Society 11th International Congress of Parkinson's Disease and Movement Disorders, Istanbul, Turkey, June 3-7, 2007.

160E. Rasagiline adjunct therapy produces marked levels of response across all Parkinson disease severities: pooled data analysis from the PRESTO and LARGO studies. *Crystal Obering, Pharm.D., M.B.A.*[1], Jack J. Chen, Pharm.D.[2]; (1)University of Missouri - Kansas City, Kansas City, Mo; (2)Loma Linda University, Loma Linda, Calif.

PURPOSE: The objective was to characterize the baseline disease and demographic traits of patients with Parkinson's disease (PD) who demonstrate the best response to rasagiline as add-on therapy. In patients with moderate to advanced PD, rasagiline 1 mg once daily has shown efficacy as adjunct to levodopa in two large randomized, placebo-controlled studies (PRESTO and LARGO), by significantly reducing mean daily OFF time.
METHODS: Pooled analysis was performed on 364 rasagiline-treated patients from the PRESTO and LARGO studies. Responders in terms of change from baseline in mean daily OFF time (primary end point) were defined in two ways: actual hours reduction and percent change from baseline. The highest quartile of responders in the "hours only" group(i.e., > 2.56 hours reduction) or the "percentage only" group (i.e., > 46% reduction) were termed "super responders." Super responders that overlapped with both groups were defined as the "overlap group." Descriptive analyses of baseline characteristics were made for the 3 super responder groups vs. non-super responders.
RESULTS: Overall, rasagiline super responders (n=119) had a longer disease duration than other patients (n=245). However, those in the "percentage" only group (i.e., no overlap with "hours" group; n=29), had lower mean daily OFF time, UPDRS-Motor ON, and UPDRS-ADL OFF scores (i.e., milder disease) at baseline, than the non-super responders. In contrast, super responders in the "hours" only group (i.e., no overlap with "percentage" group; n=28) had more severe disease at baseline than non-super responders in terms of OFF time. The overlap group (n=62) displayed baseline characteristic values in between these extremes.
CONCLUSIONS: Once-daily rasagiline, as adjunct therapy, can produce a high-level response across a spectrum of levodopa-treated PD patients with varying degrees of disease severity. Besides a tendency for longer PD duration, no clear picture emerged for the profile of moderate to advanced PD patients that respond best to rasagiline.

161. **Neurocognitive and behavioral factors associated with antiepileptic drug non-adherence.** *Collin A. Hovinga, Pharm.D.*[1], Stephanie J. Phelps, Pharm.D.[1], James W. Wheless, M.D.[1], Miya R. Asato, M.D.[2], J. Eric Pina-Garza, M.D.[3], Raj D. Sheth, M.D.[4], Ranjani Manjunath, MSPH[5], Lisa S. Haskins, M.P.A.[6]; (1)University of Tennessee Health Science Center, Memphis, Tenn; (2)Division of Child Neurology, Pittsburgh, Pa; (3)Vanderbilt University, Nashville, Tenn; (4)University of Wisconsin-Madison, Madison, Wis; (5)GlaxoSmithKline, Research Triangle Park, NC; (6)Harris Interactive, Rochester, NY.

PURPOSE: The specific patient factors associated with non-adherence in epilepsy are not well published. This study assessed the relationship between cognitive and behavioural function and non-adherence in adults with epilepsy.
METHODS: Individuals (ages 18–64 years) diagnosed with epilepsy and prescribed an antiepileptic drug (AED) were recruited between April 19 and May 10, 2007. All participants completed an online survey including validated scales for cognition (MOS-COG) and quality of life (SF-12). Non-adherent patients were defined as those who self-reported missing or stopping an AED within the last month. Data were weighted to represent the general U.S. population of people with epilepsy. Data are presented as mean ± SEM and $p<0.05$ was statistical significance.
RESULTS: Data were analyzed from 408 adults with epilepsy; 110 were classified as non-adherent. Non-adherent patients scored significantly lower on overall cognition (39% scored 1–3 of 6 on MOS-Cog) and mental health assessment (54% below the mean SF-12 MNBS) compared with adherent patients (18%, 37% respectively). Over the past 4 weeks, non-adherent patients forgot things that happened recently (3.5 ± 0.17; 4.5 ± 0.09 on a 6-point scale), had trouble maintaining attention on an activity (4.2 ± 0.16; 4.8 ± 0.08), and accomplished less due to emotional problems than adherent patients (57%, 35% respectively). Productivity issues at work occurred significantly more for non-adherent patients than for adherent patients during the past week including: becoming restless (5.4 ± 0.30; 3.1 ± 0.19 on 10-point scale) and difficulty concentrating (4.8 ± 0.34; 3.1 ± 0.21). Non-adherent patients were more likely to report feeling downhearted and blue (3.8 ± 0.14 on 6-point scale) compared with adherent patients (4.3 ± 0.08). CONCLUSION: These findings indicate that non-adherence to AEDs is associated with impairments in cognitive and emotional functioning and lowered productivity. Addressing these adherence issues through medication counseling may improve productivity and overall health outcomes.

Nutrition

162E. **Actual aluminum content of parenteral nutrition is lower than the estimated content.** *Rex Speerhas, R.Ph., BCNSP*; Cleveland Clinic, Cleveland, Ohio.

PURPOSE: In 1994, the Food and Drug Administration set a mandate that all manufacturers must label ingredients used to make parenteral nutrition (PN) solutions with the maximum concentration of aluminum. Pharmacies who prepare PN solutions must attempt to prepare these solutions so that they provide less than 5 mcg/kg/day of aluminum because of the toxicity risk for this compound. We decided to measure a series of PN solutions to determine the actual content of aluminum and clinical exposure and to compare this with the calculated value.
METHODS: Fifty samples from both adult and pediatric PN solutions and controls of plain IV fluid were sent to two different analytic laboratories. The aluminum content of these samples was measured by inductively coupled plasma mass spectrometry. Seven of the samples were duplicate measurements sent to the same laboratory. Using the labeled concentration of aluminum for the PN ingredients and the patient's weight, the estimated amount of aluminum was calculated for each sample. The difference between the measured and estimated aluminum for each solution was compared using Wilcoxon rank sum test.
RESULTS: Ten samples sent for analysis were lost, including four duplicate samples. The aluminum concentration of all controlled samples was < 25 mcg/L. Twenty three values were used in the final analysis. The median of the difference between the estimated and the actual aluminum concentrations was 25.9 mcg/kg ($p<0.0001$). Using actual concentrations, 65% of the PN solutions did not exceed the FDA toxicity level of 5 mcg/kg. Using the estimated concentrations, all solutions exceeded the FDA toxicity level.
CONCLUSIONS: The actual aluminum exposure from PN solutions is markedly less than the estimated amount. PN ingredients with the lowest amount of aluminum should be used to prepare solutions because pediatric patients are at risk for toxic exposure of this element.
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Oncology

163. Piperacillin/tazobactam hypersensitivities in patients with hematologic malignancies. *Katherine D. Mieure, Pharm.D.*[1], Craig A. Martin, Pharm.D.[1], Daniel A. Lewis, Pharm.D.[1], Kelly M. Smith, Pharm.D.[1], Susanne E. Liewer, Pharm.D.[2]; (1)University of Kentucky HealthCare, Lexington, KY; (2) Children's Mercy Hospital, Kansas City, Mo.

PURPOSE: Hypersensitivity reactions to ß-lactam antimicrobials are common. The risk factors for developing ß-lactam hypersensitivities are often present in patients with hematologic malignancies, yet the incidence for this patient population is unknown. We compared the incidence of new-onset piperacillin/tazobactam hypersensitivity in adults with hematologic malignancies to controls, characterized the reactions, and assessed the congruency of reaction documentation between our computerized physician order entry, pharmacy information and adverse drug reaction databases.
METHODS: Adult patients with hematologic malignancies at a university hospital who received piperacillin/tazobactam over a 12-month period were retrospectively compared to hospitalized controls in a 1:2 ratio. Patient demographics, diagnosed malignancy, drug allergy documentation, type and onset of hypersensitivity, and concomitant corticosteroid therapy were documented.
RESULTS: Compared to controls (n=212), study patients (n=106) experienced significantly more suspected hypersensitivities (4.3% and 17.0% respectively, p<0.001). All 18 suspected piperacillin/tazobactam hypersensitivities in the study group were mild in nature and probable in cause (Naranjo probability scale). Sixteen of the reaction types were rashes. The majority of these patients were males (55.6%), and average age was 48.4 ± 15.1 years. The most common diagnosis was leukemia (61.1%). Fifteen study patients (83%) with hypersensitivities received concomitant corticosteroids, and 10 (55.6%) had documented allergies to non-cross reacting medications. Mean number of days to onset of reaction to piperacillin/tazobactam was 8.9 ± 4.8. Congruency of documentation in all three clinical information systems was noted for only one reaction (control).
CONCLUSIONS: In this pilot study, adults with hematologic malignancies had a greater incidence of suspected piperacillin/tazobactam hypersensitivities than other hospitalized patients, yet reaction documentation in both groups needs improvement.

164E. Safety and efficacy of high-dose busulfan by 90-hour continuous infusion in hematologic malignancy patients undergoing allogeneic stem cell transplants. *Christine M. Walko, Pharm.D.*[1], Thomas Shea, M.D.[2], Kamakshi Rao, Pharm.D.[1]; (1)University of North Carolina School of Pharmacy, Chapel Hill, NC; (2)University of North Carolina, Chapel Hill, NC.

PURPOSE: Busulfan is used in allogeneic stem cell transplantation for patients with hematologic malignancies. We have previously demonstrated the benefit of using a test-dose of IV busulfan to predict the systemic exposure of this drug and report here on this approach in patients receiving a 90-hour continuous infusion of full-dose busulfan.
METHODS: All patients received a 0.8 mg/kg test dose administered over 2 hours and PK sampling at times 0, 2.5, 4, 5, and 6 hours. Patients began treatment with 30 mg/m^2 fludarabine daily x 5 and either 0.8 mg/kg ABW IV busulfan (18) or targeted busulfan to achieve an AUC of 4800 (6), 5760 (6), or 6912 (2) umol*min/hr per day on days -7 to -3. PK sampling was done at hours 0, 12, 16, 18, 48, 60, 72, and 89.5. The initial 18 patients were studied without dose adjustments, followed by dose escalation with targeted systemic exposure of the busulfan and dose adjustments as needed in the last 14 patients treated.
RESULTS: Thirty-two patients ages 18–55 (median 39) with high-risk AML (17), ALL (6), CML (2), MDS (2), or other disease (5) were enrolled. All patients engrafted with a median of 14 days. No regimen-related deaths were observed in the first 100 days post-transplant. Four patients had grade 3 mucositis, two patients had transient grade 3 hepatitis, two patients had grade 3 infections of unclear etiology, one patient had grade 3 pneumonia, and one patient had grade 3 veno-occlusive disease of the liver. Three non-relapse related deaths have occurred for a non-relapse mortality rate of 9%. Fourteen patients have relapsed at a median of 121 days (range 70–512) post-transplant.
CONCLUSIONS: This approach permits accurate delivery of a target systemic exposure to IV busulfan, is well-tolerated, and will allow additional dose escalation.
Presented at the Bone Marrow Transplant Tandem Meetings (ASBMT and CIBMTR), Keystone, Colo, February 8-12, 2007.

165E. Treating the anemia of MDS with erythropoietin: impact of higher dose vs. combination with G/GM-CSF. *Victor Moyo, M.D.*[1], Patrick Lefebvre, M.A.[2], Mei-Sheng Duh, M.P.H., Sc.D.[3], Behin Yektashenas, Pharm.D.[1], Suneel Mundle, M.D.[1]; (1)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (2)Groupe d'Analyse, Ltée., Montreal, Quebec, Canada; (3)Analysis Group, Inc, Boston, Mass.

PURPOSE: EPO is used to improve erythropoiesis and reduce transfusions in anemic MDS pts. The addition of G/GM-CSF to EPO-alfa or beta has been associated with higher erythroid response (ER) rates vs. EPO alone. Studies suggest that higher ER rates could be achieved with EPO monotherapy if higher initiation doses were used. To study this, a meta-analysis was performed on studies of patients with MDS treated with EPO-alfa or beta+G/GM-CSF.

METHODS: Data extraction was performed on studies from PubMed, ASCO, and ASH proceedings from 1990-2006 in patients with MDS treated with EPO-alfa or beta±G/GM-CSF. To allow for cross comparisons, only studies including IWG or IWG-like ER criteria were selected. Pooled ER rate estimates were calculated using fixed-effect(F-E) meta-analysis methods. Results were stratified by: 1)EPO-alfa at standard doses, 2)EPO-alfa at high doses, 3)EPO-alfa+G/GM-CSF, and 4)EPO-beta+G/GM-CSF.

RESULTS: Nineteen studies were included. Most patients (> 55%) had RA/RARS.Studies using EPO-alfa at standard doses showed comparable ER rates to studies using EPO-alfa+G/GM-CSF (49.0% vs. 50.6%; p=0.731). Among EPO-alfa studies, those using higher EPO doses had higher ER rates vs. studies using standard EPO doses (p<0.001) or EPO+G/GM-CSF combination (p=0.007). Overall ER rates were not available for studies using EPO-beta+G/GM-CSF. However, 52 pts (37.7%) had major ER, similar to that observed in all EPO-alfa monotherapy studies (195/589=33.1%).

CONCLUSION: Results suggest that increasing EPO-alfa dose may have a greater impact on ER than addition of G/GM-CSF. Further validation is warranted.

	EPO-alfa standard dose	EPO-alfa high dose	EPO-alfa+ G/GM-CSF	EPO-beta+ G/GM-CSF
Starting EPO dose, Units/week	30,000–40,000	60,000–80,000	30,000–40,000	30,000–70,000
Studies(n)	5	4	6	4
Evaluable pts(n)	393	196	152	138
Overall ER F-E % (95%CI) Crude % (95%CI)	49.0(44–54) 47.8(43–53)	64.5(58–71) 63.3(57–70)	50.6(43–58) 50.7(43–59)	N/A N/A
Major ER, Crude % (95%CI)	27.2(23–32)	44.9(38–52)	30.5*(23–38)	37.7(30–46)

*Major ER rate was not available for 1 study(11 patients)

166. **Dosing patterns and costs of erythropoiesis-stimulating agents for chemotherapy-induced anemia using FDA-approved fixed dosing regimens: real-world data from an observational study.**

Tanya Burton, M.S.[1], Kay Larholt, Sc.D.[1], Cyrus Peake, M.S.[1], Chris Pashos, B.S.[1], Brahim Bookhart, M.B.A., M.P.H.[2], Roxanne Meyer, Pharm.D.[2], Catherine Tak Piech, M.B.A.[2], *R. Scott McKenzie, M.D.*[2]; (1)Abt Associates Clinical Trials, Lexington, Mass; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: Currently, there are 2 FDA-approved fixed dosing regimens for erythropoiesis-stimulating agents (ESAs) in patients with cancer and chemotherapy-induced anemia (epoetin alfa [EPO] 40K Units, darbepoetin alfa [DARB] 500 mcg). To better characterize dosing patterns and ESA-specific costs in cancer patients, data were analyzed from the D.O.S.E. Registry, an ongoing prospective observational study.

METHODS: Data collected from US outpatient practices between 1/1/06 and 4/11/07 were analyzed. Adult chemotherapy patients with non-myeloid malignancies and ≥ 2 doses of either agent were analyzed. Outcomes assessed were mean administered dose per injection, mean cumulative dose, and respective cost (based on 1/07 wholesale acquisition cost, EPO $12.52/1000 Units, DARB $4.576/mcg), treatment duration, and hematologic outcomes.

RESULTS: 244 patients (204 EPO, 40 DARB) from 21 sites were included. The two patient groups were similar with respect to mean baseline characteristics, including age, gender, weight, hemoglobin, and tumor type. Mean administered dose per injection was 42,981 Units for EPO and 484 mcg for DARB with a mean time between injections of 10.6 days EPO and 24.8 days for DARB. The mean cumulative dose was 329,088 Units for EPO and 1705 mcg for DARB, corresponding to cost per treatment episode of $4,120 and $7,802 (p<0.0001) respectively. Mean treatment duration was 84.0 days for EPO versus 72.1 days for DARB (p=0.0638). Mean Hb levels were

significantly higher in the EPO treated group at Week 12 (EPO 11.5, DARB 10.5, p=0.0169) and Week 16 (EPO 11.3, DARB 10.1, p=0.0311).

CONCLUSION: Data from this prospective observational study showed that the mean cumulative drug cost was $3682 lower in the EPO group than in the DARB group, representing a 47% cost savings with EPO. Little change from the starting dose to the mean administered dose per injection was observed for either drug.

167E. Impact of delaying tumor progression on patient-reported outcomes and survival: results from a randomized phase 3 trial of panitumumab vs best supportive care (BSC) in metastatic colorectal cancer (mCRC) patients. Salvatore Siena, M.D.[1], Marc Peeters, M.D., Ph.D.[2], Eric Van Cutsem, M.D., Ph.D.[3], Yves Humblet, M.D., Ph.D.[4], *Giovanna Devercelli, Ph.D.*[5], Michael Wolf, M.S.[5], Rafael Amado, M.D.[5]; (1)Ospedale Niguarda Ca' Granda, Milan, Italy; (2)Ghent University Hospital, Ghent, Belgium; (3) University Hospital Gasthuisberg, Leuven, Belgium; (4)St-Luc University Hospital, Brussels, Belgium; (5) Amgen Inc., Thousand Oaks, Calif.

PURPOSE: In a phase 3 trial, panitumumab plus BSC significantly improved progression-free survival (PFS) compared with BSC in refractory mCRC. This analysis evaluates the association of achieving disease control (delaying disease progression) in mCRC with respect to overall survival, health-related quality of life (HRQoL), and CRC symptoms.

METHODS: Patients had documented disease progression after treatment with fluoropyrimidine- irinotecan- and oxaliplatin- containing chemotherapy regimens. Patients were randomized 1:1 to receive BSC + panitumumab 6 mg/kg Q2W or BSC alone. HRQoL (EQ-5D) and CRC symptoms (NCCN/FACT CRC symptom index, FCSI) were assessed at prespecified timepoints. The patient-reported outcomes (PRO) analysis set comprised patients with at least one post-baseline PRO assessment. Patients who were alive at week 8 from randomization were included in the analysis to minimize potential lead-time bias associated with response evaluation. Patients were categorized based on tumor progression (No PD [best response of partial response or stable disease] vs PD). Imputation of missing data incorporated last value carried forward and slope methods.

RESULTS: In the panitumumab arm (n=231), 36% of patients had disease control (PR or SD); in the BSC arm (n=232), 10% of patients had SD (no PRs). The PRO analysis set included 207 panitumumab patients and 184 BSC patients. Of the PRO analysis set, patients alive at week 8 were: for FCSI, panitumumab (n=181) and BSC (n=166); for EQ-5D, panitumumab (n=179) and BSC (n=164). Significantly higher HRQoL and CRC symptom scores (indicating better HRQoL and less CRC symptomatology) were observed in the No PD panitumumab patients vs, PD patients (p<0.03 and p<0.002, respectively). For BSC, significant differences in CRC symptom scores were also observed in No PD vs PD patients. A survival advantage was observed in the No PD vs PD panitumumab patients.

CONCLUSIONS: Delaying tumor progression with panitumumab was associated with better HRQoL, symptom control, and overall survival.

Presented at American Society of Clinical Oncology, Chicago, Ill, June 1-5, 2007.

168E. Phase I evaluation of tipifarnib in combination with low dose Ara-C in high risk myelodysplastic syndrome or acute myeloid leukemia: interim results. Jorge Cortes, M.D.[1], Eric Feldman, M.D.[2], Dan Douer, M.D.[3], Azra Raza, M.D.[4], *Victor Moyo, M.D.*[5]; (1)MD Anderson Cancer, Houston, Tex; (2)New York Presbyterian Hospital, New York, NY; (3)University of Southern California, Los Angeles, Calif; (4) UMASS Medical Center, Worcester, Mass; (5)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: Tipifarnib(T) is a farnesyltransferase inhibitor with clinical activity in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Low dose Ara-C (LDAC) has utility in the elderly with MDS/AML; hence its use in combination with investigational agent T to improve outcomes is warranted.

METHODS: The primary objective of this ongoing phase I, dose-finding, multicenter, open-label study was to determine the maximum-tolerated dose (MTD) based on dose-limiting toxicities (DLT) of T+LDAC observed during the first 28-day cycle. MDS (IPSS Int 1, 2 or High) and untreated AML patients (age ≥ 75 years or ≥ 65 years with preceding MDS) or relapsed/refractory AML (age > 18) were included. Planned sample size was up to 57 patients with a traditional 3+3 dose-escalation and a minimum of 3 patients enrolled per cohort. T(Dose Level 0) was administered initially at 200 mg PO BIDx21 days in combination with LDAC 10 mg SC BIDx10 days, both repeated every 28 days. Efficacy will be assessed by bone marrow and peripheral blood count studies.

RESULTS: 15 patients have been enrolled to date: 2 MDS (Int 1 n=1, High n=1) and 13 AML (7/13 patients with no previous therapy); all 15 patients were evaluable. Mean baseline characteristics for the entire cohort were: age 76.2, 67% men, Hb 9.4 ± 0.9g/dL, WBC 8.7 ± 11.3x10³/mL, platelets 96.8 ± 96.6x10³/mL. The observed DLT for T+LDAC was generalized rash seen at Dose Level 3. The MTD was therefore determined to be T 300 mg and LDAC 15 mg. The most common grade 3/4 adverse events were neutropenia, thrombocytopenia, anemia, and rash.

CONCLUSION: These interim findings show the combination of T 300 mg PO BIDx21 days and LDAC 15 mg SC BIDx10 days to be the MTD in this study. Efficacy assessment is ongoing.

Dose Level	T (mg PO BID)x21 days every 28 days	LDAC (mg SC BID) x10 days every 28 days
3	300 mg	20 mg
2	300 mg	15 mg
1	300 mg	10 mg
0	200 mg	10 mg

169E. **Severity of skin toxicity (ST) is associated with clinical outcomes and health-related quality of life (HRQoL) with panitunumab in patients with metastatic colorectal cancer (mCRC).** Marc Peeters, M.D., Ph.D.[1], Salvatore Siena, M.D.[2], Yves Humblet, M.D., Ph.D.[3], Eric Van Cutsem, M.D., Ph.D.[4], *Giovanna Devercelli, Ph.D.*[5], Michael Wolf, M.S.[5], Rafael Amado, M.D.[5]; (1)Ghent University Hospital, Ghent, Belgium; (2)Ospedale Niguarda Ca' Granda, Milan, Italy; (3)St-Luc University Hospital, Brussels, Belgium; (4)University Hospital Gasthuisberg, Leuven, Belgium; (5)Amgen Inc., Thousand Oaks, Calif.

PURPOSE: Skin toxicities (ST) are associated with epidermal growth factor receptor (EGFr) inhibition. Studies of anti-EGFr inhibitors have shown associations between severity of ST per clinical toxicity grading and progression-free survival (PFS) and overall survival (OS).
METHODS: In a phase 3 randomized study of mCRC patients with disease progression after treatment with standard chemotherapy, patients were randomized to best supportive care (BSC) plus panitumumab 6 mg/kg Q2W or BSC alone. ST was measured using modified NCI-CTC v3.0 grading criteria (CTCAE) and a modified Dermatology Life Quality Index (mDLQI). HRQoL (EQ-5D and EORTC QLQ-C30 Global QoL subscale) and CRC symptoms (NCCN/FACT CRC symptom index, FCSI) were also measured. The patient-reported outcome (PRO) subset comprised patients with ≥ 1 post-baseline PRO assessment. Analyses of ST were restricted to panitumumab patients who were progression-free ≥ 28 days to allow for onset of ST and had a ST ≥ grade 1. Hazard ratios (HR) and correlation analyses were used to determine relationships between HRQoL, PFS, and OS to ST.
RESULTS: Panitumumab (n=231) prolonged PFS vs BSC alone (n=232; p<0.0001). The incidence of grades 2–4 ST was higher in the panitumumab arm. OS was significantly prolonged in patients with more severe ST (grades 2-4 vs. grade 1; HR=0.67; p=0.0235). Lower mDLQI scores (worse ST) also predicted improved OS (Cox model, p<0.0001). Similar results were seen with PFS. Pearson correlation coefficients showed that the minimum post-baseline mDLQI score was inversely associated with post-baseline median HRQoL and CRC symptom scores, suggesting that panitumumab patients with more severe ST have a higher (better) HRQoL (p=0.0006, 0.0148, 0.2487) and improved CRC symptom scores (p=0.0649).
CONCLUSIONS: Patients with grades 2–4 ST appear to experience longer PFS and OS compared to those with grade-1 ST. Patients reporting the greatest bother from their ST also tend to report better overall HRQoL and reduced CRC symptoms.
Presented at American Society of Clinical Oncology, Chicago, Ill, June 1-5, 2007.

170. **Significance of FLT3 mutations in chronic myelogenous leukemia (CML) progression and imatinib response.** Kyung Im Kim, M.S.[1], *Ji Eun Park, B.S.*[1], Kwang Sung Ahn, Ph.D.[2], Sung Soo Yoon, M.D., Ph.D.[3], In Ja Son, Ph.D.[4], Wan Gyoon Shin, Pharm.D., Ph.D.[1], Jung Mi Oh, Pharm.D.[1]; (1)Clinical Pharmacy, College of Pharmacy, Seoul National University, Seoul, South Korea; (2)Seoul National University Hospital, Cancer Research Institute, Seoul, South Korea; (3)Cllege of Medicine, Seoul National University, Seoul, South Korea; (4)Seoul National University Hospital, Department of Pharmacy., Seoul, South Korea.

PURPOSE: The incomplete explanation of CML progression and the emergence of imatinib resistance in a significant number of patients, especially with advanced stage, necessitate studies for important prognostic factors that determine the progression and drug response.
METHODS: Microarray analysis of 10 CML patients' DNA in chronic and blast crisis phase was performed to examine global gene expression changes of tumor cell. Real-time PCR was performed on each top 10 ranking genes of increasing and decreasing pattern in microarray analysis to select significant progression-associated genes. 102 CML patients were evaluated by PCR and gel electrophoresis for FLT3 mutation that induces constitutive activation of the protein to examine the possibility as a prognostic marker in CML. Imatinib response according

to FLT3 genetic variation was analyzed in 33 patients to determine the implications of FLT3 mutations on drug response.

RESULTS: Overall genetic expression decrement from chronic to blast crisis phase that could determine the behavior of tumor cell was found. RT-PCR results demonstrated that expressions of FLT3, FGCR3A and MYD88 were significantly different between the phases (p<0.05). A total of 21 patients (14 of chronic phase, 2 of accelerated phase, 5 of blast crisis phase) were found to have FLT3 ITD genetic variations. The imatinib non-responder group had higher ratio of the patients having FLT3 ITD mutation than the responder group in all disease phase (42% vs. 14%, p=0.07). Especially in chronic phase, the ratio of patients with FLT3 ITD mutation was about 2 times higher than in responder group (42% vs. 14%).

CONCLUSIONS: This study found FLT3 ITD genetic variations in CML chronic phase and more incidences of FLT3 mutation in imatinib non-responder patients at first. This result suggested that FLT3 ITD genetic variations could be a significant prognostic marker for determining the transition from chronic to blast crisis and imatinib response in CML patients.

171E. Serious Arterial Thromboembolic Events in Patients with Metastatic Colorectal Cancer Treated with Bevacizumab: Results from the BRiTE Registry. Mark Kozloff, M.D.[1], Mary M. Sugrue, M.D., Ph.D.[2], *Amy Gelhorn, Pharm.D.*[2], Rick Hippert, Pharm.D., M.B.A.[2], David Purdie, Ph.D.[2], Wei Dong, Ph.D.[2], Axel Grothey, M.D.[3]; (1)Ingalls Hospital, Harvey and the University of Chicago, Chicago, Ill; (2)Genentech, Inc., San Francisco, Calif; (3)Mayo Clinic, Rochester, Minn.

PURPOSE: Bevacizumab (Avastin®) prolongs overall survival and progression-free survival when added to 1st-line or 2nd-line chemotherapy in metastatic colorectal cancer (mCRC). A retrospective pooled analysis of 5 randomized trials showed an association of arterial thromboembolic events (ATEs) with bevacizumab (3.8%, versus 1.7% with chemotherapy alone), with age ≥ 65 years and history of ATE identified as risk factors (Skillings et al, in press, JNCI). The BRiTE mCRC registry—a bevacizumab treatment registry initiated in February 2004—evaluated bevacizumab-associated serious adverse events, including serious ATEs, in a general practice setting.

METHODS: Data were collected prospectively via electronic data capture at baseline and then quarterly for up to 3 years per patient. Potential risk factors for ATE were collected at baseline. History and timing of serious ATEs before starting bevacizumab and use of anti-platelet therapy were summarized. The definition of serious ATE included myocardial infarction (MI), cerebral vascular accident (CVA), transient ischemic attack (TIA), and peripheral arterial disease. Fisher's exact test and multiple logistic regression were used to assess univariate and multivariate associations.

RESULTS: Of 1953 evaluable patients, 18.0% (n=352) had history of serious ATE, and 11.2% (n=219) received anti-platelet therapy. A total of 39 serious ATE [CVA (n=15), MI (n=11), angina (n=1), TIA (n=7), and other (n=5)] were reported in 35 (1.8%) patients. Median time to serious ATE was 3.7 months. Serious ATE frequency for ECOG performance status (PS) 0/≥1 (8 [1.0%] versus 23 [2.4%]) and for ATE history (yes/no) (13 [3.7%] versus 22 [1.4%]) were significant.

CONCLUSIONS: In this uncontrolled observational study of bevacizumab-treated mCRC patients, the incidence of serious ATEs associated with bevacizumab use was comparable to that reported in previous controlled trials of bevacizumab in mCRC. Prior history of serious ATE and ECOG PS were significantly associated with an increased risk of serious ATE during bevacizumab therapy.

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172E. Safety and effectiveness of bevacizumab plus chemotherapy in elderly patients with metastatic colorectal cancer: results from the BRiTE registry. Mary M. Sugrue, M.D., Ph.D.[1], Mark Kozloff, M.D.[2], *Amy Gelhorn, Pharm.D.*[1], Rick Hippert, Pharm.D., M.B.A.[1], Wei Dong, Ph.D.[1], David Purdie, Ph.D.[1], Axel Grothey, M.D.[3]; (1)Genentech, Inc., San Francisco, Calif; (2)Ingalls Hospital, Harvey and the University of Chicago, Chicago, Ill; (3)Mayo Clinic, Rochester, Minn.

PURPOSE: Bevacizumab (Avastin®) prolongs overall survival (OS) and progression-free survival (PFS) when added to chemotherapy for first-line and second-line treatment of metastatic colorectal cancer (mCRC). Phase III trials show similar bevacizumab efficacy in patients < age 65 and ≥ 65 years; however, certain safety issues are more frequent in older patients. We report safety and efficacy of bevacizumab in patients ≥ 65 years in a large community-based bevacizumab treatment registry (BRiTE) for patients with mCRC. METHODS: Data were collected prospectively via electronic data capture at baseline and then quarterly for up to 3 years per patient. Multiple logistic regression analysis was used to assess univariate and multivariate associations.

RESULTS: Of 1953 evaluable patients, 896 (45.9%) were ≥ age 65 at baseline, compared with 32% in the mCRC pivotal trial AVF2107 and the SEER general population estimate of 60% for mCRC. FOLFOX and FOLFIRI were the most common 1st-line regimens; 5 FU bolus/leucovorin was more common in patients ≥ age 65. Shown below

are selected bevacizumab-associated safety events, median PFS, 1-year survival rates, and median OS for patients < age 65 versus ≥ 65 years.

< 65 (n=1057): GI perforations, 2.3%; bleeding/wound healing complications, 2.1%; Grade 3/4 bleeding, 2.1%; ATE, 1.3%; estimated median PFS (months), 10.3; estimated 1-year survival rate, 77.3%; estimated median OS (months), not estimated.

≥ 65 (n=896): GI perforations, 1.1%; bleeding/wound healing complications, 1.0%; Grade 3/4 bleeding, 2.9%; ATE, 2.2%; estimated median PFS (months), 9.9; estimated 1-year survival rate, 71.6%; estimated median OS (months), 21.8.

Multiple regression analyses showed that age was not a significant factor for predicting incidence of gastrointestinal (GI) perforation, bleeding/wound healing complications, or arterial thromboembolic events (ATE), nor for predicting PFS.

CONCLUSIONS: In the BRiTE registry, the safety and effectiveness (PFS and 1-year survival) of bevacizumab in patients ≥ age 65 and < age 65 were similar, and comparable with results from controlled bevacizumab trials in mCRC.

Presented at the 2007 Gastrointestinal Cancers Symposium, co-sponsored by the American Society of Clinical Oncology (ASCO), the American Society for Therapeutic Radiology and Oncology (ASTRO), the AGA Institute and the Society of Surgical Oncology (SSO), Orlando, Fla, January 19-21, 2007.

173E. Management of hypertension in patients with metastatic colorectal cancer treated with bevacizumab plus chemotherapy. Mark Kozloff, M.D.[1], Wei Dong, Ph.D.[2], *Rick Hippert, Pharm.D., M.B.A.*[2], Amy Gelhorn, Pharm.D.[2], David Purdie, Ph.D.[2], Jing Yi, Ph.D.[2], Mary M. Sugrue, M.D., Ph.D.[2], Axel Grothey, M.D.[3]; (1)Ingalls Hospital, Harvey and the University of Chicago, Chicago, Ill; (2) Genentech, Inc., South San Francisco, Calif; (3)Mayo Clinic, Rochester, Minn.

PURPOSE: Bevacizumab (Avastin®) prolongs survival when added to standard chemotherapy for first-line or second-line treatment of metastatic colorectal cancer (mCRC). Following FDA labeling approval of bevacizumab in 2004, a large community-based registry (BRiTE) was initiated in patients with mCRC receiving bevacizumab in combination with first-line chemotherapy to evaluate bevacizumab-targeted safety events and effectiveness of bevacizumab in combination with commonly used chemotherapy regimens. Grade 3 hypertension has been identified in all bevacizumab clinical trials as a bevacizumab-related toxicity. However, the outcome and effective management of bevacizumab-associated hypertension have not been determined. This report from the BRiTE registry describes the impact of bevacizumab-associated hypertension development and treatment in a population-based observational study that had no prespecified patient characteristics for study participation.

METHODS: Data on hypertension requiring medication and specific classes of anti-hypertensive medications were collected using an electronic data capture system at baseline and quarterly thereafter for up to 3 years. Blood pressure readings were not collected. Hypertension was defined as the requirement for anti-hypertensive medication, and "increased hypertension" as any anti-hypertensive dose increase or addition.

RESULTS: Of 1953 evaluable patients, 827 (42.3%) had hypertension at baseline; 155 (18.7%) patients developed increased hypertension. The rate of increased hypertension was lowest in patients with more than 3 anti-hypertensive medication classes at baseline. At baseline, 1126 patients were without hypertension; 207 (18.4%) developed hypertension, and 48.3% of these de novo hypertension patients required modification of anti-hypertensive medication due to increased or uncontrolled hypertension. Use of specific classes of anti-hypertensive medication was similar for patients with or without baseline hypertension.

CONCLUSIONS: These findings suggest that hypertension at baseline does not increase the risk of developing increased hypertension associated with bevacizumab use. In BRiTE, the rate of hypertension is comparable to rates seen in randomized, controlled bevacizumab trials, suggesting that bevacizumab use in the general patient population remains well tolerated.

Presented at the 2007 Gastrointestinal Cancers Symposium, co-sponsored by the American Society of Clinical Oncology (ASCO), the American Society for Therapeutic Radiology and Oncology (ASTRO), the AGA Institute and the Society of Surgical Oncology (SSO), Orlando, FL, January 19-21, 2007.

Parkinson's Disease

174. Re-evaluating dose conversions when switching between dopamine agonists. *Andrea Eggert, Pharm.D., BCPP*, Chris Bretzmann, Pharm.D.; Schwarz Pharma, Mequon, Wis.

PURPOSE::Switching between dopamine agonists (DAs) in Parkinson's disease (PD) may be an option to enhance treatment benefit in individual patients; however, switching regimens for DAs are not well studied. To evaluate outcomes in rotigotine-treated subjects previously maintained on ropinirole, a post hoc analysis of an open-label extension to a double-blind placebo- and comparator-controlled rotigotine trial (SP513) was performed.

METHODS: Subjects randomized to the active-comparator (ropinirole ≤24 mg/day) in the 6-month, double-blind trial who elected to enroll in an open-label extension with rotigotine were evaluated. Following double-blind maintenance, ropinirole was tapered and rotigotine then titrated weekly in 2mg/24hour increments up to an optimal dose (≤8mg/24h). For this post hoc analysis, subjects were divided into three groups based upon previous daily ropinirole dose (≤9mg, >9mg to ≤18mg, or >18mg). UPDRS(II+III) scores were used to assess patient outcome, defined as improvement (≥5-point decrease), worsening (≥5-point increase) or no change.

RESULTS: Most patients (115/160;72%) were titrated to the maximum rotigotine dose allowed (8mg/24h). The percentage of patients with improvements or no change in UPDRS did not directly correlate with previous ropinirole dose (80%, 65%, and 73% for the ≤9mg[n=56], >9mg to ≤18mg[n=34], and >18mg groups[n=63], respectively). Subject withdrawal for lack of efficacy (6%) did not show bias towards prior ropinirole dose.

CONCLUSIONS: In this post hoc analysis, prior ropinirole dose was not highly predictive of therapeutic outcome following switch to rotigotine in early PD patients, suggesting that a beneficial outcome was possible with rotigotine across a broad range of previous doses of ropinirole.

175. **Patients' preference for rotigotine transdermal patch for treatment of Parkinson's disease. Results of a single-arm, multinational trial.** *Nir Giladi, M.D.*[1], Babak Boroojerdi, Ph.D.[2]; (1)Movement Disorders Unit, Tel-Aviv Sourasky Medical Center, Tel Aviv, Israel; (2)Schwarz Pharma AG, Monheim, Germany.

PURPOSE: Rotigotine (Neupro®) is approved in the EU for treatment of all stages of Parkinson's disease (PD). This trial investigated the patients' satisfaction with this treatment.

METHODS: In this open-label, multinational trial with up to 12 weeks duration, subjects received rotigotine doses up to 16 mg/24 hours. Baseline and end of maintenance UPDRS (motor score) were performed in the morning after being at least 12 hours off medication. In addition, patients' preference for the treatment was measured using a questionnaire.

RESULTS: A total of 54 patients were treated in this trial. Compared to baseline, there was a mean improvement of 11.5 ± 6.8 points in the early morning UPDRS scores. A majority of subjects (95%) were either "satisfied" or "very satisfied" with the patch treatment compared with the satisfaction of treatment with oral medication (41%). A total of 82% "agreed" or "strongly agreed" that they preferred using a patch over oral medication. The aspects of the patch that subjects liked the most were "do not have to remember to take medicine during the day" (87%) and "applying the patch once a day" (85%). The two aspects of the patch that subjects liked the least were "did not stay on for the entire day" (56%) and "symptom relief did not last all day" (28%). This was in contrast with the patch adhesiveness data, where only 4% of patches were observed to be detached.

CONCLUSIONS: In this trial, patients were much more satisfied with the rotigotine transdermal patch than with conventional oral PD therapies.

Pediatrics

176E. **Delayed administration of Filgrastim (G-CSF) following autologous peripheral blood stem cell transplant (APBSCT) in pediatric patients does not change time to neutrophil engraftment and reduces use of G-CSF.** *Vinita Pai, Pharm.D.*[1], Soledad Fernandez, Ph.D.[2], Melissa Laudick, R.N., M.S., CPNP[3], Robin Rosselet, R.N., M.S., CPNP[3], Amanda Termuhlen, M.D.[4]; (1)College of Pharmacy, The Ohio State University and Children's Hospital, Columbus, Ohio; (2)Center for Biostatistics, College of Medicine and Public Health, Columbus, Ohio; (3)Children's Hospital, Columbus, Ohio; (4)College of Medicine and Public Health and Children's Hospital, Columbus, Ohio.

PURPOSE: The use of G-CSF after APBSCT significantly reduces the time to neutrophil engraftment (TNE) compared to no G-CSF. Optimal timing to initiate G-CSF after stem cell infusion is not well established. In adults, no significant difference in TNE was observed between delayed (day +4 to +8) and early administration (day +1) of G-CSF. The objective was to compare the effect of delayed (day +6) versus early (day +1) G-CSF administration on TNE in pediatric APBSCT.

METHODS: Medical records of 65 children receiving APBSCT for solid tumors or lymphoma, receiving G-CSF and surviving until neutrophil engraftment (NE) were retrospectively reviewed. Median tests, chi-square tests and multivariate regression analysis were conducted.

RESULTS:

Variables	Early Group	Delayed Group	p value
N	19	46	
Age at transplant (years)	4.7 (1.7–22.7)	5.3 (0.9–27.4)	
Female (%)	11 (57.9)	21 (45.7)	
G-CSF Dose mcg/kg/day*	5 (1.6)	5 (2.3)	
Stem Cell Dose (x 10⁶/kg CD34)	6.73 (2.3–54.8)	5.67 (1.6–46.7)	0.77
Time to NE⁻*	10 (1.4)	11.5 (1.1)	0.06
G-CSF duration⁻*	12(3)	7 (3)	0.003
G-CSF duration to NE⁻*	10 (1.7)	5.5 (1.1)	<0.0001
Time to platelet engraftment⁻*	38 (28)	35 (76)	0.5
Bacteremia (%)	6 (32)	9 (20)	0.3
# of febrile days*	11 (8)	7 (8)	0.41
Duration of neutropenia⁻*	9 (2)	10 (2)	0.34
Duration of hospitalization⁻*	31 (10)	28.5 (13.5)	0.01

*Median (Std. Dev); ⁻Days

TNE, platelet engraftment, bacteremia, and the number of febrile days were similar between the two groups. Duration of G-CSF administration and total hospital stay were significantly shorter in the Delayed Group. Multivariate regression analysis showed that duration of G-CSF administration had no effect on TNE.
CONCLUSIONS: Delaying G-CSF administration to day +6 after APBSCT does not adversely affect TNE, risk of bacteremia, or the number of febrile days, and is associated with a shorter hospital stay.
Presented at the 2007 Pediatric Academic Societies' Meeting, Toronto, Ontario, Canada, May 5-8, 2007.

177. **Evaluation of 15-versus 30-minute application of lidocaine 4% for pediatric procedural pain.** *Anita Siu, Pharm.D.*[1], Lance Lazatin, M.D.[2]; (1)Rutgers University, The State University of NJ, Piscataway, NJ; (2)Jersey Shore University Medical Center, Neptune, NJ.

PURPOSE: Topical agents have become a popular vehicle for achieving analgesia in children, particularly for IV insertions and blood draws. The faster these procedures are done, the quicker the diagnostic and therapeutic interventions are made. There is anecdotal evidence that topical lidocaine 4% is effective at 15 minutes after application, but most protocols have a 30-minute application period. This study aims to assess the efficacy of a 30-minute versus a 15-minute application prior to venipuncture.
METHODS: All patients 3–18 years admitted to the K. Hovnanian Children's Hospital at the Jersey Shore University Medical Center were asked to participate in the study. They were then randomly selected to receive either a 15-minute or 30-minute application of topical lidocaine 4%. Pain scores were assessed using visual pain rating scales before, during, and after the procedure. The unpaired t- test was used to compare the pain scores during the procedure.
RESULTS: Fifty patients agreed to participate in this study with 25 participants enrolled in each group. During the procedure, Group A (30 minutes) had a pain score of 2.84, and Group B (15 minutes) had a pain score of 2.34. The mean pain score difference was -3.8 with the standard error difference of 0.688. Both groups were compared using the t-test at 95% confidence interval and a p-value of 0.583.
CONCLUSION: This study demonstrates that there is no difference in pain scores between Group A and Group B. A 15-minute application is therefore as effective as a 30-minute application of topical lidocaine 4%.

178E. **Assessment of daptomycin use in pediatric patients.** Darren Culshaw, Pharm.D., *Lawrence V. Friedrich, Pharm.D.*, Luke Mendez-Vigo, Pharm.D., Kenneth Lamp, Pharm.D.; Cubist Pharmaceuticals, Lexington, Mass.

PURPOSE: MRSA, particularly community-associated strains, is emerging as an important pathogen in pediatric patients. The objective of this study was to describe patterns of daptomycin use in this population.
METHODS: The Cubicin® Outcomes Registry and Experience (COREsm) program is a retrospective analysis conducted annually to assess clinical outcomes in patients treated with daptomycin. For this analysis patients < 18 years of age who were evaluable for clinical outcome were selected from 2004 through 2006. Outcomes were assessed as cure, improved, or failure at the end of therapy. Success was defined as cure + improved.
RESULTS: 32 patients met the criteria for inclusion. 31 patients were 12–18 years of age and 1 was age 7–11. The median weight was 75 kg (range, 37–110). Only 2 patients were < 50 kg. Most patients were located in the community 48 hrs before daptomycin therapy (63%). 5 patients had a CrCl < 30 mL/minute, and 2 of these

required hemodialysis. Overall, clinical success (cure + improved) was reported in 97% of patients. Infections treated were uncomplicated skin (44%), complicated skin (25%), bacteremia (19%), osteomyelitis (9%), and other (3%). Pathogens were cultured in 81% of patients and included staphylococci (85%) and enterococci (15%). More than half (59%) of the staphylococci were MRSA. The median (range) daptomycin dose and duration of therapy were 4 mg/kg (range, 3.5–6) and 10 days (2–66), respectively. Daptomycin was given once daily in 97% of patients. Concomitant antibiotic use was reported in 88% of patients. Vancomycin and TMP/SMX were most common (16% each). Median (range) time to clinical response, reported in 22 patients, was 7 days (1–14).

CONCLUSIONS: These data indicate that clinicians are choosing daptomycin to treat selected pediatric patients. In this cohort of predominantly older adolescents, daptomycin appeared to be an effective treatment option. These data require confirmation via prospective clinical trials.

Submitted to IDSA 45th Annual Meeting, Infectious Disease Society of America, San Diego, Calif, Oct 4-7 2007.

179. **Relationship between patient, caregiver, and asthma characteristics, responsibility for management, and indicators of asthma control.** *Paul J. Munzenberger, M.S., Pharm.D.*[1], Elizabeth Secord, M.D.[2], Ron Thomas, Ph.D.[2]; (1)Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, Mich; (2)Children's Hospital of Michigan, Detroit, Mich.

PURPOSE: The purpose was to explore the relationship between children with asthma, caregivers, and asthma characteristics, responsibility for management tasks, and indicators of asthma control.

METHODS: Fourteen patient, caregiver and asthma characteristics and 7 indicators of control were collected. Patient and caregiver responsibility was determined from a questionnaire containing 10 asthma management tasks scored from 1, indicating caregiver responsible all the time through 5 indicating child responsible all the time. Multiple Pearson correlations were used to determine relationships between mean responsibility scores, study characteristics and indicators of control. Linear regression determined the influence of selected predictor variables on mean responsibility scores.

RESULTS: One-hundred and four children and their caregivers completed the study. The mean responsibility scores for the patients and caregivers were 2.97 and 2.27, respectively. Characteristics and indicators of asthma control with significant correlations (r) with both the mean patient and caregiver responsibility scores included patient age, academic grade level, and number of years with asthma. In addition, the number of hospital admissions, number of adults in the home, and peak expiratory flow (PEF) had a significant correlation with the mean patient responsibility score. Regression analysis indicated that patient age (r = 0.587), number of hospital admissions (r = 0.229) and PEF (r = 0.326) had the best predictive strength for the mean patient responsibility score. The combined r squared was 0.44. Only patient age (r = 0.486) was a significant predictor for the mean caregiver responsibility score. The r squared was 0.49.

CONCLUSIONS: Patient age, number of hospitalizations, and PEF were the best predictors of patient responsibility, and patient age was a significant predictor for caregiver responsibility. Factors such as caregiver education, age or marital status, family income, asthma severity, years with asthma, number of medications had no significant relationship with the patient or caregiver responsibility.

180. **Antibiotic prescribing errors in neonatal late onset sepsis.** *Lizbeth Hansen, Pharm.D.*, Sandra Garner, Pharm.D., Toby Cox, Pharm.D., Michael Irving, M.S., Robin Bissinger, MSN, RNC, NNP, W. Michael Southgate, M.D., David Annibale, M.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Errors are more common in pediatric medication orders with the neonatal population being considered the most vulnerable. The purpose of this project was to quantify and classify prescribing errors in antibiotic orders for neonatal late onset sepsis (LOS) to serve as a baseline for evaluating a newly developed computerized prescriber order entry (CPOE) system.

METHODS: For 2 months, LOS antibiotic orders for the neonatal intensive care units (NICU) (n=150) were independently evaluated by two pediatric clinical pharmacists for prescribing errors, potential errors, and omissions. Prescribing errors were defined as overdoses or underdoses (> 10% deviation from recommended doses), inappropriate route or schedule, inappropriate antibiotic selection, drug-drug or drug-disease state interactions, and contraindications. Potential errors were those including error-prone abbreviations either listed in our institution's pediatric order writing policy or the Institute for Safe Medication Practices (ISMP) ideal components of a pediatric order. Omissions were defined as those orders missing information either required by our institution's policy or recommended by ISMP. Omissions were divided into critical and non-critical with critical omissions defined as those missing any information other than date, time, and pager number.

RESULTS: Overall, prescribing errors were identified in 26.1% of orders. The frequencies of error categories were: overdoses 7.8%, underdoses 4.6%, scheduled too frequently 3.9%, scheduled too infrequently 11.8%, inappropriate antibiotic selection 8.5%, and drug-disease state interactions 0%. Potential errors were identified in 54.2 % of orders. Critical omissions were found in 2.6% of orders, and 14.4% of orders contained non-critical

omissions. In addition, 9.2% of orders were considered illegible, and 24.8% were not ordered STAT, a routine recommendation in our NICU when initiating antibiotics.
CONCLUSIONS: Prescribing errors commonly occur in neonatal LOS antibiotic orders. These results will be used as a baseline for evaluating a newly developed CPOE system designed to minimize antibiotic prescribing errors.

Pharmaceutical Stability

181. **Effects of the space environment on medications flown on the Space Shuttle and International Space Station (ISS).** *Vernie R. Daniels, M.S., R.Ph.*[1], Jianping Du, Ph.D.[1], Phillip R. Satterfield, B.S.[2], Camille Crady, C.Ph.T.[1], Lakshmi Putcha, Ph.D.[3]; (1)Wyle Laboratories Life Sciences Group, Houston, Tex; (2)Enterprise Advisory Services, Inc., Houston, Tex; (3)NASA - Johnson Space Center, Houston, Tex.

PURPOSE: Assess physical changes and chemical degradation of select pharmaceutical formulations flown in Space Shuttle and ISS medical kits.
METHODS: Eleven pharmaceuticals dispensed as different dosage forms were selected based on physical and chemical characteristics, and susceptibility to environmental factors such as temperature, humidity, and light sensitivity. When available, ground controls with matching brand and lot numbers were used for comparison. Samples retrieved from flight were stored along with their matching controls in a temperature and humidity controlled environmental chamber. Temperature, humidity, and radiation data from the Shuttle and ISS were retrieved from onboard HOBO® U12 Temp/RH Data Loggers, and from passive dosimeters. Physical and chemical analyses of the pharmaceuticals were conducted using validated United States Pharmacopeia (USP) methods.
RESULTS: Preliminary results have indicated degradation in 6 of the 11 formulations returned from space flights. Four formulations, Amoxicillin/Clavulanate, promethazine, sulfamethoxazole / trimethoprim, and ciprofloxacin tablets, have included samples that were discolored after flight. Chemical content analyses using High or Ultra Performance Liquid Chromatography (HPLC/UPLC) methods revealed that some dosage forms of Amoxicillin/Clavulanate, promethazine, sulfamethoxazole/trimethoprim, lidocaine, ciprofloxacin, and mupirocin contained less than 95% of the label claim of active drug compound.
CONCLUSION: Shuttle and ISS environments affect the stability and shelf life of certain medications. Studies are in progress to examine the effect of specific space flight environmental factors on pharmaceutical stability. The degradation profiles generated from ground studies in analog environments will be useful in establishing predictive shelf-life profiles for medications intended for use during long-term space exploration missions.

Pharmacoeconomics/Outcomes

182. **Erythropoiesis-stimulating agents in cancer patients receiving chemotherapy: real-world dosing, hematologic outcomes and costs.** Tanya Burton, M.S.[1], Kay Larholt, Sc.D.[1], Cyrus Peake, M.S.[1], Chris Pashos, B.S.[1], Brahim Bookhart, M.B.A., M.P.H.[2], Roxanne Meyer, Pharm.D.[2], Catherine Tak Piech, M.B.A.[2], *R. Scott McKenzie, M.D.*[2]; (1)Abt Associates Clinical Trials, Lexington, Mass; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: To better characterize dosing patterns, hematologic outcomes, and treatment costs of erythropoiesis-stimulating agents (ESAs) in chemotherapy-treated cancer patients, data were analyzed from the D.O.S.E. Registry, an ongoing nationwide prospective observational study.
METHODS: Data collected between 12/03 and 4/07 from 21 outpatient practices were analyzed. Chemotherapy-treated patients with cancer ≥ age 18 years and who received ≥ 2 doses of epoetin alfa (EPO) or darbepoetin alfa (DARB) were included. Mean dose per injection, dosing frequencies, mean treatment duration, mean cumulative dose, number of injections, hematologic outcomes, treatment costs (using 1/07 wholesale acquisition cost, EPO:$12.52/1000 Units, DARB:$4.576/mcg), and office visits were studied.
RESULTS: 670 DARB and 481 EPO patients were included. Mean baseline characteristics, including hemoglobin and tumor type, were similar between both groups. Mean dose per injection was 44,914 Units for EPO and 245 mcg for DARB. Weekly and extended dosing frequencies were observed with both agents, EPO (QW:65%, Q2W:32%, ≥ Q3W:3%) and DARB (QW:8%, Q2W:63%, ≥Q3W:29%). At each monthly timepoint, EPO patients had a significantly larger mean change in hemoglobin compared with DARB patients (Weeks 4 [0.7 vs 0.4], 8 [0.8 vs 0.5], 12 [0.9 vs 0.3], and 16 [1.0 vs 0.4]). Mean treatment duration was 57 days for DARB and 58 days for EPO. Mean cumulative dose was 363,734 Units for EPO and 1189 mcg for DARB yielding a mean cost per treatment of $4,554 and $5,440, respectively (p<0.0001). EPO patients received more injections than DARB patients (mean 7.8 vs 4.9, p<0.0001), but had fewer office visits (EPO 7.1 vs DARB 10.2, p<0.0001).

CONCLUSION: This observational study of real-world practice and outcomes suggests that extended dosing for both ESAs is common among these patients. Furthermore, significantly better hemoglobin improvements were seen in the EPO group compared to the DARB group, while also being associated with a 16% cost savings in EPO-treated patients compared with DARB patients.

183E. The economic burden of chronic obstructive pulmonary disease (COPD) in a U.S. Medicare population. Luke Boulanger, M.A.[1], Homa Dastani, Ph.D.[2], Lisa Guadagno, M.S.[1], Jeno Marton, M.D.[3], Riad Dirani, Ph.D.[3], Amy Phillips, Pharm.D.[2], *Hemal Shah, Pharm.D.*[2], Joseph Menzin, Ph.D.[1]; (1)Boston Health Economics, Inc., Waltham, Mass; (2)Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Conn; (3)Pfizer Global Pharmaceuticals, New York, NY.

RATIONALE: Although the economic burden of COPD has gained attention in recent years, data on the costs of COPD among Medicare beneficiaries are lacking.
METHODS: This study used administrative claims and eligibility records from a large multistate Medicare managed-care database. Study patients were 65+ years of age with paid claims during 2004. The COPD cohort comprised patients with 1+ inpatient/ER claims or 2+ outpatient claims (> 30 days apart) for COPD (ICD-9-CM codes 491.xx, 492.x, 496). The comparison cohort included patients without COPD matched 3:1 to the COPD cohort on age, sex, months of enrollment, and Medicare plan. Excess costs of COPD were estimated as the difference in overall health plan payments between the two study cohorts during 2004. Attributable costs were calculated using medical claims with listed diagnoses of COPD or other respiratory-related conditions and pharmacy claims for respiratory medications.
RESULTS: A total of 8,370 patients were included in the COPD cohort and were matched to 25,110 comparison cohort patients. For both groups, mean (SD) age was 78 (8) years, 54% were female, and duration of eligibility was 11 (2) months. COPD patients were more likely to use health care services and had excess costs about $20,500 higher (p<0.0001) than the comparison cohort. Comorbidities were high in the COPD cohort, accounting for 46% of the observed excess cost. The attributable cost of COPD averaged about $6,300; other respiratory-related costs averaged about $4,400.
CONCLUSION: In this Medicare managed-care population, COPD was found to pose a substantial burden in terms of both respiratory-related and total health care costs.
Presented at the International Conference of the American Thoracic Society, San Francisco, Calif, May 18-23, 2007.

184. Annual total medical costs for women treated with two commonly prescribed combination oral contraceptives. *Susan Pagano, Ph.D.*[1], Amy Grogg, Pharm.D.[2], Katherine D. LaGuardia, M.D., M.P.H.[1]; (1)Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ; (2)Xcenda, Palm Harbor, Fla.

PURPOSE: To examine annual resource utilization and total medical costs for women treated with commonly prescribed oral hormonal contraceptives.
METHODS: A retrospective analysis of a national managed care claims database (PharMetrics) that identified users of two commonly prescribed oral contraceptives, norgestimate [NGM] 180/215/250 mcg/ethinyl estradiol [EE] 25 mcg and drosperinone [DRSP] 3 mg/EE 30 mcg, between January 2001 and April 2004 (n=18,982); and examined annual resource utilization and non-pregnancy-related, non-pharmacy-related total medical costs. Patients with at least 6 months of insurance coverage prior to their first index prescription and 12 months afterward were included in the analysis. Those who switched regimens or had a diagnosis of pregnancy, cancer, liver disease, heart attack, stroke or deep venous thrombosis were excluded. Medical costs were identified from resource utilization, measured by office visits; inpatient and outpatient hospitalizations; emergency room visits; and other services (e.g., laboratory, unassigned, home). Utilization and costs were compared using a linear regression model and log-transformation of cost variables, adjusted for age, health plan type, comorbidities, concomitant medication use, and pre-index costs.
RESULTS: Mean age in the NGM/EE cohort was 26.75 years, compared to 29.14 years in the DRSP/EE cohort (p<.0001). Compared to the DRSP/EE cohort (n=11,126), the NGM/EE users (n=4,397) had a significantly lower number of office visits (8.81 v. 11.22; p<.0001) and outpatient hospitalizations (1.96 v. 2.99; p<.0001), but a significantly higher number of other services utilized (6.68 v. 5.39; p<.0001). Total medical costs for the NGM/EE group were significantly lower compared to DRSP/EE ($1,682.54 v. $1,930.26; p=.0052).
CONCLUSIONS: This analysis indicated significantly different total annual medical costs and rates of office visits, outpatient hospitalizations, and other services associated with use of different oral contraceptives. Further research is needed to determine whether these data signify underlying differences between patients who select certain contraceptives.

185E. **Cost-effectiveness of telavancin versus vancomycin for the treatment of complicated skin and skin structure infections.** *Somvadee Laohavaleeson, Pharm.D.*[1], Steven L. Barriere, Pharm.D.[2], David P. Nicolau, Pharm.D., FCCP[1], Joseph L. Kuti, Pharm.D.[1]; (1)Center for Anti-infective Research and Development, Hartford Hospital, Hartford, Conn; (2)Theravance, Inc., South San Francisco, Calif.

PURPOSE: Telavancin, a new lipoglycopeptide antibiotic, was compared with vancomycin for the treatment of complicated skin and skin structure infections (cSSSI) in clinical trials. This study evaluated the cost-effectiveness of telavancin versus vancomycin during these trials.
METHODS: Cost-effectiveness was assessed from the hospital's perspective. Clinical outcome and treatment data were collected for patients enrolled at North American sites from the randomized, double blind, ATLAS trials. Costs for cSSSI specific diagnosis related groups were collected from a single hospital's 2006 billing database and applied to each infection-related hospital day (LOS-AR). Data were analyzed for all clinically evaluable (CE) patients and the subset infected with methicillin resistant *S. aureus* (MRSA). Incremental cost-effectiveness ratios (ICER) with a $25,000 bootstrap were calculated while holding the price of telavancin equal to vancomycin, and then at $25, $50, and $100 per day more costly than vancomycin.
RESULTS: Of 1350 total patients, 823 were hospitalized with LOS-AR calculated; 643 were CE, and 280 were infected with MRSA. Among CE patients with an outcome of "cure," median (25th–75th percentile) costs were $5080 ($2553–$8890) for telavancin and $5080 ($2550–$8510) for vancomycin (p=0.77). Costs for patients who were not cured in both groups ($7640 and $6579) were greater than cures (p=0.03). At equivalent prices, telavancin ICER was $3323 to achieve one additional success over vancomycin. In the MRSA group, hospital costs were similar between telavancin and vancomycin (p=0.854). However, ICER was $-410 due to a lower success rate for vancomycin. As telavancin price was raised in the MRSA group to $25, $50, and $100 above vancomycin, ICER increased to $3522, $7454, and $15,320 per additional success, respectively.
CONCLUSIONS: In these patients, telavancin was cost-effective over vancomycin for the treatment of cSSSI, particularly in those with MRSA. The extent of cost-effectiveness will depend on the final telavancin acquisition cost when available.
Presented at the 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, Ill, September 17-20, 2007.

186E. **Clinical outcomes associated with daptomycin, vancomycin, and linezolid usage in the treatment of methicillin-resistant *Staphylococcus aureus* complicated skin and skin structure infections.** *Carl Fossaceca, PharmD*; Humility of Mary Health Partners, St. Joseph Health Center, Warren, Ohio.

PURPOSE: To compare outcomes and costs associated with cSSSI, a retrospective review of patients treated at our institution with either daptomycin, linezolid, or vancomycin was performed.
METHODS: Patients with MRSA cSSSI who were treated with daptomycin, linezolid, or vancomycin were identified chronologically beginning with January 1, 2006, admissions. A total of 150 charts (daptomycin, n=50; linezolid, n=50; and vancomycin, n=50) were reviewed. Data collection included the following information: demographic information, medical history, laboratory results, infection details, dosing and outcomes, cost of therapy, clinical outcomes, adverse events (AEs) associated with antibiotic therapies, concomitant medications, and discharge information.
RESULTS: Clinical cure rates were 92%, 68%, and 76% for patients treated with daptomycin, vancomycin, or linezolid, respectively. In those patients with a positive resolution of infection, the average length of antibiotic treatment was 4.3 days in daptomycin-treated patients compared with 7.7 days for vancomycin and 6.8 days for linezolid. The length of the hospital stay for these patients (5.2 days, 8.9 days, and 7.9-days in daptomycin, vancomycin, or linezolid-treated patients, respectively) closely coincided with the duration of antibiotic therapy. No patient discontinued daptomycin therapy due to an adverse drug reaction; however, 22% (11) and 14% (7) of patients treated with vancomycin or linezolid, respectively, experienced AEs that resulted in either a change in antibiotic therapy or additional medication therapies to treat the adverse event. The overall cost of therapy (drug expenditures plus hospital charges) was lowest for daptomycin patients ($8,170) compared with vancomycin ($13,860) and linezolid ($12,920).
CONCLUSION: In this single-center retrospective chart review, treatment with daptomycin resulted in a higher cure rate, shorter hospital stays, lower overall costs, and fewer AEs as compared with vancomycin or linezolid.
Presented at the ASHP 2007 Summer Meeting and Exhibition, American Society of Health-System Pharmacists, San Francisco CA, June 24-27, 2007.

187E. **Burden of postoperative ileus (POI) in colectomy surgery patients in the United States.** *Shrividya Iyer, Ph.D.*[1], William B. Saunders, Ph.D.[2]; (1)Wyeth Research, Collegeville, Pa; (2)Premier Healthcare Informatics, Premier Inc., charlotte, NC.

PURPOSE: To assess the impact of postoperative ileus (POI) on health care utilization and costs in colectomy surgery patients in the United States.

METHODS: A retrospective cohort study design was used. Adult patients with a principal procedure code for colectomy (ICD-9 codes 45.71–45.79), discharged between January 2004 and December 2004 were identified from Premier's Perspective Comparative Database, an inpatient records database from more than 500 hospitals in the United States. The colectomy patients were further classified for the presence of POI, by the presence of paralytic ileus (ICD-9 code 560.1) and/or digestive system complications (ICD-9 code 994.1) during the study period. Hospital length of stay (LOS), ICU LOS, ventilator usage, and hospitalization costs were compared using t-tests and chi-square tests as appropriate.

RESULTS: A total of 17,896 patients with primary procedure code for colectomy were identified, of which 3115 (17.4%) patients were classified for presence of POI, including paralytic ileus (n= 2732; 15.3%) and digestive system complications (n=1899; 10.6 %), with significant overlap between the two (n=1516; 8.5%). A majority of the patients with POI were male (54.9%), Caucasian (70.9%) and in the 51–64 year age group (51%). The average hospital LOS was significantly higher (p<0.001) in patients with POI (13.6 ± 13.3 days) compared with patients without POI (8.9 ± 9.5 days). The average ICU LOS was significantly higher (p<0.001) in patients with POI (2.4 ± 8.6 days) compared with patients without (1.4 ± 6.0 days). Ventilator usage was found to be significantly higher (p<0.001) in the POI group (17.0%) compared with those without (12.4%). Average hospitalization costs were significantly higher (p<0.001) in the patients with POI ($25,089 ± 35,386) than those without POI ($16,907 ± 29,320).

CONCLUSION: Postoperative ileus in colectomy patients is associated with increased hospital resource utilization. Prevention of POI could reduce hospital length of stay and costs.

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188. **Therapeutic and financial optimization of anemia management in cancer patients with chemotherapy-related anemia through low-molecular-weight (LMW) iron dextran administration.** *Michael Auerbach, M.D.*[1], Jennifer A. Pappadakis, Ph.D.[2], Edmund H. Doherty, Pharm.D.[2]; (1)Auerbach Hematology-Oncology, Baltimore, Md; (2)Watson Laboratories, Inc., Morristown, NJ.

PURPOSE: A retrospective review of cancer patients receiving chemotherapy was conducted to assess use of erythropoietic stimulating agents (ESA) and intravenous low-molecular-weight (LMW) iron dextran (InFed®) to manage anemia in a private practice setting and to estimate the effectiveness of LMW iron dextran in reducing the cost of ESA treatment and decreasing transfusion requirement.

METHODS: Charts of living patients who recently received IV iron were screened for inclusion criteria: anemic, diagnosis of cancer < 3 years prior, received chemotherapy, and ≥ 1 dose IV iron, with data for ≥ 12 weeks from first dose. Data collected from this private practice were analyzed and compared to pooled transfusion rates from large, phase III epoetin alpha trials and to published per patient per week costs of anemia management using ESA and oral/no iron.

RESULTS: Forty patients met the inclusion criteria: 58% received platinum-containing chemotherapy, and most the common cancer diagnoses were lung (38%) and breast (40%). Fifteen percent of patients (6; all receiving platinum-chemotherapy) required blood transfusions at some point annually versus published expectations of 25%. Anemia management using ESA and IV iron in this private practice resulted in an average cost per 12 weeks of $8,275 vs. $9,576 reported in literature. Among patients with lung cancer, the financial benefit of managing anemia with IV iron and ESA was even greater: $10,223 for this practice vs. $15,458 from literature. Cost savings overall were $1,301/patient/12-week cycle for unspecified cancer and $5,235 per lung cancer patient. These cost savings were most likely driven by the ESA-sparing effects of IV iron reported in the published oncology and dialysis literature.

CONCLUSIONS: Administration of LMW iron dextran in conjunction with ESA therapy in patients receiving chemotherapy resulted in decreased blood transfusions and decreased anemia costs. These findings are financially and therapeutically important. Further studies are needed to confirm these results.

189. **Hospital costs and outcomes of patients discharged with a diagnosis of pulmonary aspergillosis in the United States.** *Aryun Kim, Pharm.D.*, David P. Nicolau, Pharm.D., FCCP, Joseph L. Kuti, Pharm.D.; Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, Conn.

BACKGROUND: Pulmonary aspergillosis is a devastating mould infection often associated with severe immunosuppression and high mortality; however, data regarding cost of hospitalization, with a focus on contribution of antifungals, are sparse.

METHODS: Hospital billing data from a private insurance company were searched for adult patients discharged with pulmonary aspergillosis between 01/2000 and 09/2006, and who received ≥ 3 days of the following antifungals during hospitalization: conventional amphotericin B (AmB), lipid complex amphotericin B (ABLC), liposomal

amphotericin B (L-AmB), caspofungin, or voriconazole. Patients were grouped by the first antifungal received. The following were analyzed: mortality at discharge, total length of stay (LOS), infection-related LOS (ID-LOS), total hospitalization cost, antifungal drug cost, percentage of hospital costs related to antifungals (%Cost$_{drug}$), and receipt of other licensed antifungal therapy in combination or after the first agent (OLAT).

RESULTS: 320 US hospitals contributed data for 3149 patients receiving AmB (n=343), ABLC (n=467), L-AmB (n=160), caspofungin (n=633), or voriconazole (n=1,546). Population mortality, LOS, ID-LOS, hospital costs, and antifungal costs were 25.5%, 23.5 ± 24.6 days, 14.7 ± 21.4 days, $55,090 ± $77,082, and $4,363 ± $10,610, respectively. Mean %Cost$_{drug}$ was ≤ 12.5% for all agents, except L-AmB (21.4%, p<0.05). Accordingly, L-AmB patients had the highest antifungal costs ($11,921 ± $17,170, p<0.05). Overall, OLAT was received in 27.4% of patients; LOS and costs were significantly greater in patients receiving OLAT, but mortality was not affected.

CONCLUSIONS: In this large US study, end of hospital mortality and hospital costs for patients discharged with pulmonary aspergillosis were substantial. However, antifungal costs accounted for a small percentage of overall costs for all agents except L-AmB. Finally, LOS and costs were greater in those patients who received OLAT, which requires further exploration.

190. Evaluation of the nutritional status of inner patients on oral supplements and active enteral nutritional support. *Branca Teixeira, Pharm.D.*, Teresa Cunha, Pharm.D., M.Sc., Bárbara Santos, Pharm.D., Gustavo Dias, Pharm.D., José Das Neves, Pharm.D., Jorge Brochado, Pharm.D.; Pharmacy Department St Antonio General Hospital, Porto, Portugal.

PURPOSE: Detection of malnourished patients in St. Antonio General Hospital (SAGH). Identifying and characterizing the patients' population treated with oral supplements and active enteral nutritional support in SAGH. Audit the nutritional status of inner patients on oral supplements and active enteral nutritional support. Establish the economical impact of enteral feeding in inner patients in SAGH. Establish guidelines on the pharmacist role in ensuring the best use of oral supplements and active enteral nutritional support in SAGH.

METHODS: Retrospective analysis of pharmaceutical records of inner patients treated oral supplements and active enteral nutritional. Analysis of clinical data and pharmacotherapeutical follow up of 40 patients treated with oral supplements and active enteral nutritional between April 1 and June 1, 2007. Assessment of inner patients' nutritional status using the "Nutritional Risk Screening – NRS 2002" Literature review.

RESULTS: Between January 1 and June 1, 2007, 1246 inner patients were provided with oral supplements and active enteral nutritional support is with a direct cost of 56,147 (Euros). From the patients observed, 18 were moderately undernourished, and 4 were severely undernourished. None of these patients had a nutritional care plan in their medical records.

CONCLUSIONS: Hospital pharmacists have a specific role in nutritional hospital policy. About 30% of all patients in hospitals are undernourished. It is unacceptable that nutritional problems causing significant clinical risk are not identified. Pharmacists must ensure the best use of oral supplements and active enteral nutritional. Clinical pharmacists are responsible for the quality of care and the efficient use of resources.

191E. **A description of patients in palliative care or hospice on warfarin therapy.** *Robin R. Hill, Pharm.D., BCPS*[1], Kerri D. Martinez, Pharm.D.[1], Thomas Delate, Ph.D.[1], Daniel M. Witt, Pharm.D., FCCP, BCPS, CACP[2]; (1)Kaiser Permanente, Aurora, Colo; (2)Kaiser Permanente, Lafayette, Colo.

PURPOSE: To compare the frequency of INR monitoring, anticoagulation control, and anticoagulation-related complications among warfarin-using patients receiving and not receiving palliative care or hospice.

METHODS: This retrospective analysis examined adult patients receiving warfarin between January 1, 2002 and December 31, 2005, who had at least two recorded INR measurements during the study period, and did and did not receive palliative care or hospice. Palliative care/hospice (PCH) patients were matched up to 1:6 on age, warfarin indication, and time on warfarin therapy to non-palliative care/hospice (NPCH) patients. Matched patients were observed the last 6 months the PCH patient received palliative care/hospice while on warfarin or until PCH patient death/plan termination. Primary outcome was frequency of INR monitoring. Secondary outcomes included percent of time spent within, above, and below patient-specific targeted INR range and occurrence of anticoagulation-related complications.

RESULTS: Included were 101 and 484 PCH and NPCH patients, respectively. Cohort characteristics were equivalent (p>0.05) except that PCH patients were more likely to have life-threatening co-morbidities (p<0.05). Mean count of INR measurements per 30 days was 2.2 and 1.7 for PCH and NCPH patients, respectively (p<0.01). PCH patients were less likely to be within (39% vs. 55%, p<0.01) but more likely to be above (30% vs. 20%, p=0.04) and below (30% vs. 25%, p=0.03) range than NPCH patients. Anticoagulation-related bleeding occurred in 1% and 3% of PCH and NPCH patients, respectively (p=0.25). Anticoagulation-related deaths occurred in 2% and 1% of PCH and NPCH patients, respectively (p=0.19).

CONCLUSIONS: Patients at the end of life endured more frequent monitoring but were less likely to remain in therapeutic range with similar risk for anticoagulation-related complications. These factors may affect these patients' quality of life and should be considered when making a decision about continuing warfarin at the end of life.

Presented at the Western States Residency Conference, Pacific Grove, Calif, May 29-June 1, 2007.

192. **Economic evaluations of clinical pharmacy services from 1988 to 2005: setting, service type, and methodology.** Fred Doloresco, Pharm.D.[1], *Alexandra Perez, Pharm.D.*[2], Patrick D. Meek, Pharm.D., M.S.[3], Daniel R. Touchette, Pharm.D., M.A.[2], James M. Hoffman, Pharm.D., M.S.[4], Lee C. Vermeulen, M.S.[5], Glen T. Schumock, Pharm.D, M.B.A.[2]; (1)University of Wisconsin Hospital and Clinics, Madison, Wis; (2)University of Illinois at Chicago, Chicago, Ill; (3)Albany College of Pharmacy, Albany, NY; (4) St. Jude Children's Research Hospital, Memphis, Tenn; (5)University of Wisconsin Hospital and Clinics; School of Pharmacy, University of Wisconsin-Madison, Madison, Wis.

PURPOSE: The purpose of this analysis was to systematically review original evaluations of the economic impact of clinical pharmacy services (CPS) published from 1988 to 2005. Characteristics of setting, type of service, and study design over the period are described.

METHODS: Articles published in each of three time periods (1988-1995 [P1], 1996-2000 [P2], and 2001-2005 [P3]) were identified using a structured search of available literature databases and randomly assigned to two reviewers for independent data abstraction. Setting, type of service, and study methodology were recorded for each article. Frequencies were used to calculate percentages of each characteristic for each time period. Publication trends and study characteristics were compared over time.

RESULTS: A total of 104, 59, and 93 articles were included in P1, P2, and P3, respectively. Regarding the most recent period [P3], economic evaluations of CPS were published in the following settings: hospital (43%), community pharmacy (22%) and clinic (15%). The types of services studied in P3 included general pharmacotherapy (32%), target drug (29%), and disease management (23%). Controlled designs were used in 43% of studies in P3. The following trends were noted over time: a greater proportion of economic evaluations were conducted in clinics, community pharmacies, and non-US sites in P3, compared with P1 and P2. In P3, evaluations of disease management services were more common, whereas evaluations of target drug and pharmacokinetic services were less common. The proportion of studies using a controlled design rose from P1 (30%) to P2 (58%), and declined from P2 to P3. Most economic evaluations of CPS over the period showed positive financial benefits.

CONCLUSIONS: Over nearly 20 years, practice settings in which economic evaluations of CPS were conducted have become more diverse, and the services evaluated have become more comprehensive. Opportunities still exist to use more rigorous methods to evaluate the value of CPS.

Pharmacoepidemiology

193. **Evaluation of clinical characteristics as predictors for the inappropriate prescribing of acid suppressive therapy in internal medicine inpatients.** Lindsay B. Palkovic, Pharm.D.[1], *Denise R. Sokos, Pharm.D., BCPS*[2], Kim C. Coley, Pharm.D.[2]; (1)University of Pittsburgh Medical Center, Pittsburgh, Pa; (2)University of Pittsburgh School of Pharmacy, Pittsburgh, Pa.

PURPOSE: Acid suppressive therapy (AST) is used in 50%–70% of inpatients and is frequently prescribed for inappropriate indications. This case-control study compared inpatients receiving inappropriate AST to inpatients not prescribed AST to determine characteristics that were predictors of inappropriate AST use.

METHODS: A random sample of adult internal medicine inpatients admitted between July 2005 and June 2006 was screened for AST use. Patients with ICU charges, an appropriate indication for AST, or those transferred from an outside hospital were excluded. Patients receiving inappropriate AST and those not prescribed AST were included in case and control groups, respectively. Indications consistent with FDA labeling or clinical practice guidelines were considered appropriate. Significant patient and clinical characteristics (p<0.1) from separate univariate regression models were entered into a multivariate logistic regression to determine predictors for inappropriate AST use.

RESULTS: Of 2368 patients screened, 242 were included (108 cases and 134 controls) in the analysis. Cases were older (mean age 57 vs. 52 years, p=0.03), had a longer median length of stay (4 vs. 3 days, p<0.001), a higher median number of medications at admission (6 vs. 4, p=0.001), and higher rates of cirrhosis (9.3 vs. 1.5%, p=0.007). Predictors of inappropriate AST use were proton pump inhibitor (OR = 15.3; 95% CI = 4.1–56.3) or histamine$_2$ receptor antagonist use prior to admission (OR = 14.5; CI = 2.8–74.8), longer length of stay (OR = 1.1; CI = 1.1–1.3), use of anticoagulants (OR = 2.7; CI = 1.4–5.2), and cirrhosis (OR = 6.4; CI = 1.02–39.5).

CONCLUSION: The strongest predictors of inappropriate use were AST before admission, a diagnosis of cirrhosis, and concomitant prescribing of anticoagulants. Possible reasons include undocumented appropriate indications,

continuation of home medications without investigating indications, and inappropriate gastrointestinal bleeding prophylaxis. These findings will enable prevention of inappropriate use through physician education, order entry flagging, and pharmacist intervention.

194E. Prescribing patterns and utilization of erythropoiesis-stimulating agents (ESAs) in hospitalized patients. *Jerry Siegel, Pharm.D., FASHP*[1], James Jorgenson, R.Ph., M.S., FASHP[2], Philip E. Johnson, M.S., R.Ph., FASHP[3], Donald F. Brophy, Pharm.D., M.Sc.[4], Thomas Comstock, Pharm.D.[5], Pramod Lal, Ph.D.[5], Amy Feng, Ph.D.[5], Paul Audhya, M.D.[5]; (1)The Ohio State University Medical Center, Columbus, Ohio; (2)University of Utah Hospitals and Clinics, Salt Lake City, Utah; (3)H. Lee Moffitt Cancer Center & Research, Tampa, Fla; (4)Virginia Commonwealth University School of Pharmacy, Richmond, Va; (5) Amgen Inc, Thousand Oaks, Calif.

PURPOSE: To evaluate inpatient uses, prescribing, and utilization patterns of ESAs.
METHODS: A retrospective chart audit of 2558 patients hospitalized in October 2005 or January 2006 who received an ESA. Hospitals were identified by DDD ESA sales from IMS Health Inc.; an equal number of hospitals were randomly chosen from each sales decile. The last 5 inpatients who received 1 ESA product, darbepoetin alfa (DA) [Aranesp®] or Epoetin alfa (EA) [Epogen®/Procrit®], for any reason were identified by pharmacy records. If a hospital did not use all 3 ESAs, 5 additional patients/ESA were identified for a maximum of 10patients/product; a maximum of 20 charts/hospital were abstracted.
RESULTS: 191 hospitals were analyzed; US geographic region for 186 (5 missing regional data) were: 11%West, 24%Midwest, 32%Northeast, and 33%South. Predominant uses of DA were end-stage renal disease(ESRD)/chronic dialysis(29%), chemotherapy-induced anemia(CIA)(13%), chronic kidney disease(CKD) not on dialysis(12%), anemia of other chronic disease(9%), and anemia of cancer(7%). Once-weekly(QW) was the most common DA dosing regimen(67%). Administered QW doses were 13–500 mcg. The median(IQR) QW dose/patient/administration was 100 (60, 110) mcg. Predominant uses for EA were ESRD/chronic dialysis(28%), CKD not on dialysis(16%), CIA(12%), anemia of other chronic disease(11%), and surgery(7%). Thrice-weekly (TIW) (37%) and QW(30%) were the most common dosing regimens. EA TIW dosing was most frequently prescribed in patients with ESRD/chronic dialysis and CKD not on dialysis; QW dosing was most frequently prescribed in patients with CIA and CKD not on dialysis. Administered EA doses for TIW were 88–60,000 Units; for QW, doses ranged from 513 to 80,000 Units. The median(IQR) TIW EA dose/patient/administration was 10,000 (7,000; 12,000) Units; median (IQR) QW EA dose/patient/administration was 40,000 (15,000; 40,000) Units.
CONCLUSION: These data describe current ESA utilization and prescribing patterns in a sample of US hospitals. The broad dosing range for DA and EA suggests an opportunity for pharmacists to assess ESA use at their institutions and develop standardized dosing guidelines.
Presented at the ASHP 2007 Summer Meeting and Exhibition, American Society of Health-System Pharmacists, San Francisco, Calif, June 24-27, 2007.

195. National aggregate database documents antimicrobial resistance at www.armprogram.com. *John G. Gums, Pharm.D.*; University of Florida, Gainesville, Fla.

PURPOSE: The ongoing Antimicrobial Resistance Management (ARM) program comprises a queriable Web-based surveillance system (www.armprogram.com) that tracks resistance patterns among U.S inpatient/outpatient isolates.
METHODS: Each institution provides a minimum of 3 years of antibiogram/sensitivity report data, which are reviewed to create a customized analysis of antimicrobial susceptibility trends benchmarked against national/regional comparators. The data, in a HIPAA-compliant non-identifying format, comprise a national aggregate database comprising 374 institutions and 30.7 million drug-isolate combinations, categorized by 51 antibiotics and 19 organisms. We reviewed *E coli* isolate reports in the database from 2006-2006 for resistance to extended-spectrum cephalosporins and fluoroquinolones and *P aeruginosa* to gentamicin, tobramycin, amikacin, imipenem, piperacillin, and piperacillin/tazobactam and fluoroquinolones.
RESULTS: For *E coli*, resistance to ciprofloxacin increased from 6.6% in 2000 to 19.5% in 2006 (n=430,170), from 6.5% to 17.8% to levofloxacin (n=372,361), 5.5% to 11.8% to ofloxacin (2005; n=16,361), and 10% to 19.7% to gatifloxacin (n=28,053). Resistance to cefotaxime was 0.7% in 2006, compared with 3.6% in 2006 (n=70,663); for ceftriaxone, it increased from 1% to 3.1% (n=420,690) and to cefepime, 0.5% to 2.5% (n=233,045), respectively. For *P. aeruginosa*, resistance decreased from 29.1% to 21.3% to gentamicin (n=184,149), from 12.4% to 10.7% tobramycin (n=161,332), from 7.5% to 6.2% for amikacin (n=125,200), from 18% to 14.7% to imipenem (n=155,768), from 15.3% to 5.9% to piperacillin (n=103,825), and from 10.7% to 9.9% to piperacillin/tazobactam (n=105,910). For each of the 6 antibiotics, *P. aeruginosa* isolate resistance declined below 2000 rates in 2002/2003 before increasing in 2004-2006. *P. aeruginosa* isolate resistance decreased from 36% in 2000 to 31.1% in 2006 to ciprofloxacin (n=149,181) and from 38.2% in 2000 to 29.4% in 2006 to levofloxacin (n=117,493).

CONCLUSIONS: Web-based surveillance programs can play an important role in the management of antimicrobial resistance by tracking patterns over time, allowing modification of therapy as necessary.

196E. **Utilizing intrastate surveillance to determine antimicrobial resistance patterns for *Staphylococcus aureus*: results from the Florida cohort of the Antimicrobial Resistance Management (ARM) Program.** *John G. Gums, Pharm.D.*; University of Florida, Gainesville, Fla.

PURPOSE: The Centers for Disease Control and Prevention recommends treating effectively by targeting the pathogen and using antimicrobials based on local data. The Antimicrobial Resistance Management (ARM) Program is an antibiogram-based surveillance system that can benchmark local antibiotic use and resistance rates.
METHODS: To test the hypothesis that *S aureus* resistance within the State of Florida is not homogenous, Florida hospitals enrolled in the ARM program were grouped into North, Central, and South regions for comparison. *S aureus* isolates (n=1,082,963) from Florida hospitals in the ARM aggregate database were reviewed for each year from 1997-2003 for resistance to nafcillin/oxacillin, clindamycin, and erythromycin as surrogates for rates of MRSA, methylation (erm), and efflux pump-mediated (mef) drug resistance.
RESULTS: From 1999-2003, *S aureus* isolate resistance to nafcillin/oxacillin increased from 36% to 58% in North and 36% to 46% in the South; in Central, rates decreased from 28% to 25% (2002). For clindamycin, erm increased from 32% to 39% in North; 4% to 7% in Central; and 29% to 39% in South. Resistance to erythromycin decreased from 52% to 70% in North; 39% to 46% in Central, and 52% to 61% in South; mef was variable, especially in Central, as follows: from 1998-2003, rates were 28%, 28%, 34%, 32%, 45%, and 39% (data not available for 1997). Rates for North for 1997-2003 were 20%, 20%, 26%, 25%, 30%, 31%, and 31%, respectively. In South, rates for 1997-2003 were 23%, 25%, 21%, 25%, 27%, 27%, and 22%, respectively.
CONCLUSIONS: Awareness of heterogeneous differences in resistance patterns for *S aureus*, as demonstrated within the State of Florida, can allow better allocation of strategic resources. These data may be useful in adjusting empiric therapy.
Published in 46th ICAAC Abstracts 2006.

197. **Adverse drug reactions leading to emergency care.** *A. Thomas Taylor, Pharm.D.*[1], Patrick F. Pratt, M.B.A., RPH[2]; (1)University of Georgia College of Pharmacy, Augusta, Ga; (2)Doctors Hospital - Augusta, Augusta, Ga.

PURPOSE: The purpose of this study was to analyze the details associated with the emergency care of community-based outpatients seeking treatment for possible ADRs.
METHODS: While tracking ADRs, a pharmacist investigator retrospectively reviewed the medical records of outpatients presenting to the emergency department (ED) of a community hospital from January through April 2007. The investigator identified patients with an ICD-9-CM code between E930.0 and E949.9 placed on their charts following an ED visit. The reviewer compiled data and prepared the report for presentation to the hospital's pharmacy and therapeutics committee.
RESULTS: Thirty-one patients, 18 female and 13 male, ages 9 months to 66 years, presented for ED care. Chief complaints were categorized as: Dermatologic (16), Neurologic (6), Hematologic (3), Endocrine (2), Cardiac (2), Respiratory (1), and Gastrointestinal (1). Fourteen patients presented with rash. Patients primarily reported ADRs to antibiotics (10) and anti-inflammatory (5), antihistamine-decongestant (3), anticonvulsant (3), and anticoagulant (2) agents. Patients' clinical conditions ranked by nursing assessment and triage level were designated as urgent (18), less urgent (12), and nonurgent (1). Onset of ADRs was categorized by time since the last dose as Fast, less than 15 minutes (0); Moderate, 15 minutes to 3 hours (6); or Slow, more than 3 hours (25). Using standardized definitions, investigators classified ADRs by causation as likely (11) or possible (20); by severity as negligible (2), moderate (28), or severe (1); and by outcome as minor (25) or serious (6) discomfort. Medical evaluations required radiological examinations, urine and blood tests, electrocardiograms and urine drug screens. Common treatments included diphenhydramine and methylprednisolone.
CONCLUSION: Outpatients experienced a wide variety of ADRs, documenting the need for continued pharmacovigilance and follow-up.

Pharmacogenomics

198. **A Haplotype in the 5-Lipoxygenase Activating Protein Gene Confers Reduced Risk of Cardiovascular Events in the INternational VErapamil SR/ trandolapril STudy - GENEtic Substudy (INVEST - GENES).** *Anzeela M. Schentrup, M.S., Pharm.D.*[1], Yan Gong, Ph.D.[1], Rhonda M. Cooper-DeHoff, Pharm.D.[2], Carl J. Pepine, M.D.[2], Julie Johnson, Pharm.D.[1]; (1)University of Florida, Gainesville,

Fla; (2)College of Medicine, Division of Cardiology, University of Florida, Gainesville, Fla.

PURPOSE: Previous *in vitro* and genetic association studies suggest a role for the arachidonic acid 5-lipoxygenase (5LO) pathway in cardiovascular (CV) disease. In particular, there is conflicting evidence for an association between variants in the *ALOX5AP* gene, encoding 5-lipoxygenase activating protein, and cardiovascular events. We tested the relationship between a haplotype in *ALOX5AP* and CV events within a nested case-control study of a high CV risk population.
METHODS: In INVEST, hypertensive subjects with coronary artery disease were randomized to either atenolol or verapamil-SR-based treatment strategies with trandolapril and hydrochlorothiazide added as needed for blood pressure control. We conducted a nested case-control study within INVEST-GENES, a genetic substudy of INVEST, where subjects who experienced a primary outcome (all-cause death, nonfatal myocardial infarction or nonfatal stroke) were frequency-matched based on age, race and gender to event-free control subjects. We genotyped a haplotype of *ALOX5AP* consisting of the G, T, and C alleles of the three single nucleotide polymorphisms, rs10507391, rs9551963, rs17222814, respectively. Genotyping was conducted using TaqMan allelic discrimination assays. Genetic associations with the primary outcome were assessed using the β2 test and logistic regression.
RESULTS: Overall, the GTC haplotype frequency was 0.13. Subjects with two copies of the GTC haplotype had a decreased risk of the primary INVEST outcome (OR 0.544, CI 0.32-0.94). Furthermore, the haplotype was associated with a further decreased risk of events in Caucasians (OR 0.409, CI 0.21-0.79), in whom the haplotype is most frequent (0.18).
CONCLUSIONS: The GTC haplotype in *ALOX5AP* was found to confer a protective effect on the risk for CV events in the INVEST-GENES. Furthermore, this benefit is more pronounced in the subgroup of Caucasians. Our results are in agreement with some previous findings in Caucasians and may contribute to understanding why previous studies of this variant have had conflicting results.

199. **Gene-guided warfarin dosing: a prospective comparison of two protocols.** *Gloria R. Grice, Pharm.D.*[1], Brian F. Gage, M.D.[2], Elena Deych, M.S.[2], Paul E. Milligan, Pharm.D.[2], Howard L. McLeod, Pharm.D.[3], Susan Gatchel, CCRC[2], Petra Lenzini, MSC[2], Leonard Grosso, M.D.[4], John Clohisy, M.D.[2], Robert L. Barrack, M.D.[2], Charles Eby, M.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, Mo; (2) Washington University, St. Louis, Mo; (3)University of North Carolina School of Pharmacy, Chapel Hill, NC; (4)Saint Louis University School of Medicine, St. Louis, Mo.

PURPOSE: In patients chronically taking warfarin, certain polymorphisms in the cytochrome P4502C9 (CYP2C9) and vitamin K epoxide reductase (VKORC1) genes are associated with lower maintenance doses. How clinicians should use this knowledge when initiating warfarin therapy is unknown. Our goal was to compare two approaches to pharmacogenetic-guided warfarin initiation.
METHODS: In the first cohort, we initiated warfarin (target INR 2.5) in 46 orthopedic patients based on clinical factors and CYP2C9 genotype. In the second cohort, we initiated warfarin in 73 orthopedic patients based on these factors and VKORC1 genotype. Also in the second cohort only, dose refinements after the third warfarin dose were gene-guided and typically targeted a slightly lower target INR (2.2). The primary endpoint was a composite one: time to major hemorrhage, INR > 3.5, or symptomatic venous thromboembolism within 30 days of warfarin initiation.
RESULTS: The first cohort was older (mean: 61 years) than the second (mean: 55 years), but the two cohorts were otherwise similar. No participant had a major hemorrhage. Compared to cohort 1, the adjusted hazard ratio for the composite endpoint in cohort 2 was 0.36 (95% CI: 0.18, 0.73; p = 0.003). The warfarin-sensitive VKORC1 G>A genotype tended to be associated with an increased risk of an adverse event in cohort 1, but not in cohort 2 (P = 0.05 for genotype interaction).
CONCLUSION: Gene-guided therapy, perhaps using a lower target INR, may improve the safety of warfarin initiation, at least in orthopedic patients with the warfarin-sensitive VKORC1 genotype.

200E. **Genetic Variation in UDP-Glucuronosyltransferases and Metabolism of Mycophenolic Acid in Heart or Lung Transplant Recipients.** *Lillian S. L. Ting, B.S.c, M.Sc.(Pharm), Ph.D.-student*[1], Marie-Odile Benoit-Biancamano, DMV, M.Sc., Ph.D.-Candidate[2], Olivier Bernard, B.Sc.(Pharm), M.Sc.[3], Chantal Guillemette, Ph.D.[3], K. Wayne Riggs, B.Sc.(Pharm), Ph.D.[4], Mary H. H. Ensom, Pharm.D., FASHP, FCCP, FCSHP[5]; (1)University of British Columbia, Vancouver, British Columbia; (2)CHUQ Research Centre, Laval University, Quebec City, Quebec; (3)CHUL Research Center, Laval University, Quebec City, Quebec; (4)University of British Columbia, Vancouver, British Columbia; (5)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada.

PURPOSE: Mycophenolate mofetil (MMF), the prodrug of mycophenolic acid (MPA), is an immunosuppressive agent used in solid organ transplantation. MPA is metabolized by the UDP-glucuronosyltransferase (UGT) enzymes to the major metabolite mycophenolic acid glucuronide (MPAG) and the minor metabolite acyl glucuronide of MPA (AcMPAG). Wide inter-patient variability is observed in MPA pharmacokinetics in thoracic transplant recipients, however, little is known regarding the contribution of UGT polymorphisms to such variability. This study aims to assess associations between polymorphisms in UGT genes with pharmacokinetic parameters of MPA, MPAG and AcMPAG

METHODS: Following written informed consent, blood samples were obtained at 0, 0.3, 0.6, 1, 1.5, 2, 4, 6, 8, 10 and 12 hours after MMF administration to 19 heart and 23 lung transplant subjects from British Columbia. Concentrations of MPA, MPAG and AcMPAG were determined by a validated high-performance liquid chromatography method with ultraviolet detection. Polymorphisms in the UGT1A8, UGT1A9 and UGT2B7 genes were identified by direct sequencing of polymerase chain reactions. Heterozygous and homozygous polymorphisms were pooled as one group. Heart or lung transplant subjects were analyzed separately. Stepwise multiple regression analysis was applied to assess the contribution of UGT polymorphisms to the inter-individual variability of MPA pharmacokinetic parameters.

RESULTS: Polymorphisms investigated: UGT1A8*2 (Ala[173]Gly) and *3 (Cys[277]Tyr), UGT1A9 [-2152, -275, *2 (Cys[3]Tyr), *3 (Met[33]Thr)], and UGT2B7*2 (His[268]Tyr). While these polymorphisms had no significant impact on MPA AUC in either group, we observed the following significant findings in lung transplant subjects: • Increased AcMPAG AUC, dose-normalized AcMPAG AUC and AcMPAG/MPA in UGT1A8*2 carriers (p=0.01, 0.025 and 0.01, respectively) • Increased AcMPAG AUC and AcMPAG/MPA in UGT2B7*2 carriers (p=0.045 and p=0.043, respectively)

CONCLUSIONS: Specific UGT polymorphisms have an impact on the pharmacokinetics of MPA. This prompts a larger study to profile UGT1A8, UGT1A9 and UGT2B7 genotypes for individualizing MMF therapy.

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201. **Gender-specific association of CRHR1 polymorphisms and bone density in long-term ALL survivors.** *Terreia Jones, Pharm.D.*[1], Sue Kaste, Ph.D.[2], Wei Lui, Ph.D.[2], Cheng Cheng, Ph.D.[2], Wenjian Yang, Ph.D.[2], Scott Weiss, M.D.[3], Ching-Hon Pui, M.D.[2], Mary V. Relling, Pharm.D.[2]; (1)University of Tennessee, Memphis, Tenn; (2)St. Jude Children's Research Hospital, Memphis, Tenn; (3)Harvard Medical School, Boston, Mass.

PURPOSE: Children with acute lymphoblastic leukemia (ALL) are at high risk for low bone mineral density (BMD) after therapy. Corticosteroids and antimetabolites are commonly used as post-remission therapy and can cause bone loss. Because there is tremendous variation in bone density in ALL patients after therapy, and corticotropin releasing hormone receptor-1 (CRHR1) is an important regulator of endogenous steroids, we studied whether CRHR1 single nucleotide polymorphisms (SNPs) were associated with bone loss in children treated for ALL.

METHODS: Clinical factors important to BMD (gender, race, body mass index, and treatment protocol) and nine CRHR1 polymorphisms were tested for association in 311 long-term ALL survivors. A classification and regression tree (CART) analysis using multiple regression modeling was applied to determine the interaction of clinical factors and CRHR1 SNPs on BMD. A CART was also applied to the estimated CRHR1 haplotypes using multiple regression models. Treatment group was the strongest predictor of BMD (p<0.0001) and was taken as the first node in the CARTs.

RESULTS: We found that gender, race, body mass index, and treatment intensity group were significantly associated with BMD (p<0.05). In patients who received intense corticosteroids and moderately intense antimetabolites, the rs1876828 SNP predicted higher BMD in males (p=0.018) but lower BMD in females (p=0.015). One haplotype (Hap3) had a similar gender-specific correlation to the SNP analysis. Hap3 copy number was positively correlated with BMD in males (p=0.03), but inversely correlated to BMD in females (p=0.027).

CONCLUSION: Although treatment intensity was the most important factor associated with BMD among ALL survivors, CRHR1 SNPs predicted BMD in a gender-specific manner.

202E. **ß₁-Adrenergic receptor polymorphisms and antihypertensive treatment outcomes in the international verapamil sr/ trandolapril study – GENEtic Substudy (INVEST-GENES).** *Michael Pacanowski, Pharm.D.*[1], Yan Gong, Ph.D.[1], Taimour Langaee, Ph.D., MSPH[1], Rhonda Cooper-DeHoff, Pharm.D.[1], Nicholas Schork, Ph.D.[2], Carl Pepine, M.D.[1], Julie Johnson, Pharm.D.[1]; (1)University of Florida, Gainesville, Fla; (2)University of California, San Diego, La Jolla, Calif.

PURPOSE: Common polymorphisms in the β1-adrenergic receptor gene (*ADRB1*) are associated with the antihypertensive response to β-blockers. The aim of this study was to evaluate the impact of *ADRB1* polymorphisms

on clinical outcomes in patients with treated hypertension and explore their interaction with antihypertensive drug therapy.

METHODS: In the INVEST, hypertensive patients with documented coronary artery disease (CAD) were randomly assigned to an atenolol- or verapamil SR-based antihypertensive strategy, with hydrochlorothiazide and/ or trandolapril added as needed for blood pressure control. A subset of patients (n=5,979) were genotyped for two polymorphisms in *ADRB1* (S49G, R389G). Cox regression was used to model the effects of drug exposure, *ADRB1* haplotypes, and their interaction on the primary outcome (composite of all-cause mortality, nonfatal myocardial infarction, and nonfatal stroke).

RESULTS: After an average follow-up of 2.8 years, 258 patients (4.3%) experienced a primary outcome event. The primary outcome did not differ by randomized treatment strategy (adjusted hazard ratio [HRadj] 0.91, 95% confidence interval [95% CI] 0.72–1.17, p=0.49). Carriers of the 49S-389R haplotype were at greater risk of having a primary outcome event (HRadj 1.57; 95% CI = 1.12–2.20, p=0.02), which was driven by a higher mortality rate (HRadj 3.60; 95% CI = 1.68–7.82, p=0.001). The influence of this haplotype on mortality was less pronounced in patients treated with atenolol (HRadj 2.32; 95% CI = 0.82–6.58, p=0.11) as compared to verapamil SR (HRadj 8.00; 95% CI = 1.93–33.07, p=0.004), suggesting a potential pharmacogenetic relationship.

CONCLUSION: β1-adrenergic receptor gene variants (49S-389R haplotype) may be of prognostic importance in hypertensive patients with CAD. Antihypertensive drug therapy did not significantly alter adverse haplotype effects for the composite outcome, although β-blocker therapy attenuated the adverse effect of this haplotype on mortality.

Presented at the Cold Spring Harbor Laboratory/ Wellcome Trust conference on Pharmacogenomics, Cold Spring Harbor, NY, November 15-18, 2006.

203E. Liver X Receptor-α (LXRA) haplotype and C-reactive protein response to atorvastatin. *Elvin T. Price, Pharm.D.*[1], Amber L. Beitelshees, Pharm.D., M.P.H.[2], Issam Zineh, Pharm.D.[1]; (1)University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, Fla; (2)Washington University School of Medicine, St. Louis, Mo.

PURPOSE: Statin therapy has been shown to reduce morbidity and mortality associated with cardiovascular disease (CVD) independently of lipid-lowering effects. Reduction in C-reactive protein (CRP) levels has been observed as a beneficial anti-inflammatory effect of statins. Liver X receptor-alpha is a transcription factor involved in cholesterol homeostasis, and we previously found an association between a single nucleotide polymorphism (SNP1, rs2221497) in LXRA and CRP response to atorvastatin. We thus considered whether a second SNP2 (rs7120118;) or LXRA haplotypes (using the two SNPs) would be more informative than consideration of single SNPs alone.

METHODS: Subjects were eligible if they were at least 18 years old, normocholesterolemic, without coronary heart disease. Subjects received atorvastatin 80 mg/day for 8 weeks. Baseline and 8-week high-sensitivity CRP concentrations were measured. Genotype determination was performed by pyrosequencing. Haplotypes were constructed with PHASE software. Percent change in CRP was compared by genotype groups by analysis of covariance controlling for age and baseline CRP.

RESULTS: A total of 58 subjects (60% women; 79% white) were analyzed. Baseline age, total cholesterol, LDL, HDL, triglycerides, and CRP were 32 ± 14 years, 183 ± 38 mg/dL, 101 ± 32 mg/dL, 61 ± 18 mg/dL, 99 ± 55 mg/dL, and 2.2 ± 3.5 mg/L, respectively. SNP1 and SNP2 variant allele frequencies were: A=14% and C=27%. SNP1 and SNP2 variant allele carriers experienced attenuated CRP reductions compared to wild-type homozygotes (-1.5% vs -17.9% and -10.6% vs -16.2% respectively). Attenuated CRP response was driven by the SNP1 variant A allele, and consideration of haplotypes was no more informative than consideration of SNP1 genotype alone (data not shown).

CONCLUSIONS: Consistent with our previous report, LXRA SNP1 genotype appears to be associated with CRP response to atorvastatin. Consideration of SNP2 or derived haplotypes was not more informative. Our analysis was limited by small sample size and requires further investigation in larger cohorts.

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204E. *LTA4H* variant confers drug therapy-dependent reduced risk of cardiovascular events in INVEST (INternational VErapamil SR/ trandolapril STudy). *Anzeela M. Schentrup, M.S., Pharm.D.*[1], German Nino, B.S.[1], Yan Gong, Ph.D.[1], John J. Lima, Pharm.D.[2], Rhonda M. Cooper-DeHoff, Pharm.D.[3], Carl J. Pepine, M.D.[3], Julie Johnson, Pharm.D[1]; (1)University of Florida, Gainesville, Fla; (2)Nemours Children's Clinic, Jacksonville, Fla; (3)College of Medicine, Division of Cardiology, University of Florida, Gainesville, Fla.

PURPOSE: Recent studies suggest a role for the arachidonic acid 5-lipoxygenase pathway in cardiovascular disease. We tested pharmacogenetic relationships between a polymorphism of the *LTA4H* gene that encodes leukotriene A4 hydrolase and cardiovascular events based on drug-treatment.

METHODS: In INVEST, hypertensive subjects with coronary artery disease were randomized to either atenolol or verapamil-SR-based treatment strategies with trandolopril and hydrochlorothiazide added as needed primarily for blood pressure control. We conducted a nested case-control study within INVEST, where subjects who experienced a primary outcome (all-cause death, nonfatal myocardial infarction, or nonfatal stroke) were matched based on age, race, and gender to event-free control subjects. We genotyped the *LTA4H* SNP rs2660845 and analyzed its effect and interaction with antihypertensive drug treatment on the primary outcome with the χ^2 test and logistic regression.

RESULTS: There was no difference in the overall event risk between carriers of the *LTA4H* G-allele and AA homozygotes. However, among AA homozygotes atenolol treatment was associated with a decreased risk for events compared with verapamil SR treatment. Subjects who carried a LTA4H G-allele showed no modification of risk based on antihypertensive treatment.

Genotype	Number of Events		Adjusted Odds Ratio	95% Confidence Interval	p
	Atenolol	Verapamil SR			
All subjects (n=932)	113	137	0.82	0.60-1.11	0.23
LTA4H G-carriers (n=464)	61	62	1.14	0.74-1.75	0.58
LTA4H AA (n=468)	44	66	0.57	0.36-0.91	0.03

CONCLUSIONS: Carriers of the *LTA4H* AA genotype may have better cardiovascular outcomes when treated with atenolol, whereas carriers of the G-allele may have similar outcomes with either atenolol or verapamil SR. Pharmacologically, this effect may be mediated by increased cysteinyl leukotriene production, leading to increased protein kinase C activation and subsequent α-adrenergic receptor modulation. Published in Clin Pharmacol Ther 2007;81(Supp.1):S35.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

205. **Development and evaluation of two gentamicin dosing interval nomograms for neonates receiving large dose, extended interval dosing.** *John E. Murphy, Pharm.D.*, Anthony M. Roether, Pharm.D.; University of Arizona College of Pharmacy, Tucson, Ariz.

PURPOSE: To create nomograms for the prediction of dosing intervals for large-dose, extended interval gentamicin dosing in neonates.

METHODS: Two nomograms were developed to predict intervals for desired troughs of either < 1 mg/L or < 0.5 mg/L. A 0.45 L/kg volume of distribution and 4 mg/kg dose were used to determine the peak concentration. Concentration-time curves were then created from the peak to the trough concentrations of 0.5 and 1 mg/L for 24, 36, and 48 hours intervals. A fixed dose of 4 mg/kg was applied to pharmacokinetic data from previous studies of 331 neonates to simulate individual concentration curves. Concentration data at 1 hour intervals from 6 to 22 hours were then applied to the nomograms and evaluated for the number of correct intervals predicted. When the trough concentration cutoff was achieved based on the interval suggested, it was deemed successful. Failures occurred whenever the indicated interval had not achieved the desired trough of < 0.5 mg/L or < 1 mg/L or when the interval chosen by the nomogram was longer than necessary for the desired trough.

RESULTS: At 15–21 hours post infusion the 0.5 mg/L and 1 mg/L nomograms led to the correct interval for 81.0%–92.1% and 85.5%–92.7% of neonates. Greater accuracy was achieved the longer the time that elapsed before a concentration was drawn post infusion. Concentrations drawn at 18 hours or later after a dose for both nomograms yielded almost 90% accuracy. The 18-hour time point would give a laboratory up to 6 hours before the next dose to report a concentration.

CONCLUSIONS: The use of these nomograms allows reasonably accurate prediction of dosing intervals for gentamicin in neonates and could help save hospital resources through use of a single concentration measurement to determine dosing interval.

206E. Evaluations of the human COX-2 inhibition for amfenac, bromfenac, diclofenac, and ketorolac.
Tetsuo Kida, Ph.D.[1], Takahiro Ogawa, Ph.D.[2], Timothy R. McNamara, Pharm.D.[3], *Clara K. Song, Pharm.D.*[3], James A. Gow, M.D.[3]; (1)Research Laboratory for Drug Development Senju Pharmaceutical Co., Ltd., Kobe, Japan; (2)Senju Pharmaceutical Co., Ltd., Woodland Hills, Calif; (3)ISTA Pharmaceuticals, Inc., Irvine, Calif.

PURPOSE: To compare the cyclooxygenase-2 (COX-2) inhibitory activity of the four commercially available ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs), amfenac, bromfenac, diclofenac, and ketorolac, using recombinant human COX-2 enzymes.
METHODS: Standard enzyme assays for evaluating the inhibitory activities of each compound using human recombinant COX-2 were used. Microsomal preparations of human recombinant COX-2 were prepared using insect sf21 cells. Tests were run with seven different concentrations of each NSAID to construct a dose-response curve and determine half the maximal COX-2 inhibition (IC50) relative to control values. Quantitation of PGE2 was measured using EIA.
RESULTS: Comparative results are expressed as IC50s, the concentration of enzyme in nanomoles (nM) necessary to inhibit 50% of the enzyme activity. Bromfenac had the greatest activity against COX-2 (IC50 = 7.5 nM) versus the other test compounds. In order of relative activity for COX-2 inhibition versus bromfenac: amfenac = 37% (20.4 nM); ketorolac = 27% (27.9 nM) and diclofenac = 25% (30.7 nM).
CONCLUSION: This is the first study directly comparing the relative potencies of the four commercially available ophthalmic NSAIDs. Bromfenac is about 3–4 times more potent than the other NSAIDs in COX-2 enzyme inhibition. This may explain why bromfenac is the only NSAID indicated for 2 times/day administration in treating post-cataract ocular inflammation and pain.
Presented at proceedings of the American Society of Cataract and Refractive Surgery (ARCRS) Meeting, San Diego, Calif, April 27-May 2, 2007.

207. **Population pharmacokinetics and exposure-response modeling and simulation to support quinolone phase iia dose selection.** *Prachi K. Wickremasingha, Pharm.D.*[1], Shashank Rohatagi, Ph.D.[1], Christine Falcoz, Ph.D.[2], Smita Kshirsagar, Ph.D.[2], Tatiana Khariton, Ph.D.[2], Helen Kastrissios, Ph.D.[2], Timothy J. Carrothers, Ph.D.[2], Jon Kuwabarra-Wagg, M.D., Ph.D.[2]; (1)Daiichi Sankyo Pharma Development, Edison, NJ; (2)Pharsight, Mountain View, Calif.

PURPOSE: The objective was to establish a quantitative framework to support Phase IIa dose selection for a novel quinolone, Q.
METHODS: Preclinical and Phase I Q data were used to develop: 1) a population PK model; 2) an exposure-efficacy response model based on preclinical data scaled to humans to predict the cumulative fraction of response (CFR); and 3) exposure-tolerability response models for QTc prolongation and liver function test (LFT) and serum creatinine elevations. Models were used to simulate likely efficacy and tolerability outcomes for dosing regimens of interest.
RESULTS: The final Q PK model was a three-compartment model consisting of a single central compartment and two peripheral compartments. QTc prolongation was modeled as an additive combination of baseline, placebo, active treatment and residual variability (ε) effects: $QTcF = Base + PCB + Eff^q + \varepsilon$. LFT elevation was modeled using logistic regression equations: $Logit(Pr(Day\ 13\ LFT\ Elevation => 1)) = K*EM + Int$. A physiological, non-linear time dependent model of creatinine dynamics was used to model serum creatinine elevations.
RESULTS: For gram-positive infections, Q 400 mg/day IV was identified as the target dose. The predicted CFR was 90.4%, 88.3%, and 85.2% for a bacteriostatic, 1 log and 2 log kill, respectively. This dose was predicted to have an acceptable safety profile.
CONCLUSIONS: Given the safety and efficacy profile, an optimal dose range for IV Q administered once a day for gram-positive infections was identified.

208E. Intravenous iron is associated with increased cytochrome P-450 3A4 (CYP3A4) activity in hemodialysis (HD) patients. *Amy Pai, Pharm.D.*, Jeffrey Norenberg, M.S., Pharm.D., Alex Boyd, B.S., Dominic Raj, M.D., Lingtak-Neander Chan, Pharm.D.; University of New Mexico, Albuquerque, NM.

PURPOSE: CYP3A4 is an enzyme responsible for metabolizing many commonly used drugs. CYP activity is dependent on the reduction of heme iron; therefore, iron deficiency may reduce CYP3A4 activity. HD patients use complicated, multidrug regimens and are frequently iron deficient. The purpose of this study was to investigate the effects of IV iron supplementation of CYP3A4 activity.
METHODS: Twelve iron-deficient (TSAT < 20% or ferritin <100 ng/mL) hemodialysis (HD) patients on stable medication regimens were enrolled in the study. To probe for hepatic CYP3A4 activity, an Erythromycin Breath Test (ERMBT, Metabolic Solutions, Merrimack, NH) was administered prior to and after 1 gram of IV iron

sucrose (100 mg x 10 HD sessions). The test uses ^{14}C labeled erythromycin that is *N*-demethylated by CYP3A4 and ^{14}C appears in breath as [14]CO2. CYP3A4 activity is estimated by the percentage of administered radiolabel exhaled in a single breath collection after the test dose of erythromycin. The ERMBT was also administered to 5 normal controls.

RESULTS: Seven HD patients (60%) had increased CYP3A4 activity after IV iron (mean ± SEM, 120 ± 67%). These patients had significantly lower CYP3A4 activity prior to IV iron compared with controls (0.86 ± 0.24 vs 2.25 ± 0.34 ^{14}C metabolized/hr, p= 0.006) and had higher mean iron indices at baseline than HD patients who did have increased CYP3A4 activity. After IV iron, CYP3A4 activity increased and was not statistically different from controls. There was a significant correlation between the percent increase in ferritin and ERMBT ($r^2 = 0.5$, p=0.014).

CONCLUSION: IV iron is associated clinically significant increases in CYP3A4 activity in some HD patients. Further studies are needed to clarify predictors of this interaction.

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209. **Lipoic acid content in different brands of dietary supplement α-Lipoic acid and its effect on human CYP1A2.** *Sompon Wanwimolruk, Ph.D.*, Matthew A. Alexander, Pharm.D.; School of Pharmacy, Loma Linda University, Loma Linda, Calif.

PURPOSE: α-Lipoic acid (ALA), an antioxidant dietary supplement, offers protection against diabetic neuropathy, cataracts, and cardiovascular disease. Despite its wide use, potential interactions with conventional drugs are unknown. Because dietary supplements are not subject to the same FDA regulations as prescription drugs, the contents of ALA may vary between different brands. The present study aims to determine ALA content in products from different manufacturers and to evaluate the effect of ALA on human CYP1A2, one of the important drug metabolizing enzymes.

METHODS: The content of ALA in 11 brands (n=6 each) was measured by an HPLC method. The content equivalent to one capsule or tablet was extracted with methanol, and extracted aliquots were used to determine the effect on CYP1A2. Human liver microsomes (0.1 mg/mL), the specific probe for CYP1A2 (7-ethoxyresorufin, 500 nM) and 1 mM NADPH in phosphate buffer were incubated at 37°C with and without ALA extract (n=4 each). Formation of metabolite resorufin was monitored by HPLC.

RESULTS: Of 11 brands tested, 3 products had ALA content < 90% of the claimed content: Metabolic Response Modifier (87.2 ± 5.8%); Loma Linda Market (83.9 ± 4.1%) and Source Naturals (72.6 ± 6.0%). The other 8 brands had ALA content that met the FDA requirement, which is > 90% of the claimed amount. None of the products except Jarrow Formulas had a significant effect on human CYP1A2 activity. Jarrow Formulas ALA brand also contains biotin and produced a strong inhibition (55.5%) on CYP1A2 activity. Pure ALA (2 mg/mL and 6 mg/mL) had no effect on CYP1A2 activity.

CONCLUSIONS: These results indicate that, unlike prescription drugs, the content in currently marketed products do not always meet FDA regulations. Lack of effect on CYP1A2 suggests that use of ALA supplements is unlikely to cause interactions with drugs metabolized by CYP1A2.

210. **Successful transdermal delivery of a skin-impermeable molecule using microneedles.** *Daniel P. Wermeling, Pharm.D.*[1], Stan Banks, Ph.D., candidate[1], Harvinder Gill, Ph.D., candidate[2], Mark Prausnitz, Ph.D.[2], Audra Stinchcomb, Ph.D.[1]; (1)University of Kentucky College of Pharmacy, Lexington, Ky; (2) Georgia Institute of Technology, Atlanta, Ga.

PURPOSE: The therapeutic utility of transdermal drug delivery is historically limited to medications exhibiting optimal physicochemical properties. Micron-scale microneedles (MN) have been used to pierce the skin of animals and thereby enable transdermal delivery of small molecules, proteins, DNA and vaccines for systemic action. However, no human proof of concept experiment has demonstrated successful transdermal delivery of a skin-impermeable drug that was enhanced by MN pretreatment of the skin.

METHODS: Nine healthy human subjects were recruited following approval from the University of Kentucky IRB. Using laser micromachining, 750 μm long microneedles were prepared in 50-needle arrays. Six subjects were each treated with two MN arrays (100 microneedle insertions) on the upper arm prior to patch application (4 patches total per patient). The prototype NTX patch was a 16% NTX•HCl gel. Three control subjects were treated with 4 patches containing 16% NTX•HCl gel without MN pretreatment of the skin. Plasma samples were collected for 72 h of patch administration in both groups and analyzed by LC-MS.

RESULTS: Pretreatment of skin with MN achieved average steady-state plasma concentration within 2 hours of patch application and was maintained for at least 48 hours. Control subjects had undetectable plasma concentrations. The MNs and naltrexone patch were well-tolerated, with mild systemic adverse effects associated with naltrexone and erythema or urticaria localized at the application site. Subjects reported no pain during MN administration. The MN arrays were not damaged during insertion, and no MNs were broken off in the skin.

CONCLUSIONS: This first human proof-of-concept study demonstrates clinically relevant systemic administration of a drug by microneedle-enhanced transdermal delivery that was well tolerated by the subjects. These findings set the stage specifically for novel naltrexone substance abuse therapies using MNs and, more broadly, for future human studies of other drugs and biopharmaceuticals for clinical applications.

211. **Pharmacokinetics of Mycophenolic Acid and its Phenolic-Glucuronide and Acyl-Glucuronide Metabolites in Stable Thoracic Transplant Recipients.** *Lillian S. L. Ting, M.Sc.(Pharm), Ph.D. student*[1], Nilufar Partovi, BSc(Pharm), PharmD[2], Robert D. Levy, MD, FRCPC[3], Andrew P. Ignaszewski, MD, FRCPC[3], K. Wayne Riggs, B.Sc.(Pharm), Ph.D.[4], Mary H. H. Ensom, Pharm.D., FASHP, FCCP, FCSHP[5]; (1)University of British Columbia, Vancouver, BC; (2)University of British Columbia and Vancouver General Hospital, Vancouver, BC; (3)University of British Columbia, St. Paul's Hospital, and BC Transplant Society, Vancouver, BC; (4)University of British Columbia, Vancouver, BC; (5)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: To characterize the pharmacokinetics (PKs) of mycophenolic acid (MPA) and its glucuronidated metabolites, MPAG (phenolic-glucuronide) and AcMPAG (acyl-glucuronide), in stable thoracic transplant recipients.
METHODS: Following written informed consent and upon administration of a steady-state morning mycophenolate mofetil (MMF) dose, blood samples were collected at 0, 0.3, 0.6, 1, 1.5, 2, 4, 6, 8, 10, and 12 hours. Total MPA, MPAG, AcMPAG, and free MPA (fMPA) concentrations were measured by a validated high-performance liquid chromatography method with ultraviolet detection and PK parameters calculated by non-compartmental analysis (WinNonlin 4.1).
RESULTS: Patients were: 54 thoracic (27 heart and 27 lung) transplant recipients; 36 males and 18 females; mean(± SD) 5.0 ± 5.5 years post-transplant; age 54.4 ± 13.5 years; and weight 74.9 ± 15.9 kg. In addition to MMF, 26 subjects were on cyclosporine, 26 on tacrolimus, and 2 on sirolimus. All lung and 3 heart transplant recipients were on prednisone. Albumin concentration was 4.1 ± 0.8 g/dL and serum creatinine 1.4 ± 0.4 mg%. MMF dosage ranged from 0.5 g to 3 g daily. Mean fMPA was 4.3 ± 4.1% (n=33). Mean(± SD) MPA PK parameters in heart vs. lung transplant groups, respectively, were: area-under-the-curve$_{0-12h}$ (AUC) 54.35 ± 36.14, 42.98 ± 36.58 µg*hr/mL; dose-normalized AUC 85.09 ± 54.74, 37.02 ± 28.35 µg*hr/mL/g; dose-normalized maximal concentration (Cmax) 19.01 ± 11.34, 9.78 ± 8.65; time-to-Cmax 3.0 ± 3.6, 1.7 ± 2.0 hours; dose-normalized minimum concentration (Cmin) 2.37 ± 2.11, 1.02 ± 0.95 µg/mL; MPAG/MPA AUC ratio 10.66 ± 7.06, 19.33 ± 13.22; AcMPAG/MPA AUC ratio 0.57 ± 0.79, 1.25 ± 2.75. Heart transplant subjects had significantly higher dose-normalized AUC, Cmax, Cmin, and lower MPAG/MPA than lung transplant subjects.
CONCLUSIONS: Large interpatient variability was observed in MPA PK parameters and metabolic ratios in thoracic transplant recipients. Differences in MPA PKs between heart and lung transplant recipients could be due to factors such as prednisone use, serum albumin, kidney and liver function, and comorbidities (e.g., cystic fibrosis). Population PK and pharmacogenetic studies are under way to identify other factors that contribute to the variability in the thoracic transplant population.

212. **No meaningful pharmacokinetic drug-drug interaction between saxagliptin and glyburide in healthy subjects.** *Chirag Patel, Ph.D.*, Li Li, Ph.D., Bernard Komoroski, Pharm.D., Ph.D., David Boulton, B.Pharm., Ph.D.; Bristol-Myers Squibb Co. R&D, Princeton, NJ.

PURPOSE: Saxagliptin is a potent dipeptidyl peptidase-4 (DPP-4) inhibitor being developed for the treatment of type 2 diabetes mellitus.
METHODS: This was an open-label, randomized, 3-period, 3-treatment, crossover study in 30 healthy males aged 21–45 yrs. Each subject received three treatments in random order: a single oral dose of 10 mg saxagliptin, a single oral dose of 5 mg glyburide, or a combination of saxagliptin and glyburide. There was > 87% power to conclude absence of interaction for saxagliptin or its major active metabolite or glyburide with respect to Cmax and AUCinf. Safety and tolerability were monitored throughout the study.
RESULTS: Point estimates [90% CIs] for ratios of population geometric means for saxagliptin Cmax and AUCinf, with and without glyburide, were 1.08 [1.02, 1.14] and 0.98 [0.95, 1.01], respectively, which met prespecified criteria to conclude an absence of interaction. The geometric mean (%CV) of Cmax for BMS-510849 with and without glyburide was 62(19) and 65(20), respectively, and AUCinf was 488(21) and 488(21), respectively. Point estimates [90% CIs] for ratios of population geometric means for glyburide Cmax and AUCinf, with and without saxagliptin, were 1.16 [1.06, 1.28] and 1.06 [1.00, 1.13], respectively. The 90% CI of Cmax of glyburide extended above, whereas that of AUCinf fell within the prespecified criteria to conclude absence of an interaction. Hypoglycemia was reported in 1 subject taking glyburide alone and 3 subjects taking saxagliptin + glyburide. All hypoglycemic events were associated with glyburide, and no subject experienced hypoglycemia on saxagliptin alone.

CONCLUSION: Coadministration of glyburide, a CYP2C9 substrate, did not alter the pharmacokinetics [Cmax or AUCinf] of saxagliptin or BMS-510849. The 16% increase in Cmax of glyburide in the presence of saxagliptin was considered unlikely to be of clinical consequence. No dosage adjustment is needed for either saxagliptin or glyburide when coadministered.

213. **No meaningful pharmacokinetic drug-drug interaction between saxagliptin and metformin in healthy subjects.** *Chirag Patel, Ph.D.*, Li Li, Ph.D., Bernard Komoroski, Pharm.D., Ph.D., David Boulton, B.Pharm., Ph.D.; Bristol-Myers Squibb Co. R&D, Princeton, NJ.

PURPOSE: Saxagliptin is a potent dipeptidyl peptidase-4 (DPP-4) inhibitor being developed for the treatment of type 2 diabetes mellitus.
METHODS: This was an open-label, randomized, 3-period, 3-treatment, crossover study in 16 healthy males aged 19–42 yrs. Each subject received 3 treatments in random order: a single oral dose of 100 mg saxagliptin; a single oral dose of 1000 mg metformin (MET); and coadministration of single doses of 100 mg saxagliptin and 1000 mg MET. There was > 95% power to conclude no interaction for saxagliptin or its major pharmacologically active metabolite, BMS 510849, or MET with respect to Cmax and AUCinf. Safety and tolerability were monitored throughout the study.
RESULTS: Point estimates [90% CIs] for the ratios of population geometric means for saxagliptin Cmax and AUCinf, with and without MET, were 0.79 [0.71, 0.87] and 0.98 [0.93, 1.04], respectively, and those of BMS-510849 were 0.88 [0.82, 0.94] and 0.99 [0.96, 1.02], respectively. The corresponding values for MET Cmax and AUCinf, with and without saxagliptin, were 1.09 [1.01, 1.19] and 1.20 [1.16, 1.24], respectively. Except for saxagliptin Cmax, the prespecified criteria to conclude absence of interaction were met for BMS-510849 and MET Cmax and the AUCinf of all 3 analytes. The most common adverse events reported in subjects who were administered saxagliptin alone or with MET were headache, chills, and upper respiratory tract infections. No subject experienced hypoglycemia.
CONCLUSION: Coadministration of MET decreased the Cmax of saxagliptin. This effect was considered unlikely to be of clinical consequence, and MET did not alter the overall exposure of saxagliptin or BMS-510849. Coadministration of saxagliptin, did not alter the pharmacokinetics of MET, a hOCT-1 and hOCT-2 substrate. No dosage adjustment is needed for either saxagliptin or MET when given together.

214. **Evaluation of Bleeding Events in Patients with Renal Insufficiency Who Received Eptifibatide for Percutaneous Coronary Intervention.** *Jeannette M. Ploetz, Pharm.D.*, William Alvarez, Pharm.D., BCPS, David R. Thiemann, M.D., Kenneth M. Shermock, Pharm.D.; The Johns Hopkins Hospital, Baltimore, Md.

PURPOSE: Eptifibatide produces a dose-dependent inhibition of platelet aggregation and is indicated in patients with unstable angina and non-ST-segment elevation myocardial infarction, who are managed medically or undergo percutaneous coronary intervention. Fifty-percent of eptifibatide is renally excreted. Patients with a creatinine clearance (CrCl) < 50 mL/min are known to have higher serum levels of eptifibatide and may experience bleeding. The intention of this study is to determine the rate of red blood cell transfusion and change in hemoglobin in patients with moderate-severe renal impairment (CrCl < 50 mL/min) compared to patients with mild renal impairment (CrCl 50–75 mL/min) or normal renal function (CrCl ≥ 75 mL/min).
METHODS: A retrospective cohort analysis of patients who underwent cardiac catheterization and received eptifibatide prior to January 2004 was conducted. Patients were excluded if they underwent emergent cardiac surgery. Patients were allocated into groups by CrCl (<50 mL/min, 50–75 mL/min, and ≥ 75 mL/min). CrCl was estimated using the Cockcroft Gault equation. Categorical outcomes were analyzed with Fisher's exact test, Chi-square test, Wilcoxin rank sum, and Kruskal-Wallis tests. ANOVA and Scheffé's test were used to assess continuous outcomes. A p-value <0.05 was considered statistically significant.
RESULTS: A total of 1185 patients were allocated (CrCl < 50 mL/min, n=76; CrCl 50–75 mL/min, n=228; CrCl ≥ 75 mL/min, n=881). A greater proportion of patients were transfused in the CrCl < 50 mL/min group compared to CrCl 50–75 mL/min and CrCl ≥ 75 mL/min (19.7% vs. 11.4% vs. 3.5%, p<0.0001). Transfused patients required 2.5–3 transfusions (p=0.99). The average reduction in hemoglobin was greatest in the CrCl < 50 mL/min group (-1.6g/dL vs. -1.5g/dL vs. -1.2g/dL, p<0.0001).
CONCLUSIONS: A higher proportion of patients with moderate-severe renal impairment (CrCl < 50 mL/min) were transfused. Transfused patients required a similar number of transfusions regardless of renal function. Reduction in hemoglobin was similar in the moderate-severe (CrCl < 50 mL/min) and mild renal impairment (CrCl 50–75 mL/min) groups, but both were significantly different from the normal renal function group (CrCl ≥ 75 mL/min).

215. **Pharmacokinetic characteristics of enteric-coated mycophenolate sodium in 16 renal transplant recipients.** *David I. Min, Pharm.D.*[1], Jeff Wang, Ph.D.[2], Jae-Wook Yang, Ph.D., Pharm.D[3], Edwina Chiang, M.S.[4], Anjela Tsirunyan, M.D.[4], Ian V. Hutchinson, Ph.D.[5], Gilbert J. Burckart, Pharm.D.[6], Vera Pravica, Ph.D[4], Tariq Shah, M.D.[7]; (1)Western University of Health Sciences, Pomona, Calif; (2)Western University of Health Sciences, College of Pharmacy, Pomona, Calif; (3)Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Los Angeles, Calif; (4)National Institue of Transplantation, Los Angeles, Calif; (5)USC School of Pharmacy, Los Angeles, Calif; (6)University of Southern California, Los Angeles, Calif; (7)National Institue of Transplantation and St. Vincent Medical Center, Los Angeles, Calif.

PURPOSE: Mycophenolic acid sodium is an enteric-coated formulation of mycophenolic acid, which is widely used in organ transplantation. This study aims to characterize the pharmacokinetics of mycophenolic acid (MPA) and its glucuronide metabolite (mycophenolic acid 7-O-glucuronide, MPAG) following oral administration of enteric-coated mycophenolate sodium (EC-MPS, myfortic®) at the steady state among 16 renal transplant patients.
METHODS: Eight blood samples were collected over a 12-hour period after overnight fast. All doses of EC-MPA were given as twice daily dosing schedule. Blood samples were analyzed by LC/MS/MS.
RESULTS: A total of sixteen patients (9 males and 7 females) have completed the study. Twelve patients were taking tacrolimus, EC-MPS, and prednisone; four patients were taking cyclosporine, EC-MPS, and prednisone as a part of their maintenance immunosuppression. The mean age of the patients was $55.3 \pm 8.5(24–62)$ years. The MPA was rapidly absorbed (Tmax, 2.0 ± 1.3) with peak concentration of 17.1 ± 16.5 µg/ml, but 12 out of 16 patients (75%) showed the second peak at 7.6 ± 3.5hrs after the dose. The second peak was not as high as the first peak, and the mean concentration of the second peak was 9.1 ± 6.3 µg/ml. The MPA was slowly converted to MPAG (Tmax, 5.5 hr) after absorption with relatively high plasma concentration of MPAG 179.7 ± 165.9 µg/ml. The apparent oral clearance of MPA was about 0.3 L/hr/kg. The drug exposure of MPA measured by AUC was 99.8 ± 92.8 mg/hr/L, and the AUC of MPAG was about 14 times higher than that of MPA (1408 ± 1337 mg/hr/L). There is no difference except MPAG AUC in any of the parameters between tacrolimus group and cyclosporine group. In case of MPAG, cyclosporine group showed high MPAG AUC compared with tacrolimus group ($p<0.05$).
CONCLUSION: This study showed that the pharmacokinetics of EC-MPA in renal transplant recipients are variable, and most patients exhibit the second peak concentrations.

216E. **Lack of pharmacokinetic drug interaction between amlodipine besylate and olmesartan medoxomil during coadministration.** Daniel Salazar, Ph.D.[1], James Lee, Ph.D.[1], Magdy Shenouda, M.D.[2], *Shashank Rohatagi, Ph.D.*[1]; (1)Daiichi Sankyo, Inc., Parsippany, NJ; (2)MDS Pharma Services, Neptune, NJ.

PURPOSE: The majority of hypertensive patients require a multiple drug-regimen to achieve blood pressure goal. The calcium channel blocker amlodipine besylate (AB) and the angiotensin receptor blocker olmesartan medoxomil (OM) are efficacious monotherapies with complementary mechanisms of action. This study investigated the pharmacokinetic (PK) drug interaction between AB and OM during coadministration.
METHODS: The PK interaction between these agents was investigated in an open-label, multiple-dose, 3-way crossover study in healthy subjects under fasting conditions. Subjects were assigned randomly to receive 1 of the following 10-day regimens on three occasions (each regimen separated by ≥ 21 days): treatment A, OM 40 mg/day (n=23); treatment B, AB 10 mg/day (n=23) and treatment C, OM 40 mg/day + AB 10 mg/day (n=24).
RESULTS: All dosing regimens were well tolerated. There was no significant PK interaction between amlodipine (AML) and olmesartan (OLM). Following treatments A and C, mean steady-state AUC_{0-t} and C_{max} of OLM were 6793.9 and 6890.9 ng·h/mL and 1083.8 and 1038.1 ng/mL. Respective values for AML following treatments B and C were 359.2 and 388.7 ng·h/mL and 19.8 and 20.1 ng/mL. The 90% CIs for the ratio of geometric least squares mean for AUC_{0-t} and C_{max} of AML and OLM were within the 80.0%–125.0% limit (combined treatment vs each monotherapy). Coadministration had no effect on the mean $t_{½}$ of either agent (OLM: 13.7h [A] and 13.5h [C]; AML: 51.2h [B] and 50.6h [C]). The tolerability profile of combination therapy was similar to that of each monotherapy. There were no serious AEs or AE-related discontinuations. Most TEAEs were mild; the most frequent was headache (n=10/24). Drug-related AEs occurred in 5 subjects during combination therapy and in 7 subjects with each monotherapy.
CONCLUSIONS: Coadministration of AB and OM did not affect the rate or extent of exposure of AML or OLM and was well-tolerated.
Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, May 19-22, 2007, Chicago, Ill.

217. **Population pharmacokinetics of Cyclosporine in Korean adult patients receiving living-donor renal transplantation.** Mi Young Kim, M.S.[1], *Ji Eun Park, M.S., candidate*[2], Eun Hee Ji, M.S.[2], Tae Kyung Kim, B.S.[2], Wan Gyoon Shin, Pharm.D., Ph.D[2], In Ja Son, Ph.D[1], Jung Mi Oh, Pharm.D[2]; (1)Department of Pharmacy, Seoul National University Hospital, Seoul, South Korea; (2)College of pharmacy, Seoul National University, Seoul, South Korea.

PURPOSE This study was designed to investigate the population pharmacokinetics of cyclosporine (CsA) in Korean adult patients receiving ling-donor renal transplantation and to identify the factors that elucidate the sources of variability in CsA apparent clearance (CL/F).
METHODS A total of 2394 retrospective CsA whole blood concentrations in 74 patients who had undergone kidney transplant (KTP) surgery at Seoul National University hospital and had received oral CsA microemulsion formulation were analyzed using mixed effects-modeling (NONMEM) with first-order absorption and elimination. And a number of clinical covariates during 12 months after KTP were screened for their influence on these pharmacokinetic parameters.
RESULTS The constant of absorption was fixed at 1.28 hr-1 and the population estimates for CsA clearance (CL/F, 43.6L/hr), V/F (1990L), and interpatient variability (CV%=17.69%) for CL/F were achieved. The final regression model for CsA CL/F with the influence of five significant covariates, comprising postoperative days (POD), prednisolone dose (PDD, mgs/day), total bilirubin level (TBIL, micromolar concentration), current body weight (WTKG, kgs), and concurrent metabolic inhibitor of cyclosporine (amlodipine, ALD), has been established and expressed as CL/F(L/hr) =(43.6-3.67*POD)*e0.11*PDD-0.044*TBIL/0.9+0.296*WTKG/59-6.18*ALD, if POD=2, CL/F=(43.6-1.67*POD/2)*e-0.1*TBIL/0.9+0.372*WTKG/59-6.44*ALD; where POD=0 for post-operative day <2 weeks, POD=1 for 2 weeks postoperative day < 4 weeks, POD=2, 4 weeks°Üpost-operative day; PDD=1 for predinoslon dose > 20 mg/day, otherwise, PDD=0; ALD=1 if the patient was taking concomitant amlodipine; otherwise 0 and TBIL, WTKG factors were adjusted by their respective median values.
CONCLUSIONS The population pharmacokinetic model developed identified some sources of variability in CsA pharmacokinetics; however, further studies are required to determine the optimum CsA dosage regimen in the Korean population.

218. **Analysis of population pharmacokinetics of Cyclosporine after hematopoietic stem cell transplantation in Korean leukemic patients.** Seunghee Kim, M.S[1], *Ji Eun Park, M.S., candidate*[2], Kyung Im Kim, M.S.[2], Yoo Jin Moon, B.S.[2], In Ja Son, Ph.D[1], Wan Gyoon Shin, Pharm.D., Ph.D[2], Jung Mi Oh, Pharm.D[2]; (1)Department of pharmacy, Seoul National University Hospital, Seoul, South Korea; (2) College of Pharmacy, Seoul National University, Seoul, South Korea.

PURPOSE: This study was to identify the factors affecting Cyclosporine (CsA) PK parameters after HSCT in Korean adult leukemia patients and to develop a model that would estimate individual dose requirement.
METHODS: A total of 757 cyclosporine steady-state whole blood concentrations in 46 leukemic patients were analyzed. CsA dosing history and trough level was obtained up to 1 year post oral CsA after HSCT. The influence of clinical covariates on the CsA PK was tested with nonlinear mixed effects modeling (NONMEM). A number of covariates were included such as basic demographic data, co-medications. After developing a base model without covariates, a final model was made through stepwise forward inclusion and backward elimination.
RESULTS: The final regression model for the estimation of CsA apparent clearance (CL) is: CL (L/hr) = 85.6*e-0.646*HCT/28.9+0.0464*SEXF. CsA CL increased as HCT decreased and as patients were male. Interindividual variability in CL was 36.02%. And another estimated parameters is: absorption rate (Ka) (hr-1) = 0.0787(27.92% CV), intercompartmental clearance (Q) (L/kg/hr)=57.1 (19.265 %CV), apparent central volume (V2) (L) =1100 and apparent peripheral volume (V3) (L) = 2.13E+05.
CONCLUSIONS: A model was developed that incorporates HCT and gender to predict CsA CL. Understanding CsA PK and the clinical events that lead to alterations in CL in this study would be useful in estimating individual dose requirement and Therapeutic drug monitoring(TDM). Cyclosporine dose requirements in individual HSCT patients to achieve the desired therapeutic blood level can be estimated using this model.

219. **Impact of Actual and Simulated MIC distributions on daptomycin pharmacodynamics against MRSA.** *Roger L. White, Pharm.D.*; South Carolina College of Pharmacy, Charleston, SC.

PURPOSE: Monte Carlo (MC) analysis can be used to assess the impact of changing MIC distributions on PD in patient populations.
METHODS: Daptomycin (D) MICs (Etest) were determined for 662 MRSA blood isolates from 2001-05. MIC distributions (median MICs of 0.38, 0.5, 0.75, and 1.0 mg/L) were simulated (based on the 2005 distribution when median MIC=0.25 mg/L). Total serum AUCs were simulated for D 4 and 6 mg/Kg (using population PK, tertiary-care hospital CrCl distribution, interval per package insert). MC (10,000 simulations) at AUC/MIC ≥ 100–≥ 500

was performed for each study year and MIC distribution. PD targets are based on microbiological/clinical end points in animal models (protein binding similar to humans).

RESULTS: In the clinical MIC distribution, D MICs were 0.19–0.75 mg/L with no changes over time. In the simulated distributions, MICs were 0.25–4 mg/L. Median (range) 24 hr AUCs were: D 4 mg/Kg = 436 (328–650), D 6 mg/Kg = 654 (493–975).

TA (%) for daptomycin 4mg/Kg (6 mg/Kg)

AUC/MIC	Median MIC = 0.38	Median MIC = 0.5	Median MIC = 0.75	Median MIC = 1
≥500	96 (100)	86 (98)	65 (89)	35 (72)
≥400	99 (100)	94 (99)	80 (94)	56 (82)
≥300	100 (100)	99 (100)	92 (99)	76 (94)
≥200	100 (100)	100 (100)	100 (100)	94 (99)

TA was 100% for both doses of D for all study years. In the simulated distributions, TA was high (≥ 86%) when the median MIC ≤ 0.5 mg/L. For the 6 mg/Kg dose, TA was high (≥ 89%) when the median MIC ≤ 0.75 mg/L. A 4-fold increase in the 2005 median MIC was necessary for TA to decline below 65%.

CONCLUSION: In this MRSA population, TA rates were 100% for D from 2001 to 2005. In simulated distributions with higher MICs, TA rates remained high until the median MIC increased dramatically from current values.

220E. **Evaluation of population pharmacokinetics after coadministration of amlodipine besylate and olmesartan medoxomil.** *Shashank Rohatagi, Ph.D.*[1], Timothy Carrothers, Sc.D.[2], Smita Kshirsagar, Ph.D.[2], Tatiana Khariton, Ph.D.[2], James Lee, Ph.D.[1], Daniel Salazar, Ph.D.[1]; (1)Daiichi Sankyo, Inc., Parsippany, NJ; (2)Pharsight Corporation, Mountain View, Calif.

PURPOSE: A novel fixed-dose combination of amlodipine besylate (AB) and olmesartan medoxomil (OM) may increase efficacy over monotherapy in patients with hypertension and also improve ease of administration and compliance. We evaluated population pharmacokinetics (POP PK) after coadministration of AB + OM.

METHODS: Data from phase I studies in 170 healthy volunteers (HV) and from a subset (n≈546) of patients with hypertension in a phase III trial were used to create POP PK models and subsequent analyses of amlodipine (AML) and olmesartan (OLM).

RESULTS: Both AML and OLM were characterized by 1st order elimination/absorption and an absorption time lag in a 1-compartment model for AML and a 2-compartment model for OLM. For AML, oral clearance (CL) decreased for patients with higher vs lower baseline ALT (10% increase would decrease CL by 1.4%), older vs younger patients (10% increase would decrease CL by 3.7%) or patients with lower vs higher bodyweight (10% decrease would decrease CL by 2.1%). In the OLM model, covariate analyses indicated decreased CL for patients with hypertension vs HV (1.7 L/h lower), female patients (0.878 L/h lower), patients with higher baseline serum creatinine (SeCr) vs lower SeCr (10% increase would decrease CL by 2.7%) or those with lower vs higher bodyweight (10% decrease would lower CL by 3.3%). Gender-based differences were independent of bodyweight and other covariates. Similarly, association between age and AML exposure was due to an effect on AML CL that was independent of age-related changes in bodyweight or other covariates. Combination therapy did not modify the effects of covariate status on CL of AML or OLM.

CONCLUSIONS: Neither compound had a clinically significant impact on the CL of the other. The impact of covariates on the CL of AML and OLM did not change between monotherapy and combination therapy. Presented at the American Society of Hypertension 22nd Annual Scientific Meeting and Exposition, May 19-22, 2007, Chicago, Ill.

221. **The pharmacokinetics and pharmacodynamics of clevidipine after prolonged continuous infusion in patients with essential hypertension.** *William B. Smith, M.D.*[1], Thomas C. Marbury, M.D.[2], Steven F. Komjathy, M.D.[3], Mark Sumeray, M.D.[4]; (1)New Orleans Center for Clinical Research, Knoxville, Tenn; (2)Orlando Clinical Research Center, Orlando, Fla; (3)PRA International Clinical Pharmacology Center, Lenexa, Kan; (4)The Medicines Company, Parsippany, NJ.

PURPOSE: Clevidipine is a novel, third-generation, arterioselective dihydropyridine calcium channel blocker used intravenously for the treatment of acute and severe hypertension. Clevidipine has an ultra-short half life of ~1 min and is characterized by its unique rapid-on and rapid-off pharmacologic profile. The objectives of this

study were to evaluate the pharmacologic and safety profile of clevidipine after a prolonged infusion in patients with hypertension.

METHODS: This was a randomized, placebo-controlled study in patients 18–80 years old with a history of essential mild to moderate hypertension. Treated patients withdrew from their oral antihypertensive medications 8–14 days prior to study drug administration. Patients were allocated to one of five cohorts: clevidipine 2.0 mg/hour, clevidipine 4.0 mg/hour, clevidipine 8.0 mg/hour, clevidipine 16.0 mg/hour, or placebo. Clevidipine was administered at an initial infusion rate of 2.0 mg/hour and force titrated by doubling increments every 3 minutes to the respective target dose. The target dose was maintained continuously for 72 hours.

RESULTS: A rapid onset of drug effect was seen for all dose levels of clevidipine. No evidence of tolerance was observed during continuous prolonged clevidipine infusion with the decrease from baseline in SBP being maintained at relatively constant levels throughout the 72-hour infusion period at all four dose levels of clevidipine. The percent change from baseline in SBP following termination of the clevidipine infusion did not show evidence of rebound, but showed a rapid return to baseline SBP following cessation of drug treatment across all doses. No SAEs occurred during this study. Clevidipine was safe and well tolerated.

CONCLUSIONS: After prolonged infusion of clevidipine, no drug tolerance developed and the decrease from baseline in SBP was maintained at relatively constant levels with no evidence of rebound hypertension upon discontinuation.

222E. Effect of olmesartan medoxomil and benazepril on plasma renin activity in patients with stage 2 hypertension. *Henry Punzi, M.D.*[1], Dean Kereiakes, M.D.[2], Joel M. Neutel, M.D.[3], Findlay Walker, M.D.[4], Robert Dubiel, Pharm.D.[4], Jianbo Xu, M.S.[4]; (1)Punzi Medical Center and Hypertension Research Institute, Carrollton, Tex; (2)The Heart Center of Greater Cincinnati and The Lindner Center at The Christ Hospital, Cincinnati, Ohio; (3)Orange County Research Center, Tustin, Calif; (4)Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: Plasma renin activity (PRA), measured under controlled conditions, has been used as a marker of the degree and persistence of renin-angiotensin system blockade. The effect of the angiotensin receptor blocker olmesartan medoxomil (OM) on PRA was assessed in a subgroup of a randomized, double-blind, multicenter titration study in patients with Stage 2 hypertension.

METHODS: After a 3–4 week placebo run-in, 190 patients with Stage 2 hypertension were randomized to increasing doses of OM (20 mg week 0–2 and 40 mg week 2–4) or benazepril (BN) [10 mg week 0–2 and 20 mg week 2–4]. Primary end point results are reported elsewhere. In the PRA substudy, 42 patients (OM=21; BN=21) were evaluated. End points included mean change in PRA from baseline (ΔPRA) after 24 hours and 2 weeks of low-dose OM or BN and after 24 hours (week 2+1 day of study) and 2 weeks (or week 4) of high-dose OM or BN.

RESULTS: Baseline mean PRA was 1.0 ng/mL/h in both groups. Mean ΔPRA was higher after 2 weeks than after 24 hours with OM 20mg (2.3 vs 0.4 ng/mL/h) and OM 40mg (2.5 vs 1.9 ng/mL/h). Mean ΔPRA was higher after 2 weeks than after 24 hours with BN 10 mg (0.6 vs 0.2 ng/mL/h) but not for BN 20 mg (0.6 vs 1.0 ng/mL/h). Correlations between PRA and BP reductions were significant for OM at week 2+1 day and week 4, whereas the correlation between PRA and sitting SBP was significant for BN only at week 4. Doubling the dose of either monotherapy did not significantly increase the PRA level at the end of the high-dose monotherapy treatment.

CONCLUSIONS: The greater mean ΔPRA after 2 weeks indicates more prolonged AT$_1$ receptor blockade with chronic than with acute OM monotherapy and, consequently, may also indicate a more prolonged reduction in BP.

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223. A double-blind, placebo-controlled dose escalation study of the safety, tolerability and pharmacokinetics of a single oral dose of KP-1461 in HIV-negative healthy adults. *Patrick G. Clay, Pharm.D.*[1], Jeff Parkins, M.S.[2], John Reno, Ph.D.[2]; (1)Kansas City University of Medicine and Biosciences, Kansas City, Mo; (2)Koronis Pharmaceuticals, Inc., Redmond, Wash.

PURPOSE: KP-1461, a deoxy-cytidine analog prodrug, works by Viral Decay Acceleration,TM inducing mutations randomly throughout the viral genome. In vitro, once a tolerable mutation threshold is exceeded, viral extinction is observed. Viral ablation was demonstrated in vitro treating HIV-infected cells with the active moiety of KP-1461, KP-1212.

METHODS: KP-1461-101, a Phase 1, randomized, double-blind, placebo-controlled, dose-escalation study evaluated safety, tolerability, and pharmacokinetics (PK) of KP-1461 of six doses. Each subject in the first 6 dose cohorts was randomized (4:2 ratio) to a single oral fasting dose (100–1600 mg or placebo). Subjects in the

seventh cohort received 800 mg following a high-fat/high-calorie meal. All subjects were evaluated for safety and tolerability following dosing and 14 days later.
RESULTS: 42 subjects (38 males, 28 KP-1461, 14 placebo) completed the study. Safety: There were no serious adverse events (SAE) or discontinuations due to an AE. Overall, 24 (57.1%) subjects reported AEs (8 placebo and 16 KP-1461-treated subjects). Pharmacokinetics: Under fasting conditions mean plasma concentrations of KP-1461 increased in a dose-related manner. Pharmacokinetics of KP-1461 appeared linear with respect to the extent of absorption (AUC (0-∞) and t½). Mean values for t½ ranged from 0.75 to 1.35 h. The rate of absorption (Cmax and Tmax) appeared to decrease with increasing KP-1461 dose. Mean KP-1212 plasma concentrations increased in a dose-related manner as did mean values for Cmax, AUC (0-t), and AUC (0-∞). Median Tmax ranged from 0.88 to 2.0 h and mean t½ ranged from 1.08 to 2.06 h.
CONCLUSIONS: Single oral doses of KP-1461 were generally well tolerated in healthy adult volunteers. Pharmacokinetics of KP-1461 and KP-1212 (the active metabolite of KP-1461) appeared to be linear. A substantial reduction in the rate and extent of absorption of both KP-1461 and KP-1212 occurred following a high-fat/high-calorie meal.

224. **Evaluation of a simple in vitro model for screening of mucosal drug delivery.** Shu Wang, B.Sc., Yan-feng Wang, Ph.D, Zhong Zuo, Ph.D, *Moses S. S. Chow, Pharm.D.*; School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong.

PURPOSE: Mucosal drug delivery can provide improved onset of action and bioavailability over oral route. Screening of suitable compounds is critical for developing such drug delivery. The purpose of the present study was to evaluate a simple hexadecane artificial membrane (HAM) model in comparison to the well-accepted cell line models for potential screening of mucosal drug delivery.
METHODS: The apparent permeability coefficient (P_{app}, average of N=3 for each determination) of a representative weak base or acid (i.e., propranolol (P) or meloxicam (M)) at different pH values was determined using HO-1-u-1 and Calu-3 cell lines and compared to HAM after proper validation of each model using standard approach.
RESULTS: When pH increased from 5 to 9, the P_{app} of P increased from 0.26 ± 0.02 to $0.54 \pm 0.01 \times 10^{-5}$ cm/s through the cell line, and from 0.19 ± 0.02 to $13.70 \pm 2.61 \times 10^{-5}$ cm/s across HAM ($r^2 = 0.99$ for the two models). In contrast, with similar pH change, the P_{app} of M declined from 3.41 ± 0.31 to $1.61 \pm 0.10 \times 10^{-5}$ cm/s through the cell line, and from 7.48 ± 1.36 to $0.35 \pm 0.07 \times 10^{-5}$ across HAM($r^2 = 0.84$ for 2 models).
CONCLUSION: The HAM model provided similar trend of change in P_{app} to that from the cell line and was consistent with what is expected of a weak base and acid. The HAM model may be a suitable and simple alternative to above cell line models for screening purposes. Further studies with more compounds, however, are needed to confirm this finding.

225. **Evaluation of an in vitro model for studying first-pass gut metabolism.** *Zisheng Xu, Ph.D.*, Joan Zhong Zuo, Ph.D., Dexing Kong, Ph.D., Francis K. L. Chan, M.D., Moses S.S. Chow, Pharm.D.; School of Pharmacy, Chinese university of Hong Kong, Hong Kong.

PURPOSE: Herbal products containing isoflavones can undergo metabolism not only in the liver, but also in the gut. Although in vitro methods for human liver metabolism are well known, an in vitro human gut metabolism model is lacking. The purpose of the present work is to provide initial validation and feasibility of such a model using daidzin, a main isoflavone component from *Pueraria lobata*, as a representative compound.
METHODS: Because daidzin is known to be hydrolyzed to daidzein (D) in human as well as rat gut, in this research rat stomach and duodenum tissues with standardized protein concentrations were collected and incubated with different concentrations of daidzin at 37°C for 60 min. Intrinsic clearance (CL_{int}), V_{max} and K_M were calculated from metabolite formation data. Similarly, studies were performed with human stomach or duodenum tissue as well as their respective fluids obtained via biopsy in suitable subjects undergoing endoscopy.
RESULTS: No D was formed in human or rat stomach tissues or human gut fluids (N=6 each). The V_{max}, K_M,and CL_{int} from the rat/human duodenum tissues (n=6 each) were 0.044/0.060 nmole/min/mg protein, 0.613/0.082 mM, and 4.3/8.8 μL/hr/mg protein respectively (p<0.05 human compared to rat).
CONCLUSIONS: Human gut metabolism of daidzin appeared to occur in the intestinal tissue, but not stomach or gut fluids. In view of the differences obtained between human and rat data, these initial results indicate that the human duodenum tissue biopsy may offer an in vitro approach for studying gut metabolism.

226. **No meaningful pharmacokinetic drug-drug interaction between saxagliptin and pioglitazone in healthy subjects.** *Chirag Patel, Ph.D.*, Li Li, Ph.D., Bernard Komoroski, PharmD., Ph.D., David Boulton, B.Pharm., Ph.D.; Bristol-Myers Squibb Co. R&D, Princeton, NJ.

PURPOSE: Saxagliptin is a potent dipeptidyl peptidase-4 (DPP-4) inhibitor being developed for the treatment of type 2 diabetes mellitus.
METHODS: This was an open-label, non-randomized, sequential study in 30 healthy males aged 22–42 years. Each subject received daily oral doses of 10 mg saxagliptin for 3 days, then 45 mg pioglitazone (PIO) once daily for the next 5 days. Thereafter, subjects continued receiving daily doses of 45 mg PIO and 10 mg saxagliptin for 5 days. There was > 87% power to conclude absence of interaction for saxagliptin or its major pharmacologically active metabolite, BMS-510849, or PIO with respect to Cmax and AUCtau. Safety and tolerability were monitored throughout.
RESULTS: For unknown reasons, 1 subject had very low exposure to saxagliptin and BMS-510849 when saxagliptin was administered alone. Data from this subject were excluded from the saxagliptin statistical analysis. Point estimates (PE) [90% CIs] for the ratios of population geometric means for saxagliptin Cmax and AUCtau, with and without PIO, were 1.11 [1.03, 1.20] and 1.11 [1.06, 1.16], respectively. Prespecified criteria to conclude absence of an interaction for saxagliptin were met for both parameters. The geometric means (%CV) of Cmax of BMS-510849, with and without PIO, were 119(25) and 120(28) ng/mL, respectively, and AUCtau were 588(23) and 628(28) ng.h/mL, respectively. In the presence of saxagliptin there was a 14% increase in the Cmax of PIO, which was not considered clinically meaningful and AUCtau did not change (PE [90% CI] of 1.08 [0.99, 1.17]). No subject experienced hypoglycemia with any treatment.
CONCLUSION: Coadministration of PIO, a CYP2C8 and CYP3A substrate, did not alter the pharmacokinetics of saxagliptin or BMS-510849. The effects of saxagliptin on pharmacokinetics of PIO were considered unlikely to be of clinical consequence. No dosage adjustment is needed for either saxagliptin or PIO when coadministered.

227. **Model-based dose selection of a quinolone to minimize drug induced serum creatinine elevation.** *SaeHeum Song, Ph.D.*[1], Shashank Rohatagi, Ph.D.[1], Prachi K. Wickremasingha, Pharm.D.[1], Tatiana Khariton, Ph.D.[2], Smita Kshirsagar, Ph.D.[2], Timothy J. Carrothers, Ph.D.[2], Jon Kuwabara-Wagg, M.D., Ph.D.[2]; (1)Daiichi Sankyo Pharma Development, Edison, NJ; (2)Pharsight, Mountain View, Calif.

PURPOSE: To use preclinical and phase I PK/PD data from a new quinolone (Q) and relevant public domain data to develop exposure-response model for serum creatinine level increase by Q to support dose selection for subsequent clinical studies.
BACKGROUND: Reversible serum creatinine elevations were observed during development of a novel Q that may confound clinical safety monitoring. Glomerular filtration rate (GFR) remained constant whereas creatinine urinary clearance decreased, suggesting that the Q selectively inhibits creatinine renal tubular secretion.
METHODS: A population PK model was linked to a PD model of creatinine dynamics assuming competitive inhibition, consistent with preclinical data suggesting competitive inhibition of creatinine transport by Q. The PD model was consisted of the following equation: $d[Crn]/dt = ([Crn].GFR + RateCrnIn - RateCrnSec*[Crn])/VolCrn$; where [Crn], GFR, RateCrnIn, RateCrnSe, and VolCrn denote serum creatinine concentration (mg/dL), glomerular filtration rate (dL/Hour), Zero order creatinine production rate (mg/Hour), creatinine tubular secretion rate (dL/Hour), and creatinine volume of distribution (dL). RateCrnSe described as $RateCrnSec = Vmax*[Crn]/(Km*(1 + [Q]/Ki) + [Crn]))$ where [Q] denotes the Q serum concentration. The resulting model was used to simulate Q dose-dependent increase in serum creatinine. Creatinine dynamics parameters were derived from the literature.
RESULTS: Model-supported competitive inhibition of serum creatinine secretion (Ki 156 ng/mL, ED50, 40 mg) by Q simulations showed that maximum serum creatinine increase occurred at Q doses of 200 mg IV QD.
CONCLUSION: Q may competitively inhibit serum creatinine secretion with maximum increase at 200 mg IV QD. Hence IV Q doses above 200 mg will not produce additional increase in serum creatinine level.

Pharmacy Administration

228. **Assessment of eptifibatide dosing in renal impairment: before and after education in-service by pharmacists.** *Jennifer L. Donovan, Pharm.D.*[1], Walter S. Schroeder, Pharm.D.[2], Maichi T. Tran, Pharm.D.[3], Keith Foster, Pharm.D.[2], A. Forrest, Pharm.D.[2], Tamara B. Lee, Pharm.D.[2], Pritesh J. Gandhi, Pharm.D.[4]; (1)Massachusetts College of Pharmacy and Health Sciences, Worcester, Mass; (2)University at Buffalo, University at Buffalo, Buffalo, NY; (3)UMass Memorial Medical Center, Worcester, Mass; (4) Genzyme Corporation, Cambridge, Mass.

PURPOSE: Antithrombotics frequently cause medication errors and patient harm; renal impairment may further exacerbate. Eptifibatide is often administered without pharmacist evaluation due to the acute nature of therapy. Our objective was to assess the impact of pharmacist education on prescriber adherence to eptifibatide renal dosing guideline at two academic tertiary medical centers (referred to as Site A and Site B).

METHODS: Our Institutional Review Board approved study was conducted retrospectively at both sites to identify eligible patients receiving eptifibatide with a creatinine clearance less than 50 mL/minute. Patients were excluded if they required renal replacement therapy. We reviewed medical records for demographics, concomitant medications, hematologic status, and actual eptifibatide dose administered. Our study was divided into pre-education and post-education phases. Site A employed a global educational campaign on acute coronary syndrome management completed via institution-wide in-services, pocket reference cards, and preprinted order forms. Site B employed a focused educational strategy, which involved in-service presentations to cardiologists only. All education described renal dosing of eptifibatide. The primary outcome was improvement in renal dosing of eptifibatide. Secondary outcomes included the difference in the improvement in dosing adherence between the sites.

RESULTS: A total of 148 patients were included: 106 and 42 in the pre-education and post-education, respectively. Patient demographics were similar between phases (p=NS). We found that education improved renal dosing of eptifibatide (pre-education 36.7% vs. post-education 69.0%; p=0.0005) regardless of the educational strategy employed. When patients were dosed inappropriately in the pre-education phase, 57.5% patients received greater than recommended eptifibatide doses, whereas in the post-education phase this was reduced to 26.2%. No difference was detected in bleeding events between phases.

CONCLUSION: Pharmacist-provided educational programs improved prescriber adherence to renal dosing recommendations for eptifibatide. Such programs may be useful in improving dosing for other medications when pharmacist review or computerized dosing aid is unavailable.

229. **Survey of pharmacist opinion and comfort level of current and future job functions.** *Molly E. Graham, Pharm.D.*, Melissa M. Blair, Pharm.D., BCPS, FCCP, CDE; New Hanover Regional Medical Center, Wilmington, NC.

PURPOSE: The role of pharmacists in health care is evolving. To help establish minimum priorities, competencies, and areas for training programs, pharmacists were surveyed at a community teaching hospital. The purpose of the survey was to determine pharmacists' opinion and comfort level of current and future job functions at a community teaching hospital.

METHODS: A survey was developed based on ASHP 2015 and departmental goals, which focused on perceived job priorities and comfort level in performing tasks. Questions were reviewed by pharmacy administration and teaching faculty for completeness, and IRB approval was obtained. Pharmacists were asked to rate their job priority using a 6-point Likert scale and their comfort level using a 5-point Likert scale. The voluntary, anonymous survey was electronically circulated to pharmacists via Surveymonkey.com. Follow-up reminders were electronically sent to those who had not yet completed the survey weekly for 2 weeks after the first distribution.

RESULTS: A total of 88% (43/49) of pharmacists responded and completed the survey. The top perceived job priorities included screening medication therapies for allergies and interactions (98%), identifying and resolving therapeutic duplications (93%), verbally communicating with health care professionals (98%), and applying formulary guidelines (85%). The job priorities with at least 50% of respondents believing the task is low priority or not part of their job included discharge medication counseling (70%), providing formal in-services (73%), smoking cessation counseling (80%), and vaccination screening (76%). The pharmacists surveyed were most comfortable with IV to PO switches (73%), and most uncomfortable with dosing anticoagulation therapies (39%).

CONCLUSION: Pharmacists at this institution are comfortable with and believe that currently implemented tasks are their top job priorities. Conversely, tasks that are not yet implemented are perceived to be a low priority. Information gathered will be used to address educational needs and development of future pharmacist roles.

230. **Impact of direct-to-consumer television advertising of medications on consumer behavior.** Nile M. Khanfar, M.B.A., Ph.D., *Kevin A. Clauson, Pharm.D.*; Nova Southeastern University, College of Pharmacy, West Palm Beach, Fla.

PURPOSE: The objective of the study was to explore the relationship between direct-to-consumer television advertising (DTCA) of prescription medication and its impact on consumer behavior.

METHODS: A 68-item email survey was sent to US residents assessing medication use for asthma, gastroesophageal reflux disease (GERD), and social anxiety disorder (SAD). The survey captured data regarding the influence of DTCA on consumer medication use practices. Questions explored consumer advertisement viewing, consumer-posed inquiries to physicians regarding advertised medications, and regimen changes during subsequent visits that occurred due to DCTA. Inferential tests, frequency counts, percentages, and descriptive analyses were used to analyze the data. The key tests included crosstab analysis and binomial tests with the Z approximation.

RESULTS: The percentages of the 478 responders who currently took a prescription were 7.5% (asthma), 24.1% (GERD) and 11.3% (SAD). Those who had seen a television advertisement for a drug for those conditions

reported at: 76.7% (asthma), 86.1% (GERD), and 75.9% (SAD). The most frequently observed advertised drug by consumers for each condition was Singulair for asthma (36.1%), Nexium for GERD (75.3%), and Zoloft for SAD (67.9%). The percentages of responders who reported discussing the brand of medication they saw on television was 6.1% (asthma), 8.4% (GERD), and 5.2% (SAD). Responders confirmed that a discussion of the DTCA drug with their physician resulted in a regimen change to the advertised medication in 44.8% (asthma), 50.0% (GERD), and 36.0% (SAD) of the cases.

CONCLUSIONS: The influence of television advertisements on patient behavior is considerable, with a change of medication directly due to DTCA likely in a high percentage of patients who are diagnosed with three common medical conditions.

231. **Impact of antifungal use at a tertiary-care hospital.** *Raymond Cha, Pharm.D.*, Sheila M. Wilhelm, Pharm.D., George J Alangaden, M.D., Pranatharthi H. Chandrasekar, M.D.; Wayne State University, Detroit, Mich.

PURPOSE: The evolving antifungal armamentarium continues to represent a significant expenditure for health systems. The advent of newer antifungal agents continues to affect cumulative drug acquisition costs. With multiple agents that can be used as first-line therapy for a variety of infections, we investigated the current financial impact of intravenous antifungal use on our system.

METHODS: This study was performed in a tertiary-care institute and the adjacent Karmanos Cancer Institute. Pharmacy databases on intravenous fluconazole (FLU), voriconazole (VOR), caspofungin (CAS), and amphotericin (AMP) billing between January 2003 and December 2005 were generated. Data on unit doses (intravenous vials billed to patients) and duration of therapy were compiled. Financial impact was assessed yearly and quarterly by drug acquisition cost per unit doses, and by patient.

RESULTS: Yearly, cumulative billed units for FLU, VOR, CAS, and AMP for 2003/2004/2005 was 2431/1755/2690, 372/552/1293, 209/243/1107, and 668/474/253, respectively. A 5-fold reduction was noted in AMP use between the 2nd and 3rd quarters of 2004. A 3-fold increase in CAS use was observed between the 4th quarter of 2004 and 1st quarter of 2005. A 4-fold increase in VOR use was noted between the 1st and 2nd quarters of 2005. Total antifungal acquisition costs more than doubled to more than $500,000 USD from 2004 to 2005. Mean duration of therapy in 2005 was 6.5, 12.2, 10.9, 6.8 days for FLU, VOR, CAS, and AMP respectively across 687 patients.

CONCLUSIONS: The substantial increase in cumulative VOR and CAS use was disproportionate to the decrease use of AMP. These increases were also independent of persistent FLU utilization. As a result of the increased use of newer agents and the increasing number of patients treated with antifungals, a significant increase in total drug expenditures was observed.

Psychiatry

232E. **Efficacy and safety of doxepin 3 mg and 6 mg in adults with primary insomnia.** *H. Heith Durrence, Ph.D.*[1], Alan Lankford, Ph.D.[2], Steven Hull, M.D.[3], Martin Scharf, Ph.D.[4], Howard Schwartz, M.D.[5], David Seiden, M.D.[6], Phillip Jochelson, M.D.[1], Roberta Rogowski, BSN[1], Thomas Roth, Ph.D.[7]; (1)Somaxon Pharmaceuticals, Inc., San Diego, Calif; (2)Sleep Disorders Center of Georgia, Atlanta, Ga; (3)Vince and Associates Clinical Research, Overland Park, Kan; (4)Tri-State Sleep Disorders Center, Cincinnati, Ohio; (5)Miami Research Associates, Miami, Fla; (6)Broward Research Group, Pembroke Pines, Fla; (7)Henry Ford Hospital Sleep Disorders Center, Detroit, Mich.

PURPOSE: The efficacy and safety of doxepin (DXP) 3 mg and 6 mg were evaluated in adults with primary insomnia.

METHODS: This was a randomized, double-blind, placebo-controlled study of adults with insomnia. Subjects reported ≥ 3 months of DSM-IV-TR primary insomnia, with confirmation by polysomnography (PSG). Subjects were randomly assigned to nightly doses of placebo (PBO; n=73), DXP 3 mg (n=75) or DXP 6 mg (n=73) for 35 days. Efficacy was evaluated objectively (PSG) and subjectively; data from the first and last PSG assessment points, nights 1 (N1) and 29 (N29), are reported. PSG end points included wake-after-sleep-onset (WASO), latency-to-persistent-sleep (LPS), and sleep efficiency (SE; overall and by third-of-the-night). Primary end point was N1 WASO.

RESULTS: Compared with PBO, DXP 3 mg and 6 mg statistically significantly improved WASO at N1 ($p < 0.0001$) and N29 (3 mg p=0.0299; 6 mg p=0.0012), LPS at N1 (3 mg p=0.0110; 6 mg p=0.0018), and overall SE at N1 ($p < 0.0001$) and N29 (3 mg p=0.0262; 6 mg p=0.0003). The significant differences on N1 LPS were not observed on N29, primarily due to PBO improvement. DXP 3 mg and 6 mg generally demonstrated statistically significant improvements in SE by third-of-the-night on N1 and N29. There were no significant group differences in next-day residual sedation, incidence of adverse events was similar between groups, and sleep architecture was generally preserved.

CONCLUSIONS: In adults with insomnia, DXP 3 mg and 6 mg were well-tolerated and produced significant improvement on the primary end point WASO and on multiple secondary end points on N1; these improvements were maintained on N29 for sleep maintenance and duration end points. On sleep onset, there was significant improvement in LPS at N1 with no loss of drug effect at N29, although statistical significance was not maintained. In addition, the incidence of adverse events was comparable to PBO; there were no reports of amnesia, no reports of anti-cholinergic effects, and no significant hangover/next-day residual effects. Presented at the American Psychiatric Association's annual meeting in San Diego, Calif, May 22nd, 2007.

233E. **Association between the methylenetetrahydrofolate reductase (MTHFR) 677C/T variant and atypical antipsychotics (AAPs) associated metabolic syndrome and insulin resistance in subjects with schizophrenia.** *Vicki l. Ellingrod, Pharm.D., BCPP*[1], Del D. Miller, Pharm.D., M.D.[2], Stephan F. Taylor, M.D.[3], Jessica Moline, B.S.[4], Timothy Holman, M.A.[2], Jane Kerr, B.S.[2]; (1)University of Michigan, College of Pharmacy and School of Medicine, Department of Psychiatry, Ann Arbor, Mich; (2)University of Iowa, Carver College of Medicine, Department of Psychiatry, Iowa City, Iowa; (3)University of Michigan School of Medicine, Department of Psychiatry, Ann Arbor, Mich; (4)University of Michigan, College of Pharmacy, Ann Arbor, Mich.

INTRODUCTION: The metabolic syndrome and insulin resistance represent growing concerns related to cardiovascular mortality and have been increasingly associated with AAP use. Metabolic syndrome and sudden cardiac death rates in AAPs users are 2–4 greater than the general population. The methylenetetrahydrofolate reductase (MTHFR) 677C/T variant, resulting in reduced folate metabolism and hyperhomocysteinemia, is linked to cardiovascular disease and unstudied in relation to AAP associated metabolic complications.
PURPOSE: To examine the relationship between MTHFR, metabolic syndrome, and insulin resistance in schizophrenia subjects receiving AAPs for ≥ 12 months.
METHODS: Fifty-eight subjects were included in this cross-sectional analysis and screened for the metabolic syndrome, insulin resistance and MTHFR 677C/T genotype.
RESULTS: Overall, 23 subjects (40%) met metabolic syndrome criteria. There were no differences in age, gender, race, or AAP exposure between genotype groups. For the 677 T allele carriers, 53% met metabolic syndrome criteria, compared with 23% in the CC genotype group (OR = 3.7; 95% CI = 1.24–12.66, p=0.02). Thus, for T allele subjects, the risk was almost four times greater, despite similar antipsychotic exposure. Both waist circumference and MTHFR genotype significantly predicted insulin resistance (F = 8.35, df = 5, 51, p<0.0001), with these two terms interacting (F = 8.6, df = 2, p=0.0006) suggesting that TT subjects are at greater risk for insulin resistance with increasing central adiposity, which is independent of age, gender, BMI, or metabolic syndrome diagnosis.
CONCLUSION: Results should be taken cautiously due to the small sample size, but suggest the MTHFR 677C/T variant may predispose patients to AAP metabolic complications.

234E. **Long-term efficacy and safety of lisdexamfetamine in school-age children with attention-deficit/hyperactivity disorder.** Robert L. Findling, M.D.[1], Ann C. Childress, M.D.[2], Suma Krishnan, M.S.[3], James J. McGough, M.D.[4], *Stacey Curtiss, PharmD*[3]; (1)University Hospitals Case Medical Center, Cleveland, Ohio; (2)Center for Psychiatry and Behavioral Medicine, Inc., Las Vegas, Nev; (3) Shire Development Inc., Wayne, Pa; (4)Neuropsychiatric Institute and David Geffen School of Medicine of UCLA, Los Angeles, Calif.

PURPOSE: To evaluate the effectiveness and safety of long-term lisdexamfetamine dimesylate (LDX) treatment in children ages 6–12 years with attention-deficit/hyperactivity disorder (ADHD).
METHODS: This long-term, open-label, single-arm study enrolled children ages 6–12 years with DSM-IV-TR® diagnosis of ADHD (combined and hyperactive/impulsive subtypes). Most subjects were previously enrolled in a double-blind clinical study and may or may not have received prior LDX treatment. Subjects were started on 30 mg/day and maintained on this dose or titrated to 50 mg/day or 70 mg/day LDX over 4 weeks. Treatment was maintained for up to 11 more months, during which time the dose could be adjusted to maintain optimal efficacy and tolerability. The primary efficacy measure was the ADHD Rating Scale (ADHD-RS). Secondary efficacy was measured by the Clinical Global Impression (CGI) scale. Safety assessments included adverse events (AEs), physical examinations, vital signs, laboratory evaluations, and electrocardiograms.
RESULTS: At end point, the mean (±SE) change in ADHD-RS total score in intent-to-treat (ITT) population (n=272; 189 boys, 83 girls) was −27.2 (± 12.8) (p<.0001), a > 60% reduction from the baseline value of 43.3 (± 7.7). Reductions from baseline were observed at each postbaseline visit through 12 months. No differences were

found between subjects who were or were not previously treated with LDX. Investigators rated > 80% of the ITT subjects improved on the CGI scale at end point, and > 95% of subjects were rated improved after 12 months. Most AEs (> 95%) were mild to moderate and occurred during the first 8 weeks of treatment. The most common AEs were decreased appetite, insomnia, weight decrease, headache, abdominal pain, irritability, upper respiratory tract infection, and nasopharyngitis.

CONCLUSIONS: Long-term treatment with 30 mg/day, 50 mg/day, and 70 mg/d LDX resulted in persistent improvement in ADHD symptoms and was generally well tolerated in children.

Supported by funding from Shire Development Inc. Presented at the American Psychiatric Association, San Diego, Calif, May 19-24, 2007.

235. **Guanfacine extended release: in vitro permeability, metabolism, inhibition, and induction studies.** *Michael Pennick, B.Sc.*; Shire Development, Inc., Basingstoke, United Kingdom.

PURPOSE: Guanfacine extended release (GXR) is a novel formulation of guanfacine, a selective $_{2A}$-adrenoceptor agonist, for the treatment of attention-deficit/hyperactivity disorder. The permeability, metabolism, and potential of guanfacine to inhibit and/or induce various cytochrome P450 (CYP450) isozymes were evaluated in vitro.

METHODS: The transport of guanfacine through intestinal cells and its effect on $[^{14}C]$-paclitaxel transport was investigated using Caco-2 cell monolayers. To determine the involvement of specific CYP450 isozymes in guanfacine metabolism, 1) human hepatic microsomes were incubated with guanfacine and CYP-isozyme selective inhibitors, and 2) selected cDNA-expressed human hepatic CYP450 were incubated with guanfacine. The effect of guanfacine on CYP450 activity was assessed in human hepatocytes and hepatic microsomes.

RESULTS: Guanfacine was highly permeable. Its apparent apical-to-basolateral permeability coefficient, P_{app}, was comparable to testosterone. P_{app} values for basolateral-to-apical and apical-to-basolateral transport were similar. Guanfacine did not affect $[^{14}C]$-paclitaxel transport through Caco-2 cells. CYP2E1- and CYP3A4-selective inhibitors (diethyldithiocarbamate and ketoconazole, respectively) significantly inhibited guanfacine metabolism, while only cDNA-expressed CYP3A4 metabolized guanfacine. Guanfacine did not substantially inhibit CYP450 activities in hepatic microsomes. In human hepatocytes, incubation with guanfacine (0.04–4 μM) for 48 hours did not induce CYP1A2, CYP2B6, or CYP3A4. Cells from 1 donor had small, clinically unimportant increases in CYP2C9 and CYP2C19 activities at the highest guanfacine concentration of 4 μM (~100 times the maximum plasma steady-state concentration $[C_{ss,max}]$ in 6–12-year old children given multiple daily doses of 4 mg GXR).

CONCLUSIONS: Guanfacine was efficiently transported through Caco-2 cell monolayers, primarily by a passive transcellular pathway, and may therefore exhibit significant absorption in vivo. Guanfacine was not a substrate or a potent inhibitor of the P-glycoprotein pump. Guanfacine is metabolized primarily by CYP3A4 and is not a reversible or irreversible inhibitor or inducer of the major human hepatic CYP450 isozymes. Supported by funding from Shire Development Inc.

236E. **Improved interpatient pharmacokinetic variability of lisdexamfetamine dimesylate compared with mixed amphetamine salts extended release in children ages 6–12 years with attention-deficit/hyperactivity disorder.** James C. Ermer, M.S.[1], Amir H. Shojaei, Pharm.D., Ph.D.[2], Joseph Biederman, M.D.[3], Suma Krishnan, M.S.[1], *Hilary Mandler, Pharm.D.*[1]; (1)Shire Development Inc., Wayne, Pa; (2)AGI Therapeutics, Inc. (formerly employed by Shire Development Inc., Wayne, Pa), Columbia, Md; (3)Clinical and Research Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Harvard Medical School, Boston, Mass.

PURPOSE: To evaluate the variability in pharmacokinetic parameters of lisdexamfetamine dimesylate (LDX) compared with mixed amphetamine salts (MAS XR) in children ages 6–12 years with attention-deficit/hyperactivity disorder (ADHD).

METHODS: This Phase II, randomized, multicenter, double-blind, 3-treatment and 3-period crossover study evaluated the efficacy and safety of LDX (30 mg/day, 50 mg/day, or 70 mg/day) and MAS XR at equivalent d-amphetamine base doses (10 mg/day, 20 mg/day, or 30 mg/day) with placebo in children with ADHD. Subjects were titrated to optimum dose of MAS XR, after which medication was administered in a randomized fashion for 1 week. At the last visit of the double-blind period, blood was drawn predose and at 1, 2, 3, 4.5, 6, 8, 10, and 12 hours postdose for measurements of plasma drug concentration and pharmacokinetic parameters. Pharmacokinetic parameters were calculated using noncompartmental methods.

RESULTS: Safety and efficacy results have been presented previously. Pharmacokinetic data were available for 8 patients administered 70 mg/d LDX and for 9 administered 30 mg/d MAS XR. The mean (±SD) C_{max}, T_{max}, and AUC_{last} of d-amphetamine following 70 mg/d of LDX were 155±31.4 ng/mL, 5.06±0.78 h, and 1326±285.8 ng•h/mL, respectively, with percent coefficients of variation (%CV) of 20.34%, 15.33%, and 21.56%, respectively. For

30 mg/day MAS XR, the mean ±SD C_{max}, T_{max}, and AUC_{last} of d-amphetamine were 119±52.5 ng/mL, 6.56±3.46 h, and 1019±436.2 ng•h/mL, respectively, with %CV of 43.96%, 52.77%, and 42.83%, respectively.
CONCLUSIONS: These results indicate that interpatient variability in d-amphetamine pharmacokinetics following LDX is considerably lower than that observed following MAS XR. These results are thought to be due to a rate limiting hydrolysis of the prodrug used in delivering the active moiety compared with an extended-release drug delivery formulation.
Supported by funding from Shire Development Inc. Presented at the American Psychiatric Association, San Diego, Calif, May 19-24, 2007.

237. **A randomized, double-blind, placebo-controlled study of guanfacine extended-release in children and adolescents with attention-deficit/hyperactivity disorder.** *Joseph Biederman, M.D.*[1], Raun Melmed, M.D.[2], Anil Patel, M.D.[3], Keith McBurnett, Ph.D.[4], Jessica Donahue, M.P.H.[5], Andrew Lyne, MSC, CStat[6]; (1) Clinical and Research Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Harvard Medical School, Boston, Mass.A; (2)Melmed Center, Scottsdale, Ariz; (3)Psychiatric Centers at San Diego, San Marcos, Calif; (4)University of California-San Francisco, San Francisco, Calif; (5)Shire Development Inc., Wayne, Pa; (6)Shire Pharmaceutical Development LTD, Basingstoke, United Kingdom .

PURPOSE: Guanfacine is an α_{2A}-adrenoceptor agonist believed to improve cognition via selective effects in the prefrontal cortex. The immediate-release formulation of guanfacine has demonstrated efficacy in treating symptoms of attention-deficit/hyperactivity disorder (ADHD). This study assessed the efficacy and safety of a new formulation, guanfacine extended-release (GXR), compared with placebo, for the treatment of children and adolescents with ADHD.
METHODS: In this multicenter, double-blind, placebo-controlled, fixed-dose study, subjects ages 6–17 years were randomized to 2 mg, 3 mg, or 4 mg GXR or placebo daily for 8 weeks. Efficacy measures included physician ADHD-RS-IV ratings, physician and parent ratings on the Clinical Global Impressions-Improvement Scale (CGI-I) and Parent Global Assessment (PGA). The Conners' Parent and Teacher Rating Scales-Revised (CPRS-R, CTRS-R) measured duration of effect. Post hoc analysis determined the effect size of GXR doses.
RESULTS: Three hundred forty-five subjects were randomized to placebo (n=86), GXR 2 mg/day (n=87), 3 mg/day (n=86), or 4 mg/day (n=86). End point CGI-I and PGA scores and total mean changes from baseline in CPRS-R and CTRS-R scores were significantly improved vs placebo for all GXR groups. Effect sizes, measured by ADHD Rating Scale (ADHD-RS-IV) and analyzed by weight-adjusted actual dose, were 0.44 (0.01–0.04 mg/kg), 0.58 (0.05–0.08 mg/kg), 1.19 (0.09–0.12 mg/kg), and 1.34 (0.13–0.17 mg/kg). Adverse effects were mostly mild to moderate in severity, the most common being sedative in nature.
CONCLUSIONS: Change in ADHD-RS-IV score from baseline was significant for the overall study population. All GXR-treated subjects showed significant improvements in CGI-I and PGA scores and significant duration of effect, measured by CPRS-R and CTRS-R scores, over placebo-treated subjects. ADHD-RS-IV effect sizes for weight-adjusted actual GXR doses ranged up to 1.34.
Supported by funding from Shire Development, Inc.

Pulmonary

238. Evaluation of the relationship between body composition, adipocytokines, and bone mineral density in men with severe chronic obstructive pulmonary disease. *Sheryl F. Vondracek, Pharm.D.*[1], Connie Valdez, Pharm.D.[1], Norbert F. Voelkel, M.D.[2], Michael T. McDermott, M.D.[3]; (1)University of Colorado at Denver and Health Sciences Center, School of Pharmacy, Denver, Colo; (2)University of Colorado at Denver and Health Sciences Center, School of Medicine, Denver, Colo; (3)University of Colorado at Denver and Health Sciences Center, School of Medicine, Aurora, Colo.

PURPOSE: To identify the relationship between body composition, adipocytokines, and bone mineral density (BMD) in men with severe, stable chronic obstructive pulmonary disease (COPD).
METHODS: Cross-sectional pilot study of 25 men, age 45 years or older, with severe, stable COPD (forced expiratory volume in 1 sec [FEV_1] < 50% predicted). The following were prospectively obtained on all subjects: dual energy x-ray absorptiometry for determination of body composition and BMD, urinary N-telopeptide, and serum concentrations of testosterone, estradiol, 25-hydroxyvitamin D, osteocalcin, tumor necrosis factor-alpha (TNF-alpha), TNF receptor 1, TNF receptor 2, leptin, adiponectin, and resistin. Linear regression analysis was used to evaluate the relationship between the adipocytokines, total body mass (TBM) and total hip BMD (THBMD). Continuous variables were compared between subjects with or without osteoporosis using the Wilcoxon Test. Data evaluating the relationship between body composition and BMD have been previously presented.
RESULTS: Twenty-four subjects completed the study (average age = 65 ± 9 years, average FEV_1% predicted = 33 ± 11%). TBM (r2=0.505; p=0.0001), adiponectin (r2=0.192; p=0.032) and leptin (r2=0.337; p=0.003) were

significantly related to THBMD in univariate analyses. After adjustment for TBM, the relationship between adiponectin, leptin and THBMD was no longer significant. When subjects with osteoporosis (n=10) were compared to subjects without osteoporosis (n=14), there was no statistically significant difference in TNF-alpha, TNF-alpha receptors, or resistin. However, there was a trend towards lower leptin (4.4 ± 4.8 vs. 9.8 ± 8.7; p=0.078) and higher adiponectin (8202.7 ± 7929.6 vs. 3333.2 ± 1788.8; p=0.051) concentrations in subjects with osteoporosis.
CONCLUSIONS: These pilot data suggest a possible relationship between adiponectin, leptin, and osteoporosis in men with severe COPD. The small sample size limits the power of this study to detect any true associations. Larger studies are needed to further evaluate this relationship.

239E. **Self-reported inhaler use in patients with chronic obstructive pulmonary disease.** *Kory VanderSchaaf, Pharm.D.*[1], Kari Olson, Pharm.D., BCPS[1], Sarah Billups, Pharm.D., BCPS[1], Melissa Rice, Pharm.D., BCPS[1], Cindy Hartsfield, Ph.D.[2]; (1)Kaiser Permanente Colorado, Denver, Colo; (2)Abbott Laboratories, Denver, Colo.

PURPOSE: The primary objective of this study was to determine the extent of patient-reported variability in inhaler use for chronic obstructive pulmonary disease (COPD) compared to prescribed instructions for use. Patient-reported reasons for non-adherence and their understanding of COPD and its treatment were also evaluated.
METHODS: A 17-item survey was mailed to 600 ambulatory patients with spirometry-defined COPD. The survey included items about inhaler use, reasons for not using inhalers as prescribed, and patient beliefs about COPD (using a Likert-type scale). Pharmacy and medical records were reviewed for pertinent study-related data for all survey respondents. Likert-type responses were grouped (strongly agree/agree/neutral vs. strongly disagree/disagree). Differences in responses based upon disease severity were compared using chi-squared.
RESULTS: The response rate was 45.8% (51.6% male; mean age: 73 ± 8 yrs). The majority (82%) had either moderate or severe COPD. A total of 39% of respondents were not taking inhalers as prescribed. Patients with moderate COPD varied inhaler use more than those with severe disease (48% vs. 28%, p=0.006). The most common reasons patients reported not taking inhalers as prescribed were as follows: feeling the inhalers did not help breathing (20%), forgetting to use inhalers (19%) and cost (15%). The majority (77%) reported good understanding of COPD and its treatment. Fifty-five percent stated they varied their inhaler used based on how they felt. Most respondents indicated they would like to learn more about how to better manage their COPD.
CONCLUSION: Patients with moderate COPD appear to vary inhaler use more than those with severe COPD and may not be taking their medications as prescribed. Given that patients stated they would like more information on how to manage their COPD, further evaluation of educational programs for patients with COPD and the impact these programs have on adherence to inhalers are needed.
Presented at Western States Residents Conference, Pacific Grove, Calif, May 30, 2007.

Regional Chapter Issues

240. **Utilization of an online survey process to better focus regional chapter resources**. *Amie Taggart Blaszczyk, Pharm.D, CGP, FASCP*, Ronald Hall, Pharm.D., BCPS, Krystal Edwards, Pharm.D., BCPS, Sachin Shah, Pharm.D., BCOP, Marissa Quinones, Pharm.D.; Texas Tech University Health Sciences Center School of Pharmacy, Dallas, Tex.

PURPOSE: To better understand the educational needs and desires of the membership of the regional Dallas-Fort Worth chapter of ACCP in order to better utilize chapter resources. The Dallas-Fort Worth area presents many unique arenas for clinical pharmacists to practice. Academic medical centers, Veterans Affairs Hospitals and Clinics and Children's hospitals are among the many varied practice atmospheres where clinical pharmacists practice. The Dallas-Fort Worth (DFW) regional chapter of ACCP was established in 1998 to meet the unique and diverse needs of these clinical pharmacists. However, during its existence, both membership and executive board involvement have waxed and waned, with the most recent executive board attempting to rebuild membership and chapter involvement. The executive board believed that better knowing the needs of clinical pharmacists in DFW would help to build a stronger regional chapter able to withstand these fluctuations and will also help with focusing limited chapter resources. A survey was employed to gather information regarding these needs and also to better understand the demographics of the clinical pharmacists served by the DFW regional chapter.
METHODS: From 9/13/06-11/13/06 a survey through the Internet website www.surveymonkey.com was made available to current membership of DFW ACCP, as well as individuals on the DFW ACCP mailing list and those clinical pharmacists working in DFW who could be reached by word-of-mouth. Questions were included in the survey regarding degrees, practice arenas and specialties, national and local organization membership, preferences in regards to locations and topics, as well as the type of programs the individual pharmacist was able to attend based on their facility policy (promotional programs vs. unrestricted educational grants, etc.).

RESULTS: 73 unique respondents took the survey online from 9/13/06-11/13/06, and results of the survey are currently being tabulated. The results of the survey will be presented at the conference.

Transplant/Immunology

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

PURPOSE: To evaluate the predictive performance of mycophenolic acid (MPA) limited sampling strategies (LSSs) previously developed in lung transplant recipients when applied to heart transplant recipients at our centre, and to compare performances of LSSs for heart transplant published in the literature.
METHODS: Optimal MPA LSSs were developed from lung transplant recipients via multiple regression analysis with backward stepwise elimination at our centre previously. The best LSSs were:
Equation 1: $LogAUC=0.241 LogC0+0.406 LogC2+1.140$
Equation 2: $LogAUC=0.202 LogC0+0.411 LogC1.5+1.09$
Equation 3: $LogAUC=0.153 LogC0+0.327 LogC0.6+0.354 LogC2+1.000$
Equation 4: $LogAUC=0.131 LogC0+0.320 LogC0.6+0.333 LogC1.5+0.974$
Published LSSs developed by Baraldet et al. (2005) for heart transplant recipients included:
Equation 5: $AUC=5.568+0.902 C1.25+2.022 C2+4.594 C6$
Equation 6: $AUC=3.80+1.015 C1.25+1.819 C2+1.566 C4+3.479 C6$
Following written informed consent and upon administration of a steady-state mycophenolate mofetil dose, 11 blood samples were collected over 12 hours from 27 heart transplant recipients. Plasma MPA concentrations were measured by a validated high-performance-liquid-chromatography method with ultraviolet detection and pharmacokinetic parameters analyzed by non-compartmental modeling (WinNonlin 4.1). The heart transplant group data were used to test the predictive performance of LSSs (equations 1–6).
RESULTS: The predictive performance of LSS equations 1–6, listed as bias, precision, and number (%) of profiles within ±15% bias and precision, were:
Equation 1: -7.99%; 11.27%; 17/27 (63%)
Equation 2: -9.92%; 12.27%; 19/27 (71%)
Equation 3: -7.68%; 10.40%; 23/27 (85%)
Equation 4: -9.36%; 12.29%; 20/27 (74%)
Equation 5: -14.43%; 20.36%; 10/27 (37%)
Equation 6: -13.60%; 17.30%; 14/27 (52%)
CONCLUSIONS: LSSs developed in lung transplant recipients at our centre performed well when applied to the heart transplant population for prediction of MPA AUC. However, application of the only other published LSSs developed in heart transplant recipients yielded less optimal results when applied to our population. LSSs appear to be center-specific and should be revalidated before use.

242. **Lung transplant patients' antibody responses to influenza vaccine viruses between seasons.** *Mary S. Hayney, Pharm.D., M.P.H.*[1], John Moran, B.S.[1], Nicholas A. Wiegert, B.S.[2]; (1)University of Wisconsin, Madison, Wis; (2)NeoClone, Madison, Wis.

PURPOSE: Lung transplant patients are at high risk of morbidity and mortality from influenza infection because of altered lung physiology and immunosuppression. Annual influenza immunization is recommended because antibody concentration wanes and vaccine composition changes each year. Vaccine antibody response may be limited by immunosuppression. We hypothesized that lung transplant patients would mount poorer antibody responses to new influenza vaccine antigens than healthy individuals or individuals waiting for lung transplantation.
METHODS: Twenty-three healthy individuals, 41 lung transplant patients, and 13 patients waiting for lung transplantation participated in both the 2004-05 and 2005-06 influenza seasons. Serum for influenza antibodies measured by hemagglutination inhibition assay was collected before and 2–4 weeks after immunization. A 4 fold increase in antibody concentration (seroconversion) in both seasons was considered vaccine response.
RESULTS: The A/H3N2 vaccine viruses were different between seasons while the other two vaccine viruses remained the same in both seasons. Seroconversion rates to A/H3N2 viruses were lower in lung transplant patients

than healthy or those waiting for lung transplants. (Table) Pre- and post-antibody concentrations were similar among groups.

Seroconversion	Healthy	Post-transplant	Pre-transplant	p value
A/New Caledonia	1/23 (8%)	5/40 (13%)	3/13 (23%)	0.25
A/H3N2	7/23 (30%)	2/41 (5%)	3/13 (23%)	<0.03
B/Shanghai	3/23 (13%)	3/40 (8%)	2/13 (15%)	0.11

CONCLUSION: The seroconversion rate to the new influenza vaccine virus antigens is lower in lung transplant patients than in healthy and those waiting for lung transplant patients. Alternate immunization strategies may be required for this high-risk population.

243. **The efficacy and safety of ezetimibe in cardiac transplant recipients.** *Kathy M. Makkar, Pharm.D.*[1], Cynthia A. Sanoski, Pharm.D.[2], Lee R. Goldberg, M.D., M.P.H., FACC[3], Sarah A. Spinler, Pharm.D., FCCP, BCPS[4]; (1)University of the Sciences in Philadelphia, Phiadelphia, Pa; (2)Jefferson School of Pharmacy, Thomas Jefferson University, Philadelphia, Pa; (3)Hospital of the University of Pennsylvania, Philadelphia, Pa; (4)University of the Sciences in Philadelphia, Philadelphia, Pa.

PURPOSE: Statins are used routinely to treat dyslipidemias and prevent accelerated graft atherosclerosis in cardiac transplant recipients; however, statins may increase the risk of myopathy when used with calcineurin inhibitors (CI). The addition/substitution of ezetimibe may help patients achieve LDL goal, but a drug interaction between ezetimibe and CI has been reported and there is only one published report of experience with ezetimibe in cardiac transplant recipients. The purpose of this study was to assess the safety and efficacy of ezetimibe in cardiac transplant recipients.
METHODS: This study was a retrospective chart review. Patients were included in the efficacy analysis if they had a baseline LDL-C concentration recorded within 1 year before and 4 weeks to 1 year following initiation of ezetimibe, with no change in other lipid-lowering therapy. Patients were included in the safety analysis if they received ≥ 1 dose of ezetimibe. The primary outcome was the mean/median change in fasting LDL-C. Secondary outcomes included the percentage of patients achieving LDL-C<100 mg/dL, incidence of adverse effects, and mean changes in serum trough concentrations and doses of CIs following ezetimibe treatment.
RESULTS: Seventy-one of 541 clinic patients were treated with ezetimibe and included in the safety analysis. Thirty-five (49%) patients were included in the efficacy analysis. After a mean of 19.7 months, total cholesterol, LDL-C, and triglycerides decreased (mean 236 vs. 200 mg/dL, p<0.0001; 129 vs. 96 mg/dL, p<0.0001; 242 vs. 207, p<0.03, respectively). Median HDL-C did not significantly change. The proportion of patients who achieved LDL-C < 100 mg/dL increased (11.5% vs. 60.5%, p<0.0001). Ezetimibe had no significant effect on serum CI concentrations or doses. Adverse effects occurred in 11 (15.5%) patients. Only 3 patients discontinued ezetimibe.
CONCLUSIONS: Ezetimibe appears to be safe and effective for the treatment of dyslipidemia in cardiac transplant recipients and may help achieve an LDL-C < 100 mg/dL.

244E. **Use of polymerase chain reaction (PCR) for a preemptive approach to CMV infection in pediatric liver transplantation.** *Gregory A. Smallwood, Pharm.D.*[1], Todd Pillen, PA[2], Rochelle Schmidt, Pharm.D.[2], Carlos Fasola, M.D.[3], Rene Romero, M.D.[3], Thomas Heffron, M.D.[3]; (1)Emory Healthcare, Atlanta, Ga; (2)Childrens Healthcare of Atlanta, Atlanta, Ga; (3)Emory University School of Medicine, Atlanta, Ga.

PURPOSE: Pediatric solid organ transplant recipients are considered to be at highest risk of developing cytomegalovirus (CMV) infection. Approach to CMV in solid organ transplant consist of prophylaxis for 3–6 months after transplant or a preemptive approach that monitors patients and treats CMV infection only when CMV DNA is isolated. The objective was to evaluate our 10-year experience with preemptive PCR monitoring and treating CMV in pediatric liver transplantation.
METHODS: Patients were routinely followed by weekly, serial blood draws for CMV by PCR and did not receive prophylactic antivirals. At time of seroconversion, patients were started on ganciclovir IV 5mg/Kg Q12H and continued to be followed by polymerase chain reaction (PCR) to monitor treatment. All patients received the same immunosuppressive protocol, which included induction.
RESULTS: From February 1997 until present, 187 pediatric patients received 210 liver grafts. A total of 66 (35.2%) patients seroconvert with 72.7% (48/66) of patients seroconverting once, 22.7% (15/66) seroconverting twice, and 3 (4.5%) patients had 3 episodes of seroconversion. Mean time to initial seroconversion was 51.6 ± 62.6 days with secondary re-conversion occurring 177.2 ± 206 days following transplant. Tissue invasive disease occurred in 22.7% (15/66) of CMV+ patients, which included CMV hepatitis (n=8), CMV gastroenteritis (n=6), and one pneumonitis. Based on CMV seroconversion, patients were similar in respect to age at transplant (6.9 ±

6.4 yr. vs 6.7 ± 6.6; p=0.876). CMV seroconverters had longer hospitalization (36.6 ± 30.8 days vs. 26.1 ± 24.1 days; p=0.02), with similar 1 year survival (90.8% vs, 93.1%; p = 0.306).
CONCLUSION: Patients can be preemptively followed by PCR for CMV without the use of antiviral CMV prophylaxis without increased incidence of mortality in our series. By utilizing a preemptive approach, all patients are not exposed to ganciclovir. Abstract published in Am J Ttransplant, Vol. 7, Sup 2, pg 382.

245E. **Analysis of hormone values in cirrhotic males prior to liver transplantation.** *Tiffany E. Kaiser, Pharm.D.*, Victoria Zacharias, PA-C, Nick Parrish, Pharm.D., Rosann Giesting, R.N., DiLynn Russell, R.N., Jill Martin, Pharm.D., Nyingi Kemmer, M.D., Guy Neff, M.D.; University of Cincinnati, Cincinnati, Ohio.

PURPOSE: The correlation of muscle wasting with the degree of cirrhosis-related morbidity and mortality is significant. Liver transplantation (LTx) as its primary treatment modality, often requires significant rehabilitation secondary to preoperative de-conditioning. Severe malnutrition and muscle wasting at time of LTx affects recovery time, leading to suboptimal outcomes and increased hospital stays. The magnitude of male hypogonadism (low free testosterone levels) is presumed to correlate with the degree of muscle wasting in cirrhotics. The aim of this study is an observational review to assess the magnitude of hypogonadism in our patient population.
METHODS: A retrospective review from January 2004 to November 2006 was performed on adult (> age18), male cirrhotic patients. Cirrhosis was defined using the abbreviated CPT score or based on liver biopsy results. Baseline patient demographics were evaluated. The following serum hormone values were included: total, free, and percent testosterone, LH, FSH, DHEA, SHBG, and estriols. Secondary to the wide variation in hormone level reporting, our institutional standard lab values were used to determine deviance from normal. To assess the magnitude of difference, low was defined as below the lower limit of normal.
RESULTS: 93 patients were included in this analysis, with an overall mean age of 54 + 9 years. Percent free testosterone levels were low in 72% (67/93), 97% (70/72) had elevated SHBG levels, 97% (70/72) had low DHEA, and 100% of estrogen levels were sub-therapeutic. However, LH and FSH were within the normal limits.
CONCLUSION: This analysis suggests that patients with cirrhosis suffer from hypogonadism. More importantly, these results 1) provide baseline estimates for the incidence and frequency of hypogonadism in our patient population, and 2) support the need for pharmacologic investigation of androgen restoration in cirrhotic patients, both of which will assist with further studies.
Presented at the American Transplant Congress, San Francisco, Calif, May 5-10, 2007.

246E. **Long-term daclizumab use in an outpatient liver transplant clinic for calcineurin sparing.** *Gregory A. Smallwood, Pharm.D.*[1], Carlos Fasola, M.D.[2], Andrei Stieber, M.D.[2], Thomas Heffron, M.D.[2]; (1)Emory Healthcare, Atlanta, Ga; (2)Emory University School of Medicine, Atlanta, Ga.

PURPOSE: The monoclonal antibodies to the CD-25 (daclizumab/basiliximab) cell are currently used for induction therapy following solid organ transplant. These agents have been used for short term use to spare the use of calcineurin inhibitors during initial hospitalization. The aim of this study was to evaluate stable liver transplant patients receiving daclizumab on an outpatient basis while sparing the use of tacrolimus for greater than 2 weeks.
METHODS: Patients unable to tolerate tacrolimus due to adverse events (renal or other reasons) were begun on daclizumab 1mg/kg given intravenously weekly in an outpatient liver transplant clinic. This is an IRB approved study with inclusion criteria requiring that the patients had to be off of tacrolimus for at least 2 weeks. Patients were evaluated for both renal and transplant outcomes.
RESULTS: From May 2003 until October 2006, 51 patients received daclizumab while sparing the use of tacrolimus. Patients receiving daclizumab was 50.7 ± 12.9 years of age, 331 ± 432 days from transplant. Patients' mean calcineurin free time was 39.8 ± 17.8 days. The renal group (n = 34) had improved GFR [28.3±9.7 mL/min/1.73m², vs. 44.4±14.4 mL/min/1.73m², p<0.0001], improved sr. cr. [2.07 ± 0.7 mg/dLvs. 1.37 ± 0.36 mg/dL,p<0.0001], while maintaining liver function as described by ALT (p=0.326), AST (p=0.375), and T. bili (p= 0.781). Only one patient (1.9%) had histological proven rejection. Patients having rejection episodes prior to daclizumab use (n=4) did not experience rejection when off tacrolimus. Patient survival was 88.3% and graft survival was 86.3%.
CONCLUSIONS: Liver transplant patients can safely be immunosuppressed with weekly daclizumab dosing on an outpatient basis while holding tacrolimus for up to 40 days. With the use of daclizumab, adverse events from calcineurin inhibitors have the opportunity to resolve. Abstract published in Am J Transplant 2007, Vol. 7, Sup. 2, pg 164.

247. **Tolerance of mycophenolate mofetil in intestinal transplant patients: a case series.** *Megan A. McCartan, PharmD.*[1], Wendy J. Grant, M.D.[2], Jean F. Botha, M.D.[2], Debra L. Sudan, M.D.[2], Alan N. Langnas, D.O.[2]; (1)The Nebraska Medical Center, Omaha, Neb; (2)University of Nebraska Medical Center, Omaha, Neb.

PURPOSE: Mycophenolate mofetil (MMF) is approved for use in heart, kidney, and liver transplantation to prevent rejection. Little information is available about the use of MMF in intestinal transplant patients and whether adverse effects of the drug (i.e., diarrhea, leucopenia) complicate their clinical management. A primary marker for rejection in intestinal transplant patients is diarrhea. The purpose of this case series is to report the use and tolerance of adverse effects of MMF in intestinal transplant patients.
METHODS: We reviewed four pediatric intestinal transplant patients who were initiated on MMF in combination with tacrolimus post-transplant due to renal dysfunction. The MMF was initiated at low doses and gradually increased. After initiation of MMF, tacrolimus levels were maintained at lower levels than the standard protocol.
RESULTS: All of the patients tolerated the MMF without experiencing adverse effects that required discontinuation. Stool output did not change significantly after initiation or dosage increases. None of the patients required dosage adjustments due to leucopenia. None of the patients had rejection while on combination therapy. See table.
CONCLUSIONS: MMF can be tolerated by intestinal transplant patients and may be a viable option for combination therapy with calcineurin inhibitors in these patients. Further studies are needed.

Day of MMF Therapy	MMF dose (mg)	Dose/BSA (mg/m2)	Stool Output (ml/kg/day)	White Blood Cell Count
Patient #1				
1	500 BID	435	6.2	22.3
12	500 BID	435	7.2	17
22	750 BID	652	11	12.8
Patient #2				
1	250 BID	300	25	6.6
8	250 BID	300		5.2
20	300 BID	361	40	4.9
Patient #3				
1	200 BID	540	42	10.5
17	200 BID	540	12.8	11.6
65	300 BID	810	28.5	4.1
Patient #4				
1	200 BID	357	31.6	22.6
38	300 BID	536	28.3	14.6
86	400 BID	714	24	7.5

248. **Effects of hyperglycemia on the development of new onset diabetes after liver transplantation**. *April L. Anderson, Pharm.D.*, Daniel A. Lewis, Pharm.D., BCPS, Dinesh Ranjan, M.D., Kelly M. Smith, Pharm.D., FASHP, Timothy M. Clifford, Pharm.D.; University of Kentucky HealthCare, Lexington, Ky.

PURPOSE: New onset diabetes after transplantation, NODAT, may lead to cardiovascular and thrombotic complications, acute rejection, and infection. NODAT in kidney transplantation is well described; however, data are lacking in the liver transplant population. We hypothesized that previously non-diabetic patients with poor glycemic control within the first 2 weeks post-transplantation have an increased risk of NODAT within 6 months.
METHODS: Patients who underwent a liver transplantation at our institution between January 2004 and December 2005 were retrospectively evaluated. NODAT was defined according to the American Diabetes Association/World Health Organization diagnostic criteria, persistent hyperglycemia (i.e., serum glucose > 200 mg/dL > 2 weeks after initial steroid induction and persisting for more than 2 weeks), or the need for hypoglycemic agents upon discharge. The primary end point was the incidence of NODAT within 6 months post-transplantation in patients with poor glycemic control within the first 2 weeks post-transplantation. Secondary endpoints included acute rejection episodes, infections, hospital readmissions, and cardiovascular and thrombotic events.
RESULTS: Forty-five patients were evaluated. Within the first 6 months post-transplantation, 11 (24.4%) developed diabetes. Serum glucose on post-operative days 1 and 2 was similar between NODAT and normoglycemic patients; however, the NODAT group had a mean fasting serum glucose > 126 mg/dL postoperative days 7–180. There were no differences between NODAT and normoglycemic patients in acute rejection (27.3% vs. 26.5%, p=0.301), infectious episodes (36.4% vs. 23.6%, p=0.208), hospital readmissions (58.8% vs. 36.4%, p=0.122), cardiovascular events (27.3% vs. 5.9%, p=0.085), and thrombotic events (11.8% vs. 2.9%, p=0.418).

CONCLUSION: Elevated fasting blood glucose throughout the first 2 weeks following liver transplant was associated with an increased incidence of NODAT. More studies are needed to determine the impact of recognition and treatment of hyperglycemia in newly transplanted patients.

249. **Clinical and genetic risk factors for a new onset post-transplant diabetes mellitus in kidney transplant patients.** *Jaewook Yang, Ph.D., Pharm.D.*[1], Yi-Chun Chiang, M.S.[2], Ian V. Hutchinson, Ph.D.[3], Vera Pravica, Ph.D.[4], Gilbert J. Burckart, Pharm.D.[3], David I. Min, Pharm.D.[1]; (1)Western University of Health Sciences, College of Pharmacy and National Institute of Transplantation, Los Angeles, Calif; (2) School of Pharmacy, Taipei Medical University, Taipei, Taiwan; (3)USC School of Pharmacy, Los Angeles, Calif; (4)USC/National Institute of Transplantation, Los Angeles, Calif.

PURPOSE: A new onset posttransplant diabetes mellitus (PTDM), is an important complication after transplantation and is associated with reduced overall patient and graft survival. Objectives were to determine the clinical and genetic risk factors for post-transplant diabetes mellitus in kidney transplant patients.
METHODS: A total of 830 patients who have received kidney allograft at St. Vincent Medical Center, between January 1, 2001, and September 30, 2005, were retrospectively reviewed. The univariate analysis and multivariate analysis were done for each recipient's risk factors and odd ratios were calculated. Recipients' DNAs were genotyped for a total of 15 diabetes-associated genes reported in the literature and incorporated for analysis to determine the association. P<0.05 was regarded as of statistical significance.
RESULTS: A total of 236 patients (28.4%) was fit to our definition of PTDM (fasting glucose greater than126 mg/dL on two occasions). The following factors were found to be significant in the Univariate analysis: age at transplantation(p<0.001)p, BMI(p=0.004, tacrolimus use,(p=0.041) sirolimus use, prednisone use(p<0.001), and number of transplantation(p=0.033). Multivariate analysis included only age (OR = 1.037, 95% CI = 1.009–1.067, p=0.011), BMI (OR = 1.113, 95% CI = 1.002–1.235, p=0.045), numbers of immunosuppressants used (OR = 1.943, 95% CI = 1.243–3.037, p=0.004), which were significantly associated with PTDM. In the case of genotypes, significant associations were found between the development of post-transplantation diabetes and the distributions of mutant alleles in hepatocyte nuclear factor1-alpha(HNF1-alpha/TCF1) (p<0.0001), peroxisome proliferator-activated receptor-gamma(PPAR-gamma) (p=0.015) and sulfonylurea receptor (ABCC8) (p<0.0005) genes. All other genes were not significantly associated with PTDM.
CONCLUSION: This study confirmed that older age at transplantation, higher BMI and more immunosuppression were important clinical risk factors PTDM. In addition, HNF1-alpha, PPAR-gamma and ABCC8 gene mutant alleles were associated with PTDM.

250. **Rotigotine patch is effective in the treatment of idiopathic RLS: results of a 6-month, multicenter, double blind, placebo controlled trial in Europe.** *Wolfgang Oertel, M.D.*; Philipps-Universität Marburg, Marburg, Germany.

PURPOSE: To evaluate efficacy and safety of rotigotine transdermal patch in moderate to very severe idiopathic RLS patients with moderate to very severe idiopathic RLS over a period of 6 months.
METHODS: Multicenter, randomized, double-blind, placebo-controlled, fixed-dose, 4-arm parallel-group trial with rotigotine 1, 2, and 3mg/24h (5-15cm2). Primary efficacy parameters were IRLS and CGI item 1 (severity of illness) scores. Secondary parameters included RLS-6 and QoL-RLS scores.
RESULTS: 458 patients (58 ± 11 years, 73% female) were randomized at 49 sites in 8 European countries. Forty-two percent of placebo and 28% of rotigotine patients withdrew from the study. The mean baseline IRLS score was 28.1±6, and the mean baseline CGI score was 5.0 ± 0.8. Improvement from baseline in IRLS score was significantly greater than placebo in all 3 rotigotine groups The net effects versus placebo of the improvements after 6 month were (-5.1, -7.5, and 8.2, p<.0001). CGI item 1 scores were also significantly improved versus placebo (-0.76, -1.07, and -1.21, p<.0001). Comparable effects were observed in the RLS-6 and QoL-RLS.
Fifty-five percent and 78% of patients on placebo and rotigotine, respectively, reported at least 1 adverse event. The most common side effects were application site reaction (1.7%, 42.5%), nausea (5.1%, 16.4%), headache (9.4%, 15.8%), and dizziness (2.6%, 5.8%) for placebo and rotigotine, respectively. AEs were usually transient and mild to moderate in intensity.
CONCLUSION: 6-month therapy with rotigotine transdermal patch (1, 2, and 3 mg/24 hours) was significantly superior to placebo and well tolerated.

Urology

251. **Impact of solifenacin on health-related quality of life, work productivity, medical resource utilization, and health utility in working-age adults.** Les Noe, M.P.A., RPh[1], *Thomas Marshall,*

Pharm.D., M.S.[2], Raafat Seifeldin, Ph.D.[2], Lawrence Rasouliyan, M.P.H.[1], Norman Zinner, M.D.[3]; (1) Ovation Research Group, San Francisco, Calif; (2)Astellas Pharma US, Inc., Deerfield, Ill; (3)Western Clinical Research, Torrence, Calif.

PURPOSE: Overactive bladder (OAB) can negatively affect health-related quality of life (HRQoL), work and activities, and medical care use. We assessed changes in HRQoL, resource utilization, work and activity impairment, and health utility among working-age adults with OAB receiving 12 weeks of solifenacin succinate (SOL) therapy, after switching from tolterodine tartrate extended-release (TOL) due to residual urgency episodes.

METHODS: A prospective, multicenter, open-label US study assessed the efficacy and safety of SOL. Subjects ≥ age 18 years, who switched from TOL to SOL due to residual urgency episodes (≥ 3/24 hour), with or without urge incontinence, usually with frequency and nocturia, were enrolled. The Overactive Bladder Questionnaire (OABq), Work Productivity Assessment Index (WPAI), Medical Care Use Index (MCUI), and Health Utilities Index (HUI) were administered at Pre-Washout and Week 12 post-SOL treatment. The OABq measures symptom bother and HRQoL. The WPAI assesses work and activity impairment. The MCUI captures information on medical resource utilization. The HUI assesses nine functional health status areas. Analyses were performed on subjects under age 65 who received at least one dose of SOL and completed questionnaires at both visits. A paired t-test was used to test change scores, using two-sided tests at =0.05 significance level.

RESULTS: 240 subjects under age 65 met analysis criteria. Subjects experienced significant improvement on the OABq symptom bother scale, all four HRQoL subscales (concern, coping, social interaction, sleep); and total HRQL score after 12 weeks of treatment with SOL. The number of physician office visits, urinary tract infections, and pads and diapers used were significantly reduced. Subjects reported a significant reduction in work loss, work impairment, and activity impairment while taking SOL. There were no significant differences in HUI scores.

CONCLUSION: Overall, SOL significantly improved symptom bother, HRQoL, work- and activity-related outcomes, and reduced medical resource utilization in working-age subjects with OAB.

252. **Comparative bioavailability and metabolism of transdermal oxybutynin (OXY-TDS) applied to the buttocks and back.** *Lawrence A. Hill, Pharm.D.*, Kim E. Caramelli, M.S., Heather M. Thomas, Ph.D.; Watson Laboratories, Inc., Salt Lake City, Utah.

PURPOSE: Use of the back as an alternative application site for OXY-TDS (currently approved for application to the hips, buttocks, and abdomen) would provide more flexibility in dosing.

METHODS: Healthy volunteer subjects ages 18–45 years (26 male, 19 female) participated in a single-center, open-label, randomized, two-way crossover study. Each wore one OXY-TDS (Oxytrol® transdermal system 3.9 mg/day) on the buttocks or back for 96 hours in a randomized sequence, with a minimum 7-day washout period between each treatment period. Blood samples were collected for measurement of oxybutynin (OXY) and N-desethyloxybutynin (DEO) concentrations during the TDS wear period and for 48 hours after patch removal. Pharmacokinetic variables $AUC_{[0-96]}$ and C_{max} were calculated from plasma OXY and DEO concentrations. Adverse events and vital signs were monitored. Skin tolerability was evaluated using a standardized scale for erythema. Average bioequivalence between application sites was determined using an analysis of variance model to compare the back:buttocks ratios of C_{max} and $AUC_{[0-96]}$ for OXY and DEO.

RESULTS: For OXY, the 90% confidence interval (90% CI) for the ratio of the geometric means of $AUC_{[0-96]}$ fell within strict bioequivalence criteria (80-125%). The upper bound of the 90% CI for C_{max} was 131%, slightly exceeding the 125% boundary. For DEO, the ratio of geometric means of $AUC_{[0-96]}$ and C_{max} met strict bioequivalence criteria. No significant safety differences were noted between the two application sites. However, a more frequent presentation of mild erythema was noted when the TDS was applied to the back versus the buttocks (19.1% versus 10.9% 1 hour after patch removal, and 14.9% versus 0.0% after 24 hours).

CONCLUSIONS: Application of Oxybutynin TDS to the back appears to be a feasible and convenient alternative to the buttocks, missing strict bioequivalence criteria by a clinically meaningless degree for OXY only, while conferring no additional safety risk.

253E. Transdermal-oxybutynin improves continence and urodynamics in neurogenic bladder following spinal cord injury. Michael J. Kennelly, M.D.[1], Gary E. Lemack, M.D.[2], Cynthia S. Trop, M.D.[3], Jennelle E. Foote, M.D.[4], *Naomi V. Dahl, Pharm.D.*[5]; (1)Carolinas Medical Center, Charlotte, NC; (2)UT Southwestern Medical Center, Dallas, Tex; (3)VA Medical Center, Bronx, NY; (4)Shepherd Center, Atlanta, Ga; (5) Watson Laboratories, Morristown, NJ.

PURPOSE: Overactive bladder resulting from spinal cord injury (SCI) is typically treated with clean-intermittent-catheterization (CIC) and pharmacotherapy. Oral oxybutynin (15–30 mg/day) improves continence; however, anticholinergic adverse effects such as dry mouth and constipation often limit tolerability. Transdermal delivery offers several advantages over oral, including less frequent dosing, and lower incidence and severity

of anticholinergic adverse effects. Objective was to evaluate efficacy and safety of transdermal-oxybutynin (Oxybutynin-TDS), at doses ≤ 11.7 mg/day.

METHODS: Adult patients with neurogenic bladder (NGB) secondary to SCI, with urinary incontinence between scheduled catheterizations were eligible for this multicenter, open-label, dose-titration study. Oxybutynin-TDS dose could be adjusted every 2 weeks by increasing/decreasing one level, as appropriate, based on patient symptoms. Number of catheterizations/day was kept constant. Efficacy was measured by change from baseline to end-of-study in average number of daily leakage-free catheterization intervals (collected in a 3-day diary) and with standardized urodynamic testing. Significance of changes from baseline to week-8 or last observation was evaluated using paired t-tests.

RESULTS: Most of the 22 participants (age 42.2 ± 10.77 years; 9.2 ± 8.55 years since SCI) were male (19; 86.4%), and classified SCI ASIA A (most severe) (15; 68.2%). Overall mean CIC interval was 4.4 ± 1.5 hours and catheterization frequency/24 hours was 5.3±1.4. %. Final titrated doses were 7.8, 9.1, and 11.7 mg/day, respectively for 3, 8, and 11 patients. Mean number leakage-free catheterization intervals per day increased from 2.4 ± 1.8 to 3.9 ± 1.9 (p=0.0036). Mean urine volume per catheterization increased from 260.8 ± 124.8 mL to 315.5 ± 140.0 mL (p=0.0029). Urodynamic parameters, including maximum cystometric bladder capacity, reflex volume, and detrusor pressure at maximum capacity, improved significantly. No patient discontinued the study due to a drug-related adverse event. Adverse event rates did not increase with increasing dose.

CONCLUSIONS: Oxybutynin-TDS was well tolerated at doses up to 11.7 mg/day in patients with NGB secondary to SCI, and significantly improved urodynamic parameters and continence between scheduled catheterizations.

Presented at American Paraplegia Society Annual Conference, Orlando, Fla, August 27-29, 2007.

Women's Health

254. **Calcium intake and osteoporosis awareness among female pharmacy students.** *Misti M. Houck, Pharm.D.*, Renee M. DeHart, Pharm.D., BCPS; Samford University McWhorter School of Pharmacy, Birmingham, Ala.

PURPOSE: To assess calcium intake and knowledge regarding osteoporosis prevention in female pharmacy students.

METHODS: Current calcium intake was assessed by conducting a survey of student pharmacists at Samford University's McWhorter School of Pharmacy. The surveys were analyzed by calcium intake per day and knowledge of the importance of calcium intake and other osteoporosis prevention measures. Subgroup analyses were made based on smoking history, family history of osteoporosis, and by academic classification. Nominal data was analyzed by Fischer's exact test, and continuous data was analyzed by the student's t-test. Statistical significance was defined as a p-value less than 0.05.

RESULTS: Of the 200 participants, the daily calcium intake averaged 964 mg (range 0–2558 mg/day). Only 31% (n=62) of participants had calcium intake greater than 1200 mg of elemental calcium per day. Twenty-four percent (n=47) of participants reported a family history of osteoporosis. Participants with a family history of osteoporosis achieved adequate daily intake of calcium more often (47% of participants with a family history versus 26% of participants without a family history, p=0.0111). While only 4% of participants reported smoking cigarettes, no smokers were found to have adequate calcium intake. Calcium intake did not differ among first, second, and third year students. When asked the appropriate daily calcium requirement, 69% of participants answered correctly. Only 10% had discussed osteoporosis prevention and only 11.5% had discussed calcium intake with their physician.

CONCLUSION: Although female pharmacy students have higher calcium intake than similarly aged women in prior studies, 69% fail to achieve a daily calcium intake of 1200 mg of elemental calcium. Family history is predictive of higher calcium intake, and a positive smoking history is predictive of lower calcium intake among female pharmacy students. Few female pharmacy students discuss calcium or osteoporosis prevention with their physicians.

255. **A Two-Center Study on the Pharmacokinetics of Intravenous Immunoglobulin (IVIG) Before and During Pregnancy.** *Mary H. H. Ensom, Pharm.D., FASHP, FCCP, FCSHP*[1], Lillian S.L. Ting, B.Sc., M.Sc.(Pharm), Ph.D. student[2], Mai Al-Khatib, B.Sc.(Pharm), M.Sc. student[2], Patricia A. Schultz, R.N., M.H.A.[3], Edwina Houlihan, R.N.[4], Mary D. Stephenson, M.D., M.Sc.[5]; (1)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia, Vancouver, BC; (3)University of Chicago, Chicago, Ill; (4)Children's & Women's Health Centre of British Columbia, Vancouver, BC; (5)University of Chicago, University of British Columbia, and Children's & Women's Health Centre of British Columbia, Vancouver, BC.

PURPOSE: To characterize intravenous immunoglobulin (IVIG) pharmacokinetics in women with recurrent miscarriages.

METHODS: Of 29 enrolled women enrolled at 2 centers (randomized placebo-controlled trial for idiopathic secondary recurrent miscarriage, n=19; open-label pharmacokinetic study for treatment of antiphospholipid antibody syndrome, n=10), 20 received IVIG (GamimuneN 5%) 500–1000 mg/kg and 9 placebo over a 2–10-hour period every 4weeks pre-pregnancy until up to 18–20 weeks gestation. Serum IgG concentrations were measured by rate nephelometry before and at 0.5h and 1, 2, 3, and 4 weeks following each dose (pre-pregnancy, 1st and 2nd trimesters).

RESULTS: Mean(±SD) age was 34.4 ± 4.5 yr and 35.7 ± 4.8 yr; number of spontaneous abortions was 4.7 ± 1.6 and 3.4 ± 0.7 for IVIG and placebo groups, respectively. Pharmacokinetic parameters (mean±SD), listed as IVIG vs. placebo, were:

     1. Pre-pregnancy (n=18,IVIG; n=9,placebo)
        • Maximum concentration (Cmax, g/L) 25.0±4.6, 11.2±2.8
        • Minimum concentration (Cmin, g/L) 12.1±2.0, 9.5±2.6
        • Area-under-the-curve (AUC_{0-}, g*h/L) 10947.1±2010.6, 6158.1±1258.2
     2. 1st trimester (n=10,IVIG; n=4,placebo)
        • Cmax (g/L) 30.0±7.6, 11.1±2.8
        • Cmin (g/L) 12.6±2.6, 9.2±2.1
        • AUC_{0-} (g*h/L) 11816.2±2416.1, 5913.5±2488.8
     3. 2nd trimester (n=8,IVIG; n=3,placebo)
        • Cmax (g/L) 26.2±4.6, 9.31±1.99
        • Cmin (g/L) 11.8±2.6, 8.0±2.5
        • AUC_{0-} (g*h/L) 11226.7±1695.5, 6033.6±1280.6

[All parameters p>0.05; repeated measures ANOVA (Student-Newman-Keuls) or paired t-test]

Dosages (mg/kg) and AUCs did not differ significantly within the IVIG group between the 3 sampling periods. Roughly-estimated contributions of exogenously-administered IVIG to total AUC_{0-} [AUC_{0-} (IVIG) minus AUC_{0-} (placebo)] were 4789.0 g*h/L (pre-pregnancy), 5902.7 g*h/L (1st trimester), and 5193.1 g*h/L (2nd trimester). Inter-patient variability in IVIG exposure was ~20%.

CONCLUSIONS: Considerable inter-patient variability in IVIG pharmacokinetic parameters was observed. Pregnancy did not have a significant effect on exposure to the same dosage of exogenously-administered IVIG. The estimated contribution of exogenous IVIG (i.e.,~5300g*h/L) to total AUC_{0-} was similar to, albeit slightly lower than, endogenous IgG (i.e.,~6000g*h/L). These preliminary data warrant further study in larger groups of patients.

256E. Women's health outcomes in an ethnic population: the Asian Women's Health Clinic. *Elaine Chong, Pharm.D., BCPS*[1], Lenore Riddell, R.N., M.S.N., ANP[2], Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP[3]; (1)University of British Columbia, Vancouver, BC, Canada; (2)BC Women's Hospital and Health Centre, Vancouver, BC; (3)University of British Columbia, BC Women's Hospital and Health Centre, Vancouver, BC.

BACKGROUND: Historically, women (especially non-Caucasians) have been underrepresented in clinical trials. Consequently, researchers across all disciplines have generally had a limited understanding of the impact of gender and ethnicity on health. With a growing recognition and interest in this knowledge gap, the Asian Women's Health Clinic (AWHC) was established in 1994 to address cultural and linguistic barriers limiting access to preventative health services for Chinese women in Greater Vancouver. In 1985-1988, the incidence of invasive cervical cancer among Chinese women in British Columbia was almost 4 times higher than in age-matched Caucasian women.

PURPOSE: To describe breast and cervical cancer screening, and oral contraceptive and hormone replacement use among females attending the AWHC. To determine whether there is a potential role for pharmacists at the AWHC.

METHODS: All women who visit the AWHC are required to complete a medical or recall history form. The current database contains more than 10 years of data, and a retrospective analysis of this dataset was performed. Additional prospective analyses are planned.

RESULTS: There have been a total of 7655 patient-encounters at the AWHC (1994-2006). The majority of patients are perimenopausal (52.8% between the ages of 40 and 54). Most women had normal Pap smears (mean ± standard deviation 82.3% ± 4.7%), and normal breast exams (86.2% ± 8.8%). Approximately 18.9% of women reported taking oral contraceptives, and 7.8% reported taking hormone replacement therapy. There may potentially be a primary health care role for pharmacists.

CONCLUSIONS: The extensive database at the AWHC is unique to the female Chinese population in Greater Vancouver and will shed light on unanswered questions relating to ethnicity and women's health. In the near

future, it is hoped that pharmacists will be able to explore the potential for a primary health care practice at the AWHC.

Preliminary results from this project were presented at the Canadian Society of Hospital Pharmacists Professional Practice Conference (January 31, 2007 in Toronto, Ontario), and the Canadian Pharmacists Association Annual National Conference.

257. Treatment with desvenlafaxine succinate results in a sustained reduction in number of moderate-to-severe hot flushes in menopausal women up to 12 months. *Liza Takiya, Pharm.D., BCPS*[1], Ken Muse, M.D.[2], Sophie Olivier, M.D.[1], Ginger Constantine, M.D.[1]; (1)Wyeth Research, Collegeville, Pa; (2) University of Kentucky Medical Center, Lexington, Ky.

PURPOSE: Desvenlafaxine succinate (DVS), an SNRI, has been shown to significantly reduce moderate-to-severe hot flushes (HFs) in postmenopausal women. This analysis assessed the long-term effect of DVS with placebo in treating moderate-to-severe menopausal HFs.

METHODS: Postmenopausal women with ≥ 50 moderate-to-severe HFs/week were enrolled in 2 double-blind, placebo-controlled trials. Subjects were randomized to receive placebo or DVS 100 or 150 mg/day in a 26-week trial (N=541; Study A) and to placebo or DVS 50, 100, 150, or 200 mg/day in a 52-week trial (n=689; Study B). Reduction from baseline in number of moderate-to-severe HFs was assessed weekly during the initial 12 weeks of therapy and by 4-week periods thereafter in response to DVS and placebo and evaluated using analysis of covariance.

RESULTS: The frequency of moderate-to-severe HFs was significantly reduced from baseline with all DVS doses and placebo at all time points studied up to week 26 in Study A and week 52 in Study B (all comparisons p<0.001). The reductions were significantly greater compared to placebo at most time points with DVS 100 mg and 150 mg through week 26 in Study A and week 52 in Study B (Table).

CONCLUSION: DVS, a nonhormonal treatment, was effective in reducing moderate-to-severe HFs and this reduction was sustained for up to 12 months.

TABLE: Adjusted mean change from baseline in number of moderate-to-severe HFs

Week	DVS 100 mg Mean* (SE)	P Value	DVS 150 mg Mean* (SE)	P Value	Placebo Mean* (SE)
Study A					
4	-6.42 (0.32)	<0.001	-6.80 (0.34)	<0.001	-4.44 (0.30)
13-16	-6.65 (0.34)	0.020	-7.22 (0.35)	<0.001	-5.61 (0.31)
25+	-6.46 (0.40)	0.061	-7.19 (0.41)	0.001	-5.48 (0.37)
Study B					
4	-6.92 (0.34)	0.003	-6.68 (0.36)	0.014	-5.31 (0.44)
13-16	-7.69 (0.34)	<0.001	-7.26 (0.37)	0.006	-5.70 (0.45)
49-52	-8.26 (0.37)	0.024	-7.81 (0.40)	0.142	-6.93 (0.49)

258. Rapid onset of effect of desvenlafaxine succinate for the treatment of moderate-to-severe vasomotor symptoms in postmenopausal women. *Liza Takiya, Pharm.D., BCPS*[1], Brian Cowan, M.D.[2], Ginger Constantine, M.D.[1], Palma Seljan, M.D.[1]; (1)Wyeth Research, Collegeville, Pa; (2)University of Mississippi Medical Center, Jackson, Miss.

PURPOSE: To compare the efficacy of desvenlafaxine succinate (DVS), a nonhormonal therapy, with placebo during the first week of treatment for moderate-to-severe vasomotor symptoms (VMS).

METHODS: Postmenopausal women with ≥ 50 moderate-to-severe hot flushes (HFs)/week were enrolled in 2 double-blind, placebo-controlled trials. Women were randomized to receive placebo or DVS 50, 100, 150, or 200 mg/day in a 52-week trial (n=689; Study A), and to placebo or DVS 100 or 150 mg/day in a 26-week trial (n=541; Study B). Reduction from baseline in number and severity of moderate-to-severe HFs and number of nighttime awakenings due to HFs was assessed using a mixed-model repeated measures analysis. Onset of effect was defined as the first day of statistically significant reduction in number of VMS compared with placebo.

RESULTS: In both studies, DVS 100 and 150 mg were associated with a significantly greater reduction from baseline in HF frequency compared with placebo at day 1 (DVS 100 mg, -22% to -24%; DVS 150 mg, -18% to -24%; placebo, -9%; all comparisons, p<0.01), and these reductions were maintained during week 1. HF severity scores were significantly reduced compared with placebo in both studies for DVS 100-mg and 150-mg groups by day 2 (DVS 100 mg, -8% to -16%; DVS 150 mg, -9% to -13%, placebo, -2% to -3%, p<0.05). Nighttime awakenings were significantly reduced in both studies by day 2 in the DVS 100-mg group -28% to -35%; (placebo,

-13% to -20%, both comparisons, p<0.05) and by day 5 for DVS 150 mg -43% to -44%; (placebo, 18% to 28%, both comparisons, p<0.05).
CONCLUSION: Postmenopausal women taking DVS, an effective nonhormonal therapy for the treatment of moderate-to-severe HFs, experienced a rapid onset of effect (within 1 week) compared with placebo in 2 clinical trials. Frequency of HFs was significantly reduced by day 1.

259. **Contribution of clinical inertia to uncontrolled hypertension and hyperlipidemia in women's health clinic patients.** *Noelle E. Daugherty, Pharm.D.*[1], Douglas T. Steinke, Ph.D.[2], Lynne Jensen, Ph.D., ARNP[1], Aimee G. Adams, Pharm.D.[1], Mikael D. Jones, Pharm.D.[2]; (1)University of Kentucky HealthCare, Lexington, Ky; (2)University of Kentucky College of Pharmacy, Lexington, Ky.

PURPOSE: Clinical inertia includes the failure to titrate or combine medications and to reinforce lifestyle modifications, despite knowing that a patient's disease state is uncontrolled. Our primary goal was to determine the contribution of clinical inertia (CI) to the prevalence of uncontrolled hypertension and hyperlipidemia in a focused-care clinic for women. Secondary aims were to determine the prevalence of uncontrolled hypertension and hyperlipidemia and to quantify the impact of CI.
METHODS: An observational, retrospective cohort study was conducted including 101 women with hypertension (n=101) and/or hyperlipidemia (n=54) that had greater than or equal to three visits between May 2005 and August 2006 at a women's health clinic. To quantify CI, a mean CI score using expected minus observed medication change rates, with higher scores reflecting greater CI, was calculated for both hypertension and hyperlipidemia.
RESULTS: Patients with hypertension were controlled 53 percent (SD 36.3) of the time and patients with hyperlipidemia achieved their LDL goal 57 percent (SD 43.5) of the time. The mean CI score for hypertension was 0.32 (SD 0.22) and hyperlipidemia 0.46 (SD 0.32). This means that changes to blood pressure or lipid therapy were made in 32 percent and 46 percent fewer visits than expected respectively.
CONCLUSIONS: This study confirms the high prevalence of uncontrolled hypertension and hyperlipidemia. Women who received routine medical care (i.e., greater than or equal to three visits per year within our time frame) were more controlled compared to other national data. CI was a contributor to the prevalence of uncontrolled hypertension and hyperlipidemia in the women's health clinic. Further research is needed to assess the contribution of patient and health-system factors on control rates.

260E. **Evaluation of antihypertensive agents in the acute treatment of preeclampsia at a tertiary care academic medical center.** *Christopher B. Woodis, Pharm.D., BCPS*, Mary W Roederer, Pharm.D., BCPS, CPP, Sarah K Ford, Pharm.D., BCPS, CPP; University of North Carolina Hospitals, Chapel Hill, NC.

PURPOSE: This study examined the use of antihypertensive medications in the treatment of acute preeclampsia at the University of North Carolina Hospitals with respect to recommendations in the American College of Obstetrics and Gynecology (ACOG) practice guidelines for the diagnosis and management of preeclampsia.
METHODS: A report was generated by this institution's pharmacy automated dispensing system identifying female patients > age 18 years who were ordered an antihypertensive agent and admitted to Women's Hospital to either the family medicine or obstetrics services from September 2005 to September 2006. Included patients must have been diagnosed with preeclampsia either according to ACOG guidelines or admitting service and also have received at least one dose of an antihypertensive medication during hospitalization. One hundred patient charts were retrospectively reviewed and descriptive statistics were used to analyze the data.
RESULTS: Thirty-nine patients met inclusion criteria. African Americans composed 46.1% of study participants. Sixty-three percent of included patients met ACOG guidelines for the acute management of preeclampsia.
CONCLUSIONS: A variety of medications are used in the acute management of preeclampsia at this institution. Currently, there appears to be limited adherence to ACOG guidelines.
Presented at the 38th Annual Southeastern Residency Conference, Athens, Ga, April 26-27, 2007.

CLINICAL PHARMACY FORUM

Analgesia

261. **C-II opioid medication rewrite program.** *Melissa A. Dragoo, Pharm.D., BCPS*, Philip J. Eulie, M.D.; Department of Veterans Affairs Northern California Health Care System, Mather, Calif.

PURPOSE: This program is designed to allow an efficient manner for providing "refills" of C-II opioid medications for patients with chronic pain who are receiving stable doses of these medications.
METHODS: Providers submit an electronic consult within the Computerized Patient Record System (CPRS) that contains the necessary elements of a prescription. When the patient presents to the pharmacy, a pharmacist enrolls the patient in the program and provides a personalized calendar with predetermined "refill" dates and a number

to call to request a "refill" of the C-II medication(s). When the patient calls to request the medication(s), the pharmacy prints the consult and has the provider complete the prescription by adding his or her name, signature, DEA number, and date. The prescription is then returned to the pharmacy to be filled by the predetermined date. RESULTS: Current enrollment of patients through June 2007 (representative of a 1-year review) will be displayed with a breakdown of the number of patients enrolled per provider per month. Also included will be an average of days between prescription fills and the percentage of C-II opioid medications filled through the program compared to C-II opioid medications filled in the usual process.
CONCLUSION: The growth and success of this program has provided an efficient way for patients to obtain "refills" of their C-II opioid medications in a manner similar to refilling non C-II medications. Success of this program may provide justification for clinical pharmacy services to provide medications for these patients and further improve the efficiency of receiving "refills" of C-II opioid medications.

Cardiovascular

262. **Factors associated with recurrent coronary events among patients in a cardiac risk reduction service.** *Karen J. McConnell, Pharm.D.*, Kari L. Olson, Pharm.D., Thomas Delate, Ph.D., John A. Merenich, M.D.; Kaiser Permanente Colorado Region, Aurora, Colo.

PURPOSE: This study determined factors associated with recurrent coronary events in patients enrolled in a cardiac risk reduction service (CRRS).
METHODS: This retrospective, case-control study at Kaiser Permanente Colorado identified patients with an incident coronary event (IE) (acute myocardial infarction (AMI) or percutaneous coronary intervention (PCI)) between 1/96 and 6/04, survived ≥ 30 days, and enrolled in a CRRS within 90 days of IE. Cases (n=259), those with a recurrent event (AMI, PCI, CABG, or cardiac-related death) anytime through 12/05, were matched on sex, age, and IE date to controls (n=688). Multivariate, conditional logistic regression was used to identify demographic, co-morbidity, laboratory, and secondary prevention medication use data associated with the recurrent event.
RESULTS: Mean age was 62 ± 10 yrs; 68% were male. Classic cardiac risk factors were similar for both groups at the time of the IE, but mean chronic disease score (CDS), an indicator of health status, was worse in the cases (3 vs. 4, p<.001). At the time of the recurrent event, mean LDL-C, non-HDL and LDL:HDL (mg/dL) were higher (88 vs. 80; 123 vs. 111; 2.0 vs. 1.7, respectively; all p<.001) and HDL-C lower (46 vs. 51, p<.001) in cases compared to controls. There were no differences in ACE-I, ARB, or ß-blocker use. Statin use was higher (83% vs 74%, p=0.007) but the dose lower (< 40 mg simvastatin equivalent 45% vs 31%, p<0.001) in cases vs. controls. Factors associated with a recurrent event included CDS (OR = 1.1; 95% CI = 1.1–1.2), LDL:HDL ratio (OR = 2.2; 95% CI = 1.5–3.3) and statin doses < 40mg simvastatin equivalent (OR = 2.9; 95% CI = 1.8–4.9).
CONCLUSIONS: These results support that moderate to high dose statin should be the basis of therapy for secondary prevention. Attention to the LDL:HDL ratio by aggressively lowering LDL-C or increasing HDL-C may also be warranted.

263. **Implementation of clinical pharmacy services in a cardiomyopathy clinic.** *Adriana Alvidrez, Pharm.D.*, Toby Trujillo, Pharm.D., BCPS, Lori Arena, Pharm.D., BCPS; Boston Medical Center, Boston, Mass.

PURPOSE: Clinical pharmacy services have been demonstrated to improve outcomes in ambulatory heart failure (HF) patients. However, previous studies have not been conducted in an urban, indigent patient population. The objective of this project is to evaluate the impact of clinical pharmacy services on the rate of HF related emergency department (ED) visits and hospital admissions within an urban, indigent patient population.
METHODS: Clinical pharmacy services were added to the cardiomyopathy service starting November 2006. Patients were enrolled into the service if they were > age 18 years, had NYHA classification I-IV, and spoke either English or Spanish. The primary end point consisted of the rate of HF-related ED visits and hospital admissions 1 year prior to, and 1 year after implementation of clinical pharmacy services. Secondary outcomes include blood pressure control, fluid management as well as all-cause ED visits and hospital admissions. Patients served as their own controls, and statistical analysis was conducted using a t-test for continuous variables and chi-squared test for categorical data.
RESULTS: Twenty-five patients have been referred to clinical pharmacy services. A trend for a reduction in combined heart failure related ED visits/hospital admissions was observed with the addition of clinical pharmacy services (0.118 prior vs. 0.030 after, rate adjusted per patient per month, p= 0.052). Patients receiving clinical pharmacy services had significant reductions in both systolic (130 vs. 146 mm Hg, p=0.025) and diastolic blood pressure (74 vs. 83 mm Hg, p=0.04). A post-hoc analysis also demonstrated a trend for reductions in all-cause ED visits/hospital admissions (0.099 vs. 0.192, rate adjusted per patient per month, p=0.053).

CONCLUSIONS: The addition of a clinical pharmacist to multidisciplinary heart failure team resulted in a decrease in ED visits and hospitalizations in an urban, indigent patient population. Full results for 1 year post-implementation will be presented.

264. **An assessment of the relationship between hemoglobin A1C levels and recurrent cardiac events.** *Amy B. Kauffman, Pharm.D.*, Kari L Olson, Pharm.D., Tom Delate, Ph.D., Angie M. Hardy, Pharm.D., Alicia A Cymbala, Pharm.D., Kara A Hutka, Pharm.D., Sheila L Kasten, Pharm.D., Jon R Rasmussen, Pharm.D.; Kaiser Foundation Health Plan of Colorado, Aurora, Colo.

PURPOSE: This study analyzed the impact of hemoglobin A1C (HbA1C) values at the time of a first cardiac event in patients prescribed optimal secondary prevention medications (©¬ blockers, statins, ACE inhibitors, aspirin) on the incidence of recurrent cardiac events (RCE).
METHODS: This retrospective study was conducted at Kaiser Permanente Colorado. Adults followed by a clinical pharmacy specialist-managed cardiac risk service (CPCRS) with an index cardiac event (IE) [acute myocardial infarction (AMI), coronary artery bypass graft (CABG) surgery, or percutaneous coronary intervention (PCI)] between 01/01/99 and 03/31/05 and HbA1C values measured within 1 year prior or 60 days after the IE were identified. Cox proportional hazards models were constructed to assess the relationship between HbA1C levels (assessed as continuous and categorical (°Ā7, 8, 9) measures) after adjusting for potential confounding variables.
RESULTS: The cohort consisted of 1459 subjects (269 with/1190 without RCE). The mean age was 65.4 years; 68.7% were male. There was no difference in mean HbA1C (7.0, p>0.5), aspirin (96.7%) or ACE inhibitors (61.9% vs. 63.9%) use between cohorts. ©¬ blockers (83.4% vs. 75.1%) and statins (82.9% vs. 77.7%) were used more frequently in the no RCE cohort (p<0.05). There was no impact on RCE when HbA1C was evaluated as a continuous measure (adjusted HR = 0.99; 95% CI = 0.95–1.05) or evaluated as a categorical measure: (°Ā7%: HR = 1.05; 95% CI = 0.80–1.38), °Ā8%: HR = 0.98; 95% CI = 0.72–1.33), and °Ā9%: HR = 1.20; 95% CI = 0.85–1.72).
CONCLUSION: Our results suggest that an elevated HbA1C is not predictive of a recurrent cardiac event among patients with cardiovascular disease whose other cardiovascular risk factors are aggressively treated. However, larger studies are warranted to validate the findings.

Critical Care

265. **Acquired factor VIII inhibitor and resultant hemophilia in a penetrating trauma patient: a case report.** *Eric W. Mueller, Pharm.D.*[1], Bryce RH Robinson, M.D.[2], J. Bracken Burns, D.O.[2], Matthew J. MacCallum, M.D.[2], Adam P. McCarthy, M.D.[2], Porembka T. David, D.O.[2]; (1)The University Hospital, Department of Pharmacy Services, Cincinnati, Ohio; (2)University of Cincinnati, College of Medicine, Cincinnati, Ohio.

PURPOSE: Acquired hemophilia (AH) from production of factor VIII (fVIII) inhibitor is a rare and serious complication. We report a case of acquired fVIII inhibitor in a previously healthy, severely injured, critically ill trauma patient.
METHODS: AH-related information regarding diagnosis and management, including medication dosages, durations, and total costs were collected.
RESULTS: A 22-year-old man presented with a single abdominal gunshot wound to the right lower quadrant with peri-umbilical intestinal evisceration. Four weeks following initial trauma, multiple operations, and recent piperacillin exposure, the patient exhibited severe epistaxis, upper gastrointestinal bleeding, and hematuria with acutely elevated aPTT of 88.5 sec. Despite blood product administration, coagulopathy and hemorrhage continued. Upon hematology consult, circulating fVIII level was 2% normal and fVIII inhibitor was detected at 2.9 Bethesda Units. With the diagnosis of acquired fVIII inhibitor, continuous IV infusion recombinant fVIII (rfVIII) was initiated and ranged from 1000 to 3000 units/hour for 48 hours without improvement. At this time, recombinant activated fVII (rfVIIa) 6000 mcg IV every 2 hours was added with cessation of coagulopathy and hemorrhage. However, fVIII remained < 5%, and inhibitor levels remained elevated. Methylprednisolone and pulse rituximab therapy were started. After 10 days of combined factor (total rfVIII 490,000 units; rfVIIa 551,400 mcg) and pulsed rituximab, hemostasis persisted, fVIII levels rose > 70%, and fVIII inhibitor was undetectable. The patient was discharged home on hospital day 108.
CONCLUSION: To our knowledge, this is the first reported case of AH in an acute peri-trauma patient. Coordinated interdisciplinary intervention was imperative for accurate diagnosis and timely delivery of appropriate pharmacotherapy.

266. **Evaluation of an evidence-based enteral nutrition protocol in a community hospital ICU.** *Tudy M. Hodgman, Pharm.D.*, Diane Ryzner, R.N., Caryl Inglis, R.D., LDN, Melanie Atkinson, R.N.; Northwest Community Hospital, Arlington Heights, Ill.

PURPOSE: Protocols for nutrition should improve the delivery of adequate calories; they may also lower gastric residuals, decrease the percentage of aspirations, decrease ICU length of stay (LOS) and ventilator days, and decrease time to tube feed goal. However, implementation of nutrition in the ICU is frequently troublesome with many barriers. The ICU Guidelines Council, a multidisciplinary team of nurses, intensivists, dieticians, and a pharmacist, developed an evidence-based protocol on the use of enteral nutrition in the critically ill. We undertook this study to examine the outcome of implementing an enteral nutrition protocol in our community ICU.
METHODS: The overall goal of this initiative was to decrease the variation seen in prescribing of enteral nutrition. We retrospectively collected data on 52 patients before initiation of the protocol, compared to 52 patients after protocol. We hypothesized that implementation would decrease the time to initiation of feedings, decrease the time to reach goal feeding rate, decrease the frequency and extent of feeding interruptions, and increase the use of pro-kinetic agents. Mann Whitney two-tailed test was used to analyze data.
RESULTS: Data collection from two time periods, before protocol and after implementation was assessed to evaluated selected outcome measures. The number of ICU days a patient was NPO, decreased from 1.9 to 1.3-post protocol. The average time to goal rate decreased from 25.3 hours to 12.7 hours (p<0.0001). The number and time of feeding interruption remained unchanged. Use of motility agents increased from 40.3% to 52% post.
CONCLUSIONS: This descriptive study was performed to evaluate the effectiveness of implementation of an enteral nutrition protocol in our community ICU. Use of a protocol can improve the time to implementation and the amount and tolerability of enteral nutrition in the intubated critically ill patient. Multidisciplinary teams within community hospitals can effectively implement national guidelines.

Drug Information

267. **Outpatient use of ezetimibe in diabetes patients in an urban university health system.** *Lisa M. Lundquist, Pharm.D., BCPS*[1], Sabrina W. Cole, Pharm.D., BCPS[2], Julie Rafferty, Pharm.D.[3], Rondell Jaggers, Pharm.D.[2]; (1)Mercer University, Atlanta, Ga; (2)Grady Health System, Atlanta, Ga.; (3)St. Thomas Hospital, Nashville, Tenn.

PURPOSE: To evaluate outpatient ezetimibe utilization in patients with type 2 diabetes mellitus and assess formulary adherence in an urban university health system.
METHODS: A retrospective chart review of diabetes patients with a documented ezetimibe prescription was completed. From a computer-generated report, 828 patients who had attended a clinic visit between September 2005 and February 2006 were identified. 100 patients were randomized to be included in the review. A data collection tool was developed to include the following: demographics, baseline (BL) and most recent (MR) lipid parameters and liver function tests, present and previous lipid-lowering medications, and adverse drug reactions (ADRs). Adherence to the health system's ezetimibe prescribing recommendation (combination therapy with an HMG-CoA reductase inhibitor) was also assessed.
RESULTS: Of the 100 diabetes patients randomized, 80 patients were eligible for study inclusion. The mean age was 63 years, and 74% were female. The average length of ezetimibe therapy was 11 months. Nine patients (11%) were receiving ezetimibe monotherapy. Of those patients receiving combination therapy with ezetimibe, 58 (82%) were prescribed simvastatin concomitantly. Mean lipid parameters decreased from baseline: total cholesterol (BL 200, MR 174), low-density-lipoprotein (LDL) (BL 123, MR 101), and triglycerides (BL 146, MR 131). Of the patients with follow-up lipid panels (n = 64, 80%), target LDL goal was achieved in 26 patients (41%). Three patients experienced an ADR associated with ezetimibe [rash (n = 2), headache (n = 1)].
CONCLUSION: Despite the use of ezetimibe in combination with another lipid-lowering agent, target LDL cholesterol goals were not achieved in the majority of diabetes patients. However, mean lipid parameters demonstrated reductions from baseline total cholesterol, LDL, and triglycerides.

Education/Training

268. Clinical pharmacy research training program (CPRTP): a longitudinal approach to career development. *Charles McQuade, B.A.*, Alex Boyd, B.S., Todd Conner, Pharm.D., Amy Pai, Pharm.D.; University of New Mexico, Albuquerque, NM.

PURPOSE: There is a significant need to increase the number of Pharm.D. students who pursue academic clinical research careers. A recent ACCP White Paper documents the shortage of pharmacy faculty and the importance of addressing this shortage to adequately support the future contributions of clinical pharmacy scientists. Many Pharm.D. programs lack a mechanism or the necessary infrastructure to train clinical pharmacy scientists. A

longitudinal mentorship program under a research-focused faculty member could provide this training and increase exposure to research and academic careers. Program design: The CPRTP was initiated in 2002, as a stepwise training program where pre-pharmacy students work within a clinical and translational research program that provides exposure to legal and regulatory research issues, industry-sponsored clinical trials, clinical practice settings, statistical analysis and ultimately the design and conduct of an independent research protocol. Our CPRTP model is unique because it begins to develop prospective students prior to pharmacy school admission. This early exposure cultivates a broad understanding of clinical research in the field of pharmacy. CPRTP involvement continues throughout the Pharm.D. program developing students' post-pharmacy school matriculation into advanced research training.

RESULTS: A total of five prepharmacy students have entered the program since its initiation. The research productivity (5 poster presentations, 8 abstracts, 1 podium presentation, and 3 peer-reviewed manuscripts as both primary and co-authors) of the five CPRTP students now P2 through P4 offers testimony to the success of the CPRTP program. Post Pharm.D., three students intend to pursue advanced postgraduate clinical training, and two students intend to pursue Ph.D. programs in epidemiology and biomedical sciences.

Conclusion: The CPRTP developed at the University of New Mexico College of Pharmacy offers comprehensive clinical research experience to increase the likelihood of pharmacy students entering post-doctoral training and to prepare clinical scientists for careers in academia.

269. **Development and implementation of a pharmacology curriculum for a new medical college by clinical pharmacy specialists (CPS).** *Morton P. Goldman, Pharm.D., BCPS*, Jennifer K. Sekeres, Pharm.D., BCPS, Christine A. Taylor, Ph.D.; Cleveland Clinic, Cleveland, Ohio.

PURPOSE: To describe the development and implementation of the pharmacology curriculum at the Cleveland Clinic Lerner College of Medicine (CCLCM).

METHODS: CCLCM admitted the inaugural class in 2004. The CCLCM goal is to train physician investigators through innovative educational approaches, including problem-based learning, interactive seminars, labs and problem sets with basic science and research principles learned in the context of clinical relevance. Curriculum in the first 2 years is organized by organ system with six blocks in year 1 and five in year 2. Basic sciences (e.g., pharmacology, anatomy, biochemistry) are organized as threads with objectives integrated throughout. Faculty consists of physicians and basic scientists from the Cleveland Clinic. The Director of Pharmacotherapy Services was chosen as the Thread Director for Pharmacology.

RESULTS: During early development, eight CPSs attended multiple block/section meetings, curricular design meetings, faculty development, and mock practice sessions. This resulted in CPSs averaging 60 hours/year. Initial challenges were integration of basic pharmacology concepts (e.g., ADME) with organ blocks, evaluation method, and CPS self-confidence as faculty. Currently, 11 CPSs provide 32 and 68 direct student contact hours in years 1 and 2 respectively. Ongoing activities include development/refinement of student assessment tools and continual curricular revision. CPS faculty members have been recognized for best practice in the college and often acknowledged by students for excellence in teaching. USMLE-1 scores were above the national mean in pharmacology for the inaugural class.

CONCLUSIONS: CPSs can successfully develop curriculum and serve as pharmacology educators in medical colleges. Significant time is required for preparation, teaching, and faculty development activities. It is critical to recognize and value time commitments to permit on-going success of CPS pharmacology programs. Early exposure for medical students to practicing clinical pharmacist may lead a generation of physicians who increasingly value the importance of clinical pharmacy services.

270. **House calls for medication therapy management: clinical pharmacy services provided through early experiential education**. *P. David Brackett Jr., Pharm.D., BCPS*, T. Lynn Stevenson, Pharm.D., BCPS, CDM; Auburn University Harrison School of Pharmacy, Auburn, Ala.

PURPOSE: This poster describes a unique pharmacy service wherein student pharmacists provide supervised medication therapy management by visiting patients in their place of residence.

METHODS: Approximately 350 student pharmacists in their first through third professional years are divided into 24 student teams that are precepted by 52 faculty members. Student pharmacists meet weekly with assigned patients to interview them and assess their current health status. Preceptors meet weekly with students to discuss patient cases and join students on visits as required. Students document all patient care in a SOAP format. Intervention recommendations are coordinated and communicated to physicians through the clinical director of the program.

RESULTS: Approximately 300 patients receive regular pharmacy services through the early experiential program. Interventions include wellness education, patient counseling, medication reviews and monitoring. Recommendations

are discussed and finalized by students and clinical faculty in team meetings. These recommendations are then communicated to primary care physicians through telephone calls or written communication.

CONCLUSIONS: This clinical service achieves a variety of outcomes. It is an avenue to potentially improve health care in our community. It gives students a "real world" opportunity to build their skills and experience while demonstrating the impact of patient-centered pharmacy and team oriented care. It provides a primary clinical practice setting for one full-time faculty member and a secondary practice setting for several other clinical faculty. Lastly, it is a mechanism to enhance relationships between physicians and pharmacists in this community.

271. A nutrition-based competency program for clinical pharmacists and clinical dieticians at an academic teaching university hospital. *Joseph Mazur, Pharm.D.*, Cathy Worrall, Pharm.D., Mary Basel, R.D., Chris Bannister, R.D., English Barbour, R.D., Jennifer Franks, R.D., Katherine Chessman, Pharm.D., Dominic Ragucci, Pharm.D., Marc Lapointe, Pharm.D., Paul Bush, Pharm.D., Mark DeLegge, M.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: There are various competency-based nutrition programs available including one developed by American Society of Enteral and Parenteral Nutrition (ASPEN). A unique nutrition competency program was developed at the Medical University of South Carolina (MUSC) to provide consistent, multidisciplinary competency training for both clinical pharmacists and dieticians, and to educate and train new pharmacy residents, clinical dietician interns, and clinical staff to write orders and document nutrition assessments for patients receiving enteral and parenteral nutrition.

METHODS: A multidisciplinary task force, including MUSC nutrition experts, was convened to develop the competency program. A Web-based program (WebCT) was created, which included modules for nutrition assessment, adult parenteral and enteral nutrition, pediatric parenteral and enteral nutrition, special populations, and a review of institutional policies and procedures regarding nutrition. Participants completed a self assessment prior to viewing the web-based program. Following this baseline education, clinicians completed patient case studies and then attempted live discussion sessions. Finally, participants reviewed mock patient charts and completed nutrition assessment notes and nutrition orders for these cases. Clinicians who successfully completed all aspects of the program were deemed competent to write nutrition assessments and orders.

RESULTS: All clinical pharmacists and dieticians at MUSC are now required to complete the nutrition competency program in order to have privileges to write orders for enteral and parenteral nutrition.

CONCLUSIONS: This nutrition competency program has fostered team building among various disciplines, enhanced pharmacy resident and clinical dietician intern knowledge, and allowed for further refinement of other nutrition programs at MUSC.

272. Survey of class content and delivery method in team taught disease state management (DSM) and pharmacotherapy (PCTP) courses. *Robin L. Southwood, Pharm.D.*, Daniel Malcom, Pharm.D. candidate 2008, George Francisco, Pharm.D.; University of Georgia, Athens, Ga.

PURPOSE: To assess instructor compliance with intended content and delivery method in two courses. The DSM course focuses on the pharmacotherapy of a specific disease state in a lecture based format while PCTP spends 75% of time in an interactive case based course of pharmacotherapy of patients with multiple health problems.

METHODS: An electronic survey was developed to differentiate between the two courses based upon the syllabus submitted to the university curriculum committee. A link was emailed to the 27 instructors who taught in either course during the previous academic year.

RESULTS: All instructors completed the survey. Thirty-three percent were volunteer faculty, 88% of respondents had previously taught in the same course, and 27% taught in both courses with 8% teaching the same topic in both courses. Eighty-one percent had received instruction regarding class content and time allocation. In the pharmacotherapy course, 14% of instructors spent 75% of course time on patient cases. Sixty-four percent of pharmacotherapy instructors spent less than 50% or less of class time reviewing patient cases. Only 46% of DSM instructors reviewed nondrug therapy. PCTP instructors more frequently reported reviewing content areas of pathophysiology, pharmacology, and disease therapeutics. DSM instructors reported spending twice as much time on patient monitoring.

CONCLUSION: This project demonstrates a simple quality assurance effort that can be conducted to assess appropriateness of content and content delivery in team taught course. The survey revealed incorrect time allocation and overuse of lecture style delivery in the pharmacotherapy course. Faculty turnover in team-taught courses can affect both instructors and course coordinators and can result in inappropriate class content or delivery methods. The results demonstrate the important role of course coordinators remaining aware of course intent and communication of course content and delivery methods to instructors.

273. Quality assessment of a team-taught two-semester pharmacotherapy course. *Robin L. Southwood, Pharm.D.*; University of Georgia, Athens, Ga.

PURPOSE: To assess quality of course administration and teaching content in a team-taught two-semester pharmacotherapy course (PCTP I and PCTP II). The courses are intended to provide case based instruction regarding the use of medications to treat simulated patients with multiple disease states with 75% percent of class time spent discussing patient cases.
METHODS: The two pharmacotherapy courses were evaluated through processes: 1) a survey of instructors regarding class content areas, time allocation and instructional format, 2) evaluation of eight course syllabus content areas for consistency, 3) a comparison of current course syllabus to syllabus on file with university curriculum committee, and 4) review of time lapse between class topic presentation in pharmacotherapy and in background courses.
RESULTS: 1) Instructor survey results revealed overuse of lecture style content delivery (86%). 2) Moderate or minor variances occurred in 2 of 8 syllabus content areas including one numeric grade range and utilization of quizzes. Neither syllabus included statements regarding students with disabilities. 3) Both course syllabi were consistent with syllabi in the university curriculum committee database. 4) Eighty-one percent of PCTP I topics were taught in prerequisite courses within 1 year versus 17% in the PCTP II course. Sixteen percent of PCTP I and 11% of PCTP II topics were never reviewed in a prerequisite course. CONCLUSION: This project demonstrates a simple quality assurance effort that can be conducted in a two-semester team-taught course. Inconsistencies existed in course syllabi that could lead to student confusion. Evaluation of the impact of delay of greater than 1 year between coverage in PCTP course and prerequisite courses and arrangement of PCTP I and PCTP II topics to reduce time should be considered. The impact of not having a PCTP topic covered in a prerequisite class warrants further evaluation.

274. **Impact of attending educational symposium upon first year pharmacy student attitude toward providing pharmaceutical care to mentally ill patients.** Merrill Norton, R.Ph., D.Ph., *Robin L. Southwood, Pharm.D., BCPS*, Matt Perri, R.Ph., Ph.D., Henry Cobb, R.Ph., Ph.D., Nilesh Bhutada, B.S.; University of Georgia, Athens, Ga.

PURPOSE: To assess effect of attending a co-occurring disorder (mental illness and substance abuse) seminar on attitudes of first year pharmacy regarding mental illness.
METHODS: Participation in a 27-question voluntary anonymous survey was offered to students before and after attending a co-occurring disorder seminar. A Likert scale of 1–5 was used where a score of 5 indicated greater agreement. The survey assessed: 1) perception of ability to provide pharmaceutical care to mentally ill patients, 2) exposure to mentally illness, 3) feelings (compassion/comfort) regarding interactions with mentally ill patients, 4) attitude toward personal interaction with individuals with mental illness, 5) perception of professionally interactions, and 6) interest in mental health as a career path.
RESULTS: Eighty-five students completed both surveys. Respondents were 70% female and 75% Caucasian. A statistically significant change in response occurred in 44% of survey questions. 1) perception of ability to provide pharmaceutical care to patients with alcoholism, drug dependence and dementia decreased significantly, 2) exposure to mentally illness was unchanged, 3) a significant increase in the number of students expressing fear when encountering mentally ill patients occurred, 4) a significant increase in respondents stating they would never marry a person with mental illness occurred, 5) a significant increase in the discomfort with professionally interactions with mentally ill patients occurred, and 6) 20% reported disinterest in mental illness as a career path. Sixty percent of students reported change in perception of mental illness and recognition of mental illness as a disease ($p<0.05$). .
CONCLUSIONS: The survey reveals insight into student attitudes regarding mental illness and suggests that attending a co-occurring disorder conference influences students' perception of mental illness and their ability to care for mentally ill patients.

Endocrinology

275. **Impact of pharmacist intervention on diabetes in an ambulatory care setting.** *Julie A. Stading, Pharm.D., CDE*, Jamie Herrmann, B.S., Christopher Destache, Pharm.D., FCCP, Michele Faulkner, Pharm.D.; Creighton University School of Pharmacy, Omaha, Neb.

PURPOSE: This study assessed the impact of a clinical pharmacist on diabetes patient outcomes as measured by the change in their hemoglobin A1c value.
METHODS: This was a retrospective study (IRB approved), which included four patient groups. The first two groups were composed of newly diagnosed diabetes patients. Group one was seen by the clinical pharmacist for education and monitoring along with their physician (Team); group two, the Control group, was seen by physicians

only. The third and fourth groups were patients with diabetes started on insulin therapy (complex patients) seen by the Team compared to the Control. All patients had type 2 diabetes. A comparison of the hemoglobin A1c changes between the Team versus the Control was done for each arm of the study.

RESULTS: In the newly diagnosed groups, 33 patients were monitored by the Team and 57 were Control patients. The mean change in hemoglobin A1c for the Team group was (-0.633%) compared to (-0.003%) in the Control group (p>0.05). In the insulin patient groups, 36 were monitored by the Team compared to 51 in the Control. The mean change in hemoglobin A1c was significantly reduced (-0.672%) in the Team group compared to (+0.308%) in the Control group (p<0.02).

CONCLUSION: This study suggests that using a clinical pharmacist for monitoring and patient education in managing diabetes patients, especially complex patients taking insulin, will improve outcomes in an outpatient clinic setting.

276. Effect of a pharmacy glycemic management team on hyperglycemia in post-surgical orthopedic patients. *Paul Juang, Pharm.D.*[1], Danielle Field, Pharm.D.[2], John Khoury, Pharm.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, Mo; (2)Missouri Baptist Medical Center, St. Louis, Mo.

PURPOSE: Studies have shown that strict glycemic control for hospitalized patients result in decreased morbidity and mortality. Recently the in-house insulin sliding scale was converted to a basal/bolus insulin model, with a pre-prandial glucose correction scale. This study was conducted to evaluate the change in glycemic control and the effect of a pharmacy glycemic management team on the achievement of target glucose levels with the new model.

METHODS: Single-center, retrospective evaluation of patients admitted within an inpatient post-surgical orthopedic service at a major metropolitan community hospital. Glucose readings were obtained for all patients admitted to the service during a 3-month interval with glucose managed by the pharmacy management glycemic team or by the prescribing physician and were categorized into 5 groups: Blood glucose < 70, 70–79, 80–110, 111–150 and > 150, respectively. Primary outcome was glucose control while secondary outcomes were discharge disposition, infectious complications, and length of stay. Statistical analysis was performed using the student t-test, chi-square test or Fisher's exact analysis, where appropriate.

RESULTS: A total of 137 patients were evaluated, with 19 patients whose glucose was managed by the pharmacy glycemic management team and 118 control patients. No significant difference was observed in the baseline characteristic between groups, except for a greater number of control patients with a history of hyperlipidemia. Patients whose glucose was managed by the pharmacy glycemic team had more glucose readings of < 70 (0.960% vs. 4.22%, p=0.0002), 70–79 (1.36% vs. 3.31%, p=0.031), 80–110 (9.51% vs. 15.7%, p=0.002) and 111–150 (35.2% vs. 35.2%, p=1.00) while fewer patients had glucose readings of > 150 (53.0% vs. 41.6%, p=0.0003). No difference in length of stay, antibiotic duration, and discharge disposition were observed.

CONCLUSIONS: A pharmacy glycemic management team is successful in achieving target glucose control on post-surgical orthopedic patients.

277. Implementation of the aspirin, lovastatin, and lisinopril (ALL) initiative in patients with diabetes. *Mongthuong Tran, Pharm.D., BCPS, CDE*, Sarah Billups, Pharm.D., BCPS; Kaiser Permanente Colorado, Denver, Colo.

PURPOSE: In 2005, the Diabetes Advisory Council of Kaiser Permanente Colorado developed the ALL Initiative, which targeted three evidence-based goals for patients with Diabetes Mellitus: 1) document use of aspirin therapy, 2) initiate lovastatin in eligible patients, and 3) identify patients with microalbuminuria not taking lisinopril. This project aimed to implement this initiative.

METHODS: We identified patients with diabetes ages 40–80 years with a total cholesterol ≤ 135 and not taking a statin. We sorted them by clinic location and divided them into two phases. For Phase 1: We provided a patient list to each primary care provider to authorize or decline lovastatin initiation for each patient. Approved patients received a letter asking them to start lovastatin therapy and come in for appropriate lab tests. They also received a survey inquiring about aspirin use. Laboratory results and patient questions were addressed by Clinical Pharmacy Services (CPS). Primary Care CPS received monthly follow-up reports regarding lovastatin fill dates, fasting lipid test dates, and microalbuminuria test dates for patients not using an ACE-inhibitor. CPS contacted patients who were overdue for lab tests and recommended initiation of lisinopril therapy when indicated. The population management strategy was implemented in the Phase 2 cohort 3 months later.

RESULTS: We assigned 1570 patients to Phase 1 (intervention) and 1782 to Phase 2 (control). Statin initiation rates at 3 months were 24.0% and 9.9%, respectively (p<0.001). Similar rates of persistence on therapy at 1 year were observed in both groups (61.1% and 64.7%, respectively (p= 0.511)). Aspirin documentation increased from 3% to 25.4% in intervention patients. The proportion of patients with an elevated microalbumin not using ACE-I therapy was decreased by 31% in the intervention group compared with 8% in the controls (p<0.001).

CONCLUSIONS: A letter-based population management strategy managed by CPS effectively improved adherence to evidence-based clinical guidelines.

Ethics

278. **Pharmacists, Pharmaceutical Manufacturers, and Conflicts of Interest: University Health Consortium Membership Survey.** *Roy Guharoy, Pharm.D.*[1], Susan Kleppin, Pharm.D.[2], Michael A. Fotis, R.Ph.[3], G. Mark Baillie, Pharm.D., M.H.A.[4], James G. Stevenson, Pharm.D.[5], Lynda Stencel, B.S.[6], Douglas Smith, Pharm.D.[6]; (1)SUNY-Upstate Medical University, Syracuse, NY; (2)University of Wisconsin Hospitals, Madison, Wis; (3)Northwestern Memorial Hospital, Chicago, Ill; (4)MUSC, Charleston, SC; (5)The University of Michigan Health System and College of Pharmacy, Ann Arbor, Mich; (6)University Health Consortium, Chicago, Ill.

PURPOSE: Conflicts of interest (COI) have received considerable attention in the recent years. Many reports have appeared in medical journals and press describing inappropriate and unprofessional behaviors secondary to COI. Many potential COI relationships involve pharmaceutical manufacturers. The Pharmacy Practice Advancement Committee of the University Health Consortium (UHC), an alliance of 97 academic medical centers and 153 affiliated hospitals, conducted a survey among members to identify the prevalence of COI in September 2006.
METHOD: Survey indicators included pharmaceutical representative access, drug samples provided by drug manufacturers, gifts, and COI disclosure of physicians and pharmacists.
RESULT: 61 members responded. 98% of hospitals have an official policy on pharmaceutical representative access. The pharmacy department alone is responsible for enforcing the policy in 34% of the hospitals. 89% of hospitals require an ID badge and registration at a central place. However, 61% felt that their current process was not effective in enforcing hospital policy. Drug samples are allowed in 72% hospitals. 20% of hospitals use vouchers in place of samples. Gifts such as pens, books, and notepads are allowed in most hospitals. Food provided by drug manufacturers is allowed in 72% of hospitals. Disclosure from Pharmacy & Therapeutics Committee members is required in 72% of hospitals. 68% of hospitals require that members with COI be excluded from decision making. Only 25% of hospitals require pharmacists to disclose COI. Only one hospital provides pharmacist participation in drug company-sponsored advisory board or speaker's bureau. Only 14% of hospitals require physicians to disclose COI each year.
CONCLUSION: Our findings suggest that there is significant room for improvement for prevention of COI in health care facilities.

Gastroenterology

279E. **Do inflammatory bowel disease patients on home parenteral nutrition with metabolic bone disease have a poorer response to intravenous pamidronate?** *John K. Siepler, Pharm.D.*, Thomas Diamantidis, Pharm.D., Reid A Nishikawa, Pharm.D., Rod Okamoto, B.S., R.Ph.; Nutrishare, Inc, Elk Grove, Calif.

PURPOSE: Both inflammatory bowel disease(IBD) and home parenteral nutrition(HPN) are risk factors for metabolic bone disease(MBD). For HPN patients, the treatment for MBD is intravenous pamidronate(IP). IP is needed due to inadequate absorption of oral bisphosphonates. We evaluated treatment response of MBD for HPN patients with IBD and without IBD in HPN patients.
METHODS: The records of patients from one home care provider receiving HPN and IP for MBD were reviewed. All patients had a baseline DEXA prior to starting IP and > 1 follow up DEXA a year later. Data collected included baseline and most recent DEXA. Outcomes were change in Femoral neck and spine T scores and %change/year of T scores. Statistics used were Ttest and Chi Square with $p<0.05$ significant.
RESULTS: Thirty-nine patients qualified(24=IBD,15=no IBD). Mean age, gender, and duration of IP use were similar in the two groups. Mean duration of IP treatment was 5.3 ± 2.6years for the IBD group and 3.9 ± 1.8years in the no IBD group(p=ns). Baseline and final spine and femoral neck T scores were not significantly different(see tables). Mean change and %improvement in spine T scores were greater in the no IBD group. Discussion: We evaluated 39 HPN patients on IP to determine whether IBD was a factor in response. We found that HPN patients with IBD had a poorer response in spine but not femoral neck T scores than those without IBD. While this difference was significant, there were no fractures noted in any patient. More work is needed to determine risk factors in these patients.

Table1

Femoral Neck T scores Group	Initial	Final	Change	%change/yr	n(%)improve
IBD	-2.8±0.8	-2.5±0.7	0.27±0.7	1±0.05	18(75)
noIBD	-2.8±0.8	-2.2±0.8	0.63±0.8	4±0.1	14(93)

Table 2

 Spine T scores Group Initial Final Change %change/yr n(%)improve IBD -2.5±1.1 -2.4±1.0 0.1±0.8 -4±0.2 11(46) noIBD -2.8±1.0 -2.0±0.7 0.7±0.8* 9±0.12* 12(80)* •=p<0.05

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Health Services Research

280. **Establishment of a pharmacist-managed smoking cessation group clinic.** *Ann M. Philbrick, Pharm.D.*[1], Erin Newkirk, Pharm.D.[1], Karen Farris, Ph.D.[2], Beth B. Phillips, Pharm.D.[1], Deanna L. McDanel, Pharm.D.[1]; (1)University of Iowa Hospitals and Clinics, Iowa City, Iowa; (2)University of Iowa, Iowa City, Iowa.

PURPOSE: Cigarette smoking is the leading cause of preventable death in the United States. In July 2006, the University of Iowa Hospitals and Clinics (UIHC) implemented a campus-wide smoking ban. Prior to 2007, smoking cessation programs at UIHC were in the Pulmonary Rehabilitation and Employee Health Clinics. These services were limited in the number of patients served and were individual sessions. A pharmacist-managed group smoking cessation program was identified as an alternative method of smoking cessation counseling.
CLINIC DESCRIPTION: The objective of this project was to establish a pharmacist-managed group smoking cessation clinic at UIHC. The clinic was developed from August 2006 to February 2007 by reviewing the literature describing smoking cessation clinics, meeting with clinicians of other smoking cessation clinics to discuss optimal design, meeting with administrators to determine space and supplies needed, and developing appropriate advertising plans. Persons over age 18 years who smoke daily are eligible to participate. The clinic, which was established in February 2007, is administered by clinical pharmacists. The clinic meets for six 45-minute sessions over 8 weeks. Each session is spent covering a specific topic related to smoking cessation, with adequate time for patients to converse about their quit attempts. Data regarding patient perceptions about the clinic will be collected at 3 months after the patient's first clinic visit. Data regarding patient self-reported tobacco use status will be collected at 3, 6, and 12 months after the patient's first clinic visit via a phone survey.
OUTCOMES: The establishment of this clinic will provide an avenue to objectively analyze the value of clinical pharmacists within a smoking cessation group clinic by examining the quit rates and satisfaction of its participants.

281. **Assessment of self-rated health knowledge on a university campus.** *Priti N. Patel, Pharm.D., BCPS*, S. Jennifer Miranda, M.S., Mahjabeen Motiwala, Pharm.D.; St. John's University, Queens, NY.

PURPOSE: The objective of this study is to assess the current status of self-rated health knowledge on our university campus.
METHODS: Self-rated health knowledge was assessed using a 27-item questionnaire. The questionnaire included both the subjects' demographic information as well as their understanding of various important health topics based on a 5-point Likert scale. The questionnaire was distributed to all populations of the university community, including students, faculty, administrators and staff. The protocol was approved by the Institutional Review Board.
RESULTS: A total of 322 questionnaires were completed. Fifty eight percent of respondents were female. The majority of respondents were undergraduate and graduate students (58.0%), with fewer faculty (13.0%), staff (19.5%), and administrators (9.5%). Ethnicity varied as follows: Caucasian (38.0%), Hispanic (10.3%), black (27.4%), and Asian (24.3%). Most participants rated knowledge of most health topics, including high blood pressure, diabetes, high cholesterol, heart disease, and asthma, as either "some understanding" (rating 3) or lower ("very poor" or "none"). Overall health knowledge was rated most commonly as 2 ("very poor understanding") by respondents in the 18–25 year age group, but was rated most commonly as a 3 ("some understanding") in the higher age groups. In regard to ethnicity, Hispanic respondents rated their overall health knowledge lower than the other ethnic groups.
CONCLUSIONS: The survey results indicated an overall need to provide all campus community populations with health information related to a variety of disease topics. The Pharmacy Care Service at our institution will discuss topics that will assist the campus community in improving their health knowledge of important diseases such as high blood pressure, diabetes, high cholesterol, heart disease, and asthma. The service intends to generate awareness of options as individuals manage their health care, medication, and lifestyle.

282. **Evaluation of a discharge pharmacy services program.** *Constance Law, Pharm.D.*, Julie E Mannello, Pharm.D., Lindsay M. Arnold, Pharm.D., BCPS, Toby Trujillo, Pharm.D., BCPS, Gail M Burniske, Pharm.D., BCPS; Boston Medical Center, Dept of Pharmacy, Boston, Mass.

PURPOSE: Discharge from a health care setting has been recognized as a vulnerable period in the medication use process. Based on beneficial outcomes seen in previous research conducted at Boston Medical Center (BMC) and other institutions, a discharge counseling service was started at BMC in September of 2005. The purpose of this study is to evaluate the impact of a pharmacist discharge counseling service in the acute care setting. This study looks to evaluate the impact of the service on 30-day readmission and emergency department (ED) visits.
METHODS: A retrospective cohort study was conducted from November 2005 through December 2006 consisting of medicine patients counseled or not counseled by a pharmacist prior to discharge. Patients received counseling prior to discharge if they met pre-specified criteria. Telephone follow-up was also conducted by a pharmacist for English-speaking patients within 3 days of discharge.
RESULTS: The final cohort consisted of 2835 patients of which 2185 patients met inclusion criteria on discharge. On average, patients were 60 years of age, and 53.2% of patients were female. A total of 811 patients were counseled (37.1%) over the 13-month period. Inpatient readmission rates at 30 days were similar for the two groups, 24.2% and 24.7% in the counseled and non-counseled groups respectively (p=0.85). There were 100 ED visits in the counseled group compared with 226 in the non-counseled group (p=0.011). 501 counseled patients were eligible to receive a telephone call post discharge. Of the 323 patients reached via telephone, 65 patients (20.1%) had a readmission within 30 days compared with 53 patients in the group of 178 patients (29.8%) who were not reached via telephone, (p=0.02).
CONCLUSIONS: A pharmacist discharge counseling services appears to have the largest impact on ED visits. A follow-up telephone call by a pharmacist can also further reduce re-admission rate.

Hematology/Anticoagulation

283. **Enhancing venous thromboembolism prophylaxis appropriateness and usage in medicine patients: a multidisciplinary approach.** *Sarah M. Martin, Pharm.D.*[1], Anees Afroze, M.D.[2], Michael A. Weisz, M.D., FACP[2]; (1)St John Medical Center, Tulsa, Okla; (2)University of Oklahoma College of Medicine, Tulsa, Okla.

PURPOSE: Venous thromboembolisms (VTE) can be a major complication and significantly prolong a patient's hospital stay. Most clinicians associate VTEs with surgery; however, an acutely ill patient's risk is similar to that of some surgery patients. Also, many express concern about the increased risk of bleeding complications with prophylaxis despite the incidence of major bleeding being equal to placebo ($\leq 1\%$) in medical patients. Complexities and inconsistencies between various guidelines can leave the clinician uncertain when considering VTE prophylaxis. Most guidelines are directed toward surgical patients. This is one explanation as to why prophylaxis is consistently underused in the medical patient population. Our objective was to develop and implement VTE prophylaxis guidelines for medicine patients and determine their usefulness.
METHODS: A retrospective analysis of patient charts to determine use and appropriateness of VTE prophylaxis before and after guideline implementation. One month of baseline data was collected. Patient charts were assessed to determine whether they were 1) given VTE prophylaxis, 2) whether the prophylaxis was appropriate, 3) whether it was initiated in a timely manner, and 4) whether there were any contraindications to the medications. Physicians were then provided with pre-printed order sheets and a 1-hour education section. Clinical pharmacists rounding with the physician teams also emphasized the importance of prophylaxis (except during the periods around the checks.) Five months and 12 months post education, a 1-week "spot-check" of patient charts was conducted.
RESULTS: Baseline data showed that physicians used VTE prophylaxis correctly 52.6% of the time, which increased to 77.9% (p≤0.001) initially and 73.2% (p≤0.001). The inappropriate use of sequential compression devices (SCD's) decreased from 37.4% initially to 17.9% (p≤0.005) and 23.6% (NS).
CONCLUSIONS: The implementation of guidelines encompassing a short educational program, pre-printed order form and supplemented by clinical pharmacist support can significantly improve appropriate and maintain VTE prevention.

284. **Formulary management of factor VII at a university hospital.** *Phillip S. Owen, Pharm.D.*[1], Larry K. Golightly, Pharm.D., BCPS[1], Rob MacLaren, Pharm.D., FCCM, FCCP[2], Ken Ferretti, M.B.A., M.P.M., Pharm.D.[1]; (1)Universtiy of Colorado Hospital, Denver, Colo; (2)University of Colorado Health Sciences Center, Denver, Colo.

PURPOSE: This report describes the clinical and fiscal effects of implementation of guidelines for use of recombinant human coagulation factor VIIa (rVIIa, NovoSeven®) at an academic medical center.
METHODS: With advisory direction from a pharmacy-driven multidisciplinary committee, evidence-based guidelines for rVIIa were revised, approved by the Pharmacy and Therapeutics Committee, and fully implemented in 2007. Requirements for retrospective review and expert assessment of appropriateness of use for 100% of cases

were adopted simultaneously. Effects of these actions were evaluated by auditing and comparing rVIIa utilization in patients treated before and after guideline implementation.

RESULTS: The written and computerized medical records of 41 recipients of rVIIa were reviewed. Of these, 22 were treated in the latter half of 2006 (group 1) and 19 were treated in 2007 (group 2). Patient characteristics generally were similar and outcomes were comparable, with mortality occurring in 18% and 32% of patients in groups 1 and 2, respectively (chi squared=1.03; p=NS). Mean dosages of rVIIa administered were 81.8 mcg/kg and 47.0 mcg/kg in groups 1 and 2, respectively (t=3.38; 2-tailed p<0.01). Accordingly, the amounts of rVIIa purchased monthly during the periods of observation averaged 42.6 mg in 2006 and 26.4 mg in 2007, a 38% difference. If this trend continues, the hospital will realize a decrease of approximately $180,792 in expenditures for rVIIa in 2007 compared with the previous year.

CONCLUSIONS: Guidelines based on currently available evidence can serve to sustain the clinical appropriateness and safety of rVIIa therapy and substantially decrease costs.

285. **Outcomes of a pharmacist-managed erythropoietin clinic for preoperative orthopedic patients.** *Dustin E. Bezy, Pharm.D.*[1], Tricia L Patterson, Pharm.D.[1], Larry Spratling, M.D.[1], Stephen A Day, R.Ph.[1], Richard Gerkin, M.D., M.S.[2]; (1)Banner Baywood Medical Center, Mesa, Ariz; (2)Banner Good Samaritan Hospital, Phoenix, Ariz.

PURPOSE: To evaluate the impact of a pharmacist-managed erythropoietin clinic designed to reduce the number of blood transfusions and improve outcomes in orthopedic surgical patients.

METHODS: Clinic patients who received erythropoietin 600 units/kg and supplemental iron were compared with matched non-clinic patients undergoing THA or TKA between September 1, 2006 and April 4, 2007. Preoperative, postoperative, and clinic Hgb concentrations as well as transfusion rates and length of stay were documented. Complications, discharge disposition, and total hospital cost were also noted.

RESULTS: A total of 20 patients treated by the clinic were reviewed and compared to an equal number of well-matched control patients not screened or treated by the clinic. The average postoperative Hgb concentration was greater in those patients treated by the clinic (11.8 gm/dL) than the control group (9.6 gm/dL, p<0.001). Higher postoperative Hgb concentrations resulted in fewer clinic patients requiring a blood transfusion compared to those in the control group (0% versus 60% respectively, P<0.001). Clinic patients stayed an average of 2.99 days and incurred an average hospital cost of approximately $61,400, whereas control patients stayed an average 3.35 days with an average cost of $66,600. A greater number of patients in both groups were discharged to home instead of a skilled nursing facility. Control patients experienced a greater number of complications while hospitalized as well.

CONCLUSION: A pharmacist-managed erythropoietin clinic consistently and efficiently screened and treated preoperative anemia in orthopedic patients. By identifying and treating these patients in advance, postoperative blood transfusions were effectively reduced and resulted in improved patient outcomes.

286. **Technological facilitation of venous thromboembolism prophylaxis screening at a community hospital.** *Kyle Utecht, Pharm.D.*, Clyde Birringer, Pharm.D.; Meriter Health Services, Madison, Wis.

PURPOSE: Venous thromboembolism (VTE) continues to be a significant risk for hospitalized patients, with iatrogenic deep vein thrombosis and pulmonary embolism contributing to 10% of hospitalized patient deaths. This prevalence is unacceptable considering the publication of evidence-based guidelines that promote prophylaxis through pharmacologic and mechanical means. A recent initiative at our 450-bed community hospital promotes the use of appropriate VTE prophylaxis. A multidisciplinary team has developed a variety of techniques for achieving this goal, including a screening process that uses an automated report to identify patients not receiving VTE prophylaxis. Each day, this report examines the nursing documentation and pharmacy records on each patient's electronic health record and identifies those patients not ambulating regularly, not receiving pharmacologic prophylaxis, and not receiving mechanical prophylaxis. A clinical pharmacist formally evaluates each identified patient's risk of developing a VTE and provides a prophylaxis recommendation based on hospital guidelines. The clinical pharmacist then documents the evaluation and recommendation in the patient's electronic health record, which will facilitate continuity and follow-up on the recommendation the next day. The pharmacy staff provided the clinical guidance for developing this novel report that leverages the power of electronic health records to fulfill a basic clinical screening role. The pharmacy staff also created an Excel®-based program for the clinical pharmacists' use that considers a patient's demographic information, renal function, medical history, current diagnosis, recent surgical procedures, and possible contraindications when performing the VTE risk assessment and recommending a VTE prophylaxis regimen. This process provides an efficient and consistent means for promoting VTE prophylaxis and is an example of how technology can augment the scope of pharmaceutical care services in a community hospital.

287. **Impact of pharmacist-hematologist collaboration on direct thrombin inhibitor utilization in the management of heparin-induced thrombocytopenia in an academic medical center.** *Snehal H. Bhatt, Pharm.D., BCPS*[1], Diane E. Soulliard, Pharm.D., BCPS[2]; (1)Massachusetts College of Pharmacy and Health Sciences, Boston, Mass; (2)Beth Israel Deaconess Medical Center, Boston, Mass.

PURPOSE: The involvement of pharmacists in in-patient anticoagulation services continues to gain interest within the profession, with many practitioners looking to establish pharmacy-based services. Our objective is to evaluate the impact of pharmacist collaboration with hematology services on direct thrombin inhibitor (DTI) utilization in patients with documented or suspected heparin-induced thrombocytopenia.
METHODS: Patients treated with direct thrombin inhibitors argatroban and lepirudin prior to the collaborative agreement were retrospectively evaluated for total duration of DTI use; percentage of patients with greater than 7 days of DTI therapy; warfarin initiation and total days of warfarin/DTI overlap; documented hematology consultation after 48 hours of DTI usage; utilization of HIT antibody testing via platelet-factor 4 (PF-4) or serotonin release assay; and average per-patient costs associated with DTI use and total length of stay. A similar group of patients was then prospectively compared to the retrospective group after the collaboration agreement.
RESULTS: Prior to the collaborative agreement, 30 % of patients received DTI therapy for greater than 7 days, 80 % of patients were treated with overlapping DTI and warfarin, 68 % of patients received a formal hematology consult, and 88 % of patients had HIT antibody testing. Average per-patient costs associated with DTI utilization was $6188/patient and average length of stay was 7.68 days. Post collaboration, 7 % of patients received DTI therapy for greater than 7 days, 81% of patients were treated with overlapping DTI and warfarin, and 81% of patients received formal hematology consult. Average per-patient costs were $4512/patient, average length of therapy was 4.8 days, and average length of stay was 5.64 days.
CONCLUSION: Pharmacist collaboration with hematology services is cost effective and can be used to support or justify pharmacy involvement in managing hospitalized patients with suspected or documented HIT.

Infectious Diseases

288. **The incidence of carbapenem (CBP)-related seizures: a meta-analysis.** Joan P. Cannon, Pharm.D.[1], Nina M. Clark, M.D.[2], Todd Lee, Pharm.D., Ph.D.[3], Paul Setlak, Pharm.D.[4], *Shellee A. Grim, Pharm.D.*[2]; (1)Hines VA Hospital, Hines, Ill; (2)University of Illinois Medical Center at Chicago (UIMCC), Chicago, Ill; (3)Edward Hines, Jr. VA Hospital, Hines, Ill; (4)University of Illinois at Chicago College of Pharmacy, Chicago, Ill.

PURPOSE: A consensus exists that imipenem/cilastatin (IMI) is the most epileptogenic CBP, despite inconsistencies in the literature. We conducted a meta-analysis to clarify the incidence of seizures (SZ) and comparative epileptogenicity of IMI, meropenem (MER), and ertapenem (ERT).
METHODS: MEDLINE was searched from 1966 to June 2006 for English language articles using the terms "carbapenem," "imipenem," "meropenem," and "ertapenem." Randomized controlled trials (RCT) were reviewed as were secondary references. Studies were included if a systemic CBP was compared to another CBP or other antibiotic in a prospective RCT. Two independent investigators extracted the data. The Peto Method for meta-analysis of odds ratio (OR) was used to compare the SZ incidence for each CBP relative to comparators.
RESULTS: Of 258 studies identified, 95 did not meet inclusion criteria. 103 additional studies were excluded from the OR analysis due to 0 incidence of SZ in all treatment arms. SZ incidence was determined individually for each drug relative to non-CBP comparators. 28 studies compared IMI to other antibiotics, and the OR was 2.801 (1.84, 4.264). For adults, there was no difference in OR by total daily dose. Of the 8 and 4 studies in which MER and ERT, respectively, were compared to other antibiotics, the OR was 0.96 (0.55, 1.67) and 2.36 (0.32, 17.19) for the 2 drugs. There was no heterogeneity among the compared groups for the three CBPs. 20 studies directly compared IMI to MER; 7 reported > 1 SZ in either treatment arm and were included in the odds ratio calculation. There was a nonsignificant trend toward increased SZ in patients who received IMI, OR 1.48 (0.54, 4.04).
CONCLUSIONS: IMI appears to be more epileptogenic than comparator non-CBP antibiotics, unlike MER. In the RCTs of IMI vs MER there is a trend toward more SZ with IMI but with wide confidence intervals.

Medication Safety

289. **Moving beyond data collection: implementation of medication utilization quality improvements from a non-punitive reporting system.** *Roy Guharoy, Pharm.D.*, David Lehmann, M.D., Nancy Page, M.S., Karen Hirschman, B.S., Scott Murray, Pharm.D., Bruce Stalder, B.S.; SUNY-Upstate Medical University, Syracuse, NY.

PURPOSE: Medication utilization in hospitals across the United States has undergone major scrutiny since the landmark Institute of Medicine Report in 1999, reflecting the frequency of medication errors and a dire need of

systemic changes in preventing adverse events. The objective of our presentation is to describe the impact of a multidisciplinary, nonpunitive adverse events reporting system on qualitative improvements of drug utilization process at our tertiary care teaching hospital.

METHOD: By eliminating the link between staff performance and adverse medication event reporting, the average number of monthly reported events increased from 19 to 142 (p<.001). Our system involves critical analysis of the processes involved in the reported events. Insulin utilization serves as a case vignette. RESULTS: Analysis of the insulin related events demonstrated that 60% of them were physician related due to complexities in ordering the drug by algorithm (i.e., "sliding scale"). Simple standardization of the low and high blood glucose ranges with protocol implementation decreased the number of insulin-related errors from 57/4684 patients in the year prior to implementation to 2/5019 patients in the year following its use (p<.001). Various other initiatives related to medication utilization achieved similar outcome.

CONCLUSION: The non-punitive approach helped us to identify process issues related to actual and prevented adverse events. Increased amount of data helped us to develop quality improvements in medication-use based on human factor principles. We conclude that a similar process can be successfully used at any other institution.

290E. The Safety, Notification, and Follow-Up (SNAFU) Committee. *Kathleen B. Orrico, Pharm.D., BCPS*; University of California San Francisco, Palo Alto, Calif.

PURPOSE: The Safety, Notification, and Follow-Up (SNAFU) Committee was formed at the Palo Alto Medical Foundation and charged with the task of formulating and enacting concerted action plans in response to FDA safety warnings. The presentation will describe the process and development of this novel quality committee and will highlight the key role a pharmacist plays in conducting drug safety surveillance in a group medical practice setting.

METHODS: The SNAFU Committee is composed of key decision-making individuals, including pharmacists, administrators, physicians, compliance officers, a materials management director, and a communications specialist. The clinical pharmacist receives a Safety Alert from the Med Watch E-List (listserve) or other source, composes a brief email synopsis of the situation, and forwards this information, attached to the original warning, to the committee for review. Committee members contribute their expertise and formulate a strategy. The committee assesses the level of risk to patient safety, decides who will need notification, defines parameters for data searches to identify patients, decides if educational materials need to be developed, assigns tasks, and projects a time schedule. The plan is enacted, and notifications are sent to providers and patients as deemed necessary. System changes are implemented to proactively prevent future adverse events.

RESULTS: For calendar year 2006, the Committee processed 41 safety notifications involving 25 medications, 9 medical devices, 3 medical supplies, 2 contact lens cleaning agents, 1 imaging agent, and 1 diagnostic reagent. The average number of days between the time of notification receipt and time to completion was 4.6 days.

CONCLUSIONS: Forming a committee to process safety warnings within a group medical practice allows for a rapid response to drug safety notifications. A pharmacist is uniquely qualified to play a lead role on this committee.

Presented at the American Medical Group Association (AMGA) 2007 Annual Conference in Scottsdale, Aris, March 3, 2007, Improving Patient Safety Through a Novel Quality Committee.

291E. Application of pharmaceutical care principles in minimizing cardiovascular adverse effects of atypical antipsychotic drugs in a community mental health facility. *G.S. Shankar, M.S., Pharm.D., Ph.C., BCPP, CG*, Carmen Nate, M.D., Rajan Radhakrishnan, Ph.D.; Western University of Health Sciences, Pomona, Calif.

PURPOSE: Atypical antipsychotic medications can cause cardiovascular adverse effects such as tachycardia, CAD, blood pressure changes, and arrhythmias. Pharmaceutical care services provided by a clinical pharmacist in a mental health facility, with careful assessment, proper monitoring, education and counseling, can have a greater impact on total patient care, increase quality of life, and minimize healthcare expenditure for patients with schizophrenia in the long term. Primary prevention is usually the best management option for these serious adverse effects.

METHODS: The participants of the study are residents of Community Mental Health and Rehabilitation Center in Pomona, Calif, who are on at least one antipsychotic and have been identified as having cardiovascular risks as per retrospective chart review. Once identified, pharmacist(s) reassessed patients for current cardiovascular risk and made appropriate recommendations to the attending psychiatrist. Every pharmacist assessing the patient is trained to monitor pulse and blood pressure; able to listen to the heart sounds; and able to interpret ECG at least lead II as well as related laboratory values. 86 patients participated in the cardiovascular monitoring by the pharmacists for a period of 12 weeks from May 2006 to September 2006 (Six weeks during May and June and six weeks during

August and September). A total of 55 recommendations were made during this period to the medical staff, and 43 recommendations were accepted.

RESULTS: For this study period, significant cardiovascular reduction was observed through clinical pharmacy intervention in high-risk patients receiving atypical antipsychotics, noting the number of recommendations and acceptance of these recommendations by the medical staff.

CONCLUSION: Most of the pharmacy recommendations were for serum lipids and fasting blood glucose during this study period. More feasibility studies are needed for the clinical pharmacist's service in improving overall cardiovascular risk.

Presented at the Annual meeting of College of Psychiatric and Neurological Pharmacists, April 13-16, 2007.

292E. Samples: A Model for Distribution and Patient Education Involving Pharmacy Students. *Michelle L. Hilaire, Pharm.D.*[1], David Marchant, M.D.[2], Marcia Snook, R.N.[2]; (1)University of Wyoming, Laramie, Wyo, and Fort Collins Family Medicine Residency Program, Fort Collins, Colo; (2)Fort Collins Family Medicine Residency Program, Fort Collins, Colo.

PURPOSE: Sample medications have become a mainstay in some family medicine residency programs for providing care for the underserved. JCAHO accredited facilities are mandated to log medication, dose, amount, lot number, and expiration date to ensure patient safety in the event of a manufacturer recall. We have developed a sample program that follows JCAHO requirements and allows for patient counseling by pharmacy students on all medication samples dispensed.

METHODS: A pager system was developed to allow for accurate logging and dispensing of samples, which are tracked using Excel® log sheets. Providers in our clinic have found this program easier to use because an up-to-date list of current sample medications can be accessed from their computers while seeing patients instead of having to search through cabinets of medications. Pharmacy students are required to counsel all patients receiving samples and do medication reviews with each patient.

RESULTS: Patient satisfaction has improved because they are receiving individualized attention regarding their medications and are asking questions outside of their 20-minute medical appointment. Pharmacy students are enjoying the one on-one-counseling sessions and the ability to share knowledge with patients in a relaxed setting.

CONCLUSION: Although providers were somewhat reluctant at first with not having direct access to sample medications, this program has become a success. Providers have instant access to all samples available in the clinic (listed on different excel tabs by category of disease treated) without having to leave the patient's room. Also, the provider is assured that the patient is getting accurate information from pharmacy students on the use of this medication and that patients have chances to ask questions about the product. We are ensuring that we are compliant with all JCAHO rules and regulations and that our patients are protected in the event of a medication recall.

Presented at the Society of Teachers of Family Medicine Annual Conference, Chicago, Ill, April 25-29, 2007.

Neurology

293. **Implementation and impact of a pharmacist-led educational program for migraineurs.** *Monica L. Skomo, B.S., Pharm.D.*, Shane Desselle, Ph.D., Hildegarde Berdine, Pharm.D., Christine O'Neil, Pharm.D.; Duquesne University, Pittsburgh, Pa.

PURPOSE: To describe the implementation and impact of a pharmacist-led educational program for migraineurs at a university wellness clinic.

METHODS: University employees and students who suffer from recurring headaches were interviewed by pharmacists to determine whether they suffer from migraine using International Headache Society (IHS) criteria. In identified migraineurs, pharmacists assessed migraine-associated disability using the Migraine Disability Assessment (MIDAS) Questionnaire and determined physician consulting status. Identified migraineurs were categorized into 3 groups: (1) never-consulter, (2) lapsed-consulter, (3) current-consulter. Never-consulters and lapsed-consulters were asked to complete questionnaires to identify putative reasons and barriers to physician consultation. Pharmacists provided patients with written education on migraine and its treatment, offered verbal counseling, and encouraged physician follow-up in appropriate patients. Pharmacist follow-up of never-consulters occurred 3 months after the initial appointment to determine whether physician consultation occurred.

RESULTS: Of the 100 headache sufferers that participated in the program, 82 met IHS criteria for migraine, of whom 40 were current-consulters, 22 were never-consulters, and 20 were lapsed-consulters. Mean MIDAS scores were 24.79 for current-consulters, 15.27 for never-consulters, and 8.37 for lapsed-consulters. At the 3-month follow-up, 64% of never-consulters contacted their physician or had future intentions to do so. All the never-consulters who followed up with their physician were diagnosed with migraine. The top three barriers to physician

consultation as identified were as follows: unaware that their headaches were migraines (50%), satisfaction with current treatment (45%), and inconvenience of physician consultation (41%). The top three reasons for lapsing from care were reduced frequency of headache (40%), self-identification of effective therapy (40%), and physician-directed effective therapy (30%).
CONCLUSIONS: This program illustrates that pharmacists can identify migraineurs, raise awareness, provide education, encourage appropriate follow-up, and positively affect migraineur physician consultation rates. Understanding of migraine-associated disability and barriers to appropriate consultation can enhance the care that pharmacists provide to recurring headache sufferers.

Oncology

294. **Retrospective evaluation of the appropriate utilization of darbepoetin alfa and epoetin alfa in cancer patients with anemia.** *Jenny E. Lin, Pharm.D.*, Megan L. Brown, Pharm.D., Rozalin Sarkisian, Pharm.D., Siu-Fun Wong, Pharm.D., FASHP, FCSHP; Western University of Health Sciences, Pomona, Calif.

PURPOSE: This retrospective, single-center chart review compared the efficacy, safety, prescribing pattern, and cost of darbepoetin alfa and epoetin alfa in anemic cancer patients at a community oncology practice.
METHODS: Cancer patients with hemoglobin < 12 g/dL who received darbepoetin or epoetin alfa were included. Efficacy end points assessed hemoglobin response, hemoglobin correction, hematopoietic response, mean change in hemoglobin, and RBC transfusions up to 16 weeks. Secondary objectives assessed prescribing pattern, safety, and costs.
RESULTS: Of 356 patients screened, 141 (70 epoetin and 71 darbepoetin) patients with non-hematologic malignancies were evaluated (87.3% receiving chemotherapy, including 36.6% cisplatin-based). Mean age was 65 years. Gastrointestinal cancer, lymphoma, and breast cancer were most common. Hematopoietic responses were achieved in 52.8% of epoetin group and 50% of darbepoetin group. Inappropriate dosing occurred in 43% of epoetin group and 18% of darbepoetin group. RBC transfusions from week 5 to the end of treatment phase (EOTP) occurred in 11.4% of the epoetin group and 8.9% of the darbepoetin group. Baseline hemoglobin levels were significantly higher (p=0.006) and more patients received appropriate iron supplementation (p=0.020) in the darbepoetin group.Statistical significance was seen between responders and non-responders in baseline hemoglobin (p=0.003) in the epoetin group, but not in the darbepoetin group. Darbepoetin Q3W (83%) dosing had better synchronization with chemotherapy than Q2W (58%). Diarrhea was the most common adverse effect in both groups. The 2-week cost analysis comparison favored darbepoetin.
CONCLUSIONS: Similar hematopoietic response was seen between the two treatment groups, but higher incidence of RBC transfusions was seen in the epoetin group. Improved knowledge of clinicians over time may have led to earlier initiation of darbepoetin therapy. Comparing responders to nonresponders, early initiation of epoetin may improve response. Darbepoetin appears to be more cost-effective due to less frequent dosing interval, higher profit margins, and improved prescribing patterns.

295. **Assessment and management of chemotherapy-induced peripheral neuropathy in an outpatient adult oncology population.** *Stephen Harnicar, Pharm.D.*, Suzanne A. Nesbit, Pharm.D., BCPS, Amy Hatfield, Pharm.D., BCOP, Audrea Szabatura, Pharm.D., BCOP; The Johns Hopkins Hospital/Department of Pharmacy, Baltimore, Md.

PURPOSE: Chemotherapeutic agents, such as taxanes, platinum compounds, and bortezomib, have been associated with peripheral neuropathy. The primary purpose of this study was to evaluate the assessment and documentation frequency of chemotherapy-induced peripheral neuropathy (CIPN) in outpatients at The Johns Hopkins Hospital. The secondary end points were to examine the management of patients with CIPN and chemotherapy dose modification or discontinuation because of CIPN.
METHODS: A retrospective review was performed of adult oncology patients in the outpatient clinic who received their first dose of paclitaxel, docetaxel, cisplatin, carboplatin, oxaliplatin, or bortezomib in January 2006 thru March 2006. A documented physician diagnosis or two or more of the following will be needed for the designation of chemotherapy-induced peripheral neuropathy: a neuropathic pain score or numeric pain score of 3 or greater; adjuvant medications (i.e., anticonvulsants, antidepressants) used for neuropathy; and documented neuropathic symptoms. Data collected included: neuropathy assessment frequency, demographic information such as pertinent medical history and oncologic diagnosis, pain scores at the time of chemotherapy administration, and patient motor and/or sensory symptoms. Chemotherapy regimens and associated administration dates, cumulative dose of chemotherapy, and adjuvant therapy used to treat peripheral neuropathy were collected.

RESULTS: 77 patients were evaluated. Thirty-five percent had CIPN by either documentation or meeting criterion. Assessment of CIPN was documented in 64% of all patient visits. Chemotherapy modifications and adjuvant analgesic therapy occurred in 48% of the patients with CIPN.
CONCLUSIONS: CIPN was documented in more than a third of our patients receiving paclitaxel, docetaxel, cisplatin, carboplatin, oxaliplatin, or bortezomib. CIPN can affect a patient's course of treatment and quality of life. All patients receiving taxanes, platinum compounds, or bortezomib should be assessed for CIPN at every clinic visit to ensure prompt diagnosis and treatment.

Pediatrics

296. **Pediatric dosing at 14 HIV clinics in Kenya.** Jeff Shelton, Pharm.D.[1], Sarah Durham, Pharm.D.[1], *Ellen M. Schellhase, Pharm.D.*[1], Beatrice Jakait, R.Ph.[2]; (1)Purdue University, Ind; (2)AMPATH, Kenya.

PURPOSE: Academic Model for Prevention and Treatment of HIV/AIDS (AMPATH) is a comprehensive program that treats more than 50,000 patients of which 7000 are children. Care is provided in 14 mostly rural clinics located throughout western Kenya. The purpose of this project was to improve pediatric dosing of ancillary medications in AMPATH clinics by creating a pediatric dosing guide for prescriber use. In addition, this project allowed the identification of the medications that are most often dosed inappropriately.
METHODS: Prescription data from pediatric patients enrolled in AMPATH was collected for 31 days in July 2005 (prior to distribution of the dosing guides) and for 30 days in June 2006 (about 1 month after distribution). Data collected included medication dosage, age, and weight. For the 16 orally available agents, the dosing guide included recommended dose(s) by indication, maximum dose, and additional administration information.
RESULTS: Baseline data was evaluated for 1106 prescriptions. 50% were within the recommended dose, 15% were incomplete, 27% were above the recommended dose, and 8% were below the recommended dose. Follow-up data was collected for 2583 prescriptions. 51% were within the recommended dose, 10% were incomplete, 23% were above the recommended dose, and 16% were below the recommended dose. There was a 5% decrease in the number of incomplete prescriptions. Accuracy of prescribing by clinic ranged from 45% to 80%. Azithromycin and chlorpheniramine were most often overdosed. Paracetamol, ibuprofen, and griseofulvin were most often underdosed.
CONCLUSIONS: Growth in the program accounted for the increase in medications prescribed. There was a decrease in the number of incomplete prescriptions. Minimal changes in dosing accuracy were seen after distribution of the dosing guide. Additional prescriber education is needed to benefit from the implementation of the dosing guide. Using these data, interventions need to be targeted toward the most problematic medications.

Pharmacoeconomics/Outcomes

297E. **Impact of a long term comprehensive intervention program on clinical and economic outcomes.** *Ahuva Lustig, M.Sc.*; Barzilai Medical Center, Ashkelon, Israel.

PURPOSE:Antibiotics may account for up to 30% of a hospital's drug budget. We developed a comprehensive intervention program in response to a steady increase in use and costs of antibiotics since 2000.
METHOD: Barzilai Medical Center is a general hospital of 500 beds serving 400,000 inhabitants. Use of antibiotics and costs using daily defined doses (DDD) per 100 hospitalization days were analyzed during a 6-year period after program implementation. The program combined several well known methods such as formulary restrictions, special approval for restricted drugs, education of health staff, early switches from parenteral to oral therapy, and preparation of individual intravenous admixture of antibiotics by the pharmacy staff. Statistical analysis used student t test for continuous variables. For all analyses a 2-sided test was used.
RESULTS:Compared with 1999 (last year before intervention), average use/100 hospitalization days decreased by 17.2% for nonrestricted drugs and 32% (p=0.006) for restricted drugs. Costs ($)/100 hospitalization days decreased by 18.6% for nonrestricted drugs and by 37.8% (p=0.05) for restricted drugs. Usage and costs/100 hospitalization days remained fairly stable during the following 6 years compared to 1999. Overall mortality and rehospitalization didn't change significantly after the intervention program.
CONCLUSIONS:Cost-saving effects were demonstrated in a large number of studies, but the duration of the follow up was mostly short. This study is based on a long follow-up of the interventional program. The program was highly successful and had long-lasting effects.
Not published or presented yet

298. **Development and implementation of a pharmacist-managed medication adherence and medication therapy management clinic in a family practice office.** *Michele C. Miller, Pharm.D. candidate*, Monica L. Skomo, Pharm.D., Hildegarde J. Berdine, Pharm.D., BCPS; Duquesne University, Pittsburgh, Pa.

PURPOSE: The positive impact of pharmacist interventions has been described in a variety of practice settings. However, little information is currently available concerning the benefits of physician-pharmacist partnerships in family practice settings. The purpose of this project is to describe the development and implementation of a pharmacist-managed medication adherence/medication therapy management clinic in a family practice office.
METHODS: Planning and details regarding space, furniture, equipment, compensation, and the service itself were addressed with the collaborating physician 6 months before the first patient was seen. Patients are obtained through physician referral and include 1) non adherent patients taking four or more medications chronically; 2) patients with hypertension, hyperlipidemia, or diabetes who are nonadherent to their medication, dietary, or exercise regimens; and 3) patients ready for smoking cessation counseling. Initial appointments are scheduled for 1 hour and are used to collect patient information, perform physical assessments, counsel on non-adherence, and set clinical goals for future visits. PIDS (Pharmacist Intervention Documentation System) is used to document pharmacist interventions and pertinent patient information. A SOAP note is printed and placed in the patient chart for physician review. Follow-up appointments are used to assess changes in adherence, behavior related to diet and exercise, and clinical biomarkers. Data currently being collected include 1) disease specific clinical markers, 2) quality of care markers, 3) patient satisfaction, 4) patient understanding of disease, 5) medication adherence by pill count, refill records, and 6) types of pharmacist interventions.
CONCLUSIONS: The development and implementation of a pharmacist-managed medication adherence/ medication therapy management clinic in a family practice office is a tremendous opportunity for pharmacists and has the potential to enhance patient care. This type of service offered in a unique setting is an additional health care arena where pharmacists can make a positive impact and ultimately improve patient outcomes.

299. **Model for cost justification of new critical care clinical pharmacy services in a community teaching hospital.** *Amy L. Beatty, Pharm.D., BCPS*, Margaret A. Huwer, Pharm.D.; Doctors Hospital, OhioHealth, Columbus, Ohio.

BACKGROUND: Health-care systems require justifying the cost of new services to optimize expenditures. Although many clinical pharmacy activities provide value, the cost impact is difficult to document. Commercial computer programs to analyze pharmacy activities for cost savings are available, but many will be associated with an added expense to the clinical pharmacy service.
PURPOSE: To describe the development and implementation of a model for cost justification of critical care clinical pharmacy services in a community teaching hospital.
METHODS: A literature search was performed in January 2006 for studies of pharmacist intervention tracking, cost-effectiveness analysis, and supporting data for clinical pharmacy services. Guided by these studies, we developed a model for recording and analyzing the impact of these interventions. Clinical pharmacy interventions were separated into three classifications in the model: Quality of care, drug cost savings, and cost savings of avoiding adverse drug events. This model was applied to a critical care pharmacist's interventions from March 2006 to December 2006.
RESULTS: The clinical pharmacist reported a 97% acceptance rate for recommendations improving quality of care, and a cumulative drug cost savings of $18,809. The potential for cost-avoidance of adverse drug events during the review period was $1,804,800, based on literature estimates of $2400 in additional hospitalization costs per adverse event. At the end of the study, an additional financial analysis demonstrated an estimated drug cost savings of $177.29 per ICU visit compared with the previous year, totaling $164,365 for the 10-month review period.
CONCLUSIONS: This model may assist in justifying a new critical care clinical pharmacy service by providing cost, quality, and safety data to support the pharmacist's impact on drug expenditures, as well as patient safety.

Pharmacoepidemiology

300. **Self-Medication with antibiotics in the Jordanian population.** *Sayer I. Al-azzam, Pharm.D.*, Belal A Al-husein, M.sc., Firas Q Alzoubi, FRCS; Jordan University of Science and Technology, Irbid, Jordan.

PURPOSE: This survey was conducted to estimate the prevalence of self-medication with antibiotics in Jordan and to evaluate factors associated with antibiotics misuse.
METHODS: A validated questionnaire was used to collect data from a sample of 1943 households, (9281 persons), selected from different cities in Jordan.

RESULTS: Eight hundred and forty two (41.4%) of the study population had used antibiotics without a prescription within one month prior to the study. Self medication with antibiotics was found to be significantly associated with age, income, and level of education. The main reason that was indicated for the self-medication was previous experience with medication efficacy. The main source of medicines was an old medications reservoir and friends.

CONCLUSION: The prevalence of self-medication with antibiotics in Jordan is alarmingly high. Given the growing global resistance to antibiotic drugs and documented health issues related to inappropriate use of such drugs, our findings has major public health policy implications for countries like Jordan.

Pharmacy Administration

301. **Levalbuterol usage in an urban acute care teaching hospital: impact of formulary deletion and automatic therapeutic interchange to albuterol.** *Radhika Pisupati, Pharm.D.*[1], Sapna Bhambhani, Pharm.D.[2]; (1)St. Joseph's Regional Medical Center, Paterson, NJ; (2)Morgan Stanley Children's Hospital of NewYork-Presbyterian, New York, NY.

PURPOSE: A review of clinical trials and comparative product reviews indicate that data showing superior safety and efficacy of levalbuterol over racemic albuterol are either lacking or are inconclusive. Levalbuterol costs significantly more than racemic albuterol. These factors, along with high usage at our institution, prompted deletion of levalbuterol from the formulary in October 2005 after review by the Pharmacy & Therapeutics Committee and Medical Board. A therapeutic interchange of levalbuterol to albuterol was instituted in adult patients (verbal clarification is required for pediatric patients). Conversion ratio is based on the National Heart Lung and Blood Institute's Asthma guidelines (2002). The impact of these measures on levalbuterol usage is examined in this study.

METHODS: Orders for levalbuterol in adults were converted to albuterol by pharmacists using a 1:2 dosing ratio at the same frequency with the exception of q8h levalbuterol orders, which were converted to q6h albuterol. Data on inpatient use of levalbuterol and purchase reports before and after the implementation of the therapeutic interchange were analyzed.

RESULTS: Levalbuterol usage declined significantly following formulary deletion and institution of the therapeutic interchange. At baseline, ~170 patients per month received levalbuterol. Usage declined to < 10 patients/month 4 months after the interventions started (February 2006); by May 2006, ≤ 1 inpatient had received levalbuterol. Usage has remained at this level. During the 1-year period preceding the interventions (10/04–10/05), 69,000 single dose units of levalbuterol were purchased. After the interventions began (11/05), 0 units were purchased. No increases in adverse events were reported. Our interventions resulted in a cost-avoidance of ~ $80,000–$100,000/year.

CONCLUSIONS: Formulary deletion and implementation of a therapeutic interchange to albuterol were successful in reducing levalbuterol usage without compromising safety or efficacy. This is a viable cost savings measure for consideration by other institutions.

302. **Snapshot Evaluation of Clinical Pharmacists' Pharmacokinetic Monitoring.** *Carolyn K. Stephens, Pharm.D.*, John Hoeldtke, Pharm.D., BCPS; Bay Pines VA Healthcare System, Bay Pines, Fla.

PURPOSE: The pharmacy department at Bay Pines VA Healthcare system did not have a system in place to assess the quality of pharmacokinetic monitoring. The pharmacokinetic consults were completed by clinical pharmacists and documented in the electronic patient record but were not evaluated using a structured process. The goal for this project was to develop an assessment tool that could evaluate pharmacokinetic monitoring in a formalized and consistent manner.

METHODS: A group of inpatient clinical pharmacists was formed to develop the assessment tool of pharmacokinetic documentation and drug regimen design and monitoring. Using clinical guidelines and experience, the workgroup adapted the American Society of Health-System Pharmacists criteria based assessment tool ("snapshot") that was developed for use in the Residency Learning System evaluation of residency training.

RESULTS: The tool was developed and implementation took base on a trial basis. Using the one page assessment tool (ASHP RLS "snapshot"), clinical pharmacists evaluated three pharmacokinetic progress notes for each pharmacist per month. This assessment was accomplished by peer review. The data gathered from these reviews are being used for staff development and quality assurance purposes.

CONCLUSION: Adaptation of the ASHP "snapshot" evaluation form is a method available to evaluate clinical pharmacist activities.

303. **Effects of a pharmacist-to-dose computerized request on promptness of antimicrobial therapy.** *William R. Vincent III, Pharm.D.*, Craig A. Martin, Pharm.D., P. Shane Winstead, Pharm.D., Kelly M. Smith, Pharm.D., Daniel A. Lewis, Pharm.D.; University of Kentucky HealthCare, Lexington, Ky.

PURPOSE: Pharmacist-managed drug therapy for vancomycin and aminoglycosides is associated with clinical and economic benefits. Our institution implemented a pharmacist-to-dose (PTD) request within the electronic prescribing system. PTD consultations provide patient-specific dosing for medications and are frequently requested for vancomycin and aminoglycosides due to their narrow therapeutic windows. Concern was raised that these consults may delay administration of first antibiotic doses.
METHODS: A retrospective review was conducted of patients hospitalized from January 2004 to June 2006 with suspected pneumonia who received vancomycin, tobramycin, or gentamicin via PTD (study) or routine prescriber order entry (control). The primary end point was time to pharmacist completion of PTD request. Secondary end points included medication turn-around times for first doses of vancomycin, aminoglycosides, and other antibiotics, dose adjustment for renal dysfunction, medication errors, and time of order entry. Multivariate analysis was conducted to identify predictors of time to pharmacist verification and time to administration of first antibiotic doses.
RESULTS: Median time for pharmacist completion of PTD requests was 29 minutes. There was no statistically significant difference in median turn-around times for vancomycin or aminoglycosides (185 vs. 138 min, p=0.45) or for any antibiotic (134 vs. 118 min, p=0.42) between the study (n=49) and control groups (n=48), respectively. Fewer medication errors were reported in the study group (5 vs. 18 errors, p=0.002). On multivariate analysis, renal dysfunction was a significant predictor of increased time for pharmacist order entry.
CONCLUSIONS: A computerized pharmacist-to-dose request did not delay turn-around times for first antibiotic doses and decreased medication errors.

304. **Application of heuristic methods to pharmacy project evaluation by incorporating a weighted priority scale.** *Carisa J. Masek, Pharm.D.*, Erin Iselin, Pharm.D., Colleen Malashock, Pharm.D., Rick VanCura, Lori Murante, Pharm.D., Elizabeth Hermsen, Pharm.D., Stephanie Johnson, Pharm.D., BCOP, Lori Peters, Pharm.D., Sara Smith-Shull, Pharm.D., M.B.A., Lisa Worrall, Pharm.D., BCPS; The Nebraska Medical Center, Omaha, Neb.

PURPOSE: Projects or initiatives designed to improve processes or patient care compete for the same limited resources: time, human, and financial. At a large academic medical center, a panel was created to evaluate all proposed projects and initiatives that require pharmacy resources. The panel's charge was to determine the priority ranking for project initiation relative to other proposals, while accounting for ongoing projects and initiatives.
METHODS: The heuristic approach to project evaluation incorporated a weighted priority scale. Weighted priority scales are used by industry to apply standardized criteria to projects that will consume resources. The concept was applied to pharmacy by including the evaluation of resources and outcomes important within the healthcare setting. The weighted prioritization scale was organized into four main categories: safety, value, resources, and benefit. Each project was evaluated by panel members and assigned a score in the four categories. It was determined that the safety of a health care project carried as much weight as value, resources consumed, and benefit. Safety of a project was rated on a scale of 1 through 9 (1 = negative impact on safety; 9 = positive impact on safety.) The other three evaluation categories were divided into subcategories. Each subcategory had a scale of 1–3 with a maximum category score of 9. The subcategories for project value were evidence-based; innovative approach; and defined measurable outcomes. Project resources were divided into cost (non-human resources), human resources required for implementation, and human resources required for maintaining a program. The subcategories of project benefit were patient outcomes; revenue/productivity/efficiency; and staff satisfaction. The scores were combined, and the project was assigned a total score. Scores ranged from 4 to 36, and the high score indicated a higher priority project. The scale was applied to computerized physician order entry and bedside bar scanning for validation.

Transplant/Immunology

305. **Efficacy and safety of rabbit antithymocyte globulin induction in adult living-unrelated renal transplant recipients.** James T. Miller, Pharm.D., Linda J. Stuckey, Pharm.D., Curtis D. Collins, Pharm.D., M.S., Cheryl Bauzon, Pharm.D. Candidate, *Jeong M. Park, M.S., Pharm.D.*; University of Michigan, Ann Arbor, Mich.

PURPOSE: Induction with rabbit antithymocyte globulin (Thymoglobulin", TMG) is widely accepted in deceased-donor renal transplant to prevent acute rejection (AR) and delayed graft function (DGF); however, its routine use remains controversial in living-donor renal transplant due to concerns for increased risk of infection

and malignancy. Our transplant center implemented TMG induction (1.5 mg/kg IV daily for 5 days, adjusted for leucopenia) for living-unrelated renal transplant (LURT) in January 2005. This study evaluated the efficacy and safety of TMG induction in LURT.

METHODS: A retrospective review of medical records was performed on consecutive LURT recipients between January 2003 and March 2006 who met the inclusion criteria: age ≥ 18 years, first transplant, non-black, and panel reactive antibody (PRA) < 30%. Maintenance immunosuppression consisted of cyclosporine microemulsion, mycophenolate mofetil, and steroids. Data were collected for baseline characteristics of recipients/donors, biopsy-proven AR, DGF, graft loss, patient death, cytomegalovirus (CMV) disease, and malignancy during 1 year post-transplant. Chi-square or Fisher s exact test was used to analyze categorical variables and Student t-test was used for continuous variables.

RESULTS: Patients receiving no induction and TMG induction were comparable for age and gender of recipient/donor, PRA, HLA mismatch, etiology of end-stage renal disease, and CMV serostatus.

Outcomes	No induction (n = 40)	TMG induction (n = 34)	p
Biopsy-proven AR	19 (47.5%)	0	<0.001
DGF	0	0	-
Graft loss	2 (5.0%)	3 (8.8%)	NS
Patient death	2 (5.0%)	2 (5.9%)	NS
CMV disease	2 (5.0%)	2 (5.9%)	NS
Malignancy	1 (2.5%)	1 (2.9%)	NS

NS = not significant (p>0.05)

CONCLUSION: LURT is at high risk for AR, and antibody induction should be considered. Our single-center experience showed that TMG induction was efficacious in preventing AR in adult LURT recipients without substantial infectious or malignant complications within 1 year post-transplant.

306. Impact of calcineurin inhibitor conversion from cyclosporine to tacrolimus on pharmacokinetics of mycophenolate mofetil in diabetic renal transplant recipients. *Jeong M. Park, M.S., Pharm.D.*, Kathleen D. Lake, Pharm.D., Diane M. Cibrik, M.D., M.S.; University of Michigan, Ann Arbor, Mich.

PURPOSE: The effects of cyclosporine, which inhibits enterohepatic recirculation of mycophenolic acid (MPA)/ MPA glucuronide (MPAG), and tacrolimus, which may alter gastric emptying rate, on pharmacokinetics of mycophenolate mofetil (MMF) have not been documented in patients with diabetic gastroparesis. This study evaluated the changes in MMF pharmacokinetics when cyclosporine was converted to tacrolimus in renal transplant recipients with long-term diabetes.

METHODS: Renal transplant recipients with juvenile-onset diabetes were switched from cyclosporine to tacrolimus while taking MMF 1g twice daily. Twelve-hour total plasma concentration-time profiles of MPA and MPAG were obtained following a morning dose of MMF on 2 occasions: first during coadministration with cyclosporine and second at steady-state after switching to tacrolimus. MPA and MPAG concentrations were measured using HPLC, and their pharmacokinetic parameters were determined by non-compartmental methods.

RESULTS: Eight patients participated (age 46 ± 9 years, 4 males, 20 ± 14 months post-transplant, duration of diabetes 35 ± 7 years, and serum creatinine 1.2 ± 0.3 mg/dL). Concomitant medications, serum creatinine, and albumin remained stable between the studies.

	Cyclosporine	Tacrolimus	P
MPA-AUC (mg·hr/L)	45.2 ± 15.9	66.2 ± 29.2	0.012
MPA-C_0 (mg/L)	2.3 ± 2.1	4.6 ± 3.7	0.008
MPA-Cmax (mg/L)	15.0 ± 6.9	16.1 ± 9.7	0.773
MPA-Tmax (h)	1.0 ± 0.4	1.2 ± 0.8	0.461
MPA-CL/F (L/hr/kg)	0.21 ± 0.05	0.15 ± 0.05	0.004
MPAG-AUC (mg·hr/L)	1180 ± 291	913 ± 299	0.009

The change in MPA-AUC was highly variable (mean 46%, 95% CI = 24%–69%), and it was poorly reflected (r^2 = 0.39) and overestimated by MPA-C_0 (mean 121%, 95% CI = 116%–125%).

CONCLUSION: Conversion from cyclosporine to tacrolimus increased MPA exposure without changing the rate of absorption in renal transplant recipients with long-standing diabetes. Monitoring MPA-AUC, but not MPA-C_0 may be warranted to manage MMF dosing when switching concomitant calcineurin inhibitors.

307. **Valganciclovir does not affect the steady-state pharmacokinetics of mycophenolate mofetil.** *Jeong M. Park, M.S., Pharm.D.*[1], Michal J. Figurski, Ph.D.[2], Leslie M. Shaw, Ph.D.[2], Kathleen D. Lake, Pharm.D.[1]; (1)University of Michigan, Ann Arbor, MI; (2)University of Pennsylvania, Philadelphia, Pa.

PURPOSE: It has been proposed that ganciclovir may compete with glucuronide metabolites of mycophenolic acid (MPA) for renal tubular excretion, but a single-dose pharmacokinetic interaction study of two drugs did not support the hypothesis. We evaluated the effect of valganciclovir (prodrug of ganciclovir) on pharmacokinetics of mycophenolate mofetil (MMF) at steady-state.
METHODS: Renal transplant recipients taking stable doses of tacrolimus, MMF, and prednisone for immunosuppression and valganciclovir 450 mg daily for cytomegalovirus prophylaxis were enrolled. Serial blood samples were collected over 12 hours following a morning dose of MMF on 2 occasions: first while taking MMF and valganciclovir together (MMF + VGCV) and second at least 5 days after discontinuation of valganciclovir (MMF alone). Patients should remain on the same dose of MMF at least 1 week prior to first study through second study. Total plasma concentrations of MPA, MPA glucuronide (MPAG) and MPA acyl glucuronide (AcMPAG) were measured using HPLC, and their pharmacokinetic parameters were determined by non-compartmental methods.
RESULTS: Ten patients participated (age 45 ± 12 years, 6 males, 3 simultaneous kidney-pancreas transplant, 91 ± 2 days post-transplant, and serum creatinine 1.2 ± 0.2 mg/dL). Concomitant medications, serum creatinine and albumin remained stable between the studies. MPA-AUC ratio was 0.98 [90% CI = 0.82–1.17] and MPA-Cmax ratio was 0.96 [90% CI = 0.73–1.24].

	MMF + VGCV	MMF alone	P
MPA-AUC (mg·hr/L)	51.6±9.1	53.1±18.6	0.75
MPA-Cmax (mg/L)	12.0±4.4	11.9±4.9	0.96
MPA-Tmax (h)	1.2±0.7	1.6±0.9	0.37
MPA-CL/F (L/hr/kg)	14.8±2.8	15.9±6.7	0.55
MPAG-AUC (mg·hr/L)	643±243	640±205	0.94
AcMPAG-AUC (mg·hr/L)	6.2±3.6	5.9±6.7	0.64

CONCLUSION: Coadministration of valganciclovir 450 mg/day for 90 days had no significant effect on steady-state pharmacokinetics of MMF in stable renal transplant recipients. Ganciclovir from this low dose of valganciclovir does not seem to interfere with renal excretion of MPA and its glucuronide metabolites.

RESIDENTS AND FELLOWS RESEARCH IN PROGRESS

ADR/Drug Interactions

308. **Adverse serotonergic effects observed in patients receiving concomitant linezolid and serotonin re-uptake inhibitors.** *Valerie A. San Luis, Pharm.D.*[1], Michael D Kraft, Pharm.D.[1], Daryl D. DePestel, Pharm.D.[1], Daniel Streetman, Pharm.D.[1], Linda Welage, Pharm.D.[1], Ian B. Holis, Pharm.D.[1], Erica Stein, Pharm.D.[1], Christian J. Teter, Pharm.D., BCPP[2]; (1)University of Michigan Health Systems, Ann Arbor, Mich; (2)Northeastern University & McLean Hospital, Boston, Mass.

PURPOSE: The purpose of this study is to determine whether the concomitant use of linezolid and SRIs is associated with an increase in adverse effects that are consistent with serotonin excess.
METHODOLOGY: This is a retrospective, case-controlled study. Patients who received linezolid and SRI for at least 24 hours at the University of Michigan Medical Center between January 1, 2000 and December 31, 2005 were identified via electronic databases. Cases will be matched to control patients who received SRI and vancomycin or daptomycin. Medical records will be reviewed to evaluate for the presence of symptoms consistent with serotonin excess and serotonin syndrome. The primary outcome will be the incidence of tremor observed in patients who received concomitant linezolid and SRI as compared to patients who received either vancomycin or daptomycin and SRI.
RESULTS: Data collection is ongoing. Tremor was observed in 7 (6.8%) of 103 patients who received linezolid and SRI. Patients who received a longer duration of concomitant linezolid and SRI therapy were more likely to experience tremor than those with a shorter duration of therapy (13.8 vs. 9.3 days, p<0.05), as were patients who received a longer duration of linezolid therapy (15.0 vs. 12.6 days, p<0.05). Patients with a history of renal disease were more likely to experience tremor than those who did not (14.7% vs. 2.89%, p<0.05), as were patients with a history of hepatic disease (17.7 vs. 2.9, p<0.05).
CONCLUSIONS: Interim data analysis indicates that the incidence of tremor is low with concomitant linezolid and SRI therapy. Patients with a history of renal or hepatic disease may be more likely to experience tremor when

receiving concomitant linezolid and SRI therapy. Further data collection and analysis are required to confirm these results and assess the possible clinical implications.

Ambulatory Care

309. **Clinical efficacy and safety profile of ezetimibe/simvastatin (Vytorin®) 10/80 mg in patients previously receiving atorvastatin (Lipitor®) 80 mg.** *Andrea M. Mendyk, Pharm.D.*, Kim Kim, Pharm.D., Dayna Mitchell, Pharm.D., Robert Silverman, Pharm.D., Jane Third, M.D.; Edward Hines, Jr. VA Hospital, Hines, Ill.

PURPOSE: Recent literature has shown that combination therapy ezetimibe/simvastatin 10/80 mg results in a statistically significant decrease in LDL cholesterol from baseline compared to atorvastatin 80 mg (59% vs. 53%) and greater LDL goal achievement. Based clinical trials, potential cost savings and other VA experiences, the Hines VA Pharmacy and Therapeutics Committee approved patients on atorvastatin 80 mg to be switched to ezetimibe/simvastatin 10/80 mg in April 2006. The goal of this research is to validate that the switch from atorvastatin to ezetimibe/simvastatin results in the anticipated benefits of clinical efficacy, preservation of safety, and cost savings. The primary objective is to determine the percent change in LDL after patients were switched from atorvastatin 80 mg to ezetimibe/simvastatin 10/80 mg. The secondary objectives are to determine differences in safety, achievement of LDL goal in a randomized subset of patients, the percent of those patients on other concurrent lipid-lowering therapy, cost savings and medication possession ratio (MPR) prior to and after the switch.
METHODS: A retrospective study will be performed at Edward Hines, Jr. VA Hospital. Patients switched from atorvastatin 80 mg to ezetimibe/simvastatin 10/80 mg with a previously active outpatient prescription for atorvastatin 80 mg during the timeframe from March 2005 through March 2006 will be evaluated for inclusion and exclusion criteria. Outpatient charts will be reviewed using the computerized patient record system. Eligible patients had their medical record reviewed for laboratory data, goal LDL based on risk status, prescription refill history, concurrent lipid-lowering medications and reported adverse drug reactions. The first 90 eligible patients will be randomly selected for analysis.
RESULTS/CONCLUSIONS: Results, conclusions and future directions of this study will be presented at the American College of Clinical Pharmacy (ACCP) annual meeting.

Cardiovascular

310. **The effects of calcitriol (1α, 25-[OH]2 vitamin D3) on renin expression in hypertensive patients without vitamin D deficiency.** *Benjamin W. Van Tassell, Pharm.D., BCPS*, Mark A. Munger, Pharm.D., FCCP; University of Utah, College of Pharmacy, SLC, Utah.

PURPOSE: Vitamin D deficiency is associated with increasing renin-angiotensin system (RAS) activity, leading to hypertension and cardiovascular disease. Treatment with vitamin D directly inhibits renin transcription in animal models. In human subjects, vitamin D therapy reduces cardiovascular mortality in hemodialysis patients with secondary hyperparathyroidism (a surrogate marker of reduced vitamin D activity). Vitamin D therapy in RAS activated human hypertension may therefore reduce vascular pressure and potentially reduce cardiovascular events. To date, vitamin D effects on the RAS have not been systematically investigated in patients without vitamin D deficiency.
METHODS: This randomized, double-blind, placebo-controlled crossover study will measure the impact of an oral vitamin D regimen (calcitriol 1 mcg daily) on renin transcription. Eligible patients will have stage I hypertension (following discontinuation of any antihypertensive medication) without vitamin D deficiency. The primary outcome will evaluate renin transcription as measured by plasma renin activity (PRA), plasma renin concentration (PRC), and renin mRNA during a 24-hour collection period following 2-week treatment with vitamin D or placebo. Secondary end points will measure vitamin D effects on inflammatory cytokines, calcium homeostasis, and cardiovascular hemodynamics. As genetic polymorphisms in the coding and promoter regions of the vitamin D receptor (VDR) may also affect renin transcription, patients will also be genotyped for several common VDR polymorphisms.
RESULTS: Our pilot-data confirm the potential for vitamin D inhibition of renin in this patient population. A 4-day course of oral vitamin D (calcitriol 1 mcg daily) produced a 24% reduction in PRA (4 hours post-dose) in a hypertensive, but otherwise healthy, population. This result is consistent with the magnitude of vitamin D-induced PRA reductions in animal models and human subjects with secondary hyperparathyroidism.
CONCLUSION: Vitamin D inhibition of renin transcription may be a viable therapeutic option to reduce RAS activity in patients with stage I hypertension.

311. **Evaluation of appropriate beta-blocker use in patients with heart failure.** *Carleton B. Maxwell, Pharm.D.*[1], Shannon W. Finks, Pharm.D.[2], Kelly C. Rogers, Pharm.D.[2], Robert B. Parker, Pharm.D.[2]; (1)VA Medical Center at Memphis, Memphis, TN; (2)University of Tennessee College of Pharmacy, Memphis, Tenn.

PURPOSE: Beta-blocker therapy with carvedilol or sustained release (SR) metoprolol succinate reduces morbidity and mortality in patients with heart failure (HF) and reduced ejection fraction (EF). Use of one of these agents is recommended in current HF treatment guidelines since other beta-blockers (e.g., immediate release metoprolol, atenolol) have no proven benefit. Therefore, the purpose of this study is to determine the extent of appropriate (carvedilol or SR-metoprolol) or inappropriate (all other beta-blockers) beta-blocker use in patients with HF and an EF ≤ 40% and to compare the effects of beta-blocker selection (appropriate versus inappropriate) on morbidity and mortality.
METHODS: Patients prescribed beta-blockers at the Memphis VAMC with HF and an EF ≤ 40% that either presented to the emergency department (ED), an outpatient clinic, or were hospitalized between 01/01/05 and 06/30/05 were retrospectively identified. Demographic data, beta-blocker received, EF, number of ED visits, hospitalizations for any cause, concomitant medications, and mortality were recorded.
RESULTS: A total of 384 patients were identified. Patients were prescribed appropriate beta-blockers significantly (p=0.013) more often (n=218, 57%) than inappropriate agents (n=166, 43%). There was a trend toward fewer patients with at least one hospitalization (27% vs 33%) or ED visit (36% vs 47%) in the appropriate versus inappropriate therapy groups, respectively, despite a lower EF (26.4 ± 7.8% vs 31.1 ± 7.2%).
CONCLUSIONS: Carvedilol and SR metoprolol are significantly under-utilized in this patient population which is associated with trends in increasing morbidity. Additional data analysis will focus on differences in mortality and concomitant medication use between the two groups. Strategies to increase appropriate beta-blocker use should be implemented.

312. **Evaluating possible correlations with metabolic syndrome in patients with an acute coronary syndrome.** *Kathryn D. Mathews, Pharm.D.*[1], Nicholas B. Norgard, Pharm.D.[1], Toni L. Ripley, Pharm.D., BCPS[2]; (1)University of Oklahoma Health Sciences Center, College of Pharmacy, Oklahoma City, Okla; (2)University of Oklahoma College of Pharmacy, Oklahoma City, Okla.

PURPOSE: Metabolic syndrome (MS) is a constellation of risk factors predisposing individuals to cardiovascular disease and type II diabetes. It is important to recognize the specific characteristic features consistent with MS in order to prevent future complications. The World Health Organization (WHO), the National Cholesterol Education Program (NCEP), and the International Diabetes Federation (IDF) provide different definitions of MS. This study seeks to analyze possible associations between MS and clinical outcomes in acute coronary syndrome (ACS).
METHODS: The study was a prospective analysis comparing the severity of ACS in patients meeting the criteria for MS, based on the three separate guidelines. Patients admitted to the coronary care unit (CCU) for an ACS are included. Each set of guidelines were used to separate the patients into MS and non-MS groups. Groups were compared by TIMI risk score on arrival and by in-hospital and 6-month risk according to the GRACE algorithm. Data were analyzed using the t-test and chi-square test of association.
PRELIMINARY RESULTS: Of 16 patients admitted for ACS, 94% met IDF criteria, 56% met WHO criteria, and 69% met NCEP criteria. According to TIMI risk score, patients at high risk included 63.3% of the NCEP population and 66.7% of the WHO population. Based on the NCEP definition, risk of in-hospital and 6-month death/MI was not different in the MS and non-MS groups (12.6% vs 12.2%, p=NS; 21.3% vs 21.2%, p=NS). Based on the WHO definition, risk of in-hospital and 6-month death/MI was not different in the MS and non-MS groups (13.8% vs 10.9%, p=NS; 22.2% vs 20%, p=NS).
CONCLUSION: Preliminary results revealed no significant association between risk of cardiac events and MS. This finding is most likely secondary to the fact that the sample size was small. A complete analysis following enrollment of 50 patients is planned and will be presented.

313. **Evaluation of appropriate spironolactone use in patients with heart failure (HF).** *Timmye L. Edwards, Pharm.D.*[1], Robert Parker, Pharm.D.[2], Kelly C. Rogers, Pharm.D.[2], Shannon W. Finks, Pharm.D.[2]; (1)Memphis VA Medical Center, Memphis, Tenn; (2)University of Tennessee College of Pharmacy, Memphis, Tenn.

PURPOSE: Current HF guidelines recommend the addition of spironolactone to standard therapy in patients with HF and reduced ejection fraction (EF). To prevent hyperkalemia, the guidelines recommend baseline and follow-up monitoring of potassium (K+) and serum creatinine (SCr). The purpose of this study is to evaluate the use of spironolactone in patients with HF to determine whether appropriate baseline and follow-up monitoring is performed and to assess the incidence of adverse events due to spironolactone.

METHODS: Patients prescribed spironolactone at the Memphis VAMC with HF and EF°Ü40% that either presented to the emergency department or an outpatient clinic, or were hospitalized between 01/01/05 and 12/31/05, were identified. Demographic data, EF, baseline and follow-up laboratory data, concomitant medications, adverse events, and hospitalizations were recorded.

RESULTS: Baseline and follow-up data on the first 180 patients identified is reported. All patients had baseline K+ and SCr before spironolactone initiation; 11 patients (9.4%) were started on spironolactone despite having baseline K+ °Ý 5.0 mEq/L or baseline SCr °Ý 2.5 mg/dL. Appropriate follow-up laboratory monitoring was completed in 175 patients (97%). After initiation of spironolactone, 32 patients (17.8%) had subsequent SCr > 2.5 mg/dL and hyperkalemia [K+ > 5.0 mEq/L occurred in 62 (34%) patients]. Of the 90 elderly patients (age > 65), 40 (44%) had K+ > 5.0 mEq/L, 20 (22%) had SCr > 2.5 mg/dL, and 53 (59%) had a SCr > 1.6 mg/dL during spironolactone treatment.

CONCLUSION: A high rate of adherence to baseline and follow-up laboratory assessment was found. During treatment with spironolactone, hyperkalemia and renal insufficiency developed more frequently in elderly patients. However, additional data analysis will include concomitant medications, adverse events, and hospitalizations.

Critical Care

314. **Insulin Infusions: Incidence of Hypoglycemic Events and Protocol Deviation.** *Stephanie Thune, Pharm.D.*[1], Mitchell Buckley, Pharm.D.[2], Philip Fracica, M.D.[2]; (1)Midwestern University, Glendale, Ariz; (2)St. Joseph's Hospital and Medical Center, Phoenix, Ariz.

PURPOSE: Studies have shown significant decreases in morbidity and mortality when critically ill patients are kept euglycemic. Continuous insulin infusions have been shown to be safe and effective in controlling blood glucose levels in this patient population. However, hypoglycemic adverse drug events (ADEs) are a possible consequence of this therapy. The purpose of this study is to identify the incidence and causes of hypoglycemic ADEs resulting from insulin infusion protocol nonadherence in intensive care unit (ICU) patients.

METHODS: This is a prospective observational study conducted from January to April, 2006. Patients on an insulin infusion were identified from a report generated from Cerner pharmacy order entry software. Patients selected were > age 18 years and on the insulin infusion protocol at least 24 hours. Patients treated for diabetic ketoacidosis were excluded. Protocol deviation was classified into the three following categories: initiation, titration, and monitoring. Hypoglycemic events and their treatments were also recorded. The study definition of hypoglycemia was a blood glucose of < 60 mg/dL, which coordinates with our institution's IIP.

RESULTS: A total of 4874 deviations were recorded for 80 patients over 4 months. The mean daily deviation rate was 10.7 deviations per patient. Insulin infusion deviations mostly consisted of monitoring errors (55.9%), followed by titration errors (41.5%) and initiation errors (2.6%). A total of 93 hypoglycemic ADEs occurred during 11,688 drip hours (19 events per 100 patient days). Fourty-four (55%) subjects had at least one hypoglycemic ADE, and 22 (27.5%) had multiple events. Severe hypoglycemia(< 40 mg/dL) occurred in 5 (6.3%) patients.

CONCLUSION: Our study found that all insulin infusions deviated from protocol; therefore, we were unable to determine whether non-adherence contributed to ADEs. The study did allow us to quantify our IIP related hypoglycemic ADE rate, which was higher than what has been published in other IIP validation studies.

Education/Training

315. Educating the pharmacist to provide acute palliative care. *Pmela Moore, Pharm.D.*, Dorcas Letting-Mangira, Pharm.D., Kenneth Komorny, Pharm.D.; Summa Health System, Akron, Ohio.

PURPOSE: Our institution recently opened an inpatient acute palliative care unit. Recognition of the unique therapeutic needs of these patients and the staff pharmacists' lack of familiarity prompted the development of an educational program. Therapeutic issues such as alternative routes of administration, dosing regimens, monitoring, and off-label medication uses generated much concern. Given the lack of formal treatment guidelines, and randomized, controlled clinical trials, it is understandable that pharmacists would be uncomfortable with medication orders or drug information questions from the palliative care team. In addition, current hospital policies and guidelines for the administration of the medications in question do not apply to these patients and need to be revised and/or developed. Therefore, the objectives of this study were to 1) identify therapeutic and pharmacy issues related to palliative care patients, 2) participate in the writing and/or revision of hospital policies, and 3) educate the pharmacists.

METHODS: A survey was conducted to determine the inpatient pharmacists' level of familiarity with palliative care issues, diseases encountered, symptoms, medications, and drug information references. The survey results were used to determine educational topics which where presented to all pharmacists at various sessions. These included an overview of palliative care, and symptom management. Electronic notifications and key articles were provided to suppliment presentations. Following the educational series, the survey was again conducted, and the

pharmacists' familiarity and comfort level with palliative care issues were re-assessed. The Wilcoxon signed rank test was applied for statistical analysis.

RESULTS: Forty-five surveys were distributed before and after the educational series with 67% and 33% returned rates respectively. The initial survey revealed the pharmacists' lack of comfort with their knowledge base, available references, and the use of midazolam for palliative sedation.

CONCLUSIONS: Following the in-services, there was a significant increase in the pharmacists' level of comfort with palliative care issues.

316. **Predictors of readiness for self-directed learning among third and fourth year student pharmacists.** Donard D. Huynh, Pharm.D.[1], *Stuart T. Haines, Pharm.D.*[1], Deborah A. Sturpe, PharmD[1], Cherokee Layson-Wolf, Pharm.D.[1], Kristin Watson, Pharm.D.[1], Cecilia M. Plaza, Pharm.D., Ph.D.[2]; (1) University of Maryland School of Pharmacy, Baltimore, Md; (2)American Association of Colleges of Pharmacy, Alexandria, Va.

PURPOSE: Self-directed learning (SDL) is an instructional strategy that may promote lifelong learning. ACPE Standards require schools and colleges of pharmacy to support the development of self-directed lifelong learners. The objective of this study is to characterize the self-directedness of third and fourth year student pharmacists and to identify characteristics that are associated with readiness for self-directed learning.

METHODS: The Self-directed Learning Readiness Scale (SDLRS) and Baseline Characteristics Survey (BCS) were administered to third and fourth year student pharmacists. SDLRS is a validated instrument that determines the relative degree to which students have the attitudes and motivation to engage in SDL. The BCS provides data on demographics, pre-pharmacy coursework, elective interests, and leadership participation. Students' scores on the SDLRS were compared to their self-reported characteristics obtained from the BCS. Data was analyzed using the two-sample t-test and Fisher's exact test.

RESULTS: A total of 77 (67.0%) third year student pharmacists and 100 (84.7%) fourth year student pharmacists completed the questionnaires. No significant difference was found between the mean scores on SDLRS for third (157 ± 21) and fourth (154 ± 20) year student pharmacists (p = 0.39). Participation in the pharmacotherapy elective pathway was associated with higher scores (p = 0.04), and participation in the geriatric elective pathway was associated with lower scores (p = 0.04). No other baseline characteristic was found to be associated with high or low scores on SDLRS.

CONCLUSIONS: Readiness for self-directed learning may be an intrinsic characteristic that is relatively stable and not readily influenced by external factors. Characteristics of those students attracted to certain elective pathways needs to be further examined.

Endocrinology

317. **Guidelines for glycemic control utilizing basal insulin in cardiac surgery patients.** *Erin Stahl, Pharm.D.*, Norman Kwong, Pharm.D., BCPS, Jennifer Biltoft, Pharm.D., BCPS; Exempla Saint Joseph Hospital, Denver, Colo.

PURPOSE: Stress-induced hyperglycemia in hospitalized patients is no longer considered an inconsequential phenomena. The University Health-System Consortium (UHC) has developed clinical performance measures to improve glycemic control.

HYPOTHESIS: Implementation of a guideline initiating basal insulin in patients possessing two glucoses over 150 mg/dL will result in better glycemic control.

METHODS: A glucose control guideline, using continuous insulin infusion (CII), long acting insulin, oral hypoglycemics, and slide scale insulin was developed and implemented. A retrospective review of 140 cardiac surgery patients was completed. End points in both the pre-guideline group (n=63) and post-guideline group (n=73) were compared. The primary end point was average blood glucose. The secondary end points were frequency of hyperglycemia and hypoglycemia, basal insulin and oral hypoglycemics utilization, ICU and non-ICU blood glucose average.

RESULTS: Average blood glucose was reduced (133 mg/dL vs 129 mg/dL) p<0.05. Percentage of glucoses > 200 mg/dL was reduced by 40%. Hypoglycemia incidence (< 50 mg/dL) was unchanged. Utilization of basal insulin and oral hypglycemics improved after guideline implementation (CII increased by 24%, long acting insulin increased by 66%, oral hypoglycemics increased by 21%). Average ICU and non-ICU post-operative glucose were both reduced (136 mg/dL vs 129 mg/dL and 133 mg/dL vs 130 mg/dL). A sub-group analysis of the diabetic population yielded a reduction in glucose from 153 mg/dL to 137 mg/dL.

CONCLUSIONS: The implementation of a glucose control guideline reduced average blood glucoses. There was a reduction in the frequency of blood glucoses over 200 mg/dL and under 50 mg/dL. In addition, the guideline

also increased the utilization of basal insulin and oral hypoglycemics. Implementation had an even more profound impact within the diabetic subpopulation examined.

318. **Assessment of adherence to diabetic treatment guidelines in a family practice**. *Jessica M. Trompeter, Pharm.D., MBA*, Dawn E. Havrda, Pharm.D., BCPS; Bernard J. Dunn School of Pharmacy, Shenandoah University, Winchester, Va.

PURPOSE: To determine the adherence of physicians in a family practice setting to diabetic treatment guidelines and to identify opportunities for pharmacist intervention.
METHODS: Eligible patient charts were selected from a CPT code generated list of patients over an 18-month period. Eligible patients had a diagnosis of diabetes and were treated with at least one medication for diabetes, and were followed by the family practice for treatment of diabetes. Charts were reviewed for patient's age, gender, weight, height, medical conditions, medications, recent dose changes in these medications, immunizations, tobacco use, relevant laboratory values, and eye and foot exams. Treatment guidelines available in 2007 were used to assess adherence. Anticipated completion of project is July 2007.
RESULTS: Preliminary results indicated routine monitoring of HbA1c in 93% of patients with 64% at therapeutic goal and lipid panel in 90% with 43% at therapeutic goal. Blood pressure measured at every visit showed 53% of patients at therapeutic goal. For those patients not reaching adequate blood pressure control, therapeutic changes were initiated in 41.6% of patients. Routine monitoring was documented for microalbuminuria, neuropathy, and dilated eye exams in 39%, 35.7%, and 28.5% of patients, respectively. Influenza and pneumococcal vaccines were documented in 35.7% and 21.4% of patients, respectively.
CONCLUSIONS: Based on the preliminary results, adherence to treatment guidelines is greater with the macrovascular complications of diabetes when compared to adherence to microvascular complications of diabetes. Microvascular complications are a potential opportunity for pharmacist intervention.

Erythropoietin Clinic

319. **Retrospective review of the health care benefits and cost utilization of a pharmacist-managed hematopoietic clinic.** *Charles L. Quaglieri, Pharm.D.*, Scott Mambourg, Pharm.D.; VA Sierra Nevada Health Care System, Reno, Nev.

The use of hematopoietic agents significantly improves clinical outcomes and quality of life in anemic patients. These agents, however, are not without serious risk. The FDA has recently released black box warnings for the hematopoietic agents relating unmanaged anemia to serious cardiovascular complications, death, and possible tumor progression in oncology patients not receiving chemotherapy. The ongoing safety monitoring, dose optimization, and financial burden of these agents present a continued challenge to many health care systems across the country. A 2004 review at the Veteran's Affairs Sierra Nevada Health Care System elucidated that 100% of 32 anemia patients receiving hematopoietic therapy were in need of therapeutic intervention. 66% of the patients had a Hgb > 12 g/dL; 34% of the patients had a Hgb of < 10 g/dL, and only 25% had updated iron studies. The hematopoietic clinic was reestablished in November 2006 based on these 2004 findings. Currently, 90 patients with CKD or drug induced anemias who require hematopoietic therapy and iron supplementation are being monitored through the clinic. The primary outcome of this retrospective analysis is to determine how many of these anemic patients are in a Hgb range of 11–12 g/dL using a pharmacy-managed protocol. The secondary outcomes include an updated assessment of iron studies, patients requiring iron supplementation, quality of life improvements, and cost allocation.

Gastroenterology

320. **Evaluation of the relationship between gastric-acid suppression therapy and the development of *Clostridium difficile*-associated disease in hospitalized patients.** *Philip E. Grgurich, Pharm.D., MBA*, Diane E. Soulliard, Pharm.D., BCPS; Beth Israel Deaconess Medical Center, Boston, Mass.

PURPOSE: The incidence and severity of *Clostridium difficile*-associated disease (CDAD) is increasing. Recent studies have established acid suppressive therapy as a risk factor for CDAD. The purpose of this study was to determine whether intensity of acid suppressive therapy is associated with development of CDAD in hospitalized patients.
METHODS: A pharmacoepidemiologic cohort study was conducted at a large, urban, tertiary care center. Administrative data prospectively gathered during a 2-year period were analyzed. Data from the first hospitalization for all adult patients were included if the hospitalization lasted 3 or more days. Patients who developed CDAD within the first 2 days of hospitalization were excluded. Maximum acid suppression exposure in-hospital was

classified as: no acid suppression, histamine-2 receptor antagonists (H$_2$RAs), daily proton pump inhibitors (PPIs), and more frequent than daily PPIs. Antibiotics were classified as high-risk or low-risk based on medical literature. Multivariate logistic regression was used to evaluate the risk of CDAD with each acid suppression regimen after adjustment for covariates.
RESULTS: 24,366 patients were included in the study. The mean age was 53.7 years and most were female. The plurality of patients received no acid suppression; however, among those prescribed acid suppression, daily PPIs were the most commonly used agents. CDAD occurred in 4.9 per 1,000 patients. The incidence of CDAD was highest in patients prescribed more frequent than daily PPIs together with high-risk antibiotics. The adjusted odds ratio of CDAD with daily PPIs was 1.81, (95% CI = 1.10–2.97) and with more frequent than daily PPIs was 3.57 (95% CI = 1.97–6.45). H$_2$RAs were not independently associated with CDAD. Other independent risk factors were: high-risk antibiotics, renal failure, and advanced age.
CONCLUSIONS: Acid suppression with PPIs is associated with an increased risk of CDAD in hospitalized patients. More intense proton pump inhibitor regimens are associated with the greatest risk.

Hematology/Anticoagulation

321. **Sickle Cell Pain Management Database Implementation.** *Sarah B. Dehoney, Pharm.D.*, Marlea Wellein, Pharm.D., BCPS, Robert N. Axon, M.D., Anne Spencer, Pharm.D., BCPS; Medical University of South Carolina, Charleston, SC.

PURPOSE: The primary objective of this study is to determine whether patients with sickle cell disease report improved satisfaction after a patient-specific pain management database is utilized to design pain medication regimens upon hospital admission.
METHODS: Adult patients with at least 5 hospital visits/year at MUSC related to sickle cell disease were mailed an anonymous survey to assess the baseline quality of pain management at our institution. Upon admission for a pain crisis and after informed consent was obtained, data were concurrently collected regarding the patient's home pain medication regimen, hospital pain medication regimen required to achieve pain control, and other salient information affecting pain management. This information was entered into the database, which is available to health care providers during future hospital admissions. The information will then be updated during each hospital admission. The patient-perceived impact of the database will be determined by a second survey mailed one year after study initiation. An employee survey will be distributed to health care providers using the database to obtain their feedback and perceptions. In addition, the number of admissions for pain crises and the length of hospital stay before and after database initiation will be determined.
RESULTS: Sixty-three patients met inclusion criteria, and currently 9 (14%) of patients have returned the pain satisfaction survey. Preliminary results revealed that 89% (n=8) of patients experienced pain reduction, 33% (n=3) of patients achieved pain control, and 11% (n=1) of patients believed the time to pain control was acceptable while being treated for sickle cell pain at MUSC. Patient enrollment in the database is ongoing. Final patient satisfaction and employee satisfaction results will be collected within the next 12 months.

322. **An evaluation of a full-dose weight-based heparin nomogram.** *Linda H. Ghobrial, Pharm.D.*, Jeffrey Ketz, Pharm.D., BCPS, Katie Greenlee, Pharm.D., BCPS, Michael Militello, Pharm.D., BCPS; Cleveland Clinic, Cleveland, Ohio.

PURPOSE: A recent change in the reagent used to determine the activated partial thromboplastin time (aPTT) at Cleveland Clinic led to adjustments of the heparin nomogram. Primary end point was percentage of patients that achieved a therapeutic aPTT within 24 hours. Secondary end points included mean time to first therapeutic aPTT and mean time to therapeutic maintenance rate, defined as therapeutic aPTTs for 2 consecutive days. Nomogram safety and compliance were also assessed.
METHODS: Concurrent chart review and descriptive analysis of 100 patients treated with heparin. Patients were followed until therapeutic maintenance rate was achieved or for a maximum of 96 hours. Initial dosing of heparin included four groups of patients: weight-based dosing (80 units/kg bolus and 18 units/kg/hour infusion), weight-based dosing without bolus, and physician-initiated dosing with and without bolus. Assessments of nomogram compliance were determined by evaluating dosing adherence, time from lab draw to lab reporting, and time from lab reporting to dosage adjustment. Nomogram safety was assessed by incidence of major and minor bleed.
RESULTS: One therapeutic aPTT was attained within the first 24 hours in 55 (55%) patients. The mean time to first therapeutic aPTT was 27 hours. The mean time to therapeutic maintenance rate was 58 hours. There were 5 (5%) patients that did not achieve one therapeutic aPTT within 96 hours. Average bolus dose was 63 units/kg and average initial infusion was 16 units/kg/hour. The average therapeutic infusion rate was 14 units/kg/hour for patients who achieved therapeutic maintenance. Of the 252 aPTTs attained in the first 24 hours, 101 (40%) were

supra-therapeutic. Six (6%) patients experienced a major bleed (4 blood transfusions and 2 overt bleeds), and 9 (9%) patients experienced a minor bleed.
CONCLUSIONS: About half of patients reached the therapeutic goal. Assessment of adherence to dosing must be made to further explain these observations.

Infectious Diseases

323. *Clostridium difficile*-associated disease: incidence, treatment, causitive antibiotics, and mortality: using data to improve care. *Jennifer A. Platt, Pharm.D.*, Douglas D. DeCarolis, Pharm.D., BCPS, Joseph Thurn, MD, Murray Leraas, Pharm.D., BCPS, Eric Geurkink, Pharm.D., BCPS; Minneapolis Veterans Affair Medical Center, Minneapolis, Minn.

PURPOSE: Many literature reports cite an increasing incidence and severity of *Clostridium difficile*-associated diarrhea (CDAD). Concern has been raised regarding the efficacy of the standard evidence-based treatments. Many of these reports refer to high mortality either due to or associated with CDAD. These concerns have led to an increased awareness of CDAD, earlier empiric treatment, and quick adjustments to standard therapies.
METHODS: The database included patients from January 1, 2004, to December 31, 2005, with a positive culture or toxin and treatment with metronidazole or vancomycin. Charts were reviewed retrospectively. A CDAD case was defined if diarrhea, colitis, or ileus was documented. These data were compared to historical data.
RESULTS: CDAD case rate increased from 7 to 12.3 cases per 10,000 patient days. Forty nine percent of treated patients did not meet criteria for CDAD diagnosis. Of those diagnosed with a new case of CDAD, greater than 75% received metronidazole, although treatments trends revealed an increasing use of vancomycin, earlier changes to vancomycin, and other non-evidenced based approaches. Efficacy did not differ between metronidazole and vancomycin; however, treatment failure or relapse rates appear to be increasing. Fluoroquinolones were associated with the most cases by far but when analyzed in comparison to amount used, clindamycin had the highest association. There was no difference in CDAD rates between various quinolone agents. Associated and attributable mortality has increased.
CONCLUSION: Similar to other reports, we found an increased incidence and more refractory disease. We also identified that current practice includes treating many asymptomatic patients and a variation from evidence based regimens. The association of antibiotics is clouded due to multiple antibiotics used simultaneously and/or cumulatively. These data will be used as a quality improvement project to improve our institutional response to evidence based diagnosis, treatment, and surveillance of CDAD.

324. **Stratification of infecting organisms, susceptabilities, and antibiotic selection based on admitting service in a cancer center.** *Denise E. Riccobono, Pharm.D.*, Elizabeth A. Coyle, Pharm.D., Tami N. Johnson, Pharm.D., Holly L. Hogan, Pharm.D., Carmen E. Gonzalez, M.D., Kenneth V.I. Rolston, M.D.; University of Texas M. D. Anderson Cancer Center, Houston, Tex.

PURPOSE: Infections are a major cause of morbidity/mortality in cancer patients and infecting pathogens and susceptibilities can differ according to cancer type and institution. Knowledge of the pathogens infecting specific cancer types is imperative for appropriate empiric treatment. The purpose of this study was to delineate the infecting bloodstream organisms and their susceptibilities according to cancer type from patients seen in the M. D. Anderson Cancer Center(MDACC) Emergency Center(EC), and evaluate the initial antimicrobial therapy given in the EC for appropriate coverage.
METHODS: Patients from MDACC EC from 9/01/2005 to 2/28/2006 who were > age 18, who had an EC admission diagnosis of fever, and who had at least one positive blood culture either 2 weeks prior to EC evaluation, in the EC, or up to 48 hours after EC were evaluated. Data colleted included demographics, immune status, infecting organisms/susceptibilities, and initial empiric therapy. Delineation of infecting organisms were grouped by cancer type; solid tumors(S), leukemia/lymphoma(L/L), and stem cell transplant(SCT).
RESULTS: To date, 284 patients have been evaluated, 29% S, 63% L/L, and 7% SCT. In total, there were 302 bacterial infections, 55.6% gram-positive(GP) and 43.4% gram-negative(GN) with a similar delineation among cancer types. The majority of GP organisms were *Staphylococcus* spp. 56.9%, 47.2%, and 45.5% in S, L/L, and SCT, respectively, with the majority being methicillin sensitive. For GN, *Enterobacteriacae* spp. were predominant with 59.1%, 60%, and 43% in S, L/L, and SCT, respectively. Resistant organisms were primarily seen in L/L, specifically MRSA, VRE, *Pseudomonas*, and resistant *E. coli*. Neutropenia was seen in 47.5% (18.1% S, 63.9% L/L, and 23.8% SCT).
CONCLUSIONS: Preliminary data demonstrate that the majority of infecting organisms in our cancer patients at MDACC are GP, with resistance seen mainly in the L/L patients. Additional analysis is needed before final conclusions can be made and will be completed August 2007.

325. **Analysis of vancomycin dosing guidelines: a retrospective, pre-post protocol study design.** *Joyce S. Lee, Pharm.D.*, Brett Heintz, Pharm.D., BCPS, Jeff King, Pharm.D.; University of California, Davis Medical Center, Sacramento, Calif.

PURPOSE: The vancomycin guidelines in our institution have been updated to give dosing recommendations for both traditional (8–15 mcg/mL) and aggressive (15–20 mcg/mL) target blood levels. The primary objectives of this study were to determine whether patients were able to achieve target vancomycin blood levels sooner and to evaluate the compliance with these new guidelines. Secondary objectives included an assessment of the efficacy and toxicity of vancomycin comparing the pre-protocols vs. post-protocols.
METHODS: All patients receiving vancomycin for at least 5 days before (December 1, 2005, to February 28, 2006) and after (December 1, 2006, to February 28, 2007) the implementation of the new vancomycin guidelines were included. The following data were collected: serum creatinine, microbiology cultures, indication, site of infection, goal vancomycin trough, and mortality.
RESULTS/CONCLUSION: To be presented.

326. **Beta-lactam antibiotic desensitization: analysis of standardized protocols at a tertiary medical center.** *R. Wayne Shipley, Pharm.D.*, Christopher McCoy, Pharm.D., BCPS, Katherine Cunningham, Pharm.D., BCPS; Beth Israel Deaconess Medical Center, Boston, Mass.

PURPOSE: A history of allergy to beta-lactam antibiotics limits anti-infective treatment choices and may preclude the use of drugs that would otherwise be chosen for eradication of a pathogen. Despite the increased use of antibiotic desensitization protocols, an efficacy analysis of such an approach in adults is lacking. The primary objective of this study was to evaluate the efficacy and success of standardized beta-lactam antibiotic desensitization protocols.
METHODS: This retrospective analysis included all patients who underwent antibiotic desensitization with ampicillin, cefazolin, ceftriaxone, meropenem, oxacillin, penicillin, or piperacillin-tazobactam over a 4-year period. The following parameters were evaluated: completion of the desensitization protocol, lack of acute allergic reaction, and successful transition to the targeted antibiotic. Data collection included patient demographics, admitting and infectious diagnoses, microbiologic data, clinical data and safety.
RESULTS: A total of 33 beta-lactam desensitizations performed in 30 patients were assessed. The mean age was 57 years old, and 20 (61%) were male. The majority of the desensitizations were performed in an intensive care unit setting (97%). At least one adverse event was noted in 24% of the desensitizations performed. Adverse events were minor and managed with diphenhydramine. The most common pathogens requiring desensitization were methicillin-susceptible *Staphylococcus aureus*, extended-spectrum beta-lactamase producing *Klebsiella* species, and *Enterococcus* species. Successful completion was achieved in 32 of 33 (97%) of the desensitizations, 30 of which (91%) went on to complete the course of targeted antibiotic.
CONCLUSION: Beta-lactam desensitizations that were completed using the standardized protocols resulted in a low discontinuation and adverse event rates, facilitated the desensitization to many antimicrobials, and permitted the use of the preferred antimicrobial against a wide variety of organisms. Beta-lactam antibiotic desensitization is a safe and successful therapeutic option for patients with a history of allergy.

Managed Care

327. **Evaluation of diabetes outcome measures for a national employee population enrolled in a multidisciplinary diabetes management program.** *E. Thad Mick, Pharm.D.*[1], Paul J. Williams, Pharm.D., M.S., FCCP, FCP[2], Thanh Lam, Pharm.D.[1], Christine Lee, Pharm.D.[1], Nazly Westernoff, Pharm.D.[1]; (1) American Health Care, Rocklin, Calif; (2)University of the Pacific, School of Pharmacy, Stockton, Calif.

PURPOSE: Glycemic control is paramount to the successful management of diabetes and the prevention of diabetes related complications that eventuates increased morbidity and mortality. Studies have identified a strong correlation between hyperglycemia and the rate of diabetic complications. Despite strong evidence clearly mandating aggressive glycemic control, diabetes remains the leading cause of blindness, end stage renal disease, and non-traumatic lower limb amputation in the United States. The objective of this study is to determine the extent to which enrollment in an employer-sponsored multidisciplinary diabetes management program increases adherence to clinically appropriate medication regimens and testing frequencies.
METHODS: The methods of this study have been evaluated by the American Health Care Advisory Board to ensure that subject selection is equitable, provisions to protect the privacy and confidentiality of subjects are intact, and the potential risks to subjects are minimized. All selected subjects will have ICD-9 codes for diabetes during the period of August 1, 2005, to July 31, 2006. Identified subjects will be given the opportunity to participate through an opt-in process. Subjects will be assigned to a Care Manager for monthly in person meetings dedicated to patient-specific diabetes education, medication guidance, blood glucose self monitoring training, and referrals

to the primary care provider (PCP) for clinically appropriate medication modifications and laboratory monitoring. Pharmacy claims data will be evaluated upon subject enrollment, and at quarterly intervals to identify changes in medication and test strip refills. Verification of appropriate testing frequencies will be conducted through the use of current procedural terminology (CPT) codes for hemoglobin A1c (HbA1c) assessments, lipid panels, and eye examinations. A statistical comparison of baseline and interval data, utilizing repeated measures anova, will be used to determine the impact of the diabetes management program for the identified population.

Pediatrics

329. **Safety and efficacy of inhaled aminoglycoside in mechanically ventilated premature infants for the treatment of symptomatic Gram-negative bacilli tracheitis.** *Hanna Phan, Pharm.D.*[1], Vinita Pai, M.S., Pharm.D.[1], John Hayes, Ph.D.[2], Tersea Puthoff, Pharm.D.[3], Milap C. Nahata, Pharm.D., FCCP[1]; (1) The Ohio State University, College of Pharmacy and Columbus Children's Hospital & Research Institute, Columbus, Ohio; (2)Columbus Children's Research Institute, Columbus, Ohio; (3)Columbus Children's Hospital, Columbus, Ohio.

PURPOSE: The objective was to determine the safety and efficacy of inhaled aminoglycoside (IH AG) in the treatment of mechanically ventilated premature infants with symptomatic Gram-negative bacilli (GNB) tracheitis.
METHODS: The medical records of 76 mechanically ventilated (≥ 14 days) premature infants (1993-2004) with tracheal culture positive for GNB and receiving IH AG were retrospectively reviewed. Patients receiving high frequency/oscillator ventilation, peritoneal dialysis, or extracorporeal membrane oxygenation were excluded. Data were analyzed by mixed model regression analysis of variance repeated measures, one-way ANOVA with Tukey test and Post Hoc analysis, t-tests, and descriptive statistics. Review of additional medical records will be conducted prior to final analysis.
RESULTS: Premature infants of mean gestational age 29 ± 5 weeks and birth weight 1362 ± 897 g received 91 courses of IH AG for median duration of 6 days (range 1–22). The mean gentamicin (n=82) and tobramycin (n=8) doses were 15 ± 6.9 mg (10–40 mg) and 15.2 ± 4.7 mg (8–20 mg) every 8 hours, respectively. One patient received inhaled amikacin 30 mg every 8 hours. Concurrent systemic aminoglycosides, other antibiotics, or both were included in 57 of 91 courses. Among courses with available (n=63) pre- and post-treatment tracheal aspirate cultures, 35 (56%) cleared of GNB; 12 of which received no other systemic antibiotic. Increased duration of therapy was associated with decreased polymorphonuclear leukocytes (PMN) in tracheal aspirates (p=0.045) and required FiO_2 (p=0.008). Among 76 patients, 32 (42%) were extubated to nasal cannula/oxygen hood post-treatment. Serum creatinine improved (p=0.003) from baseline. IH AG did not significantly affect blood urea nitrogen, urine output, heart rate, or hearing, or cause oxygen desaturations.
CONCLUSION: Inhaled aminoglycoside was well-tolerated, with no significant nephrotoxicity, ototoxicity, or other adverse effects. This treatment also seemed potentially effective based on improved respiratory function and reduction in PMN in tracheal aspirates. Additional studies regarding optimal dosing are needed.

Pharmacy Administration

330. **Evaluation of acute decompensated heart failure management in membership hospitals of a group purchasing organization.** *Alexandra Perez, Pharm.D.*[1], Robert DiDomenico, Pharm.D.[1], Glen T Schumock, Pharm.D.[1], Jeffrey E Wojtynek, Pharm.D.[2], John C Theobald, Pharm.D.[2]; (1)University of Illinois at Chicago, Chicago, Ill; (2)Consorta Inc., Schaumburg, Ill.

PURPOSE: In 2004, the care of patients with acute decompensated heart failure (ADHF) resulted in an aggregate loss on DRG 127 of $57 million among member hospitals of a large group purchasing organization. Consequently, a review of ADHF management was performed among member hospitals to identify potential areas to improve the cost-effectiveness of caring for these patients.
METHODS: Eighteen member hospitals participated in a retrospective chart review. Patients presenting to the emergency department and hospitalized with the primary diagnosis of heart failure July 1–September 30, 2006, were randomly selected for inclusion.
RESULTS: Data were collected on 470 patients with a mean age of 72 ± 15 years and of whom 53% were female. The most common comorbidities were hypertension (75%), heart failure (70%), coronary artery disease (57%), and diabetes (48%). Clinical presentation was consistent with volume overload in most patients. The average length of stay was 4.9 ± 3.7 days, with 60 (13%) requiring ICU admission. 363 (77%) were given intravenous (IV) diuretic (time to initiation 5 ± 9 hours, therapy length 48 ± 49 hours). 58 (12%) were given IV vasoactive drugs (time to initiation 26 ± 58 hours, therapy length 39 ± 42 hours, 7% vasodilators, 4% inotropes). 68(15%) patients had an episode of hypotension (10 [15%] requiring vasopressors), 39(8%) had worsening renal function (4 [10%]

requiring hemodialysis). Overall, 460 (98%) patients were alive at discharge. JCAHO core measure adherence was 90% (421), 66% (310), and 56% (120) to documentation of discharge instructions, LVF assessment and smoking cessation counseling, respectively and 60% (280) of patients were on ACE-inhibitors/ARB upon discharge.

CONCLUSION: There may be several opportunities to improve ADHF management in these hospitals, including more timely and appropriate utilization of IV vasoactive drugs, minimizing complications (hypotension and worsening renal function), and improving adherence to JCAHO measures. To address these needs, ADHF guidelines have been developed and implemented in these hospitals, and their impact will be studied.

331. **The effect of ezetimibe dose on LDL levels is the treatment of hypercholesterolemia.** *Karmen R. Jorgensen, Pharm.D.*; Iowa City VA Medical Center, Iowa City, Iowa.

PURPOSE: Ezetimibe decreases low density lipoprotein (LDL), an important risk factor for the development of atherosclerotic vascular disease. Preclinical dose-response studies showed that about 80% of the LDL-lowering effect occurred with ezetimibe 5 mg. Therefore, 5 mg ezetimibe, particularly in combination with other cholesterol-lowering therapy could be a cost-effective option. This study was designed to confirm non-inferiority of ezetimibe 5 mg daily compared to 10 mg daily. Non-inferiority was defined as an LDL-lowering difference between ezetimibe 5 mg and 10 mg of ≥ 15%.

METHODS: The primary objective was to compare LDL lowering of ezetimibe 5 mg and 10 mg in patients on stable cholesterol-lowering regimens. A secondary objective was to determine the percent of patients achieving LDL goals. Safety and tolerability was assessed by documenting adverse drug reactions between the study groups.

RESULTS: A total of 226 patients met inclusion and exclusion criteria, 68 patients receiving ezetimibe 5 mg and 158 patients receiving ezetimibe 10 mg. Patients on ezetimibe 5 mg and 10 mg had an LDL of 128.5 ± 28.2 mg/dL at baseline and 96.9 ± 28.8 mg/dL at study end compared with 140.7 ± 36.2 mg/dL and 99.5 ± 32.9 mg/dL, respectively. Average percent LDL reduction for use of 5 mg and 10 mg was 24.1 ± 16.6 and 28.6 ± 18.2, respectively (p<0.001), demonstrating non-inferiority of ezetimibe 5 mg compared to 10 mg. LDL goal was achieved in 66.2% and 58.2% of patients on 5 mg and 10 mg ezetimibe, respectively (p=0.3). One patient included in the study receiving ezetimibe reported an adverse drug reaction, but continued therapy for minimum study duration.

CONCLUSION: Ezetimibe as monotherapy or in addition to other lipid medications effectively provides additional reduction in LDL. Results of this study demonstrate ezetimibe 5 mg, a cost effective option, provides comparable LDL-lowering to ezetimibe 10 mg.

Underserved Care

332. **Potential factors in diabetes control in a free urban clinic.** *Lauren J. Fields, Pharm.D.*[1], Sharon E. Connor, Pharm.D.[2], Tina M. Scipio, Pharm.D.[2]; (1)UPMC St. Margaret Hospital, Pittsburgh, Pa; (2) University of Pittsburgh, Pittsburgh, Pa.

PURPOSE: Diabetes complications are a significant burden to both patients and society. The medically underserved are more susceptible to complications secondary to lack of consistent access to medical and pharmaceutical care. By understanding the differences between patients in free clinics with type 2 diabetes who do and do not meet diabetes treatment goals, specific programs can be created and tailored to address specific factors affecting control and may decrease the burden of this disease.

METHODS: In this cross-sectional needs assessment analysis, patients with a diagnosis of type 2 diabetes will be stratified by A1C (A1C of ≤ 7% versus A1C > 7%), and differences in demographic, medical, medication, and socioeconomic characteristics will be compared between the groups. All English-speaking patients with type 2 diabetes who receive care at the free clinic will be eligible for inclusion in the study. Demographic data and medical history will be gathered through chart review and during a face-to-face interview with a pharmacist. Survey instruments will be administered to measure diabetes knowledge, adherence, health literacy, self-efficacy, and social support.

RESULTS: Differences between patients meeting and not meeting A1C goals will be described using descriptive statistics and will be analyzed for significance at p<0.05. Results will be presented.

CONCLUSIONS: The authors anticipate an association between poor control and low diabetes knowledge, poor adherence, low health literacy, low self-efficacy and limited social support. The knowledge obtained from this study will assist the investigators and others in creating targeted programming aimed at increasing diabetes control in this and other free clinic populations.

STUDENT SUBMISSIONS

ADR/Drug Interactions

333. Hepatotoxicity induced by a nutritional supplement marketed for osteoarthritis. *Olivia C. Rapacchietta, Pharm.D. Candidate*[1], Sunny A. Linnebur, Pharm.D., FASCP, BCPS, CGP[1], Maria V. Vejar, M.S., R.N., GNP[2]; (1)University of Colorado at Denver and Health Sciences Center, School of Pharmacy, Denver, Colo; (2)University of Colorado at Denver and Health Sciences Center, Department of Medicine, Denver, Colo.

PURPOSE: We are reporting two patients who experienced hepatoxicity after consuming "Move Free Advanced" (MFA), a nutritional supplement marketed for osteoarthritis that contains glucosamine, chondroitin, Chinese skullcap, black catechu, and hyaluronic acid.
CASE REPORT: Patient No. 1: a 71-year-old white woman with a previous history of normal liver function tests (LFTs) presented with diarrhea, fatigue, depression, and laboratory values of: aspartate aminotransferase (AST) 275U/L (normal 0–47 U/L), alkaline phosphatase (ALP) 296U/L (normal 39–117 U/L), alanine aminotransferase (ALT) 422U/L (normal 0–47 U/L), and a total bilirubin (TBili) 0.9mg/dL (normal 0.0–1.0 mg/dL). Her values peaked 1 month later: AST 483 U/L, ALP 328 U/L, ALT 645 U/L, TBili 2.0 mg/dL, direct bilirubin 0.9 mg/dL (normal 0.0–0.4 mg/dL), indirect bilirubin 1.1 mg/dL (normal 0.0–0.7 mg/dL). During this time and about 1 month before her initial visit, she was taking the product MFA. This was her only medication change and she had no other risks for hepatic injury. An abdominal ultrasound and hepatitis screening were negative. The patient discontinued the MFA, and her LFTs slowly returned to normal after 3 months. Patient No. 2: a 85-year-old white woman presented asymptomatically with slightly elevated ALP and ALT values of 144 U/L and 54 U/L, respectively; her AST and TBili were 37 U/L and 0.2 mg/dL. The patient stated that she had started MFA about 3 weeks prior and had no history of elevated LFTs, hepatitis, or risk factors for liver disease. She discontinued the MFA, and her LFTs normalized 7 weeks later.
DISCUSSION: We found no published reports of hepatoxicity associated with glucosamine, chondroitin, black catechu, or hyaluronic acid. One report of hepatotoxicity in four European patients describes a possible link to skullcap. Based on this, it appears that Chinese skullcap is potentially the cause of hepatotoxicity in our patients. Because "Move Free Advanced" is readily available over-the-counter, this product could be a health concern for Americans.

Cardiovascular

334. Vascular endothelial surface micro-vortices. *Curtis L. Prichard, Pharm.D.*; Creighton University School of Pharmacy, Omaha, Neb.

PURPOSE: I propose the existence of micro-vortices near the surface of the endothelium, specifically in arteries of humans and other mammals. The function of the vortices is to form a region of impenetrable or resistant turbulence near the surface of the endothelium. The turbulence would minimize the risk of bombardment to the endothelial surface from LDL and other damage causing macro molecules, through deflective properties inherent in turbulent flow associated with vortices. The vortices would be produced by the existence of opposite ended charged, or partially charged circulating molecules such as multi-meric proteins. The breakdown of such a system would explain the susceptibility to endothelial injury in the beginning of artery diseases. The proposal is for a procedure to establish prima fascia evidence: The vortex system on the endothelial surface would be extremely small and difficult to measure or detect.
METHODS: I recommend radio labeling a number of the causative agents (LDL) and photo recording their trajectory while flowing through a vessel in an area of known curvature. The reason for this approach is to establish the difference in deflective angles after the LDL particles hit the endothelium in the disease-susceptible versus the non disease-susceptible subjects.
EXPECTED RESULTS: The radio labeled LDL particles will show different deflection angles between study groups. The still photos of resultant deflection of the labeled particles would provide a relatively easy way to observe these angles and provide a general idea of the nature of the difference in plasma flow at the endothelial surface. This difference would give insight into the nature of the micro vortices that are causing the deflection, and provide a basis for a mathematical model.

336. The feasibility and potential value of automated online anticoagulation monitoring of warfarin-treated patients. *Brandi N. Thoma, Pharm.D., Candidate*[1], Laura Barron, Pharm.D.[2], Megan Anderson, Pharm.D.[3], Marie Walker, BBA[4], Henry I. Bussey, Pharm.D., FCCP, FAHA[5]; (1)Temple University School of Pharmacy, Philadelphia, Pa; (2)College of Pharmacy, University of Texas, Austin, Tex; (3)Drake University School of Pharmacy, Des Moines, Iowa; (4)Clotcare.com, San Antionio, Tex; (5)University of Texas HSC, San Antonio, Tex.

PURPOSE: Veeger et al recently reported that 25% of warfarin-treated patients account for most out of range INR values and the majority of adverse events. 1) Previously, Rospond et al reported that the majority of warfarin-treated patients could achieve prolonged periods of anticoagulation stability. 2) Current technology (i.e., the ClotCare Online Management System) can provide automated online anticoagulation monitoring (AOAM) which could substantially reduce the time commitment of patients and clinicians. The feasibility and value of AOAM is dependent on the extent and duration of anticoagulation stability in individual patients.

METHODS: Warfarin doses and INR values of 53 consecutive patients seen in an anticoagulation clinic were analyzed to determine the degree of INR control for the group, the number of patients with stable INRs (2 months of therapy without a dosage change), and the duration of periods of INR stability. The initial 3-month dose titration phases were excluded as were peri-procedural INRs.

RESULTS: 53 patients provided 188 patient-years of data. INR time in range was 69.8% (87.92% if the range was expanded by +/- 0.3 INR units). "X" (y%) of 53 patients achieved INR stability. These "X" patients were stable for "A" patient-years of their "B" total patient-years ("p%") of monitoring. The mean duration of stability was "C" with a range of "d" to "e". Conclusion: These data suggest that y% patients can maintain INR stability for p% of the time. Use of AOAM, therefore, could be employed for p% of the time and reduce clinic visits by a similar amount to an average of once every "s" months.

337. **Evaluation of racial differences in the treatment of veterans with heart failure (HF).** *Rebekah Kirkpatrick, B.S.*, Emily K. McCoy, B.S., Kelly C. Rogers, Pharm.D., Robert B. Parker, Pharm.D., Shannon W. Finks, Pharm.D.; University of Tennessee College of Pharmacy, Memphis, Tenn.

PURPOSE: Recent evidence documents important racial differences in HF prevalence, etiology, response to treatment, and morbidity between African-Americans (AA) and Caucasians. Racial differences in the proportion of patients with health insurance or access to care may partially account for these disparities. The purpose of this study is to evaluate racial differences in quality of care and outcomes in Veterans with HF and an ejection fraction (EF) $\leq 40\%$.

METHODS: The present results are a subset of data originally collected to assess beta-blocker prescribing patterns in patients with HF and an EF $\leq 40\%$ at the Memphis VAMC. Patients with HF and an EF $\leq 40\%$ prescribed beta-blockers who presented to the emergency department or an outpatient clinic, or who were hospitalized between 01/01/05 and 06/30/05, were retrospectively identified. Demographic data, EF, number of emergency department visits, hospitalizations for any cause, concomitant medications, and mortality were recorded.

RESULTS: A total of 427 patients were identified. Caucasians (n=274) were significantly older (72.2 + 9.5 vs. 65.2 + 11.6 years, p<0.001), had higher EFs (29.4 + 7.5 vs. 26.5 + 8.1%, p<0.001), and had fewer emergency department visits (0.9 + 1.6 vs. 1.5 + 2.5, p=0.004) compared with AAs (n=142). Trends toward lower mortality (21.9 vs. 28.2%) and fewer hospitalizations (0.5 + 1.0 vs. 0.6 + 1.2) were observed in Caucasians compared with AAs. Spironolactone was prescribed more frequently for AAs than for Caucasians (n=95; 66.9% vs. n=137; 50%, p=0.01) No differences in prescription rates for ACE inhibitors, ARBs, beta-blockers, loop diuretics, or digoxin were found.

CONCLUSIONS: Racial differences exist in patient demographics, degree of systolic dysfunction, emergency department utilization, and spironolactone use in this Veteran population. Additional data analysis will focus on differences in HF etiology and comorbid conditions.

Critical Care

338. **Sedation agent administration and outcomes following a sedation awakening trial in MICU patients.** *Dana A. Simonson, B.A.*[1], Craig R. Weinert, M.D., M.P.H.[2], Monica I Lupei, M.D.[1], Henry J. Mann, Pharm.D.[1]; (1)University of Minnesota College of Pharmacy, Minneapolis, Minn; (2)University of Minnesota School of Medicine, Minneapolis, Minn.

PURPOSE: Most of the 300,000 patients on ventilators each year in U.S. ICUs receive sedation agents. Continuous IV sedation is associated with prolonged mechanical ventilation; therefore, daily sedation awakening trials (SATs) have become the standard for practice. The purpose of this study is to identify the relationship between sedation agent administration, patient wake-up time, and subsequent sedation agent status following a daily SAT.

METHODS: MICU patients undergoing a SAT during a 12-week period were prospectively evaluated for inclusion. Demographic data, sedative agent(s) and dosing, SAT results, outcome, and final medication status were collected.

RESULTS: Data collection will be complete August 21, 2007. At week 4, 22 completed SATs were available on 10 patients (5 men, 5 women). The mean age of the patients was 48 ± 13 years. Sedation regimens were: propofol (50%), midazolam (18%), fentanyl and midazolam (14%), fentanyl and propofol (14%), and fentanyl (4%). At the start of the SAT, patients were already awake for 12 trials (55%), and in 3 trials (14%) the patient did not wake up

within 24 hours. The median time to respond to a command in the remaining 7 trials was 120 minutes. In 12 of the SATs performed (66%), patients were spontaneously awake at the start of the SAT while receiving propofol at a median dose of 35 mcg/kg/min over the previous 4 hours. Sedation was stopped following the SAT in 10 patient trials, and 5 patients were extubated. Sedation agent dose was reduced by > 50% in 6 of the remaining 12 trials following the SAT.
CONCLUSIONS: In our MICU, propofol is the most common sedation agent for patients on mechanical ventilation undergoing a SAT. A significant proportion of patients are awake before a SAT is begun. Patients who receive a SAT are likely to stop or reduce the dose of sedation agents.

Education/Training

339. **Students' perception of patient-focused roundtable discussions in the Pharm.D. curriculum.**
Tae Y. Kwak, Pharm.D. candidate, Laura Gilbert-Hayn, Pharm.D., John J. Foley, Pharm.D. candidate, Ina L. Calligaro, Pharm.D., Rachel Clark-Vetri, Pharm.D., BCOP, Nicole Sifontis, Pharm.D., BCPS; Temple University School of Pharmacy, Philadelphia, Pa.

PURPOSE: Over the past 3 years, professional student chapter organizations at our institution hosted three patient-focused roundtable discussions (PFRDs) in various specialty areas. The goal was to convey to student pharmacists the significance of clinical pharmacy services, by inviting patients to share their experiences. The purpose of this study was to evaluate the impact of a PFRD on student learning by assessing students' attitudes toward this type of teaching format.
METHODS: The program included a 10-minute overview of organ transplantation by a clinical pharmacist (CP), one 20-minute presentation by a renal transplant patient, and a 30-minute Q&A session. Attendees completed a 4-question survey, which was collected prior to the presentation and a 6-question post-presentation survey. Pre and post surveys were numbered identically so that each attendee served as his/her own control. Participation was voluntary.
RESULTS: 102 students completed the survey; (PY1, n=46; PY2, n=32; PY3, n=21; PY4, n=3). When asked to assess one's knowledge of the role of the CP as a member of the transplant team on a scale of 1 (unfamiliar) to 5 (very familiar), the mean response increased from 2 ± 0.3 (pre) to 4 ± 0.7 (post-presentation). When asked to list the 2 most common drug related problems transplant patients face, the responses were: rejection (24%)/DDI (16%) pre, and compliance (37%)/ADRs (28%) post-presentation. When asked to assess what effect PFRDs may have on student learning on a scale of 1 (no effect) – 5 (greatly enhanced), the mean response was 4.2 (pre) and 4.3 (post-presentation). The most common written comment to this question was that PFRDs served to humanize the profession early on in the learning process.
CONCLUSION: Preliminary data suggest that PFRDs may have a positive impact on student learning. Further analyses are warranted to validate the effect of this teaching strategy on pharmacy student education.

Endocrinology

340. **Influence of the PPAR-gamma Pro12Ala polymorphism on plasma resistin concentrations in nondiabetic subjects without cardiovascular disease.** *Charles J. Foster, B.S.*[1], Shannon D. Yessak, B.A.[1], Lisa A. Kosmiski, M.D.[2], Christina L. Aquilante, Pharm.D.[1]; (1)Department of Pharmaceutical Sciences, University of Colorado at Denver and Health Sciences Center School of Pharmacy, Denver, Colo; (2)Division of Endocrinology, Diabetes, and Metabolism; University of Colorado at Denver and Health Sciences Center, Denver, Colo.

PURPOSE: The peroxisome proliferator activated receptor-gamma (PPAR) plays an integral role in the differentiation of adipocytes and is involved in the transcriptional regulation of adipocyte-derived cytokines, such as resistin. A common polymorphism, Pro12Ala, exists in the PPAR gene. We sought to determine whether the Pro12Ala polymorphism is associated with plasma resistin concentrations in nondiabetic subjects.
METHODS: A blood sample was obtained from 144 nondiabetic subjects without cardiovascular disease. Pro12Ala genotypes were determined by PCR-pyrosequencing. Plasma resistin concentrations were determined using ELISA. Baseline characteristics and plasma resistin concentrations were compared between genotype groups by unpaired *t* tests (wild type homozygotes versus variant carriers). In addition, differences in plasma resistin levels were compared between genotype groups using ANCOVA, with sex, weight, and metabolic syndrome as covariates.
RESULTS: The study population consisted of 144 subjects (mean age 44 ± 7, 65% female, 84% non-black, 47% with metabolic syndrome, mean weight=94.6 kg ± 17.5, mean BMI=33.3 ± 6 kg/m^2, mean fasting plasma glucose=93 ± 11 mg/dl, mean systolic blood pressure=133 ± 16, mean diastolic blood pressure=77 ± 12; mean triglycerides=149 ± 104 mg/dl, and mean HDL = 51 ± 13 mg/dl). The frequency of the Ala12 allele was 8%.

Baseline characteristics did not differ between genotype groups. Mean plasma resistin concentrations were not significantly different between wild type homozygotes and those carrying the Ala12 polymorphism (10.9 ± 4.1 versus 12.1 ± 4.9, respectively; p=0.288). ANCOVA analysis revealed that sex (p=0.04), weight (p=0.004), and metabolic syndrome (p=0.017) were significantly associated with plasma resistin concentration, but PPARg Pro12Ala genotype was not significantly associated with plasma resistin concentrations(p=0.13).
CONCLUSIONS: Data from our cross-sectional study suggest that the PPAR Pro12Ala polymorphism does not influence plasma resistin levels in non-diabetic subjects without cardiovascular disease. Given our small sample size, this hypothesis merits investigation in a larger population of nondiabetic individuals.

341. **Influence of the PPAR-gamma Pro12Ala polymorphism on plasma resistin concentrations in nondiabetic subjects without cardiovascular disease.** *Charles J. Foster, B.S.*[1], Shannon D. Yessak, B.A.[1], Lisa A. Kosmiski, M.D.[2], Christina L. Aquilante, Pharm.D.[1]; (1)Department of Pharmaceutical Sciences, University of Colorado at Denver and Health Sciences Center School of Pharmacy, Denver, Colo; (2)Division of Endocrinology, Diabetes, and Metabolism; University of Colorado at Denver and Health Sciences Center, Denver, Colo.

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CONCLUSIONS: Data from our cross-sectional study suggest that the PPARγ Pro12Ala polymorphism does not influence plasma resistin levels in nondiabetic subjects without cardiovascular disease. Given our small sample size, this hypothesis merits investigation in a larger population of nondiabetic individuals.

342. **The safety and efficacy of sitagliptin in type 2 diabetes.** *David Aboellez, Pharm.D. Candidate*[1], Michael P. Kane, Pharm.D.[1], Robert S. Busch, M.D.[2], Gary Bakst, M.D.[2], Jill M. Abelseth, M.D.[2], Robert A. Hamilton, Pharm.D.[1]; (1)Albany College of Pharmacy, Albany, NY; (2)The Endocrine Group, LLP, Albany, NY.

PURPOSE: To evaluate the efficacy and safety of sitagliptin, the first of a new class of anti-diabetes medications, the dipeptidyl peptidase-IV inhibitors, in patients with diabetes in an ambulatory care practice.
METHODS: A review of the electronic medical records of three private-practice endocrinologists was conducted to identify patients initiated on sitagliptin during its first 3 months of availability (available October 23, 2007). Drug safety was evaluated by review of documented reports of adverse effects and drug discontinuations that occurred during sitagliptin use. Drug efficacy was evaluated by comparing each patient's baseline A1C and weight with data after a minimum 3 months of sitagliptin therapy. Each patient served as his/her own control. Paired t-tests and chi-square analysis, as appropriate, were used for statistical analysis.
RESULTS: A total of 151 patients began sitagliptin therapy prior to January 23, 2007. Follow-up information was unavailable for 16 patients. Fourteen patients discontinued therapy because of adverse drug effect (n=6) or lack of efficacy (n=8). Sitaglitin use resulted in a statistically significant A1C reduction of 0.24% (p=0.016) from a baseline of 7.29%. This improved A1C occurred despite a 63% discontinuation rate of sulfonylurea therapy and an 83% discontinuation rate of meglitinide therapy at the initiation of sitagliptin therapy (both, p<0.001). There was no difference in the use of pre-meal insulin (p= 0.558). An A1C of < 7% was attained by 55.9% of patients receiving sitagliptin, compared to 40.8% of patients prior to treatment (p=0.018). Use of sitagliptan was

associated with a non-significant 2.5-pound weight loss (p=0.068). Reported side effects were nausea (n=3), and tiredness, chest pain, and muscle aches (n=1 each). No cases of severe hypoglycemia were reported.
CONCLUSIONS: Sitaglitin use was associated with a significant A1C lowering despite marked reductions in secretagogue therapy. Overall, sitagliptin was well tolerated, although it was sometimes ineffective when substituted for high-dose secretagogue therapy.

Health Services Research

343. **Analysis of correlates of smoking in Korean adolescents.** *Yeonhong Lee, B.S.*, Myunghee Park, M.S., Jiae Hwang, B.S., Haeshil Kang, B.S., Seohyung Lee, B.S., Kwisook Choi, Ph.D., Hyesun Gwak, Ph.D., Pharm.D; Ewha Womans University, Seoul, South Korea.

PURPOSE: The objective of this study was to examine the factors influencing smoking of adolescent and elucidate the relation between cigarette smoking and insomnia.
METHODS: This study was designed as a cross-sectional survey. Total number of survey data (n=2404, boys: 54%, girls: 46%) were collected from 9 high schools both in urban and rural area of the middle and southern Korea.
RESULTS: The prevalence of smoking was 15.1% for males and 3.6% for females. The proportion of ex-smokers was 6.1% for boys and 2.7% for girls. The mean pack-years was 1.5 °" 1.7 and 7% of smokers were highly dependent on nicotine. In the analysis using polytomous logistic regression model, age, male, having less than four members of family, and alcohol consumption were positively related to smoking. When variables were adjusted, caffeinated beverage was positively and independently related to cessation of smoking. Smokers had longer nocturnal sleep duration and latency period during sleep (6.5 „b 1.7 hrs and 20.9 „b 24.3 mins, respectively) than never-smokers (6.0 „b 1.2 hrs and 14.1 „b 17.6 mins, respectively) (p<0.0001). The prevalence of taking sleeping pills for smokers, ex-smokers, and never-smokers was 3.0, 1.8, and 0.7% respectively. After adjustment for age, sex, alcohol drinking and caffeine consumption, smokers had a 50% excess in the odds of insomnia compared with non-smokers (p=0.017).
CONCLUSIONS: The results of this study suggest that an adolescent's smoking is influenced by various factors and may cause insomnia and impair the quality of sleep. The development of a health education program to promote never-smoking is recommended.

Hematology/Anticoagulation

344. **Comparison of epoetin alfa and darbepoetin alfa for anemia in cancer patients with chemotherapy and chronic kidney disease patients with hemodialysis in Korea.** *Seohyung Lee, B.S.*[1], Jinyoung Moon, M.S.[2], Suyeon Nam, M.S.[3], Yeonhong Lee, B.S.[1], Jiae Hwang, B.S.[1], Haeshil Kang, B.S.[1], Hyesun Gwak, Ph.D., Pharm.D[1]; (1)Ewha Womans University, Seoul, South Korea; (2)National Cancer Center, Seoul, South Korea; (3)Ewha Womans University Dongdaemun Hospital, Seoul, South Korea.

PURPOSE: This study aimed to compare the patterns of use and effectiveness of therapy with epoetin alfa (EPO) and darbepoetin alfa (DARB) for anemia, and investigate which patient groups, cancer patients with chemotherapy and chronic kidney disease (CKD) patients with hemodialysis, have more responsiveness to these drugs.
METHODS: This study was a retrospective chart review of cancer patients and hemodialysis patients with anemia treated with EPO or DARB in two medical centers. Eligible patients were adults (≥ age 18 years) with baseline Hb ≤ 11g/dL. Effectiveness was measured as the hemoglobin (Hb) level increase from the baseline (≥ 1g/dL). Administration frequency was 2–3 times per week in EPO and once weekly in DARB.
RESULTS: Mean baseline Hb were similar in EPO and DARB groups. Mean weekly doses of EPO and DARB were 19,014.7U (n = 64) and 68.7μg (n = 64), respectively; Dose only ratio was of EPO and DARB was 276.8 : 1. The results showed Hb increase and Hb response (≥ 1g/dL increase) rate in EPO was higher than that in DARB. Hb increase and response rate in hemodialysis patients (n=63) were higher than those in cancer patients (n=65). (p<0.05) In cancer patients, Hb increase in female was higher, while in hemodialysispatients, Hb increase in male was much higher. (p<0.05)
CONCLUSION: EPO-treated patients had a greater mean changes in Hb from baseline and Hb responses than DARB, even though it was not a statistically significant. Hb increase and response in hemodialysis patients were much higher than those in cancer patients.

345. **Analysis of anticoagulation complications in emergency center patients with mechanical heart valve replacements on warfarin therapy in Korea.** *Jiae Hwang, B.S.*[1], Hyosook Song, M.S.[1], Yeanhong Lee, B.S.[1], Seo-hyung Lee, B.S.[1], Haeshil Kang, B.S.[1], Hyesun Gwak, Ph.D., Pharm.D.[1], Byungchul Chang, Ph.D.[2]; (1)Ewha Womans University, Seoul, South Korea; (2)College of Medicine, Yonsei University, Seoul, South Korea.

PURPOSE: This study was to evaluate the factors on bleeding complications and thromboembolism in patients on warfarin with mechanical heart valves visiting emergency center.
METHODS: Among records of 560 patients who were operated at Y Cardiovascular Hospital between November 2001 and October 2006, those of 83 patients who had mechanical heart valve and visited emergency center were reviewed.
RESULTS: There were 6 major thromboembolic events, 18 major bleeding events, and 25 minor bleeding events in patients visiting emergency center. The mean international normalized ratio (INR) was 2.11 ± 1.17 in all patients, 4.30 ± 13.29 in patients visiting emergency center, 6.07 ± 3.86 in patients with major bleeding, and 5.89 ± 2.80 in patients with minor bleeding complication. There was statistically significant difference in INR between bleeding complication groups and no bleeding groups (p=0.001 in patients with major bleeding, p=0.0001 in patients with minor bleeding). However, there was no difference in time in therapeutic range (TTR) when the therapeutic target INR range was 1.8 ~ 3.0 (p=0.730). With risk analysis, serum albumin level was significantly low and weekly warfarin dose was significantly high in patients with bleeding complication (p °Ü 0.05). Among 18 patients with major bleeding, 10 patients were related to drug interaction. There was no correlation between mechanical valve position and INR (p=0.0873).
CONCLUSIONS: There was no statistically significant difference in TTR between no bleeding group and bleeding groups, meaning that there were many unknown factors of warfarin related to anticoagulation complications. To reduce anticoagulation related complications, close monitoring and systemic anticoagulation education should be offered by experienced and knowledgeable pharmacists.

346. **Assessment of the impact of various dosing intervals on the delivery of effective venous thromboembolism prophylaxis in medically ill patients.** *Nataliya Shinkazh, Pharm.D. Candidate*[1], Kate Phillips, Pharm.D.[2], Toby Trujillo, Pharm.D., BCPS[3]; (1)Northeastern University School of Pharmacy, Boston, Mass; (2)Boston Medical Center, Boston, Mass; (3)Boston Medical Center, Dept of Pharmacy, Boston, Mass.

PURPOSE: Unfractionated heparin (UFH) 5000 units every 8 hours and enoxaparin 40 mg/day are commonly used in the prevention of venous thromboembolism (VTE). UFH is often preferred due to lower cost, but the need for three daily doses may prevent optimal implementation of the regimen and compromise efficacy. The purpose of this study was to assess whether there is a difference in the ease of implementation between the UFH and enoxaparin prophylaxis regimens.
METHODS: Patients included were medically ill, receiving > 2 doses of either UFH or enoxaparin for prophylaxis. Patients on alternative prophylaxis, currently anticoagulated at an INR > 1.8, or on dialysis were excluded. The primary end point was the percentage of inappropriately administered doses (defined as a composite of all doses given too early, too late, or completely missed) with UFH and enoxaparin. Secondary end points included the percentage of patients who had > 10%, and > 25% of their total number of prophylaxis doses administered inappropriately, as well as the incidence of bleeding, VTE and heparin induced thrombocytopenia (HIT). A total of 204 doses per regimen is needed to detect a 10% difference in the percentage of inappropriately administered doses at an alpha level of 0.05 and power of 80%.
RESULTS: Currently, 46 UFH (315 doses) and 47 enoxaparin (123 doses) patients have been included. The primary end point occurred 21.27% and 6.5% of the time in the UFH and enoxaparin groups respectively (p<0.05). A higher percentage of patients receiving UFH had at least 10% (45.7% vs 17%, p<0.05) and 25% (30.4% vs 12.8%, p=NS) of their total doses given inappropriately.
CONCLUSION: Preliminary results indicate that the UFH regimen has a greater number of inappropriately administered doses compared with enoxaparin. Full results including the incidence of bleeding, VTE, and HIT will be presented.

HIV/AIDS

347. **Medication errors in hospitalized HIV-infected patients in a tertiary care teaching hospital.** *Melissa D. Dragic, Pharm.D., Candidate*, Olga M. Klibanov, Pharm.D.; Temple University School of Pharmacy, Philadelphia, Pa.

PURPOSE: To quantify and describe medication errors in hospitalized HIV-infected patients.

METHODS: We prospectively reviewed medication profiles of all hospitalized patients who were on antiretrovirals (ARVs) for a 30-day period (May 1–30, 2007) at a 600-bed tertiary care teaching hospital. Data collected included demographics (including renal function) and medication appropriateness (dosing, formulation, drug interactions). A daily assessment was performed by a pharmacy student, under the supervision of a HIV clinical pharmacist. If an error was noted, the prescribing physician was contacted, and interventions were recommended and documented.

RESULTS: During the 30-day period, 31 admissions of 28 patients patients (3 patients were admitted twice) who were on ARVs were recorded; 23 (74%) men, mean (SD) age was 49.7 (11.5) years. ARV regimens consisted of ritonavir-boosted protease inhibitors (PIs) in 15/31 (48%), unboosted PIs in 7/31 (23%), and nonnucleoside reverse transcriptase inhibitors (NNRTIs) in 9/31 (29%). Of 31 admissions, 15 medication errors were identified (48% error rate). Of 15 errors, the most common were wrong ARV dose (6/15; 40%) and significant drug-drug interactions (5/15; 33%). Other errors included wrong dose of opportunistic infections medications (2/15; 13%), wrong ARV formulation (1/15; 7%), and duplicate therapy (1/15; 7%). Pharmacist intervention resulted in 100% physician acceptance rate.

CONCLUSIONS: HIV-infected patients admitted to the hospital are at a high risk for medication errors. Awareness and education regarding medication prescribing and dispensing in HIV-infected patients needs to increase to ensure that these patients receive appropriate therapy during their hospitalizations.

348. Characterization of virologic and immunologic responses following initiation of ART in HIV-treatment naïve pregnant women. *Yat-Shing Lau, Pharm.D. Candidate*[1], Sanjivini Wadhwa, M.D.[2], Jeremy Peters, Pharm.D.[3], Susan L. Koletar, M.D.[4], Michael F. Para, M.D.[4], Michael T. Brady, M.D.[5], Jane Hunkler, R.N.[5], Patty Fan-Havard, Pharm.D.[1]; (1)School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, SUNY, Amherst, NY; (2)School of Medicine and Biomedical Sciences, University at Buffalo, SUNY, Amherst, NY; (3)College of Pharmacy, Ohio State University, Columbus, Ohio; (4)School of Medicine, Ohio State University, Columbus, Ohio; (5)Columbus Children's Hospital, Columbus, Ohio.

PURPOSE: The objectives of the study are to 1) characterize the median time to achieve undetectable HIV-1 viral load, 2) assess the change in CD4+ cell count, and 3) analyze differences in the virologic and immunologic responses based on ART regimen, trimester of ART initiation, and baseline VL and CD4+ cell counts in HIV-infected treatment-naïve pregnant women.

METHODS: HIV-infected pregnant women receiving antepartum ART chemoprophylaxis to reduce perinatal transmission were evaluated for this study. Patient demographics, ART regimens, initiation dates of ART, and virologic and immunologic data were retrospectively collected from July 2001 to April 2007. Exclusion criteria included those women who received ART prior to conception or who had changes in their antepartum ART regimens, and nonadherence to ART or clinic appointments. For each patient, the days to achieve undetectable VL and the change in CD4+ cell count during pregnancy were calculated. Mann-Whitney U and Kruskal-Wallis non-parametric tests were used to determine median differences between groups based on 1) ART regimen, 2) trimester therapy initiated, 3) baseline VL, and 4) baseline CD4+ cell counts.

RESULTS: A total of 26 patients, mean (± SD) age 25.9 (± 4.7), fit these criteria. Antepartum ART chemoprophylaxis regimes were NRTIs in 6, NNRTI-based in 15, and HIV-1 PI-based in 5 women. The median time to reach undetectable HIV VL after initiation of ART was 55 days (range 20–132 days). Following initiation of ART, the median increase in CD4+ cell count at delivery was 120/mm³ (range: -389–766/mm³).

CONCLUSIONS: This is the first report characterizing the time to undetectable HIV VL and change in CD4+ cell count during pregnancy in HIV-1 infected women treated with antepartum ART. Non-parametric analyses are under way to determine the differences in virologic and immunologic responses based on ART regimen, trimester of ART initiation, and baseline VL.

Infectious Diseases

349. **Pediatric antibacterial use at US academic health centers from 2002 to 2005.** *Holly E. Gurgle, B.S.*[1], Amy Pakyz, Pharm.D., M.S.[1], Ronald E. Polk, Pharm.D.[1], Michael J. Oinonen, Pharm.D., M.P.H.[2]; (1)Virginia Commonwealth University School of Pharmacy, Richmond, Va; (2)University HealthSystem Consortium, Oak Brook, Ill.

PURPOSE: To measure and evaluate trends in antibacterial (AB) use in pediatric patients (<age 18) at academic health centers from 2002 to 2005.

METHODS: AB usage among pediatric inpatients was determined from billing data at 21 academic health centers that participated in the University HealthSystem Consortium Clinical Resource Manager Database. AB use was measured in days of therapy per 1000 patient days (DOT/1000PD). Aggregated DOT/1000PD data was analyzed

to rank individual ABs and AB classes most commonly used. Repeated measures ANOVA determined trends in AB use from 2002 to 2005.

RESULTS: Pediatric patients contributed 385,295 discharges or 16% of total (adult and pediatric) hospital discharges between 2002-2005. Pediatric patients received 11% of total AB prescriptions. The mean percent of pediatric patients receiving at least one AB was 40% +/- 14% while the mean percent of adult patients receiving at least one AB was 64% +/- 5%. The individual ABs most commonly used in pediatric patients were 1) ampicillin, 2) gentamicin, 3) vancomycin, 4) cefazolin, and 5) ceftriaxone. Individual ABs that increased significantly in use between 2002-2005 were: amoxicillin (p=0.0492), linezolid (p=0.0010), and piperacillin/tazobactam (p=0.002). Individual ABs that decreased significantly were ampicillin (p=0.0127), azithromycin (p=0.0089), and cefazolin (p=0.0291). The AB classes most commonly used were 1) penicillins, 2) aminoglycosides, and 3) 3rd-/4th-generation cephalosporins. Although no AB classes were observed to decrease significantly, the beta-lactamase inhibitor (p=0.0174) and carbapenem (p=0.026) classes increased significantly. There was no significant change in total AB use from 2002 to 2005.

CONCLUSIONS: The use of selected narrow-spectrum ABs (ampicillin, azithromycin, cefazolin) decreased significantly. The use of individual broad-spectrum ABs (piperacillin/tazobactam), ABs for resistant organisms (linezolid), and broad-spectrum AB classes (carbapenems, beta-lactamase inhibitors) increased significantly. The total use of ABs, the individual ABs most commonly used, and the AB classes most commonly used in pediatric patients remained consistent from 2002 to 2005. Trends in the use of some individual and classes of ABs require special attention as they may generate increased rates of bacterial resistance.

350. **Predictors of pediatric antibacterial use in 35 US academic health centers in 2005.** *Holly E. Gurgle, B.S.*[1], Amy Pakyz, Pharm.D., M.S.[1], Ronald E. Polk, Pharm.D.[1], Michael J. Oinonen, Pharm.D., M.P.H.[2]; 1) Virginia Commonwealth University School of Pharmacy, Richmond, Va; 2) University HealthSystem Consortium, Oak Brook, Ill.

PURPOSE: To identify predictors of antibacterial (AB) use in pediatric patients (< age18) at academic health centers (AHC).

METHODS: Inpatient pediatric AB usage was determined from billing data at 35 AHC that participated in the University HealthSystem Consortium Clinical Resource Manager Database in 2005. AB use was measured in days of therapy per 1000 patient days (DOT/1000PD). Multivariate analysis identified independent predictors of total AB DOT/1000PD.

RESULTS: The AHC had a mean AB use of 564.8 +/- 211.9 DOT/1000PD in pediatric patients. The mean, standard deviation, and range of AHC characteristics of potential predictor variables included: case mix index (1.08 ± 0.23, 0.61–1.52); total discharges (3,808 ± 2063, 415–8008); total patient days (23,332 ± 13,948, 2,112–51,504); mean age of patients (4.2 ± 2.3, 0–17); number of inpatient surgeries/1000PD (5.15 ± 3.72, 0.48–17.5); number of bone marrow transplants/1000PD (0.14 ± 0.39, 0–2.27); number of solid organ transplants/1000PD (0.19 ± 0.27, 0–1.21); number of urinary tract infections/1000PD (3.28 ± 1.85, 0.34–8.23); number of pneumonia infections/1000PD (5.65 ± 3.45, 0–12.6); and number of bloodstream infections/1000PD (4.69 ± 3.36, 0–16.9). AHC represented the following regions: Mid-Continent (7 hospitals); Midwestern (7); Mid-Atlantic (7); Southeastern (7); Western (4); New England (3). On multivariate regression, three factors were shown to significantly predict AB use in pediatric patients: number of urinary tract infections/1000PD (p=0.0259); number of pneumonia infections/1000PD (p=0.0015); and number of solid organ transplants/1000PD (p=0.0236); overall R²adj=0.7209.

CONCLUSIONS: Demographic factors vary between AHC. Urinary tract infections, pneumonia, and solid organ transplants are significant positive predictors of AB use in AHC. Further studies should be conducted to better understand the relationships between certain infections or procedures, pediatric AB usage practices, and AB resistance rates in order to establish more effective AB use policies in pediatric populations.

351. ***In vitro* evaluation of the mutant prevention concentration (MPC) and mutant selection window (MSW) for fluoroquinolones against *Neisseria gonorrhoeae*.** *Cynthia D. Hankins, Pharm.D.*, George P. Allen, Pharm.D.; Oregon State University College of Pharmacy, Portland, Ore.

PURPOSE: The use of fluoroquinolones (FQs) for the treatment of *Neisseria gonorrhoeae* (NG) has been limited by the development of FQ resistance, yet few alternate antimicrobials are available for treatment of NG. Ciprofloxacin (CIP) and levofloxacin (LEV) are the only available FQs that have been evaluated against NG. Moxifloxacin (MXF) has activity against NG, and its C-8-methoxy substituent is known to prevent FQ resistance. The MPC is a novel susceptibility index that is defined as the minimum inhibitory concentration (MIC) of the most resistant first-step mutant in a heterogeneous bacterial population. Maintenance of FQ concentrations above MPC should prevent resistance selection, and concentrations between MIC and MPC (the MSW) will promote resistance selection. No published studies of the MPC in NG exist. We evaluated resistance induction by FQs in NG using the MPC.

METHODS: CIP, LEV, and MXF were studied. MPCs of ATCC 49226 (49226) and a *gyrA* mutant of 49226 (m-49226) were determined by culturing an inoculum of 10^{10} colony-forming units on FQ-impregnated agar. The MPC was the lowest concentration to completely inhibit growth.

RESULTS: MIC/MPC (mg/L) for 49226 were: CIP 0.008/0.03, LEV 0.008/0.125, MXF 0.015/0.06. MIC/MPC (mg/L) for m-49226 were: CIP 0.125/4, LEV 0.125/0.5, MXF 0.125/0.25. Based on population pharmacokinetics for single-dose regimens of each FQ, MXF will attain the longest time above MPC (T>MPC) for both 49226 and m-49226. All FQs will attain concentrations within the MSW for both isolates. MXF is the only FQ that will achieve a T>MPC longer than its usual dosing interval.

CONCLUSIONS: MXF is predicted to be less likely than either CIP or LEV to induce resistance in NG. However, concentrations of all FQs are predicted to fall within the MSW for both 49226 and m-49226. Use of multiple-dose FQ regimens may prevent further resistance in NG; this option warrants further study.

352. **Evaluating the effect of heparin, norepinephrine and phenylephrine on biofilm-producing Staphylococcus aureus.** *Kevin W. McConeghy, student*, Kerry L. Laplante, Pharm.D; University of Rhode Island and Veterans Affairs Medical Center, Providence, RI.

PURPOSE: *Staphylococcus epidermidis* and *S. aureus* commonly colonize indwelling catheters. Studies report that heparin and catecholamines may enhance biofilm production in these bacteria. We evaluated the effects of heparin and catecholamines on biofilm formation in *S. aureus* and *S. epidermidis* with chemical-grade and pharmacy-obtained drug stock (which contains 0.9% benzyl alcohol).

METHODS: Biofilm-producing *S. aureus* (ATCC 35556) and *S. epidermidis* (ATCC 35984) were evaluated. Biofilm mass was measured using a colorimetric assay (optical density 570) described by Christensen, et al. Clinically relevant concentrations of heparin (5,000 u/mL), phenylephrine (200 mcg/mL) and norepinephrine (8 mcg/mL) were evaluated for biofilm inhibition after 24 hours of growth. The ANOVA test was used to determine significance of the results.

RESULTS: For *S. aureus,* there was no reduction in biofilm formation in heparin 5000 u/mL chemical stock, but there was a decrease (p=0.002) of biofilm formation in the presence of the pharmacy stock. *S. aureus* biofilm formation was not affected by catecholamine in either chemical or pharmacy stock. Biofilm production by *S. epidermidis* was not significantly affected by any chemical stock, but the pharmacy stock of the catecholamines/ heparin demonstrated a decrease in biofilm growth (p=0.013).

CONCLUSION: Reduction of *S. aureus* biofilm growth in the presence of heparin and catecholamine pharmacy-stock is most likely due to the 0.9% benzoyl alcohol preservative in the solution, providing evidence that heparin and catecholamines do not support the growth of Staphylococcus.

Isolate	Growth Control (avg ±sd)	Heparin 5000 u/mL (avg ±sd)	Phenylephrine 200 mcg/mL (avg ±sd)	Norepinephrine 8 mcg/mL (avg ±sd)	Media control (avg ±sd)
S.aureus CS	0.427±0.14	0.216 ±0.07	0.267 ±0.03	0.242 ±0.03	0.00±0
S. aureus PS	0.416 ±0.17	-0.009 ±0.01	0.292 ±0.09	0.328 ±0.10	0.000 ±0.03
S.epi Chem	2.495 ±0.15	2.211 ±0.45	1.893 ±0.37	1.908 ±0.32	0.000 ±0.30
S.epi Pharm	2.79 ±0.79	2.394 ±0.79	2.181 ±0.16	2.074 ±0.19	0.00 ±0.01

Oncology

353. **Analysis of febrile neutropenia in multiple myeloma patients post-autologous hematopoietic stem cell transplantation (HSCT).** *Kendrick A, Lake B, DeRemer D, Farrow S, Ustun C, and Jillella A.*

PURPOSE: High dose melphalan (140-200 mg/m2) with autologous hematopoietic stem cell transplant (HSCT) has become standard treatment for patients with multiple myeloma. Prior to engraftment initiating at day +1, patients commonly receive fluoroquinolone prophylaxis in addition to antiviral and antifungal therapies. Despite this strategy, patients still encounter febrile neutropenia and infections. The primary objective of this study was to identify potential risk factors influencing febrile neutropenia and documented infections. Secondary objectives include antibiotic utilization and clinical outcomes.

METHODS: Retrospective chart review of multiple myeloma patients who received an autologous HSCT at the Medical College of Georgia between December 1999 and June 2007. Statistical analysis was performed using the Mantel-Haenszel Chi square test and ANOVA. Clinical outcomes were retrospectively analyzed using Kaplan-Meier survival analysis.

RESULTS: Seventy-three patients were evaluated. The mean number of CD34+ cells infused was 10.2 x 106 / kg (range: 1.63-31.2 x 106/kg). Neutrophil engraftment was achieved at 10.5 ± 1.4 days. A total of 220 days of febrile neutropenia was identified with a mean duration of 4.4 ± 4 days. No statistical association was found

between febrile days and documented infection (P=0.054), day post-engraftment (P=0.074), mobilization regimen (P=0.11), race (P=0.77), diabetes (P=0.18), number of prior regimens (P=0.27), mucositis grade (P=0.47), age (P=0.54), or number of CD34+ cells infused (P=0.89). Microbiological documented infections were found in 16/73 (22%) patients. A trend was observed for increased number of documented infections with number of pre-transplant regimens (P=0.052). Overall survival for day +30 and day +100 was 95% and 94% respectively.
CONCLUSIONS: Patients with documented infections and later neutrophil engraftment trended to have more febrile days. However, previously proposed risk factors had negligible association with neutropenic fever or infection.

Pediatrics

354. **Variable delayed clearance of methotrexate in pediatric oncology patients: a retrospective review.** *Ann R. Howell, Pharm.D./M.S. Candidate*, Tracy M. Hagemann, Pharm.D., Donald L Harrison, Ph.D.; University of Oklahoma College of Pharmacy, Oklahoma City, Okla.

PURPOSE: The purpose of this study is to identify children who exhibit variable clearance of methotrexate (MTX) and then to identify common variables that are associated with these changes in clearance. Findings will be used to evaluate processes that can be implemented to prevent delayed clearance and toxicity in these patients.
METHODS: A retrospective chart review was conducted at The Children's Hospital at OU Medical Center, including children who had received IV MTX between January 2000 and June 2006. A MTX plasma concentration of > 0.2 μM at 48 hours was classified as delayed clearance. The children were grouped as always delayed, always normal, or mixed. Patient age, sex, disease, and renal function were included for comparison. All concurrent medications received within 7 days prior to the day of the MTX dose were noted. Statistical analyses were conducted to look for associations between the variables and patients with mixed-type MTX clearance.
RESULTS: 134 patient charts were reviewed. Of these, 47 always cleared normally, 37 were always delayed, and 56 had a mixture of delayed and normal clearance. Of the 56 mixed patients, there were 516 courses of MTX with male patients accounting for 62% of the courses. Patients ranged in age from 8 months to 21 years, all with leukemia, lymphoma, or osteosarcoma. The mean dose was 5.8g (+/- 6.5). Preliminary statistics show differences between the 48-hour plasma MTX level and both MTX dose and creatinine levels; an association was recognized between MTX levels and both gender and disease.
CONCLUSIONS: Data analysis is ongoing. The results will be used to identify variables responsible for mixed-type MTX clearance. Steps can then be taken toward improving MTX clearance in susceptible patients.

Pharmacoepidemiology

355. **Antifungal prescribing and associated health outcomes among institutionalized patients.** *Christine U. Oramasionwu, Pharm.D.*, Andres D. Ruiz, Pharm.D. Candidate, Christopher R. Frei, Pharm.D., M.Sc., BCPS; The University of Texas at Austin College of Pharmacy and The University of Texas Health Science Center at San Antonio, San Antonio, Tex.

PURPOSE: Antifungal stewardship involves two key practices: appropriate antifungal selection and dose optimization. This study characterized antifungal usage patterns and health outcomes for patients admitted to a large academic health-center.
METHODS: Clinical data were collected for 80 random inpatients who received systemic antifungals at University Health-System (San Antonio, Texas) in 2006. Data included: patient demographics, admission and discharge dates, infectious diagnoses, comorbidities, antifungals, cultures, and discharge disposition. Descriptive statistics were used to determine inpatient mortality and duration of hospital and ICU stays. Antifungal-, disease-, and pathogen-specific outcomes analyses are planned.
RESULTS: Patients had a mean (±SD) age of 53±12 years, 62% were male, and 29% were admitted through the emergency department. Common comorbidities included solid organ transplant (44%), diabetes (43%), and liver disease (28%). Tobacco use (18%) and substance abuse (14%) were uncommon. Fifty percent of patients underwent surgical procedures, 45% were admitted to the ICU, 9% required hemodialysis and 8% required mechanical ventilation. Cultures were obtained from 80% of patients and 27% were culture positive. Of these, *Candida sp.* accounted for 88% of the positive cultures (10/15 *C. albicans*, 5/15 *C. glabrata*, and 1/15 *C. krusei*), followed by *Aspergillus* sp. (12%), and *Cryptococcus neoformans* (12%). Multiple mycotic species were occasionally isolated from the same patient. Fluconazole (61%), voriconazole (23%), itraconazole (20%), and amphotericin-B (18%) were frequently prescribed. Patients required a median (25th and 75th percentile) stay of 10 (7–19) hospital days and 7 (3–21) ICU days. Ten percent of patients expired. Forty-one percent of patients received antifungals at discharge: itraconazole (32%), fluconazole (29%), voriconazole (26%), and other (13%).

CONCLUSION: Fluconazole remains the therapeutic mainstay during hospitalization and at discharge; however, voriconazole use is on the rise. Future analyses will determine fluconazole doses for the various *Candida* sp. and will identify patient, disease, and pathogen factors associated with voriconazole use.

356. Characterization of continued use of antimicrobial therapy post-diagnosis of *Clostridium difficile* associated diarrhea (CDAD). *Timothy J. Inocencio, Student*[1], Spencer E. Harpe, Pharm.D., Ph.D., M.P.H.[1], Amy Pakyz, Pharm.D., M.S.[1], Michael Oinonen, Pharm.D., M.P.H.[2], Ronald E. Polk, Pharm.D.[1]; (1)VCU School of Pharmacy, Richmond, Va; (2)University HealthSystem Consortium, Oak Brook, Ill.

PURPOSE: Antibacterial drugs cause most cases of CDAD, and experts recommend discontinuation of the offending drug whenever possible. The purpose of this study was to determine if these recommendations are followed.
METHODS: Cases of CDAD in adults using a previously validated definition were identified among 26 academic medical centers that participated in the UHC Clinical Resource Manager (CRM) program during the first quarter of 2006. Four quarters of data will be included by late July. Cases were defined as those with a secondary ICD-9-CM code for pseudomembranous colitis (008.45) plus > 3 days of treatment with oral or IV metronidazole and/or oral vancomycin starting > 4 days post hospital admission. The day of CDAD diagnosis was assumed to be the day that metronidazole or vancomycin was started. Information was collected on antimicrobial drugs administered before and after CDAD diagnosis. Patient demographics included age, sex, and race.
RESULTS: A total of 209 cases were identified, with 189 patients qualifying as having prior antibiotic exposure. Overall, 55% of cases continued antimicrobial therapy for > 2 days after the day of CDAD diagnosis. Among patients receiving 1, 2, 3, or ≥ 4 antibacterial drugs before the diagnosis of CDAD, 42%, 59%, 59%, and 69% continued antimicrobial therapy on at least one drug 2 or more days beyond the day of diagnosis, respectively. The most frequently continued antimicrobials were piperacillin/tazobactam (n=18), ciprofloxacin (n=15), levofloxacin (n=12), and cefepime (n=10).
CONCLUSIONS: Despite guidelines that advise discontinuation of antimicrobial drugs upon CDAD diagnosis, a majority of patients in this sample of hospitals continued to be exposed post-diagnosis. The clinical significance of continued antimicrobial therapy on CDAD severity cannot be determined from this study.

357. Predicting antibiotic resistance in nosocomially acquired *Pseudomonas aeruginosa* bacteremia. *Timothy J. Inocencio, Student*, James R. Robles, Ph.D., Shivi Kansal, B.S., Ronald E. Polk, Pharm.D.; VCU School of Pharmacy, Richmond, Va.

PURPOSE: Increasing antibiotic resistance among clinical isolates of *Pseudomonas aeruginosa* is a cause for concern around the world. In this study, we have begun an analysis of the Cerner Health Facts Data Warehouse database as a novel source of information to identify and analyze the risk factors for antibiotic-resistant *P. aeruginosa*.
METHODS: The cases include adult inpatients identified from microbiology records with nosocomial acquired *Pseudomonas aeruginosa* bacteremia at 50 hospitals. Multiple files are being merged to create a profile of relevant predictor variables such as age, sex, concurrent comorbidities, pre-diagnosis length of stay, hospital unit (ICU or non-ICU), and prior exposure (quantitative) to specific antimicrobial drugs. CART analysis will be used to identify breakpoints in continuous variables such as the duration of antimicrobial therapy and length of hospital stay associated with susceptible versus mono- and multidrug resistant isolates of *P. aeruginosa*.
RESULTS: Data from two quarters in 2006 have been accessed, and 88 clinical isolates of *P. aeruginosa* bacteremia have been identified. Susceptibility data are under evaluation. Among the 88 patients, preliminary analysis suggests that predictor variables are available for 68. The database will eventually include years 2000–2006 by the end of Summer 2007 and is expected to yield the largest series of nosocomial bacteremia caused by *P. aeruginosa* yet collected.
CONCLUSIONS: The Cerner Health Facts Data Warehouse is a rich source of clinical information including laboratory results. However, computer scientists and bioinformaticians with specialized training are required to access these data. As with any retrospective investigation of electronic health information, several limitations are likely. Nevertheless, the large numbers of patients and the detail of information may make it possible to investigate clinically relevant topics under "real world conditions" that cannot be studied by prospective investigations.

358. Aspirin use among US adults with diabetes from 2004 MEPS database. *Patrina E. McCauley, B.S.*, Stephanie E. Cho, B.A., Weiming Zhang, M.S., Marianne McCollum, Ph.D.; University of Colorado at Denver and Health Sciences Center, Denver, Colo.

PURPOSE: To investigate population-level differences and estimate prevalence of aspirin use within the population of US adults with diabetes.
METHODS: Data were obtained from the 2004 Medical Expenditure Panel Survey (MEPS). Diabetes was identified by self report or ICD-9 code. Daily or every-other-day aspirin was identified by patient self report. Patients with aspirin contraindications were excluded. Chi square and t-tests were used to determine differences in aspirin use stratified by factors such as demographics, insurance status, and race/ethnicity for US adults with diabetes.
RESULTS: 1789 MEPS respondents met study criteria, representing 14,163,478 adults. Among adults with diabetes, those using versus not using aspirin were older, mean (SE) 63.9 (0.4) years versus 54.2 (1.2) years (p=0.006), more likely to be Hispanic versus non-Hispanic (p=0.0012), and more likely to have CHD versus not having CHD (p=0.019). Having insurance also increased the likelihood of using aspirin in this population with 58% of publicly insured and 60% of privately insured patients taking aspirin compared with 32% of non-insured patients (p=0.0013). Other factors associated with aspirin use were mean (SE) years of education 12.1 (0.27) versus 11.63 (0.23), (p=0.031), 51% of smokers versus 58% of non-smokers (p=0.0158), and 66% of those with hypertension compared with 55% of normotensive people (p=0.0336),
CONCLUSIONS: Aspirin is underused in people with diabetes who are older than age 40. The American Diabetes Association (ADA) recommendation for aspirin use is strongest for people with diabetes 40 years and older. Targeting people with diabetes 40 years and older with effective public education campaigns about appropriate aspirin use could help national compliance with the ADA guideline by reaching the uninsured populations and populations not seeing physicians regularly.

359. **Prevalence of aspirin use among US adults.** *Stephanie E. Cho, B.A.*, Patrina McCauley, B.S., Weiming Zhang, M.S., Marianne McCollum, Ph.D.; University of Colorado at Denver and Health Sciences Center, Denver, Colo.

PURPOSE: To estimate prevalence of aspirin use and examine population-level differences in aspirin usage among US adults.
METHODS: Data from the Medical Expenditure Panel Survey (MEPS) 2004 database were used. Self-reported aspirin usage among adults ≥ 18 years was estimated using chi-square and t-tests stratified by factors that included demographics, insurance status, race/ethnicity, CHD, and diabetes status. Patients with aspirin contraindications were excluded.
RESULTS: A total of 22,115 MEPS participants were eligible for these analyses, of which 4204 (19%) reported daily or every-other-day aspirin use. 63% of people with diagnosed CHD and 54% of people with diagnosed diabetes reported aspirin use, while 15% of non-CHD and 18% of people not diagnosed with diabetes used aspirin regularly. Adults using aspirin were older than those not taking aspirin, mean (SE) age 61.01 (0.32) years versus 40.73 (0.20) years (p<0.001). Factors associated with increased likelihood of using aspirin regularly were other than Hispanic ethnicity (versus Hispanic), having a history of CHD versus no CHD, and having no insurance compared with any private or public insurance (all p<0.001). People who self-identified as smokers were significantly less likely to report aspirin use versus non-smokers (p<0.0001). Mean number of education years was not significantly associated with aspirin use (p=0.460). Patients with CHD not taking aspirin regularly may be taking other anti-coagulant medications, a limitation of the current study.
CONCLUSION: Nineteen percent of all US adults and 63% of those with CHD and 54% of those with diabetes report taking aspirin every day or every-other-day. It is important from a public health perspective to identify potential barriers to regular aspirin use for primary or secondary prevention of cardiovascular events. Pharmacy practitioners can play an important role in promoting appropriate use of this inexpensive and readily accessible, other-the-counter medication.

Pharmacogenomics

360. **Serum concentration and response to fenofibrate based on genetic variability in the drug transporter SLCO1B1 (OATP-C).** *Mary Jo Zurbey, B.A.*[1], Na Li, Ph.D.[1], Michael Y. Tsai, Ph.D.[1], Naomi Q. Hanson, M.Sc.[1], Jose M. Ordovas, Ph.D.[2], Donna K. Arnett, Ph.D.[3], Robert J. Straka, Pharm.D.[1]; (1) University of Minnesota, Minneapolis, Minn; (2)Tufts University, Boston, Mass; (3)University of Alabama, Birmingham, Ala.

PURPOSE: Variability in fenofibric acid (FA) serum concentrations and triglyceride response is large for subjects taking fenofibrate. Single nucleotide polymorphisms (SNPs) in the OATP-C transporter encoded by SLCO1B1 gene have been associated with serum concentrations of statins. From the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study, we recently reported an association between carriers of SLCO1B1 521T>C and reduced triglyceride lowering response to fenofibrate and therefore hypothesized that OATP-C may affect

FA concentrations. The objective was to investigate the relationship between SLCO1B1 genotype and serum FA concentrations in GOLDN subjects.

METHODS: Fasting lipid profiles were obtained from subjects > 18 years of age on 2 consecutive days pre and post 3-week exposure to daily fenofibrate 160 mg. Trough serum FA concentration obtained on day 21 was quantified by HPLC. Response was calculated by log of the ratio of the average of two pre- and two post-fenofibrate triglyceride levels. SLCO1B1 SNPs 388A>G (*1b), 521T>C (*5) and the combined haplotype (*1b and *5) were determined by Sequenom® (MALDI-TOF mass spectrometry).

RESULTS: From 733 subjects [374 (51%) males] with a mean (±SD) age of 50 (16) years, 698 (*1b), 728 (*5) and 693 (*1b and *5) subjects had evaluable data. Mean (±SD) [range] pretreatment fasting triglyceride was 141 (98), [26-1202] mg/dL vs. 91 (66) [19-419] mg/dL at end of treatment period. Minor allele frequencies for 388A>G and 521T>C were 0.37 (G) and 0.14 (C). No statistically significant associations were found between either individual or combined SLCO1B1 SNPs and FA concentrations. Mean (±SD) serum FA concentrations for SLCO1B1 521 CC, CT and TT were 6.7 (2.3), 8.2 (5.5), and 8.0 (4.8) mg/dL.

CONCLUSIONS: In spite of our previous finding, available data provide insufficient evidence to conclude that reduced triglyceride lowering response to fenofibrate with SLCO1B1 521C carriers is associated with trough serum FA concentrations.

361. **Pharmacogenetics of intravenous busulfan in patients undergoing myeloablative hematopoietic cell transplantation.** *Nissa Abbasi, M.S.*[1], David K. Blough, Ph.D.[1], Edward J. Kelly, Ph.D.[1], Paul V. O'Donnell, M.D., Ph.D.[2], Matthew A. Pawlikowski, M.A.[3], Jeannine S. McCune, Pharm.D.[1]; (1)University of Washington, Seattle, Wash.; (2)Fred Hutchinson Cancer Research Center, Seattle, WA; (3)Seattle Cancer Care Alliance, Seattle, Wash.

PURPOSE: The alkylating agent Busulfan (BU) is an integral part of many hematopoietic cell transplantation (HCT) conditioning regimens. At our center, about 80% of our lab service with outside centers involves therapeutic drug monitoring (TDM) of IV administered BU. Less resource-intensive methods to achieve target BU concentration steady state (Css) are desirable. Therefore, we sought to determine the ability of genetic polymorphisms regulating enzymes involved in BU conjugation (i.e., glutathione-S-transferase, GST), demographics and end-organ function to predict BU clearance.

METHODS: Between 6/02 and 11/06, 59 patients received IV busulfan every 6 hours (n=20) or every 24 hours (n=39) and had pharmacokinetic sampling the morning of days 1, 2, and 3 of IV BU. Samples were quantitated by gas chromatography-mass spectrophotometry, pharmacokinetic modeling was performed to estimate the patient's IV BU clearance and Css, and the dose was adjusted as needed. DNA samples obtained from each patient prior to HCT were analyzed for GSTA1 *A/*B gene promoter polymorphisms and GSTM1 gene deletion genotypes. The ability of demographic, end-organ function, and genetic covariates to predict busulfan clearance will be evaluated.

RESULTS: GSTA1 genotype was in Hardy-Weinberg equilibrium; no association was observed between GSTA1 genotype and BU clearance. The average BU clearance for all patients was 106 mL/min/m². The average clearance determined by genotypes did not significantly differ from this value for either dosing interval (p>0.05). Additional analysis of demographic, laboratory, and GSTM1 covariates and BU clearance will be completed by September 2007.

CONCLUSION: BU dosing in HCT is an iterative process that may need daily TDM to achieve and maintain a targeted Css. Based on current results, modifying the Bu dose based on GSTA1 genotype would not be practical for BU dose optimization. However, additional population pharmacokinetic analyses may elucidate parameters to simplify BU TDM and improve patient safety.

362. **The influence of CYP2C8 polymorphisms on rosiglitazone pharmacokinetics in healthy volunteers.** *Shannon D. Yessak, B.A.*[1], Lisa A. Kosmiski, M.D.[2], Lane Bushman, B.S.[1], Lauren Burt, Pharm.D.[1], Lucille Capo Rome, ANP[1], Courtney V. Fletcher, Pharm.D.[1], Christina L. Aquilante, Pharm.D.[1]; (1)Department of Pharmaceutical Sciences, University of Colorado at Denver and Health Sciences Center School of Pharmacy, Denver, Colo; (2)Division of Endocrinology, Diabetes, and Metabolism; University of Colorado at Denver and Health Sciences Center, Denver, Colo.

PURPOSE: Rosiglitazone is a thiazolidinedione used in the treatment of type 2 diabetes. We sought to determine whether the CYP2C8*3 allele (Arg139Lys, Lys399Arg) is associated with interindividual variability in rosiglitazone pharmacokinetics.

METHODS: The study population consisted of 26 healthy Caucasian subjects (n=20, CYP2C8*1/*1 genotype; n=6, CYP2C8*1/*3 genotype). Subjects were given a single 4 mg dose of rosiglitazone, and blood was sampled over a 24-hour period. Rosiglitazone plasma concentrations were determined by HPLC and analyzed using noncompartmental pharmacokinetic methods. Pharmacokinetic parameters were compared between genotype

groups using unpaired t tests. Linear regression was used to determine the joint effects of CYP2C8 genotype, age, sex, and weight on rosiglitazone AUC.

RESULTS: The baseline characteristics of the study population were: 22 women, mean age=32 ± 9 years, mean weight=67.4 ± 11.4 kg. Rosiglitazone AUC was significantly lower, and oral clearance was significantly higher, in heterozygotes compared to wild type homozygotes (see table). There were no significant differences in C_{max}, t_{max}, or $t_{1/2}$ between genotype groups. Stepwise linear regression analysis revealed that CYP2C8 genotype (p=0.006) and weight (p=0.036) were significant predictors of rosiglitazone AUC (overall p=0.002; r^2 = 42.7%).

CONCLUSION: These data suggest that the CYP2C8*3 allele contributes to interindividual variability in rosiglitazone pharmacokinetics in healthy volunteers. It remains to be determined whether the observed differences in AUC will translate into clinically significant differences in rosiglitazone efficacy or toxicity in patients with type 2 diabetes.

	CYP2C8 *1/*1 (N=20)	CYP2C8 *1/*3 (N=6)	P value
AUC (ng*h/mL)	1815 ± 376	1345 ± 316	0.013
Oral Clearance (mL/h)	2259 ± 502	3075 ± 671	0.029
Weight-adjusted oral clearance (mL/h/kg)	34.5 ± 6.7	43.7 ± 10	0.075
C_{max} (ng/mL)	387 ± 107	324 ± 57	0.080
T_{max} (h)	1.0 ± 0.5	0.7 ± 0.3	0.111
$t_{1/2}$ (h)	4.1 ± 0.8	3.4 ± 1.3	0.237

Mean ± SD

363. **Interaction between *ADRA2C* genotype and beta-blocker response in acute coronary syndromes.** *James M. Baker, B.S.*[1], Lan Xiao, M.S.[2], David E. Lanfear, M.D., M.S.[3], Sharon Cresci, M.D.[4], Philip G. Jones, M.S.[2], Jun Wu, M.S.[4], Michael A. Province, Ph.D.[4], John A. Spertus, M.D., M.P.H.[2], Amber L. Beitelshees, Pharm.D., M.P.H.[4]; (1)Saint Louis College of Pharmacy, St. Louis, Mo; (2)University of Missouri Kansas City and Mid America Heart Institute, Kansas City, Mo; (3)Henry Ford Heart and Vascular Institute, Detroit, Mich; (4)Washington University School of Medicine, St. Louis, Mo.

PURPOSE: Polymorphisms in the 2c- and 1-adrenergic receptor genes (*ADRA2C* and *ADRB1*, respectively) have been shown to have functional consequences associated with -blocker (BB) response in heart failure (HF). We sought to determine whether the *ADRA2C* insertion/deletion (In>Del) and *ADRB1* Arg389>Gly polymorphisms are associated with BB response after an acute coronary syndrome (ACS). We hypothesized that patients carrying the Del allele and Arg389Arg genotype would have the greatest benefit from BB administration compared to other genotype groups.

METHODS: Two prospective cohorts of ACS patients with 3 years of follow-up were assessed (n=1226). *ADRA2C* In>Del and *ADRB1* Arg389>Gly were genotyped using pyrosequencing or Taqman. Kaplan Meier (KM)-estimated death rates were calculated and multivariable Cox proportional hazards models were constructed to calculate hazard ratios and 95% confidence intervals (CI).

RESULTS: The allele frequencies were 0.44 and 0.05 among blacks and whites for the *ADRA2C* Del and 0.37 and 0.26 for *ADRB1* Gly389. BB were prescribed to 91% of white patients and 77% of black patients. Among whites, KM-estimated mortality rates were 12.5% for del-carriers not discharged on BB, 2.9% for del-carriers discharged on BB, 11.4% for In/In not discharged on BB, and 10% In/In discharged on BB. Del-carriers tended to have improved survival compared to In/In patients (HR 0.269 95% CI 0.066-1.098) when discharged on BB. No difference was noted by In>Del genotype among those not discharged on BB (HR 1.06 95% CI 0.12-9.6). The interaction between In>Del genotype and BB on survival did not reach significance (p=0.20). Results were similar in black patients. Arg389>Gly genotype did not modify the effect of *ADRA2C* In>Del in this post-ACS cohort.

CONCLUSIONS: Consistent with previous findings in HF, the *ADRA2C* Del allele was associated with improved survival in BB-treated post-ACS patients. In contrast, the *ADRB1* Arg389>Gly polymorphism did not influence this association in post-ACS patients.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

364. **Clonidine pharmacokinetics during pregnancy: An OPRU Network Study.** *Megan L. Buchanan, B.S.*[1], Thomas Easterling, M.D.[1], Darcy Carr, M.D.[1], Danny Shen, Ph.D.[2], Mary F. Hebert, Pharm.D., FCCP[1]; (1)University of Washington, Seattle, Wash; (2)University of Washington and Fred Hutchinson Cancer Research Center, Seattle, Wash.

PURPOSE: To estimate the pharmacokinetic parameters of clonidine during pregnancy.

METHODS: Steady-state non-compartmental pharmacokinetic parameters were estimated in pregnant women (n=8) receiving oral clonidine for therapeutic reasons. Serial blood and urine samples were collected over one dosing interval to measure creatinine clearance and clonidine concentrations. At the time of labor and delivery, maternal and umbilical cord (venous and arterial) plasma samples were collected. A validated LC/MS assay was used to measure clonidine concentrations. Research in progress.

RESULTS: Clonidine CLrenal was significantly higher in pregnant women with CrCl ≥ 150 mL/min (11.6 ± 5.5 L/hr) vs. those with CrCl < 150 mL/min (5.8 ± 1.6 L/hr; p=0.03). Clonidine CL/F in pregnant women with CrCl ≥ 150 mL/min (26.0 ± 8.4 L/hr) trended towards being higher than those with CrCl < 150 mL/min (19.0 ± 4.8 L/hr; p=0.09). Clonidine half-lives were 8.6 ± 3.2 hrs (CrCl ≥ 150 mL/min) and 10.5 ± 2.9 hrs (CrCl < 150 mL/min). There was a good correlation between clonidine CLrenal and CrCl (r = 0.7). Cord-to-maternal plasma clonidine concentration ratios were 1.02 ± 0.13 (arterial) and 1.00 ± 0.10 (venous).

CONCLUSION: The high renal filtration (≥150 mL/min) seen in some women during pregnancy is associated with increased clonidine renal clearance. At the time of delivery, the infant is exposed to similar clonidine plasma concentrations as the mother. This finding is consistent with the case reports of newborn transitory hypertension likely to be due to clonidine withdrawal.

RESEARCH SUPPORT: NIH/NICHD grant #5U10 HD047892, NIH grant #M01RR-00037 and NIH/NCRR grant #RR-023256.

365. **Pharmacokinetics of chemotherapy in pregnancy and lactation: an OPRU network study.** *Mariska Audriani, B.S.*[1], Megan L. Buchanan, B.S.[1], Thomas Easterling, M.D.[1], Hank Kaplan, M.D.[2], Darcy Carr, M.D.[1], Stacey Berg, M.D.[3], Kathleen Scorsone, Ph.D.[3], Matthew Ames, Ph.D.[4], Joel Reid, Ph.D.[4], William Petros, Pharm.D.[5], Terry McManus, Ph.D.[5], Eddie Reed, M.D.[5], Danny Shen, Ph.D.[6], Elizabeth Swisher, M.D.[1], Jeffrey Skolnik, M.D.[7], Mary F. Hebert, Pharm.D.[1]; (1)University of Washington, Seattle, Wash; (2)Swedish Medical Center, Seattle, Wash; (3)Texas Children's Cancer Center, Houston, Tex; (4)Mayo Clinic, Rochester, Minn; (5)Mary Babb Randolph Cancer Center, West Virginia University, Morgantown, WV; (6)University of Washington and Fred Hutchinson Cancer Research Center, Seattle, Wash; (7)Children's Hospital of Philadelphia, Philadelphia., Pa.

PURPOSE: To study the pharmacokinetics of chemotherapeutic agents during pregnancy and lactation.

METHODS: Non-compartmental pharmacokinetic parameters were estimated during pregnancy for doxorubicin (n=4), vinblastine (n=1), cyclophosphamide (n=2), and dacarbazine (n=1) and repeated 2.6 weeks postpartum for doxorubicin, vinblastine, and dacarbazine (n=1). Duration of platinum excretion in breast milk was determined in one subject receiving cisplatin while lactating. Chemotherapeutic agents were administered for therapeutic reasons. Drug and metabolite concentrations were measured utilizing atomic absorption, HPLC, LC/MS and LC/MS/MS assays.

RESULTS: Doxorubicin clearance was 26.7 ± 4.1 L/hr/m² during pregnancy and 21.6 L/hr/m² postpartum. Vinblastine clearance was 18.9 mL/min/kg during pregnancy and 12.5 mL/min/kg postpartum. Cyclophosphamide clearance was 148 ± 6 mL/min during pregnancy. Dacarbazine clearance was 9.3 mL/min/kg during pregnancy and 12.8 mL/min/kg postpartum. AUCpregnancy/AUCpostpartum for dacarbazine (prodrug) was 1.3, for 5-[3-hydroxy-methyl-3-methyl-triazen-1-yl]-imidazole-4-carboxamide (active) was 0.6 and for 5-[3-methyl-trazen-1-yl]-imidazole-4-carboxamide (active) was 0.6. Platinum concentrations in breast milk were > 5 ng/mL for 13 hours and > 2.5 ng/mL for 57 hours post-cisplatin dosing.

CONCLUSION: Preliminary data suggests that pregnancy may alter the concentrations of some chemotherapeutic agents. Platinum is excreted in breast milk for a few days following a single dose of cisplatin.

RESEARCH SUPPORT: NIH/NICHD grant #5U10-HD047892, NIH grant #M01RR-0037 and NIH/NCRR grant #RR-023256.

366. **Creatinine clearance during pregnancy and postpartum: An OPRU Network Study.** *Megan L. Buchanan, B.S.*, Thomas Easterling, M.D., Darcy Carr, M.D., Mary F. Hebert, Pharm. D., FCCP; University of Washington, Seattle, Wash.

PURPOSE: 1) To evaluate the effects of obesity on creatinine clearance during pregnancy and postpartum and 2) to evaluate the effects of time postpartum on creatinine clearance in lactating women.

METHODS: Serum creatinine and a 12-hour urine were collected to estimate creatinine clearance (CrCl). CrCls were estimated in 15 non-obese (BMI < 30 kg/m²) and 19 obese (BMI ≥ 30 kg/m²) women 18–22 weeks gestation (T2), 30–34 weeks gestation (T3), and 3 months postpartum (PP). CrCls were also estimated in 11 lactating women 2–4 weeks, 3–4 months, and 6–8 months postpartum. Results are reported as mean ± SD. p<0.05 was considered significant.

RESULTS: CrCl was higher during pregnancy than postpartum in both the obese (T2 209 ± 55 mL/min, p<0.0001; T3 218 ± 50 mL/min, p<0.0001 and PP 152 ± 44 mL/min) and non-obese (T2 166 ± 41 mL/min, p<0.0001; T3 176 ± 42 mL/min, p<0.0001 and PP 120 ± 26 mL/min) populations. CrCl was higher in pregnancy (T2 p<0.02, T3 p=0.01) and postpartum (p<0.02) in the obese as compared to non-obese subjects. CrCl was higher 6–8 months postpartum (145 ± 28 mL/min) compared with the same women 2–4 weeks (133 ± 21 mL/min, p=0.01) and 3–4 months (129 ± 30 mL/min, p=0.006) postpartum.
CONCLUSION: CrCl increases during pregnancy to about the same degree in obese and non-obese women. CrCl is higher 6–8 months postpartum than 2–4 weeks and 3–4 months postpartum. Changes in renal filtration may alter dosage requirements during pregnancy and postpartum.
RESEARCH SUPPORT: FDA Office of Women's Health, NIH/NICHD grant #5U10 HD047892, NIH grant #M01RR-00037 and NIH/NCRR grant #RR-023256

367. **Pharmacodynamic evaluation of the Hartford Nomogram for dosing of aminoglycosides in Intensive Care Unit patients using Monte Carlo simulation.** *Kathryn D. Beavers, Pharm.D. Candidate*[1], Christopher G. Wilson, Pharm.D. Candidate[1], Tyree H. Kiser, Pharm.D.[2], Douglas Fish, Pharm.D., BCPS[2]; (1)University of Colorado School of Pharmacy, Denver, Colo; (2)University of Colorado Health Sciences Center, Denver, Colo.

PURPOSE: Aminoglycoside pharmacokinetics are substantially altered in critically ill intensive care unit (ICU) patients. The purpose of this study was to evaluate pharmacodynamic characteristics of gentamicin and tobramycin in ICU patients using a Hartford Nomogram (HN) recommended dosing regimen (7 mg/kg) and alternative regimens of up to 10 mg/kg.
METHODS: This retrospective study evaluated gentamicin and tobramycin pharmacokinetics in ICU patients with ≥ 2 plasma concentrations. Peak plasma concentrations (Cmax) at various doses were determined from calculated pharmacokinetic parameters. Minimum inhibitory concentration (MIC) values for *Pseudomonas aeruginosa* ICU isolates were obtained from the 2005 ISS national surveillance study (Merck & Co., Inc.). Monte Carlo simulation (Crystal Ball version 7, Decisioneering, Inc.) was used to predict the probability of target attainment (PTA) for the specified pharmacodynamic goal of Cmax to MIC ratio (Cmax/MIC) ≥ 10.
RESULTS: Pharmacokinetic data were calculated in 208 patients. Volume of distribution and clearance (mean ± SD) were 0.38 ± 0.13 L/kg and 63 ± 28 mL/minute, respectively. Calculated median Cmax after a 7 mg/kg dose was 18.3 mg/L (range 9.4 to 37.6 mg/L). The mean Cmax/MIC ratio for gentamicin 7 mg/kg was 7.8 with PTA of 26% by Monte Carlo simulation. Gentamicin 10 mg/kg achieved mean Cmax/MIC ratio of 10.9 but PTA of still only 44%. Mean tobramycin Cmax/MIC ratios and PTA were 14.1 and 66%, respectively, at 7 mg/kg and 18.9 and 74%, respectively, at 10 mg/kg.
CONCLUSIONS: HN-recommended doses of 7 mg/kg for gentamicin or tobramycin are inadequate for reliably achieving Cmax/MIC ratio ≥ 10 for *P. aeruginosa* in ICU patients. Doses up to 10 mg/kg marginally improved Cmax/MIC ratio but were still inadequate with PTA < 75%. Although combination antibiotic therapy was not evaluated, gentamicin or tobramycin doses higher than recommended by the HN appear necessary to reliably obtain pharmacodynamic targets against key pathogens in ICU patients.

368. **Evaluation of the Hartford Nomogram for dosing of aminoglycosides in critically ill patients.** *Christopher G. Wilson, Pharm.D. Candidate*[1], Kathryn D. Beavers, Pharm.D. Candidate[1], Tyree H. Kiser, Pharm.D.[2], Douglas Fish, Pharm.D., BCPS[2]; (1)University of Colorado School of Pharmacy, Denver, Colo; (2)University of Colorado Health Sciences Center, Denver, Colo.

PURPOSE: The Hartford Nomogram (HN) is commonly used for monitoring of extended-interval aminoglycosides (EIA) in the intensive care unit (ICU). However, the HN has not been specifically validated in ICU patients. The purpose of this study was to determine appropriateness of the HN for routine monitoring of EIA in ICU patients.
METHODS: A single-center, retrospective study evaluated ICU patients who had received gentamicin or tobramycin and who had ≥ 2 plasma concentrations adequate for determining pharmacokinetic parameters. Calculated parameters were used to determine peak plasma concentrations (Cmax) achieved with the HN-specified dose of 7 mg/kg. Predicted plasma levels and corresponding HN-recommended dosing intervals were determined at time points ranging from 6 to 14 hours after starting the dose. Appropriateness of HN-derived recommendations and resultant plasma concentrations were compared against individually calculated pharmacokinetic recommendations for each patient.
RESULTS: A total of 208 patients were evaluated. Volume of distribution and clearance (mean ± SD) were 0.38 ± 0.13 L/kg and 63 ± 28 mL/minute, respectively. Calculated median Cmax after a 7 mg/kg dose was 18.3 mg/L (range 9.4–37.6 mg/L). HN-recommended dosing intervals agreed with those derived from traditional methods in only 23% of patients and were ≥ 12 hours shorter in 44% of patients. In 32% of patients, HN-recommended intervals differed depending on when concentrations were evaluated within the 6-14 hour interval. Although

the HN targets a drug-free (< 0.5 mg/L) period of ≥4 hours before the next dose, 46%–64% of patients did not achieve this goal and 23%–29% had pre-dose minimum plasma concentrations > 0.5 mg/L (depending on when concentrations were evaluated).
CONCLUSIONS: HN-recommended regimens disagree with individualized pharmacokinetic dosing methods, provide inconsistent recommendations, and do not provide adequate drug-free periods in most ICU patients. Individualized pharmacokinetic dosing methods, rather than the HN, should be routinely recommended in ICU patients receiving EIA.

369. **Interpatient and interdose variability in the pharmacokinetics of intravenous and oral busulfan.** Jeannine S. McCune, Pharm.D.[1], *Jennifer A. Knutson, Pharm.D.candidate*[1], David K. Blough, Ph.D[1], Lu Yu, BS[2], Meagan Bemer, M.S.[2], Matthew A. Pawlikowski, MA[2]; (1)University of Washington, Seattle, Wash; (2)Seattle Cancer Care Alliance, Seattle, Wash.

PURPOSE: The alkylating agent busulfan is commonly administered intravenously (IV) as a component of hematopoietic cell transplantation conditioning regimens due to its potentially lower interpatient and/or interdose pharmacokinetic variability in comparison to oral (PO) busulfan. Our clinical experience with busulfan therapeutic drug monitoring has been that interpatient variability is similar between administration routes but interdose variability is lower with IV. We analyzed interpatient and interdose variability in busulfan clearance after IV or PO administration.
METHODS: We conducted a retrospective analysis of patients treated with FHCRC protocols between January 1995 and June 2007 who had three busulfan clearance measurements. All plasma busulfan concentrations were measured by gas chromatography-mass spectrometry. Concentration-time data was fit by noncompartmental or compartmental models to estimate the concentration at steady state and clearance. The clearance coefficients of variation (CV) for PO and IV groups were calculated. The proportion of patients with a clinically important change in busulfan clearance between doses was calculated. A t-test was used to compare the mean difference in clearance, oral versus IV.
RESULTS: The mean (±standard deviation) clearance of PO (n=1088) and IV busulfan (n=74) were 108.1 ± 21.6 and 103.4 ± 23.3 mL/min/m^2, respectively. This difference in clearance was not statistically significant (p=0.09). The interdose CV for PO and IV busulfan were: a mean of 8.34% (0.02%–77.2%) and 6.65% (1.58%–17.15%), respectively. A higher percentage of PO busulfan patients had a clinically important (> 10%) change in clearance between doses with 27% of PO and 20% of IV patients.
CONCLUSIONS: We seek to determine whether interpatient and interdose variability differ between IV and PO busulfan. Preliminary analysis indicates that the pharmacokinetic differences are moderate. Improved methods for individualizing IV and PO busulfan dosing are needed to achieve the target systemic exposure. The use of busulfan population pharmacokinetic models with limited sampling schedules may offer such a cost-effective strategy.

370. **Population pharmacokinetics of UCN-01 (7-hydroxystaurosporine).** *Charlene A. Baksh, Pharm.D.*[1], Kenneth S. Bauer, Pharm.D., Ph.D.[1], Martin J. Edelman, M.D.[2]; (1)University of Maryland School of Pharmacy, Baltimore, Md; (2)University of Maryland Greenbaum Cancer Center, Baltimore, Md.

PURPOSE: This study aims to provide a preliminary assessment of the pharmacokinetic profile of UCN-01 in a target population of oncology patients, to characterize interpatient and intrapatient variability, and to identify covariates that influence UCN-01 disposition.
METHODS: A population pharmacokinetic analysis will be performed using nonlinear mixed effects modeling. Using NONMEM v 1.1, concentration data obtained from 23 patients who participated in a phase I trial of UCN-01 and Carboplatin will be assessed. The data will then be evaluated by both one- and two-compartment models. Individual empirical Bayes parameter estimates will be generated to examine possible covariate relationships. Height, weight, age, race, gender, body surface area (BSA), serum creatinine (Scr), albumin, bilirubin, and $_1$-acid glycoprotein (AAG) will then be included as possible covariates. Error models to be assessed are additive, constant coefficient of variation (CCV; proportional), and both additive and CCV combined.
RESULTS: The pharmacokinetic estimates of the structural model consisted of a clearance of 0.0104L/h (coefficient of variation [CV], 11.3%), a central volume of distribution of 3.65L (CV, 10.7%), intercompartmental clearance 0.660L/h (CV, 41.8%), and a peripheral volume of distribution of 3.11L (CV, 19.5%).
CONCLUSION: The pharmacokinetic parameters of UCN-01 were adequately described by a two-compartment population model. A covariate model based on this structural model is under development. A population pharmacokinetic model will be helpful in the selection and adaptation of the most appropriate UCN-01 dosage regimen.

Psychiatry

371. **The concomitant use of anticholinergic agents with first and second generation antipsychotics.** *Ghazala A. Jafer, R.Ph.*[1], Joshus Caballero, Pharm.D.[2], Mercedes Gonzalez-Blanco, M.D.[3]; (1)Nova Southeastern University, Fort Lauderdale, Fla; (2)Nova Southeastern University, Jackson Memorial Mental Health Hospital, Fort Lauderdale, Fla; (3)Jackson Memorial Mental Health Hospital, Miami, Fla.

PURPOSE: First-generation antipsychotics (FGAs) are known for having increased extra pyramidal symptoms (EPS) compared to second-generation antipsychotics (SGAs). Anticholinergic medications are often used to treat these adverse reactions. However, limited data exist comparing the incidence of anticholinergic use with FGAs and SGAs. Also, data may have confounded results since it is unknown if patients were concomitantly taking other psychiatric medications. Therefore, the purpose of this study was to compare patients receiving FGAs or SGAs with and without an anticholinergic.
METHODS: A retrospective chart review was conducted in patients admitted to an inpatient psychiatric hospital. Inclusion criteria included schizophrenic patients, ages 18–65 years, and discharged on an antipsychotic medication with or without an anticholinergic. Exclusion criteria included any patients discharged on any other psychiatric medications. A chi square test compared the percentage of patients on a FGA or SGA concomitantly receiving anticholinergics.
RESULTS: A total of 371 patient charts were included. The most commonly prescribed FGA was haloperidol (80%) at an average dose of 16 mg/day. Risperidone was the most commonly prescribed SGA (64%) at an average dose of 5 mg/day. The most commonly prescribed anticholinergic was benztropine (95%) at an average dose of 2 mg/day. Sixty-five percent of patients on a FGA received an anticholinergic compared to 26% of patients on a SGA (p<0.05). Patients prescribed a FGA with or without an anticholinergic had a length of stay of 17 and 13 days, respectively. Length of stay of patients receiving a SGA with and without an anticholinergic was 16 and 15 days, respectively.
CONCLUSION: It appears that FGAs are associated with more anticholinergic use compared to SGAs, which may be due to increased EPS. Also, there are no statistical differences in length of stay between groups. Additional prospective studies need to be conducted to confirm our results.

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Cardiovascular

373. **UCP2 -866 G/A polymorphism influences ß-blocker response in post-acute coronary syndrome diabetic individuals.** *Amber L. Beitelshees, Pharm.D., M.P.H.*[1], Lan Xiao, M.S.[2], Sharon Cresci, M.D.[1], Philip G. Jones, M.S.[2], Jun Wu, M.S.[1], Matthew R. Minton, B.S.[1], Michael A. Province, Ph.D.[1], Daniel P. Kelly, M.D.[1], Howard L. McLeod, Pharm.D.[3], John A. Spertus, M.D., M.P.H.[2]; (1)Washington University School of Medicine, St. Louis, Mo; (2)University of Missouri Kansas City and Mid America Heart Institute, Kansas City, Mo; (3)University of North Carolina School of Pharmacy, Chapel Hill, NC.

PURPOSE: Uncoupling proteins (UCPs)are involved in insulin secretion, reactive oxygen species generation, and fatty acid transport. Neurohormonal inhibition with ß-blockers may modulate these activities with differing consequences depending on patient population. We have found UCP2 -866 G>A to influence BB response after an acute coronary syndrome (ACS) in diabetic patients. We sought to increase the sample size from previous finding by adding a second, similar cohort for analysis.
METHODS: A prospective cohort of post-myocardial infarction patients with 12-months of follow-up was assessed (n=361) and combined with a previously assessed cohort of ACS patients (n=723) who had similar data collected and were from same region of the country (total n=1084). UCP2 -866 G>A was genotyped using Taqman. Cox proportional hazards models containing prespecified covariates were constructed separately by race and stratified by genotype and discharge BB status to calculate hazard ratios and 95% confidence intervals (CI). Interaction terms between BB and genotype were calculated.
RESULTS: A total of 211 patients were diabetic and Caucasian. The -866 A allele frequency was 0.40. We identified a significant interaction between genotype and BB response on cardiac rehospitalization (p=0.02). Among those not discharged on BB, G/G individuals had an increased risk of cardiac rehospitalization compared to A-carriers (HR = 9.61; 95% CI = 1.68–55.0). Among variant A-carrier individuals, discharge BB was associated with an increased risk of cardiac rehospitalization (HR = 4.69; 95% CI = 1.04–21.26).
CONCLUSIONS: The independent population was not large enough to replicate previous findings with UCP2 and BB response in diabetic individuals. However, it did increase our sample size by 1/3 and provide findings consistent with our previous results using this larger cohort. Our findings suggest a significant interaction between

UCP2 -866 G>A genotype and BB response. We are currently attempting to replicate these findings in a larger independent population.

374. Linkage of genetic polymorphisms to vascular access thrombosis in dialysis patients. *Donald F. Brophy, Pharm.D., M.Sc.*, Bonny L. Bukaveckas, Ph.D., Erika J. Martin, M.T., Sarah Calkins, R.N., Andrea Ferrieira-Gonzales, Ph.D., Al M. Best, Ph.D., Todd W.B. Gehr, M.D.; Virginia Commonwealth University School of Pharmacy, Richmond, Va.

PURPOSE: To explore the associations between genetic polymorphisms in inflammatory and coagulation biomarkers, patient variables and the occurrence of vascular access thrombosis (VAT) in dialysis patients.
METHODS: This case-control study compared 60 cases that experienced frequent VAT (Group 1: VAT) to 42 VAT-free controls (Group 2: No VAT). Blood samples were obtained from each participant for determination of genetic variation in vascular inflammatory makers (Transforming Growth Factor-*f*"1(TGF-*f*"1), endothelial nitric oxide synthase (NOS3), angiotensin converting enzyme (ACE), endotoxin receptor CD14), homocysteine metabolism (MTHFR) and pro-coagulant clotting factors (Factor V Leiden and Factor II polymorphisms). Demographics, concomitant disease states and medications were also included in a multivariate stepwise logistic regression model that determined the odds ratio (OR) and 95% CI of these parameters to the occurrence of VAT.
RESULTS: The groups were well matched for demographics. There were no associations between the VAT group and TGF-*f*"1, ACE, CD14, MTHFR, Factor V Leiden and Factor II polymorphisms. There was a positive association between the NOS3 27 intron 4 (27 base pair tandem repeat) polymorphism (OR >100; 95% CI not estimable; p=0.03); presence of a catheter dialysis access relative to arterio-venous fistula access (OR 13.8; 95% CI 10.3, 17.4); p< 0.0001) and the use of HMG-CoA reductase enzyme inhibitors (OR = 3.7; 95% CI = 2.1–5.3; p=0.02). The use of aspirin significantly lowered the odds of being in the VAT group (OR = 0.23; 95% CI = 0.10–0.38; p=0.01).
CONCLUSIONS: The presence of the NOS3 27 intron 4 (27 base pair tandem repeat) genetic polymorphism, dialysis access catheter use, and HMG-CoA reductase inhibitor use were positively associated with the VAT group. Aspirin use appeared beneficial in lowering the odds of VAT. Future studies should explore the ability to predict VAT based on NOS3 genetic variation, as well as the role of pharmacotherapy in preventing VAT.

375. Immune responses to influenza vaccine in patients with heart failure taking carvedilol. *Orly Vardeny, Pharm.D.*[1], Nancy K. Sweitzer, M.D.[2], Maryl R. Johnson, M.D.[2], Walter G. Kao, M.D.[2], Elaine M. Winkel, M.D.[2], John J. Moran, B.S.[2], Mary S. Hayney, Pharm.D., M.P.H.[2]; (1)Pharmacy Practice Division, University of Wisconsin School of Pharmacy, Madison, Wis; (2)Division of Cardiovascular Medicine, Dept of Medicine, University of Wisconsin, Madison, Wis.
Abstract not yet available

Gastroenterology

377. Glucocorticoid therapy for acetaminophen-induced liver toxicity. *Robert MacLaren, Pharm.D*, Hao Yin, M.Sc., Cynthia Ju, Ph.D.; University of Colorado School of Pharmacy, Denver, Colo.

PURPOSE: To determine whether glucocorticoid therapy reduces inflammation and liver injury associated with acetaminophen (APAP)-induced hepatotoxicity.
METHODS: This study consisted of two portions: 1) assessing the glucocorticoid dosage regimen required to suppress inflammation and 2) combining this regimen with NAC to determine whether an additive effect is observed. In part 1, mice (C57BL6/J or BALB/CJ strains) received intraperitoneal (ip) injections of APAP 300 mg/kg and either saline (control) or dexamethasone at various dosage regimens after APAP exposure. In part 2, NAC 200 mg/kg ip was administered with dexamethasone after APAP exposure. Mice were sacrificed at 48 hours. Inflammation and liver injury were determined by serial measurements of serum tumor necrosis factor (TNF)- and alanine aminotransferase (ALT), respectively. Mann-Whitney U test was used for analyses.
RESULTS: Three doses of dexamethasone 5 mg/kg starting 4 hours after APAP was most effective for reducing TNF- . This regimen reduced ALT from 3762 ± 1241 U/L at 24 hours to 464 ± 204 U/L (p<0.05) at 48 hours in C57BL6/J strain and from 8164 ± 4373 U/L at 24 hours to 1772 ± 1673 U/l (p<0.05) at 48 hours in BALB/CJ strain. Neither magnitide of reduction was statistically different from the control groups. Combining dexamethasone and NAC had no addititive effect on TNF- . Combination therapy reduced ALT from 4280 ± 2420 U/l at 24 hours to 1724 ± 1469 U/L (p<0.05) at 48 hours in C57BL6/J strain with the magnitude of change similar to control, dexamethasone alone, and NAC alone. With combination therapy or NAC alone, ALT remained < 200 U/L for 48 hours in BALB/CJ strain. These results trended toward showing differences when compared with control or dexamethasone alone.
CONCLUSIONS: Glucocorticoid therapy may reduce inflammation associated with APAP-induced hepatotoxicity, but does not reduce liver injury beyond NAC treatment.

378. **Lipopolysaccharide increases cell surface p-glycoprotein that exhibits altered transport properties in intestinal epithelial cells.** Jayshree Mishra, Ph.D., Qiuye Zhang, M.D., Jessica L. Rosson, M.S., *Brien L. Neudeck, Pharm.D.*; University of Tennesse College of Pharmacy, Memphis, Tenn.

PURPOSE: To determine the effect of Toll-like receptor 4 (TLR4) activation on intestinal P-glycoprotein (Pgp) expression and function.
METHODS: TLR4+/Pgp+ SW480 cells and TLR4-/Pgp+ cells were employed. Cells were exposed to 100 ng/ ml lipopolysaccharide (LPS) or media control for 3, 6, and 24 hours. Polymyxin B (10 μg/mL) was used as a LPS antagonist. Intracellular accumulation of Rhodamine 123 (Rh123) was measured to characterize Pgp function. Western immunoblotting and confocal microscopy were employed to measure total and cell surface Pgp, respectively. Transepithelial electrical resistance (TEER) was measured using a Milli-Cell ERS system.
RESULTS: Activation of TLR4 in SW480 cells significantly decreased Pgp function shown by increased Rh123 uptake (Control:210 + 30 vs 450 + 20 3hr vs 440 + 40 6hr vs 580 + 27 pmoles/mg; p<0.05) Polymyxin B prevented these changes. Conversely, there was no effect of LPS in the TLR4- Caco-2 cells. No changes in TEER occurred with LPS (Control: 524 + 41 vs LPS 24 hr 496 + 28 ohms• cm2). Total Pgp amounts did not change in LPS treated cells however there was a significant 53% increase in cell surface Pgp as measured by confocal microscopy.
CONCLUSIONS: Commensal bacteria play an important role by influencing intestinal physiology. LPS led to increased surface Pgp that exhibited decreased function. Activation of intestinal TLR4 by LPS may be one environmental regulator of Pgp expression and function via yet to be determined post-translational mechanisms.

Geriatrics

379. **Guideline adherence and blood pressure control in elders.** *Jessica L. Milchak, Pharm.D.*[1], Barry L. Carter, Pharm.D.[2], Gail Ardery, Ph.D.[3], Jeffrey Dawson, Sc.D.[4], Matt Harmston, M.A.[3], Carrie Franciscus, M.A.[5]; (1)Kaiser Foundation of Colorado, Boulder, Colo; (2)College of Pharmacy, and Dept of Family Medicine, Carver College of Medicine, University of Iowa, Iowa City, Iowa; (3)College of Pharmacy, University of Iowa, Iowa City, Iowa; (4)College of Public Health, University of Iowa, Iowa City, Iowa; (5) Iowa City Veterans Administration Medical Center, Iowa City, Iowa.

PURPOSE: This study examined adherence to blood pressure (BP) guidelines using a tool comprised of explicit process elements of care to 1) compare guideline adherence in elderly and non-elderly populations, 2) examine the underlying factor structure within the adherence tool, and 3) evaluate whether identified criteria groupings (factors) predict BP control in either population.
METHODS: Medical records of participants in a 9-month study examining hypertension care at five university-affiliated family medicine clinics were abstracted. Patient demographics, medications, medical conditions, laboratory results, clinic visits and specialist consultations were included.
RESULTS: One-hundred-seventy-nine subjects (105 subjects < 65 years of age and 74 subjects >/= 65 years of age) were included. Guideline adherence scores were significantly higher in the non-elderly compared to the elderly group (59.3% vs. 56.1%, p=0.024). For each estimated decrease of 0.25 in SBP mm Hg there was a 10-unit increase in adherence scores (p=0.723) with both groups combined. A two factor pattern for the elderly and a three factor pattern for the non-elderly was demonstrated. No factors in the elderly group were significantly associated with BP control. One factor was significantly correlated with BP control in the non-elderly group, p<0.0001. Criteria composing this factor were: 1) treatment with diuretic therapy, 2) adjusting medication for uncontrolled BP, 3) documentation of uncontrolled BP at the visit, 4) documentation of correct BP goal and 5) documentation of cardiovascular risk factors.
CONCLUSIONS: Overall adherence to BP guidelines was significantly higher in the non-elderly group. There was no significant relationship between overall adherence score and BP control across all patients. However, a smaller criteria grouping was significantly correlated to BP control in non-elderly patients.

Hematology/Anticoagulation

380. **Clinical consequences of subtherapeutic anticoagulation: The low INR study (LINeRS).** *Nathan P. Clark, Pharm.D.*[1], Daniel M. Witt, Pharm.D.[1], Thomas Delate, Ph.D.[1], Melissa R. Trapp, Pharm.D.[1], David Garcia, M.D.[2], Walter Ageno, M.D.[3], Elaine M. Hylek, M.D.[4], Mark A. Crowther, M.D.[5]; (1)Kaiser Permanente Colorado, Lafayette, Colo; (2)University of New Mexico Health Sciences Center, Albuquerque, NM; (3)University of Insubria, Varese, Italy; (4)Boston University School of Medicine, Boston, Mass; (5) McMaster University, Hamilton, ON, Canada.

PURPOSE: To quantify the risk of thromboembolic (TE) complications associated with a significant subtherapeutic INR excursion in a diverse group of anticoagulated (AC) patients.
METHODS: This retrospective study utilized data collected from electronic administrative databases and medical records. Patients on warfarin were included if they had 2 INR values within or above the therapeutic range and at least 2 weeks apart. The Low INR cohort (LC) included patients with a 3rd INR ≥ 0.5 INR units below their INR range lower limit. The Therapeutic INR cohort (TC) included patients with a 3rd INR value within the therapeutic range and no INR measurement ≥ 0.2 INR units below the INR range lower limit in the ensuing 90 days. Patients were excluded if target INR range lower limit was < 2.0 or for prescribed warfarin discontinuation during the study. LC patients were matched to TC patients on index INR date, indication for warfarin, and age. The primary outcome was TE within 90 days of the index INR. Secondary outcomes were times to the first occurrence of AC-related complications (bleeding, TE, and death) within 90 days following the index INR. Conditional proportional hazards modeling estimated the hazard ratios and their 95% CIs for AC-related complications.
RESULTS: A total of 1080 LC patients were matched to 1517 TC patients. There were no differences in the proportions of TE, bleeding, or death between the cohorts (p>0.05). In the unadjusted and adjusted hazards modeling, there were no differences in the hazard of TE, bleeding, or death between the cohorts (p>0.05).
CONCLUSIONS: Patients with stable, therapeutic AC experiencing a significant subtherapeutic INR excursion of at least 0.5 INR units below their INR range have a low risk of subsequent TE that is similar to that experienced in patients without such an excursion.

HIV/AIDS

381. **Exposure to zidovudine plus sulfamethoxazole-trimethoprim alters peripheral lymphocyte function in HIV-infected subjects.** Veena Venugopalan, Pharm.D.[1], Alice C. Thornton, M.D.[2], Beth A. Garvy, Ph.D.[2], *David J. Feola, Pharm.D., Ph.D.*[1]; (1)University of Kentucky College of Pharmacy, Lexington, Ky; (2)University of Kentucky College of Medicine, Lexington, Ky.

PURPOSE: Animal studies have demonstrated that combination exposure to zidovudine (ZDV) and sulfamethoxazole-trimethoprim (SMX-TMP) depletes precursor B lymphocytes from bone marrow. We have demonstrated in human subjects that this translates into suppressed humoral responses to antigenic stimulation; however, it is not known whether this is due to B cell depletion or dysfunction. This toxicity could be contributing to the B cell functional abnormalities observed in HIV-infected individuals. The purpose of our study was to determine the effects of ZDV plus SMX-TMP exposure on peripheral B lymphocyte function in HIV-infected patients.
METHODS: HIV-infected adults receiving ZDV with CD4+ T lymphocyte counts > 350 cells/mm^{3} and undetectable viral loads were prospectively recruited. A 28-day course of SMX-TMP (1 double-strength tablet daily) was initiated in subjects meeting criteria. Venous blood collections were performed at baseline (day 0) and following exposure (day 28). Peripheral blood mononuclear cells were isolated, cultured, and stimulated separately with 3 mitogens: pokeweed (T-cell dependent B cell mitogen), *Staphylococcus aureus* Cowan (T-cell independent B cell mitogen), and phytohemagglutinin A (T cell mitogen). Lymphocyte function was assessed by analyzing cell proliferation using hemocytometric enumeration, antigen-specific antibody production using enzyme-linked immunosorbent assays, and cytokine secretion using cytometric bead array technology.
RESULTS: Upon interim data examination (n=8), *ex vivo* B and T cell proliferation were significantly reduced at the 3-day culture timepoint, whereas the proliferative capacity at day 7 of culture was not significantly different. Immunoglobulin and cytokine production data will be determined and presented at the conference.
CONCLUSION: Interim results indicate that exposure to ZDV plus SMX-TMP causes an alteration in peripheral B and T lymphocyte proliferative capacity. Additional functional tests will be completed and reported. Clinicians treating patients infected with HIV should be wary of the contribution of this drug combination to the immunodeficiency observed in this population.

Infectious Diseases

382. **Differential bronchoalveolar protein expression in critically ill patients with and without ventilator-associated pneumonia.** *G. Christopher Wood, Pharm.D.*, Joseph M. Swanson, Pharm.D., Christopher F. Heohamer, Ph.D., Martin A. Croce, M.D., P. David Rogers, Pharm.D., Ph.D., George Hilliard, Ph.D., Bradley Boucher, Pharm.D., Timothy C. Fabian, M.D.; University of Tennessee College of Pharmacy, Memphis, Tenn.
PURPOSE: This pilot study compared protein expression in bronchoalveolar lavage (BAL) fluid of critically ill trauma patients with and without ventilator-associated pneumonia (VAP). The goal of this research is to identify novel biomarkers that could be used for more rapid diagnosis of VAP.
METHODS: Eleven patients with suspected VAP underwent bronchoscopic BAL for VAP diagnosis using the standard clinical pathway in the study center. Upon final quantitative culture reporting, patients were assigned to the study group (VAP) or control group (no VAP). VAP was diagnosed if a patient had ≥ 100,000 cfu/mL of a

bacterial organism from the BAL. A portion of the diagnostic BAL fluid was collected for the study. The protein concentration was determined using the BCA assay. An equal amount of protein from each sample was analyzed using comparative 2-D polyacrylamide gel electrophoresis and visualized with SYPRO® Ruby protein stain. The gels were analyzed visually for differences in protein expression between the study and control groups.

RESULTS: Differences in BAL protein expression between the study and control groups were seen in seven potential protein spots. The study group had higher expression in 2 spots (pH ~6 and 6.5; molecular weight ~15,000 daltons). The control group had higher expression in 5 spots. Four of the five were a cluster of proteins with pH ~7-9 and molecular weight ~15,000 daltons. The other was at pH ~6.5 and molecular weight 35,000 daltons. A common protein pattern was seen in all 11 patients in an area corresponding to a pH ~6-7 and molecular weight ~95,000 daltons.

CONCLUSIONS: Protein expression in diagnostic BAL fluid differed between patients with and without VAP. The 2-D gels will be further analyzed using PDQuest software to determine the degree of differential expression, and selected protein spots will be identified using MALDI-ToF spectroscopy.

383. Antiretroviral Pharmacokinetics in the Female Genital Tract: Implications for Pre- and Post- Exposure Prophylaxis. *Julie B. Dumond, Pharm.D.*[1], Rosa F. Yeh, Pharm.D.[2], Kristine B. Patterson, M.D.[3], Amanda H. Corbett, Pharm.D.[1], Byung Hwa Jung, Ph.D.[4], Naser L. Rezk, Ph.D.[2], Arlene S. Bridges, Ph.D.[1], Paul W. Stewart, Ph.D.[5], Myron S. Cohen, M.D.[3], Angela D.M. Kashuba, Pharm.D.[1]; (1)University of North Carolina, School of Pharmacy, Chapel Hill, NC; (2)University of Houston, College of Pharmacy, Houston, Tex; (3)University of North Carolina, School of Medicine, Chapel Hill, NC; (4)Bioanalysis and Biotransformation Research Center, Korea Institute of Science, South Korea; (5)University of North Carolina, Department of Biostatistics, Chapel Hill, NC.

Pharmacoeconomics/Outcomes

385. Outcomes after discharge from a pharmacist-run secondary prevention service. *Kari L. Olson, Pharm.D.*, Jon Rasmussen, Pharm.D., John Merenich, M.D., Tom Delate, Ph.D., Tammy Humphries, Pharm.D.; Kaiser Permanente Colorado Region, Aurora, Colo.

PURPOSE: This study evaluated whether patients with cardiovascular disease (CVD) followed by a clinical pharmacy specialist-managed secondary prevention program (CPCRS) and discharged back to usual care (UC) maintain lipid goals.

METHODS: This was a 2-year, randomized controlled study conducted at Kaiser Permanente Colorado (KPCO). Patients with CVD (acute myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention) were eligible if they were enrolled in CPCRS for at least 1 year; had continuous KPCO membership; had at least 2 consecutive low density lipoprotein (LDL-C) and non-high density lipoprotein cholesterol (non-HDL) measurements at goal; and the most recent blood pressure (BP) was at goal within 6 months prior to study enrollment. Patients were randomized to remain in CPCRS (i.e., receive long-term management to ensure that evidence-based secondary prevention treatment strategies were initiated and follow-up laboratories were addressed to assist patients in achieving their therapeutic goals) or receive UC (i.e., physician-care, electronic monitoring to ensure laboratories were ordered and results sent to the physician, and laboratory reminder letters were sent to patients). The primary outcome was the maintaining of LDL-C goal at study end. Descriptive statistics were used for baseline characteristics. Student's t-tests were used to assess differences in mean values between groups; 2 tests were used for between group comparisons on dichotomous outcomes.

RESULTS: A total of 462 patients (n=231 UC, n=231 CPCRS) were randomized. The mean age was 71.6 ± 9.6 yrs; 75.2% were male. Hypertension, diabetes mellitus, and current smoking were present in 65.7%, 9.3%, and 3.7% of the population, respectively. The average baseline LDL-C, nonHDL, and systolic BP were 70.4 ± 15.2, 94.3 ± 16.9 mg/dL, and 117.6 ± 11.6 mmHg, respectively. There were no statistically significant differences in baseline characteristics between groups (p>0.05). Outcome results are under analysis and will be presented.

CONCLUSION: To be presented.

386. Diabetes and comorbid depression: health care expenditures 2000-2003. *Marianne McCollum, Ph.D., R.Ph.*[1], Lori Nichols, M.S.[2], Weiming Zhang, M.S.[2]; (1)University of Colorado School of Pharmacy, Denver, Colo; (2)University of Colorado Department of Preventive Medicine, Denver, Colo.

PURPOSE: The objective of this study was to compare health care expenditures and factors associated with expenditures for US adults with diabetes with and without comorbid depression.

METHODS: Data were obtained from the 2001 and 2003 Medical Expenditure Panel Survey (MEPS). Diabetes was identified by patient self-report or ICD-9-CM code. Depression was identified by ICD-9-CM code. Demographic, clinical, and expenditure data for annual mean office-based visits, prescriptions, hospitalizations, and emergency

department visits were examined in univariate and multivariate linear regression models adjusted for covariates. All analyses compared expenditures for US adults with diabetes with and without depression.

RESULTS: In total, 7280 respondents with diabetes were included (2000, n=1319; 2001, n=1833; 2002, n=2196; 2003, n=1932). Adults with diabetes with versus without depression were found to have higher expenditures for prescriptions in each year, by an average of 55 percent (p=0.00–0.05). Total expenditures for individuals with diabetes and comorbid depression were higher in each year by an average of 57 percent (p<0.01). Differences between the depressed and non-depressed adults with diabetes for emergency, inpatient or ambulatory expenditures were not significant. In multivariate analysis, insurance status was one of the most consistent predictors of health care expenditures. Number of comorbidities, perceived health status, age, gender, race/ethnicity, and income level were inconsistent predictors of expenditures, as significant associations between these variables and expenditures in each category varied across the four study years.

CONCLUSIONS: Among people with diabetes, those with versus without depression had consistently higher annual expenditures for prescription medications each year from 2000 through 2003. Differences in resource use in other categories were not consistently significant. Continued research in the area of diabetes and depression is warranted to examine the implication of these findings.

Pharmacogenomics

387E. **Pharmacogenetics of drug transporter OATP 1B1 (SLCO1B1) and triglyceride response to fenofibrate.** *Robert J. Straka, Pharm.D.*[1], Na Li, Ph.D.[1], Michael Y. Tsai, Ph.D.[1], Naomi Q. Hanson, M.Sc.[1], Jose M. Ordovas, Ph.D.[2], Donna K. Arnett, Ph.D.[3]; (1)University of Minnesota, Minneapolis, Minn; (2) Tufts University, Boston, Mass; (3)University of Alabama, Birmingham, Ala.

PURPOSE: Fenofibric acid, the active moiety of fenofibrate, acts on the peroxisome proliferator-activated receptor-alpha (PPAR-a) to lower triglycerides (TG) and raise high-density lipoprotein (HDL-C)- both of which mitigate cardiovascular disease risk. Given the SLCO1B1 gene coding for organic anion transporting polypeptide (OATP 1B1) affects hepatocellular influx of numerous drugs, we hypothesized that this transporter also modulates fenofibric acid access to the PPAR-a receptor, thereby affecting clinical response. The objective was to investigate the impact of common variants of the SLCO1B1 gene on TG response to fenofibrate.

METHODS: As part of the NHLBI-sponsored Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study, consenting subjects > 18 years, were analyzed for lipid response pre and post 21 days of once daily 160 mg fenofibrate. Fasting lipid profiles were ascertained on 2 consecutive days pre and post exposure to fenofibrate, and TG response was calculated by the log of the difference of the average of the 2 pre- and post-fenofibrate exposure TG determinations. SLCO1B1 SNPs 388A>G (*1b), 521T>C (*5) and the combined haplotype were determined by MALDI-TOF mass spectrometry using a sequenom.

RESULTS: 733 subjects, with a mean ± SD age of 50 ± 16 years including 374 (51%) males and 58 (8%) with type 2 diabetes, composed this analysis. Mean ± SD (range) pretreatment fasting TG was 141 ± 98, (26–1202) mg/dL vs 91 ± 66 (19–419) mg/dL at the end of the treatment period. Minor allele frequencies for 388A>G and 521T>C were 0.37 (G) and 0.14 (C) with both in HWE. Subjects carrying C allele of 521T>C variant had a moderately decreased TG response. The median post-vs pre-fenofibrate TG concentration ratio was increased by 5.8% (95% CI = 0.6%–11%, p=0.03). No statistical significant association was found between 388A>G variant or the 2-SNP haplotypes and TG response.

CONCLUSIONS: Carriers of the 521T>C variant for the SLCO1B1 gene display reduced TG lowering response to fenofibrate.

388. **Serotonin transporter gene polymorphism in HCV patients.** *Susie H. Park, Pharm.D., BCPP*, Stan G. Louie, Pharm.D., Gilbert Burckart, Pharm.D., Zheng-Yi Zhou, M.S.; University of Southern California, School of Pharmacy, Los Angeles, Calif.

PURPOSE: This is a pharmacogenomic study of hepatitis C virus (HCV)-infected patients to determine whether there is a differential development of depression dependent upon their genetic polymorphism for the serotonin transporter (5-HTT). The goals are to examine the relationship between 1.) the genotypes (e.g., L/L, L/S, S/S) of the serotonin transporter gene-linked polymorphic region (5-HTTLPR) and the development of depression in patients being treated for hepatitis C with pegylated interferon; 2.) the genotype of the 5-HTTLPR and response to an antidepressant agent for treating interferon-induced depression.

METHODS: One 8 mL blood sample was taken from each subject for DNA analysis of the serotonin transporter and genotyped. Baseline (i.e., pre-interferon) Hamilton Depression Rating Scale (HAM-D) and Inventory for Depressive Symptomatology Self-Report (IDS-SR) were administered as well as at follow-up visits at 1, 2, 3, 6, 9, and 12 months. Patients requiring an antidepressant agent were treated with open-label citalopram 10–60 mg/day.

RESULTS: Of the 46 patients enrolled, 32 (70%) completed interferon treatment. Of those who completed, there was a statistically significant difference (p=0.0113) between patients requiring an antidepressant agent and their 5-HTTLPR genotype, where patients with S/S or L/S (84%) required an antidepressant at some point during therapy. There was no clinically significant change in HAM-D or IDS-SR scores, but this could not be demonstrated statistically because no L/L patient (0%) required an antidepressant.
CONCLUSION: The serotonin transporter is considered an objective marker for depression. This preliminary investigation is the first study to find a relationship in patients infected with HCV. Genotype results suggest that it may be advisable to preemptively treat S/S and S/L patients with an antidepressant before starting interferon for HCV.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

389. **Outcomes of a pharmacist-initiated antimicrobial step-down protocol.** *Elizabeth Hermsen, Pharm.D., M.B.A.*[1], Sara S. Shull, Pharm.D., M.B.A.[1], Lisa Parizek, Pharm.D.[1], Fang Qui, M.S.[2], Joshua Wilderman, B.A.[1], Mark E. Rupp, M.D.[2]; (1)The Nebraska Medical Center, Omaha, Neb; (2)University of Nebraska Medical Center, Omaha, Neb.

PURPOSE: Intravenous (IV) to oral (PO) conversion may expedite hospital discharge. Most IV to PO programs include antimicrobials with highly bioavailable PO formulations, allowing direct interchanges. Clinical and economic benefits may be achieved by including antimicrobials with no such equivalent: a step-down protocol. Our aim is to evaluate a pharmacist-initiated antimicrobial step-down protocol.
METHODS: The study consists of three phases. A pre-intervention phase established comparability of intervention and control groups. A pharmacist-initiated step-down protocol will be implemented in the intervention phase. In the crossover phase, the intervention and control groups will be switched. Outcomes include the percent receiving step-down conversion; length of stay (total and after antimicrobial start); duration of therapy (total and IV only); IV catheter utilization, complications, and infection rates; clinical cure; and cost of antimicrobials and total hospitalization. Outcomes are reported after step-down eligibility has been met.
RESULTS: These results represent baseline data. Of 911 patients in the pre-intervention phase, 25.5% (n=232) received IV antimicrobials not in our existing direct interchange IV to PO program, and 34.9% (n=81) of those were eligible for step-down. Eight became eligible on the discharge date and were excluded. The intervention group was older (p=0.02) with more IV complications (p=0.01). No difference was seen for other outcomes. The percent of step-down eligible patients in the intervention and control groups was 36.5% and 27.2%, respectively. Of these, 30.8% (intervention) and 29.4% (control) received step-down conversion (p=0.65) without intervention. A post hoc analysis showed those receiving conversion had shorter stays (p=0.005) and decreased total cost of hospitalization (p=0.0025) than those not converted. Results from post-intervention phases will be presented.
CONCLUSIONS: Without a step-down protocol, about 70% of eligible patients do not receive step-down conversion. When conversion occurs, shorter stays and decreased hospital costs result. These data support the rationale for a step-down protocol.

Pulmonary

391. **Pretreatment with albuterol vs. montelukast in exercise-induced bronchospasm in children with asthma.** *Hengameh H. Raissy, Pharm.D.*, Michelle Harkins, M.D., Fran Kelly, B.S., Ronald Schrader, Ph.D., William Kelly, Pharm.D.; University of New Mexico, School of Medicine, Albuquerque, NM.

PURPOSE: Exercise-induced bronchospasm (EIB) is common in children. Current asthma treatment guidelines recommend inhaled short-acting beta-2 agonist prior to exercise for prevention of EIB. Montelukast was recently approved for the prevention of EIB. Presently, there is no data available comparing standard of care pretreatment with albuterol- to montelukast in children with EIB.
METHODS: We compared pretreatment with albuterol to montelukast therapy added to the current asthma regimen for protection against EIB in 11 children, 7–17 years old, with mild to moderate asthma in a double-blind, double-dummy, crossover study. Patients with EIB (defined as > 15% drop in forced expiratory volume in 1 second [FEV_1] at screening and baseline visit) were randomly assigned to 3–7 days of montelukast or 2 puffs of albuterol just prior to an exercise challenge and then crossed over to the alternate therapies for the last visit. Serial spirometry was done before and at 0, 5, 10, 15, 30, 45, and 60 minutes after the exercise challenge at each visit. The primary outcome was the maximum change in FEV_1 after exercise. The area under the curve for FEV_1 (expressed as percent change from baseline) in the first 60 minutes (AUC0–60) after exercise and number of patients with complete blocking of EIB were secondary outcomes.
RESULTS: The maximum decrease in FEV_1 was 27.5% + 7.9% at baseline. Patients on montelukast had 18.3% + 13.7% decrease in FEV_1 compared to 0.7% + 1.6% with albuterol (p= 0.002, paired t-test). EIB was blocked in 100% of the patients on albuterol compared with 50% of the patients on montelukast (p<0.05, McNemar's test).

The AUC0−60 was significantly smaller with albuterol compared to montelukast (p< 0.001, Wilcoxon signed rank test). CONCLUSION: Pretreatment with albuterol is more effective than montelukast for blocking EIB in children with asthma.

392. Phosphatase and Tensin homolog deleted on chromosome Ten (PTEN). *Daren Knoell, Pharm.D.*; The Ohio State University, Columbus, Ohio.

PURPOSE: Epithelial injury contributes to lung pathogenesis. Our work and others identified the phosphoinositide-3 kinase (PI3K)/Akt pathway as a vital axis in lung epithelia. Therefore, we hypothesized that pharmacologic inhibition of PTEN, a major suppressor of this pathway, would enhance wound closure and restore lung epithelial monolayer integrity following injury. Experimental approach: We evaluated the ability of two bisperoxovanadium derivatives, bpV(phen) and bpV(pic), in differentiated primary human airway epithelia and BEAS2B cultures for their ability to inhibit PTEN, activate the PI3K/Akt axis, and restore epithelial monolayer integrity following mechanical injury. Key
RESULTS: BpV(phen) and bpV(pic) induced Akt phosphorylation in primary and BEAS2B cells in a dose- and time-dependent manner. Minimal toxicity was observed as measured by lactate dehydrogenase (LDH) release. To verify that Akt phosphorylation is specifically induced by PTEN inhibition, the PTEN positive cell line, DU145, and two PTEN negative cell lines, LNCaP and PC3, were examined. PTEN positive cells demonstrated a dose responsive increase in Akt phosphorylation whereas PTEN negative cells showed no response indicating that bpV(phen) directly suppresses PTEN without effecting auxiliary pathways. Next, we observed that exposure to both compounds resulted in accelerated wound closure following mechanical injury. Similar effects were observed after transfection with a dominant negative isoform of PTEN and PTEN specific siRNA. Conclusions and Implications: Based on this we conclude that PTEN is a valid target for future studies directed at restoring epithelial barrier function after lung injury.

Transplant/Immunology

393. Are solid organ transplant recipients provided adequate prophylaxis to prevent fractures? *Pamela C. Heaton, Ph.D., R.Ph.*[1], Amaka Moka, Pharm.D.[2], Jill Martin, Pharm.D.[1]; (1)University of Cincinnati College of Pharmacy, Division of Pharmacy Practice, Cincinnati, Ohio; (2)VA Medical Center, Cincinnati, Ohio.

PURPOSE: Fractures are a significant comorbidity associated with solid organ transplants. The objectives of this study were to 1) examine the utilization rates of anti-osteoporotic drugs, immunosuppressive, and osteoporosis-inducing drugs in solid organ transplant patients, 2) identify predictors for use or nonuse of anti-osteoporotic drugs, and 3) calculate the risk of fracture in patients using or not using anti-osteoporotic drugs.
METHODS: We conducted a longitudinal drug utilization analysis and a case-control analysis using California Medicaid claims between January 1, 1999 and December 31, 2001. For the drug utilization analysis, we included patients (n=441) who received solid organ transplants. We identified patients who used any anti-osteoporotic drugs, defined as drugs that prevent or treat osteoporosis and included bisphosphonates, calcium, vitamin D, calcitonin and hormones, osteoporosis-inducing drugs or immunosuppressive drugs. For the case-control analysis, we selected all solid organ transplant patients who experienced a fracture after their transplant (n=70) and matched them by race and gender to a transplant patient who did not fracture. We measured their drug exposure prior to the fracture to see whether the use of anti-osteoporotic drugs conferred less risk of fracture to the patients.
RESULTS: 204 (53.7%) patients pre-transplant and 133 (30.2%) patients post-transplant received an anti-osteoporotic drug. Positive predictors for anti-osteoporotic drug use included kidney transplant, female gender, Hawaiian or Pacific Islander, age, immunosuppressive drug use post-transplant and osteoporosis. Patients who received a liver or patients with alcoholism were less likely to receive anti-osteoporotic drugs. In the case-control analysis, current use of anti-osteoporotic drugs conferred protection against fractures (OR = 0.179; 95% CI = 0.034–0.929, p=0.041). Also, current use of immunosuppressive drugs increased the risk of fracture (OR = 4.916; 95% CI = 1.363–17.730, p=0.015).
CONCLUSION: Post-transplant, the majority of transplant patients did not receive anti-osteoporotic drugs. However, the use of anti-osteoporotic drugs significantly reduced the risk of fracture.

PRN

394. **Pharmaceutical Industries PRN Abstract.** *Clara Song, Pharm.D., Diana Isom, R.Ph., EunMee Lee, Pharm.D., BCPS, Jill Chappell, Pharm.D.*

PURPOSE: To promote awareness and education about pharmacy practice in industry, the ACCP Pharmaceutical Industry PRN conducted a survey.
METHODS: Both paper-based and online formats were administered from February 2006 through February 2007. PRN members were asked to share the survey with any industry-based pharmacists who may or may not be ACCP members. Survey questions included educational background, employment history (previous industry positions and other clinical pharmacy experience), job title/role, travel requirements, duties, value of a pharmacy degree for their positions, and interactions with pharmacy students/residents/fellows.
RESULTS: 143 responses were received; 77% from PRN members and 23% from non-PRN members. Responses were grouped into 8 categories based on roles. Many positions (55%) were not field-based. Many (58%) industry pharmacists have minimal or no student contact.
CONCLUSIONS: Pharmacist opportunities are diverse in focus and rank. Pharmacy training provides knowledge that is useful and valued in the pharmaceutical industry.

395. **Highlighting the Ambulatory Care PRN**. *Sarah Shrader, PharmD; Sara Klockars, PharmD; Renee Koski, PharmD; Eric Jackson, PharmD; Mitzi Wasik, PharmD*

PURPOSE: The purpose of the poster is to increase visibility and membership of the Ambulatory Care PRN within the ACCP organization. It will, additionally, increase awareness of professional development, networking opportunities, and highlight accomplishments of current members of the Ambulatory Care PRN.
Several aspects of the Ambulatory Care PRN will be highlighted. Demographic information will be discussed, as this PRN is the largest with 1,106 current members. Activities of the Communications, Education, Networking, Nominations, Research and Scholarship, Budget and Finance, and Advocacy Committees will be described. The Ambulatory Care PRN Pilot Grant program will be featured to promote research and scholarly activity among PRN members in pharmacy-related health services or clinical and translational research. Medication therapy management services is a growing area within pharmacy; the commentary on "Medication Therapy Management Services: Application of the Core Elements in Ambulatory Settings" will be included to direct PRN members to this useful publication. A major networking opportunity is provided by the PRN list-serv. A variety of topics are posted on the list-serv, with the five most common topics this year being anticoagulation, diabetes mellitus, medication therapy management services and billing for services, smoking cessation, and medication errors. Many of the list-serv postings in these areas consist of discussions of new publications, patient cases, and development and sharing of protocols. The Ambulatory Care PRN is a large and dynamic group within the ACCP organization. Active membership and support is needed to ensure its continued success.

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